

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ARLA FOODS AMBA,
Petitioner

v.

LEPRINO FOODS COMPANY,
Patent Owner.

IPR2025-01199

U.S. Patent No. 11,825,860

**DECLARATION OF DR. MARK ETZEL
UNDER 37 C.F.R. § 1.68 IN SUPPORT OF PETITION FOR
INTER PARTES REVIEW**

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I, Mark Etzel, hereby declare as follows:

I. INTRODUCTION

1. I have been retained on behalf of Arla Foods AMBA (“Arla” or “Petitioner”) to offer technical opinions related to U.S. Patent No. 11,825,860 (“the ’860 patent”) (Ex1001). I understand that Arla is requesting that the Patent Trial and Appeal Board (“PTAB” or “Board”) institute an *inter partes* review (“IPR”) proceeding for the ’860 patent. Specifically, I have been asked to consider the validity of claims 8-9, 11-13, and 15-20 of the ’860 patent (the “Challenged Claims”) in view of prior art and obviousness considerations from the perspective of a person of ordinary skill in the art (“POSITA” or “POSITAs”) at the time of the invention as it relates to the ’860 patent.

2. I am being compensated for my time at my standard consulting rate of \$300/hour. I am also being reimbursed for expenses that I incur during this work. My compensation is not contingent upon the results of my study, the substance of my opinions, or the outcome of any proceeding involving the Challenged Claims. I have no financial interest in the outcome of this matter or in the pending litigation between Petitioner and Leprino Foods (“Patent Owner” or “PO”).

I have reviewed and considered at least the following documents in connection with my analysis of the ’860 patent:

- U.S. Patent No. 11,825,860;

- File History of the '860 patent (“’860 Pat File History”);
- PCT Application Publication No. WO2021/136785 (“Nielsen785”);
- PCT Application Publication No. WO2018/115520 (“Bertelsen”);
- PCT Application Publication No. WO2020/002450 (“Nielsen450”);
- Gulustan Ozturk, et al., “Glycoproteomic and Lipidomic Characterization of Industrially Produced Whey Protein Phospholipid Concentrate with Emphasis on Antimicrobial Xanthine Oxidase, Oxylipins and Small Milk Fat Globules,” Dairy, Vol. 3, Issue 2, April 20, 2022 (“Ozturk”);
- Y. Kawasaki, et al., “pH-Dependent Molecular Weight Changes of κ -casein Glyco-macropeptide and Its Preparation by Ultrafiltration,” Milchwissenschaft, Vol. 48, Issue 4, 191-196. April 1993 (“Kawasaki”);
- APV LeanCreme™ Microparticulation of Whey Protein with SPX Flow Technology, White Paper,” November 2012, (“LeanCreme”);
- Alexander Tolkach and Ulrich Kulozik, “Fractionation of Whey Proteins and Caseinomacropeptide by Means of Enzymatic Crosslinking and Membrane Separation Techniques,” Journal of Food Engineering, Vol. 67, Issues 1-2, 13-20, March 2005;

- Andrea Hinkova, et al., “Cheese Whey Tangential Filtration Using Tubular Mineral Membranes,” Chemical Papers, Vol. 70 (3), 325-32, December 28, 2016;
- A. V. Swaminathan, et al., “A Study of Various Chemical Pretreatments to Fractionate Lipids from Whey Protein Phospholipid Concentrate,” Journal of Dairy Sci., Vol. 104, Issue 12, 12249-12262, December 2021;
- U.S. Pat. No. 5,280,107 to Kawasaki et al., issued January 18, 1994;
- U.S. Pat. No. 4,734,287 to Singer et al., issued March 29, 1988;
- PCT Application Publication No. WO2015059245;
- Mark Johnson, “Cheese pH—What’s Behind the Rise and Fall?” Dairy Pipeline, Vol. 14, No. 4, 1-11, December 2002;
- U.S. Pat. Appl. Pub. No. US2011/0003975, published January 6, 2011;
- U.S. Pat. Appl. Pub. No. US2016/0058025, published March 3, 2016 to Christensen et al.;
- Declaration of Tanja Christine Jæger;
- J.N. De Wit and G.A.M. Swinkels, “A Differential Scanning Calorimetric Study of the Thermal Denaturation of Bovine β -lactoglobulin Thermal Behaviour at Temperatures Up to 100°C,” Biochimica et Biophysica Acta, Vol. 624, 40-50, July 24, 1980;

In forming the opinions expressed below, I have considered:

- (a) the documents listed above;
- (b) the relevant legal standards, including the standard for obviousness, and any additional authoritative documents as cited in the body of this declaration; and
- (c) my own knowledge and experience based upon my work in the field of dairy processing as described below, as well as the following materials.

3. Unless otherwise noted, all emphasis in any quoted material has been added.

4. My analysis here is based on my years of education, research, and consulting experience, as well as my investigation and study of relevant materials, including those cited herein.

5. I may rely upon these materials, my knowledge and experience, and/or additional materials to rebut arguments raised by the Patent Owner. Further, I may consider additional documents and information in forming any necessary opinions, including documents that may not yet have been provided.

6. My analysis of the materials in this proceeding is ongoing, and I will continue to review any new material as it is provided. This Declaration represents only those opinions I have formed to date. I reserve the right to revise, supplement,

and/or amend my opinions herein based on new information and my continuing analysis of the materials already provided.

II. BACKGROUND AND QUALIFICATIONS

7. My complete qualifications and professional experience are described in my Curriculum Vitae, a copy of which can be found in Exhibit 1004. The following is a brief summary of my relevant qualifications and professional experience.

8. For the last 36 years I have been a professor of Food Science at the University of Wisconsin-Madison. Wisconsin is known as America's Dairyland for a reason, and not surprisingly my research focused on dairy processing, specifically dairy protein separations. In 1989, my first research grant at UW-Madison was from the Wisconsin Center for Dairy Research on spray drying of dairy starter cultures for cheesemaking. In 1991, my first research grant on dairy protein separations was from the USDA. In 1997, I obtained my first research grant on separation of glycomacropeptide from cheese whey from Dairy Management, the research funding division of the U.S. Dairy Promotion Program. A major emphasis of my research thereafter was separation of glycomacropeptide from cheese whey for use in foods for children with phenylketonuria. That research led to the first intact protein safe for children with phenylketonuria to eat, and several patents on that technology that were licensed to the food industry. For 32 years, I taught courses on

food engineering, food and pharmaceutical separations, and food manufacture and preservation. I have consulted for the dairy industry on these topics for 36 years. I was invited to write three chapters for the Encyclopedia of Dairy Science on Membrane Processed Liquid Milk, Fractionated Proteins – Alpha-Lactalbumin and Beta-Lactoglobulin, and Fractionated Whey Protein Ingredients – Glycomacropeptide. I have published several times on the topic of denaturation and aggregation of whey proteins. One of my publications on this topic (Manufacture and Use of Dairy Protein Fractions) was cited 471 times. My educational background in chemical engineering provided me with a unique and quantitative approach to understanding dairy protein separations and whey protein manufacture using membrane separations. Few people working in the dairy protein topic area have a chemical engineering degree, especially at the PhD level, or with 36 years of academic research and teaching experience.

9. Given my background, I believe I am qualified to provide this declaration before the Patent Trial and Appeal Board.

III. LEVEL OF ORDINARY SKILL

10. I understand there are multiple factors relevant to determining the level of ordinary skill in the pertinent art, including (1) the levels of education and experience of persons working in the field at the time of the invention; (2) the

sophistication of the technology; (3) the types of problems encountered in the field; and (4) the prior art solutions to those problems.

11. I understand that the '860 patent was filed on January 13, 2023. My analysis reflects the views of a person of ordinary skill in the art ("POSITA") in the field of the '860 patent as of January 13, 2023. This would have been someone knowledgeable and familiar with the field of dairy proteins and dairy processing that are pertinent to the '860 patent. That person would have a bachelor's degree in food science, chemical engineering, biological systems engineering, chemistry, microbiology, or a related field, and two or more years of work experience or research related to processing dairy products or developing protein compositions for use in food products. Lack of work experience can be remedied by additional education, and vice versa.

12. As of January 13, 2023, I met, and in fact exceeded, the qualifications of a person of ordinary skill in the art.

13. For purposes of this Declaration, in general, and unless otherwise noted, my statements and opinions, such as those regarding my experience and the understanding of a POSITA generally (and specifically related to the references I consulted herein), reflect the knowledge that existed in the field as of the earliest proper priority date of the '860 patent (i.e., January 13, 2023). Unless otherwise

stated, when I provide my understanding and analysis below, it is consistent with the level of a POSITA prior to the earliest alleged priority date of the '860 patent.

IV. LEGAL STANDARDS

14. I am not an attorney. In preparing and expressing my opinions and considering the subject matter of the '860 patent, I am relying on certain basic legal principles that counsel have explained to me. These principles are discussed below.

15. I understand that for an invention claimed in a patent to be found patentable, it must be, among other things, new and not obvious in view of what was known before the invention was made.

16. I understand the information that is used to evaluate whether an invention is new and not obvious is generally referred to as “prior art” and generally includes patents and printed publications (e.g., books, journal publications, articles on websites, product manuals, etc.).

17. I understand that in this proceeding the Petitioner has the burden of proving that the claims of the '860 Patent are anticipated by or obvious in view of the prior art by a preponderance of the evidence. I understand that “a preponderance of the evidence” is evidence sufficient to show that a fact is more likely true than it is not.

18. I understand that prior art to the '860 patent in this proceeding includes patents and printed publications in the relevant art that predate the proper priority date of the alleged invention recited in the '860 patent.

19. I understand that terms appearing in the patent claims are to be interpreted according to their “ordinary and customary meaning” in an IPR proceeding. In determining the ordinary and customary meaning, the words of a claim are first given their plain meaning as they would have been understood by a POSITA at the time of the alleged invention, in light of the specification and file history. I understand that treatises and dictionaries may be consulted, albeit under limited circumstances, to determine the meaning attributed by a POSITA at the time of the alleged invention. I have followed this approach in my analysis and have applied the ordinary and customary meaning of those terms throughout my analysis in this Declaration.

20. I understand that there are two ways in which prior art may render a patent claim unpatentable. First, the prior art can be shown to “anticipate” the claim. Second, the prior art can be shown to have made the claim “obvious” to a person of ordinary skill in the art. In this declaration I focus on “obviousness.” My understanding of the legal standard for “obviousness” is set forth below.

21. I have been informed that a claimed invention is unpatentable as obvious if the differences between the invention and the prior art are such that the

subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains.

I have also been informed by counsel that the obviousness analysis takes into account factual inquiries including the level of ordinary skill in the art, the scope and content of the prior art, and the differences between the prior art and the claimed subject matter.

22. Specifically, I understand that the obviousness question requires consideration of four factors (although not necessarily in the following order):

- The scope and content of the prior art;
- The differences between the prior art and the claims at issue;
- The knowledge of a person of ordinary skill in the pertinent art; and
- Whatever objective factors indicating obviousness or non-obviousness may be present in any particular case.

23. I have been informed by counsel that the Supreme Court has recognized several rationales for combining references or modifying a reference to show obviousness of claimed subject matter. Some of these rationales include the following: (a) combining prior art elements according to known methods to yield predictable results; (b) simple substitution of one known element for another to obtain predictable results; (c) use of a known technique to improve a similar device (method, or product) in the same way; (d) applying a known technique to a known

device (method, or product) ready for improvement to yield predictable results; (e) choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; and (f) some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

24. I further understand that certain factors may support or rebut the obviousness of a claim. I understand that such secondary considerations include, among other things, commercial success of the patented invention, skepticism of those having ordinary skill in the art at the time of invention, unexpected results of the invention, any long-felt but unsolved need in the art that was satisfied by the alleged invention, the failure of others to make the alleged invention, praise of the alleged invention by those having ordinary skill in the art, and copying of the alleged invention by others in the field. I understand that there must be a nexus—a connection—between any such secondary considerations and the alleged invention. I also understand that contemporaneous and independent invention by others is a secondary consideration tending to show obviousness.

25. I am not aware of any allegations by the named inventor of the '860 patent or any assignee of the '860 patent that any secondary considerations are relevant to the obviousness analysis of any Challenged Claim of the '860 patent.

26. I understand that a petition must identify, for any terms with means-plus-function limitations, the specific portions of the specification that describe the structure, material, or acts corresponding to each claimed function. I also understand a rebuttable presumption exists that without use of the term, “means,” a claim term is not interpreted as means-plus-function, but that other nonce words like “component” have been found to satisfy the rebuttable presumption and invoke a means-plus-function claim construction of such a claim term.

27. I also understand that a petitioner seeking to demonstrate that the prior art discloses a means-plus-function limitation must prove that the corresponding structure—or an equivalent—was present in the prior art and performing the same claimed function.

28. I understand that the standard for determining whether the prior art discloses the corresponding structure or an equivalent is whether there are insubstantial differences, which means that if the assertedly equivalent structure performs the claimed function in substantially the same way to achieve substantially the same result as the corresponding structure described in the specification, it is equivalent.

29. I understand that proving structural equivalence does not require a component-by-component analysis, but rather that it is sufficient to show structure, materials, or acts that perform the claimed function in substantially the same way to

achieve substantially the same result because the claim limitation is the overall structure corresponding to the claimed function and not individual components.

30. I understand that for a claim to be valid, its scope must be definite, and that improperly introducing a term can lead to an unascertainable scope of a term, rendering it indefinite. I understand that any claim element first addressed in the claims by the antecedent basis, “a” may then be identified later in the claims by the antecedent basis, “the.” I understand that failing to follow this convention may lead to ambiguity in the identification of the particular claim element in question, leading to an indefinite scope of the claim’s term. For purposes of this proceeding, I identified and provided my best understanding of any such terms despite such ascertainable scope.

V. CLAIM CONSTRUCTION

31. It is my understanding that in order to properly evaluate the ’860 patent, the terms of the claims must first be interpreted. It is my understanding that for the purposes of this inter partes review, the claims are to be construed under the so-called *Phillips* standard, under which claim terms are given their ordinary and customary meaning as would have been understood by one of ordinary skill in the art in light of the specification and prosecution history, unless the inventor has set forth a special meaning for a term.

32. For the purposes of this declaration, it is my opinion that the term “native GMP” should be construed to mean “non-hydrolyzed GMP.”

33. I report that the '860 specification strongly supports such claim construction. Describing methods to reduce GMP, the specification distinguishes between “native GMP” and GMP that has been hydrolyzed through enzymatic action. For example, “GMP that has undergone at least one hydrolysis reaction, also referred to herein as enzymatically hydrolyzed GMP” does not cause the “same adverse effects as the native GMP.” Ex1001, 10:3-8, Abstract, 1:46-48. The claims reflect the same distinction. *Id.*, 23:4-7. Similarly, the specification confirms that hydrolysis reduces “native GMP” in a composition, *id.*, 7:19-39, even though resulting GMP fragments may remain, *id.*, 3:30-35, 10:1-37. In my opinion, the import is clear: GMP is no longer “native GMP” after hydrolysis. Accordingly, “native GMP” should be construed to mean “non-hydrolyzed GMP.”

34. I have given all other claim terms of the Challenged Claims their plain and ordinary meaning, as would have been understood by a person of ordinary skill in the art, at the time of the alleged invention, which I understand is January 13, 2023 for all claims.

VI. OVERVIEW**A. Overview of the Declaration**

35. The challenged claims of the '860 patent are nothing more than a collection of prior art and the claims can be met by examples pulled from prior art that produce whey protein compositions meeting the claims. Ex1001, 23:34-24:57. However, as I explained in this declaration, neither the processing steps of whey protein compositions nor the composition values were new prior to the earliest possible priority date of the '860 patent.

36. This declaration presents the following grounds of unpatentability with regards to the claims of the '860 patent:

Ground		Claims	Prior Art
1	§102	8-9, 11-13	Nielsen785
2	§103	8-9, 11, 13	Bertelsen in view of Nielsen785
3	§103	8-9, 11-13, 15-20	Nielsen450
4	§103	8-9, 11-13, 15-17, 20	Ozturk in view of Kawasaki and further in view of LeanCreme

37. Grounds 1-3 rely on patent application publications that were all filed by Arla Foods amba, namely Nielsen785 (Ex1005), Bertelsen (Ex1006), and Nielsen450 (Ex1007). These publications represent continuous cutting-edge research work performed by overlapping inventors for Arla in the same research facility. As I explained in this declaration, Bertelsen described the surprising

discovery of making novel crystalline BLG powder. Nielsen450 and Nielsen785 were built on the discovery of Bertelsen and investigated applications of the crystalline BLG powder. I see these publications as a continuation of a clear research path from discovery to applications for that discovery.

38. Ground 1 relies on Nielsen785, and in my opinion, invalidates claims 8-9 and 11-13 of the '860 patent. Nielsen785 taught using crystalline BLG powder to produce denatured whey protein compositions for use in food products. Ex1005, 1:5-11, 2:8-20. The crystalline BLG powder was produced using methods in Bertelsen (Ex1006), which I understand was incorporated into Nielsen785 in its entirety. *Id.*, 89:1-3, 18:27-31.

39. Ground 2 relies on the combination of Bertelsen and Nielsen785, and in my opinion, invalidates claims 8-9 and 11-13 of the '860 patent. Bertelsen taught making crystalline BLG powder with high BLG concentration, and Nielsen785 taught applications of such crystalline BLG powder, such as using the powder to produce denatured protein compositions for beverages. *See* Ex1005, 3:34-36; Ex1006, 4:10-23, 69:9-20.

40. Ground 3 relies on Nielsen450, and in my opinion, invalidates claims 8-9, 11-13, 15-20 of the '860 patent. Nielsen450 described preparing exemplary whey powders and beverages using BLG powders prepared through BLG crystallization. Ex1007, 95:11–113:12. The BLG powders used in Nielsen450 were

produced using methods taught by Bertelsen. *Id.*, 74:22-24. Similar to Nielsen785, Nielsen450 also incorporated Bertelsen in its entirety. *Id.*, 79:19-20. In my opinion, Nielsen450 taught all claim limitations of the challenged claims in this ground but did not expressly teach specific denaturation levels (i.e., claim limitations 8.7 and 15.5) and particle size limitations (i.e., claims 18-20). However, I was able to faithfully replicate Nielsen450's experiments and determine those values (e.g., denaturation level and particle sizes) to conclude that Nielsen450's products met those claim limitations. To achieve a faithful replication of Nielsen450's experiment, I travelled to Arla's laboratory facility in Denmark and performed Nielsen450's experiments by (1) using the same batch of sample as used in Nielsen450; and (2) using the same lab setup and equipment as those used in Nielsen450.

41. Ground 4 relies on the combination of Ozturk (Ex1008), Kawasaki (Ex1009), and LeanCreme (Ex1010), and in my opinion, invalidates claims 8-9, 11-13, 15-17, and 20 of the '860 patent. Ozturk described filtration-based processing steps applied to cheese whey to derive several types of concentrated whey-protein compositions. Ex1008, 278-79, Fig. 1. Kawasaki is in the same field of endeavor as Ozturk and taught benefits of isolating GMP from whey protein concentrates for use in food products. Ex1009, 192-93. LeanCreme—also in the same field of endeavor as Ozturk and Kawasaki—taught processing and denaturing whey protein concentrates to produce a nutritious protein composition. As I explained in detail in

this declaration, a POSITA would have been motivated to combine Ozturk, Kawasaki, and LeanCreme because of the various known benefits provided by the processes of each of the references.

B. Technology Background

1. Whey protein

42. Bovine milk contains a diverse set of bioactive components, minerals, and nutrients that promotes human health and makes it an excellent source for protein and fat and other essential nutrients. Milk casein can be precipitated from milk by acidification or enzymatic reaction, forming curd and leaving whey as the liquid supernatant. Whey contains more than half of the solids content from the original milk, including whey protein and most of the lactose and water. *See* Ex1008, 277; Ex1006,18:22-25; Ex1013, 325.

43. As I mentioned in the qualification section, I have worked in the field of biochemical engineering for 36 years, and in particular, the field of dairy protein separations and dairy foods. Research into the separation and application of whey protein started as early as 1989. Glycomacropeptide was a dairy protein of particular focus in my research.

44. Prior to the 1970s, cheese was the valued product of the dairy industry and cheese whey was discarded to the environment. The dairy industry considered whey a waste product “due to its high organic content and high biochemical oxygen

demand.” Ex1008, 278. However, developments in membrane separation processes, particularly ultrafiltration technology, enabled improved commercial recovery of whey protein concentrate (WPC). *Id.* Additionally, consumers’ desire for higher-purity whey proteins “drove further process improvements from the manufacture of conventional WPC...into higher purity protein.” *Id.* As a result of these advances in technology, the dairy industry evolved to where whey became a “novel raw material for many purposes beyond physiologically motivated concepts.” Ex1012, 14.

45. Several types of whey exist, depending on the type of casein precipitation process. *See* Ex1006, 12. For example, sweet whey “is the whey product produced by rennet-based precipitation of casein,” whereas “acid whey” is the “whey product produced by acid-based precipitation of casein.” *Id.*, 12:26-29 A major component of sweet whey proteins is beta-lactoglobulin (BLG)—a well-known source of essential amino acids that has many nutritional uses. *See* Ex1006, 4. Sweet whey also contains other major proteins, including alpha-lactalbumin (ALA), glycomacropeptides (GMP), and others. A typical protein composition of sweet whey is shown in the table below.

PROTEIN	% OF TOTAL WHEY PROTEIN
B-LACTOGLOBULIN	48-58
A-LACTALBUMIN	13-25
GLYCOMACROPEPTIDES (GMP)	12-20
IMMUNOGLOBULINS	08-12
BOVINE SERUM ALBUMIN	6
LACTOFERRIN	2
LACTOPEROXIDASE	0.05

Table 1: Typical composition of sweet whey proteins (Belitz and Grosch 1999)

Ex1010, Table 1.

2. Glycomacropeptide (GMP)

46. GMP is a small protein cleaved enzymatically from casein by the protease enzyme chymosin during production of the cheese curd. *See* Ex1012, 13. GMP is a glycosylated peptide. In other words, it has sugars attached to the peptide chain. The term “caseinomacropeptide” or “CMP” encompasses both glycosylated and non-glycosylated forms of the peptide chain, and “[i]n the scientific literature CMP is also sometimes referred to as caseinoglycomacropeptide (cGMP) or glycomacropeptide (GMP).” Ex1020, ¶16. Because the ’860 patent does not differentiate glycosylated peptide from non-glycosylated peptide, I consider CMP and GMP equivalents for the purpose of this declaration. Indeed, the ’860 patent itself explicitly uses CMP and GMP interchangeably. *See* Ex1001, 4:66–5:5.

47. GMP is the third most abundant protein in sweet whey, after BLG and ALA. *See* Ex1020, ¶31; Ex1010, Table 1. GMP is a “valuable constituent for both its functional properties as well as its specific nutritive value.” Ex1012, 14. The optimal application of GMP as a food ingredient depends on the recipient. On one hand, GMP is a unique peptide because it does not contain the amino acid Phenylalanine (Phe) which makes it “an interesting protein source for persons suffering from phenylketonuria (PKU).” Ex1020, ¶¶3-4. On the other hand, GMP “is a less desirable component due to its high content of the amino acid threonine” which causes hyperthreoninemia in infants including “premature or very new born infants.” Ex1012, 14. Additionally, GMP could impart an “off-flavor” to food, often described as a “stale” or “chemical” taste. Ex1018, 9. The ’860 patent acknowledged this shortcoming of GMP: “a high native GMP content in whey protein compositions can lead to undesirable flavor and poor process incorporation, reducing the total amount of protein capable of being fortified into the product.” Ex1001, 1:36-40.

48. Bovine milk naturally contains the 64-amino acid macropeptide GMP covalently linked to kappa-casein. Chymosin cleaves GMP from kappa-casein releasing it into the cheese whey and precipitating para-kappa casein to form cheese curd. Therefore, the dairy industry recognized that “it appears lucrative to separate CMP from whey, both in order to offer CMP free rennet whey as a raw material for baby food manufacture and to obtain CMP concentrates for extended use in food

matrix design and for functional food concepts directed towards adult nutrition.”

Ex1012, 14. CMP-free rennet whey is useful for the prevention of hyperthreoninemia in infants and CMP concentrates are useful for prevention of phenylketonuria. These facts were well known before the priority date of the '860 patent. These facts provided ample motivation for past researchers to develop numerous methods to separate CMP from whey proteins, for example, by ultrafiltration using membranes. *Id.* In particular, membranes “are especially suitable for the food industry” due to their “relatively easy scale up” capabilities and “low processing costs.” *Id.*

49. Tolkach (Ex1012) developed “a new method for the separation of caseinomacropeptide (CMP) from native whey proteins” by “pretreatment of whey protein concentrate with the enzyme transglutaminase followed by microfiltration.” Ex1012, Abstract. GMP can be crosslinked by transglutaminase whereas other “native whey proteins show much less sensitivity to be crosslinked by this enzyme due to their globular structure.” *Id.* The aggregated GMP could then be “removed by means of microfiltration or diafiltration” to “obtain a CMP-free whey protein concentrate from sweet whey, which can be further used for the fractionation of individual whey proteins after CMP removal.” *Id.*

50. Hinkova (Ex1013) studied “filtration kinetics and separation efficiency during purification and fractionation of cheese whey (sweet and salty)” as well as

“[v]arious mineral membranes’ cut-offs...” Ex1013 at 325. Specifically, Hinkova studied the impact of membrane molecular weight cut-offs and filtration factors on GMP, BLG, and ALA. *Id.*, 330. Inorganic tubular membranes with different cut-offs were investigated: “1 kDa, 5 kDa, 20 nm, 100 nm, 200 nm, and 500 nm.” *Id.*, 326. In particular, Hinkova investigated the average rejection rates of whey proteins for cut-offs of 5 kDa, 100 nm, and 500 nm. *Id.*, 330. Rejection rate refers to the percentage of solutes that does not permeate through the membrane during the filtration process. A higher rejection rate indicates that the membrane is more effective at preventing the passage. As shown in annotated Table 7 below, GMP has a lower rejection rate (70.2 ± 7.6) than BLG (81.8 ± 2.7) when using membrane cut-off size of 100 nm. *Id.* In other words, GMP permeates through the membrane more easily than BLG. As also shown in annotated Table 7 below, filtration also applied similarly to α -La (alpha-lactalbumin) which has a rejection factor of 69.7 ± 1.5 . A microfiltration process which uses a membrane cut-off of 100 nm and which reduces the content of alpha-lactalbumin therefore reduces the content of GMP in a similar manner. In other words, GMP and alpha-lactalbumin have substantially the same rejection factor when using a membrane with a 100 nm cut-off and their concentration is reduced by substantially the same rate.

Table 7. Average protein rejection on ceramic membranes

Rejection factor $\pm$ SD/%				
Protein	Protein size ^a /kDa	Membrane cut-off		
		5 kDa	<u>100 nm</u>	500 nm
CMP	7	94.6 $\pm$ 7.6	<u>70.2 $\pm$ 7.6</u>	16.3 $\pm$ 2.3
α -La	14.2	96.7 $\pm$ 5.7	69.7 $\pm$ 1.5	16.3 $\pm$ 2.8
β -Lg B	18.4	97.5 $\pm$ 4.3	<u>81.8 $\pm$ 2.7</u>	17.8 $\pm$ 2.1
β -Lg A	18.4	96.3 $\pm$ 6.5	87.2 $\pm$ 3.1	26.3 $\pm$ 0.9

a) Maubois and Ollivier (1997); R_{CMP} – rejection of casein macropeptide, $R_{\alpha\text{-La}}$ – rejection of α -lactalbumin, $R_{\beta\text{-Lg A}}$ – rejection of β -lactoglobulin B, $R_{\beta\text{-Lg A}}$ – rejection of β -lactoglobulin A, SD – standard deviation.

Ex1013, Table 7 (annotated), 330. As such, CMP is depleted more than BLG in the retentate after filtering whey solution using membrane cut-off of 100 nm.

51. Kawasaki (Ex1009) taught benefits of using GMP “as an ingredient in dietetic foods and pharmaceuticals” and developed a filtration method to separate GMP from the other whey proteins. Ex1009, 191-93. Kawasaki’s “simple procedure for isolating GMP from WPC by UF” took advantage of GMP’s pH-dependent change of molecular weight. *See id.*, 192-93. WPC solution was acidified to reduce the GMP molecular weight. When the acidified WPC solution was filtered through multiple filtration stages, GMP with decreased molecular weight was small enough to pass through the ultrafiltration membrane, but “the majority of whey proteins such as β -lactoglobulin, α -lactalbumin, immunoglobulin and bovine serum albumin were rejected by the membrane.” *See id.*, 192-93, Figs. 1, 3. The resulting retentate thus contained reduced GMP content. *Id.*

3. Whey Protein Denaturation

52. Denatured and microparticulated whey protein concentrates have long been used as a food ingredient for dairy products, such as cheese or yogurt. *See* Ex1017, 1:14-15. Higher degrees of denaturation can provide the benefit of increased particle stability, which is essential for ensuring food product qualities. *See* Ex1007, 15, 25; Ex1010, 20.

53. Heating is one of the most common methods to cause denaturation of whey proteins. BLG—the most dominant protein of sweet whey—“determines the overall denaturation kinetics.” Ex1010, 5. Heat treatments can change the structure of whey proteins with the exception of GMP. *Id.* The figure below illustrates an exemplary denaturation process, which “is a molecular process” that involves unfolding native whey proteins (step 1) and creating thiol binding sites (step 2). *Id.*, 5, Fig. 1. Denaturation is normally irreversible and creates whey protein aggregation. *Id.*

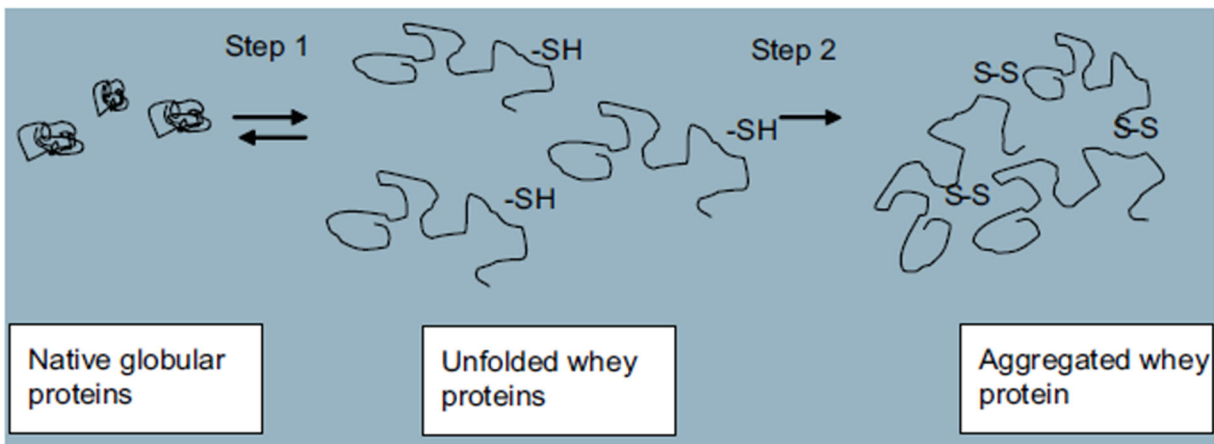


Fig. 1: Schematic drawing of aggregation of whey proteins

54. Whey protein aggregation often results in an undesirable “sandy or gritty mouthfeel.” *Id.* Therefore, the “[a]pplication of mechanical shear forces is necessary to stop the growth of whey protein aggregates.” *Id.* Simultaneous heating and mechanical shearing can be applied in one step or applied separately in two steps by “employing heat denaturation followed by mechanical creation of microparticles.” *Id.*, 4. In either scenario, “[t]ight control of the heating and shear force is necessary in order to ensure production of denatured whey protein particles with the desired smooth mouthfeel instead of a sandy or gritty mouthfeel.” *Id.*, 5.

C. Summary of the '860 Patent

55. I understand the '860 patent was filed on January 13, 2023. Ex1001, Cover. It is titled “Denatured Milk Proteins and Methods of Making Them.” *Id.*, Title. The assignee listed on the front of the patent is Leprino Foods Company. *Id.*, (73).

56. The '860 patent relates to denatured whey protein compositions and acknowledges that whey is a protein source generated in cheesemaking—casein in the milk forms curds that are collected to make cheese, leaving behind liquid whey as a byproduct. Ex1001, 1:6-8, 1:17-23. The background section of the '860 patent focuses its discussion on deriving whey protein from cheese making and using whey protein as an ingredient for food and beverages. *Id.*, 1:13-40.

57. As I explained in Section VI.B.1, whey includes fat, lactose, minerals, and a variety of milk-derived proteins. For example, familiar proteins found in whey include β -lactoglobulin (BLG), α -lactalbumin (ALA), and glycomacropeptide (GMP). *See* Ex1001, 4:36-65. GMP is a small protein cleaved enzymatically from casein during curd production. Ex1001, 4:66–5:5. The '860 patent recognizes that GMP is “considered an inferior source of protein for muscle recovery” and that “a high native GMP content in whey protein compositions can lead to undesirable flavor and poor process incorporation.” Ex1001, 1:30-40; *see also id.* 5:5-24. I can personally attest that these issues regarding GMP were well known in the dairy industry. For example, it was well known that GMP imparts an “off-flavor” to food, “described as ‘stale’ or chemical.” *See* Ex1018, 9. These issues of GMP were known in the dairy industry in the early 2000s when I conducted research on process chromatography to separate GMP from whey. *Id.*, 8.

58. To address those known problems, the '860 patent describes high-protein compositions derived from whey that have “a reduced percentage of such protein attributable to native GMP.” Ex1001, 5:25-30. The patent also describes methods for making such a protein composition that include filtering cheese whey, reducing GMP levels in the retentate, and performing a denaturation process on the reduced-GMP retentate. *See* Ex1001, 6:3-28, 6:44-59, 7:49–8:14, 8:43-59. I have annotated Figure 1 of the '860 patent to highlight those steps:

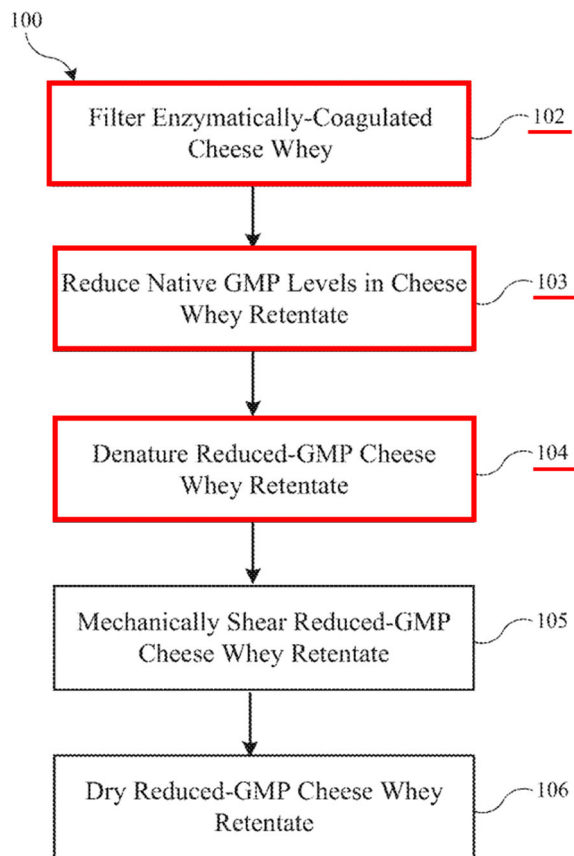


FIG. 1

59. Starting from cheese whey, the filtration can concentrate whey protein and remove lactose and minerals to form a cheese whey retentate and may be performed using ultrafiltration “or other methods as known in the art.” Ex1001, 6:14-37. The ’860 patent describes two ways to reduce GMP levels in the filtered cheese whey retentate: through enzymatic hydrolysis or microfiltration. Enzyme hydrolysis can be performed by adding “one or more enzymes that selectively reduce native GMP levels.” Ex1001, 6:44-46; see *Id.* 6:44–7:48, 15:61–16:11. Alternatively, GMP can be reduced in the filtered cheese whey retentate through a second filtration step: “a microfiltration process in which a portion of the GMP permeates the microfiltration membrane.” Ex1001 7:49-53. In contrast, denatured proteins and fat are retained by the microfiltration membrane. Ex1001, 7:49–8:14, 18:16-24. Under either approach, the resulting reduced-GMP composition is heated to denature the remaining proteins “as known in the art.” Ex1001, 8:44-52.

60. According to the ’860 patent, such denatured, reduced-GMP compositions can be used as protein additives for use in products such as protein bars, yogurts, and beverage powders. Ex1001, 11:29-49, 3:28-43.

D. Prosecution History of the ’860 Patent

61. I have reviewed the prosecution history of the ’860 patent. U.S. Patent Application No. 18/097,003 was filed on January 13, 2023 with a prioritized examination request and without a claim to earlier priority. Ex1001, Cover; Ex1002,

186. After overcoming a single prior art-based rejection and several rejections under 35 U.S.C. §112, the '860 patent issued about ten months later on November 28, 2023. Ex1002, 1-4.

62. During prosecution, the Examiner rejected as-filed claims 1-7 as being obvious over US2018/0242608 to Tikanmaki et al. *See* Ex1002, 120-22. No prior-art-based rejection was made on claims 14-20. *Id.* In response, Applicant contended that Tikanmaki fails to teach “greater than 50 wt.% **denatured** whey proteins relative to the total weight of the protein” because “the only discussion of denaturization in Tikanmaki is of β -lactoglobulin.” *Id.* at 98 (emphasis in original). The Examiner issued a final Office Action without additional prior-art-based rejections and allowed claims 14 and 18-20. *Id.*, 60-65. In view of the allowable subject matter, the Applicant amended and requested rejoinder of the withdrawn method claims. *Id.*, 50-56. The application issued as the '860 patent after the Applicant made amendments to overcome rejections under 35 U.S.C. §112. *Id.*, 10-16.

63. The Examiner’s “Reasons for Allowance” stated that Tikanmaki “fails to expressly teach the claimed composition including at least 60 wt.% whey protein on a dry weight basis; less than 8 wt.% native glycomacropeptide (GMP) and greater than 2 wt.% enzymatically hydrolyzed GMP relative to a total weight of protein in

the denatured whey protein composition; a proteolysis index of at least 8.0 wt.%.”

Id., 15.

64. None of the prior art references relied upon in my declaration were presented before the Examiner during prosecution of the '860 patent.

VII. DETAILED EXPLANATION OF GROUNDS

A. Ground 1: Anticipation by Nielsen785 (incorporating Bertelsen) (Claims 8-9, 11, 13)

1. Overview of Nielsen785

65. In my opinion, Nielsen785 (Ex1005) is analogous art to the '860 patent. Nielsen785 taught the production of denatured whey protein compositions for use in food products and is therefore directed toward the same field of endeavor as the '860 patent. *Compare* Ex1005, 1:5-11, *with* Ex1001, 1:6-8.

66. Nielsen785 described its denatured whey protein compositions as “whey protein nanogels,” which are small particles of denatured whey protein, typically spherical in shape. *See*, Ex1005, 9:16-22. Whey protein could include any or all proteins found in whey and could be a subset of those protein species or even one species. Ex1005, 7:29-32. The compositions had high protein concentrations, such as a high concentration of BLG. Ex1005, 1:30-2:6.

67. Nielsen785's production methods started with “providing a whey protein solution,” Ex1005, 2:8-20, preferably by “dissolving BLG isolate powder produced” using methods described in Bertelsen, Ex1005, 89:1-3, 18:27-31. The

whey protein solution was heated to “at least 68 degrees C.” Ex1005, 2:22-23, 19:24-20:8 (“most preferably 85-89 degrees C”). Heating should be “performed for a duration sufficient to denature at least 50%” and “most preferably at least 99%” of the BLG. Ex1005, 20:10-30.

68. I note that Nielsen⁷⁸⁵ expressly incorporated Bertelsen (Ex1006) in its entirety. Ex1005, 18:34-35 (“WO 2018/115520 A1 and PCT/EP2019/066998 are incorporated herein by reference for all purposes.”). Because Bertelsen is directed to manufacturing BLG compositions, a POSITA would have understood Nielsen⁷⁸⁵ as incorporating with detailed particularity the entire disclosure of Bertelsen because the examples taught by Bertelsen (e.g., Examples 1-14) all involved processing BLG compositions and/or investigating their properties. *See* Ex1006, 56-87. At a minimum, disclosures related to Bertelsen’s BLG isolate powder are expressly incorporated with particularity, which is the material I relied upon below

2. Overview of Bertelsen

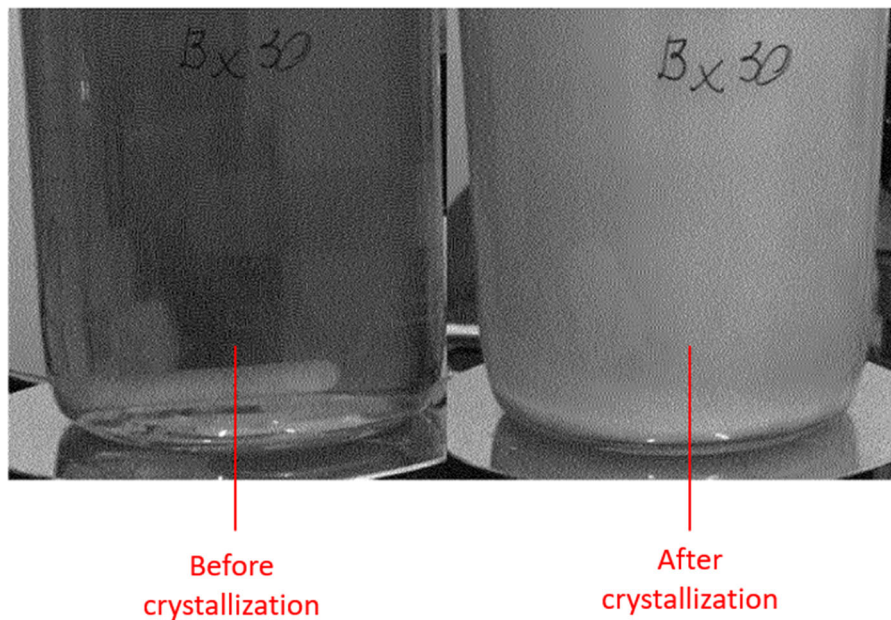
69. In my opinion, Bertelsen (Ex1006) is analogous art. Bertelsen is directed to preparing highly purified BLG compositions from whey protein solutions to be used as a food ingredient. *Compare* Ex1006 3:11-25, 4:19-20, *with* Ex1001, 2:26-32, 3:28-43.

70. Bertelsen described “producing isolated beta-lactoglobulin compositions...containing crystallised beta-lactoglobulin.” Ex1006, Abstract.

Bertelsen's method allowed efficient production of "highly purified BLG which is safe to use as a food ingredient." *Id.*, 3:11-13, 4:10 ("BLG is well known to be a great source of essential amino acids...").

71. Bertelsen's "highly pure BLG crystals" were directly obtained from "crude whey protein solution." Ex1006, 3:4-6. BLG crystals were prepared by "providing a whey protein solution comprising BLG and at least one additional whey protein," with the solution being "supersaturated with respect to BLG." Ex1006, 3:19-21. For example, cheese whey was filtered to obtain a concentrated retentate containing BLG. Ex1006, 57:1-15, 60:30-62:5. BLG was then crystallized in the solution, as illustrated below in annotated Figure 12 of Bertelsen. Ex1006, 3:23, 57:17-18, 60:30-65:9.

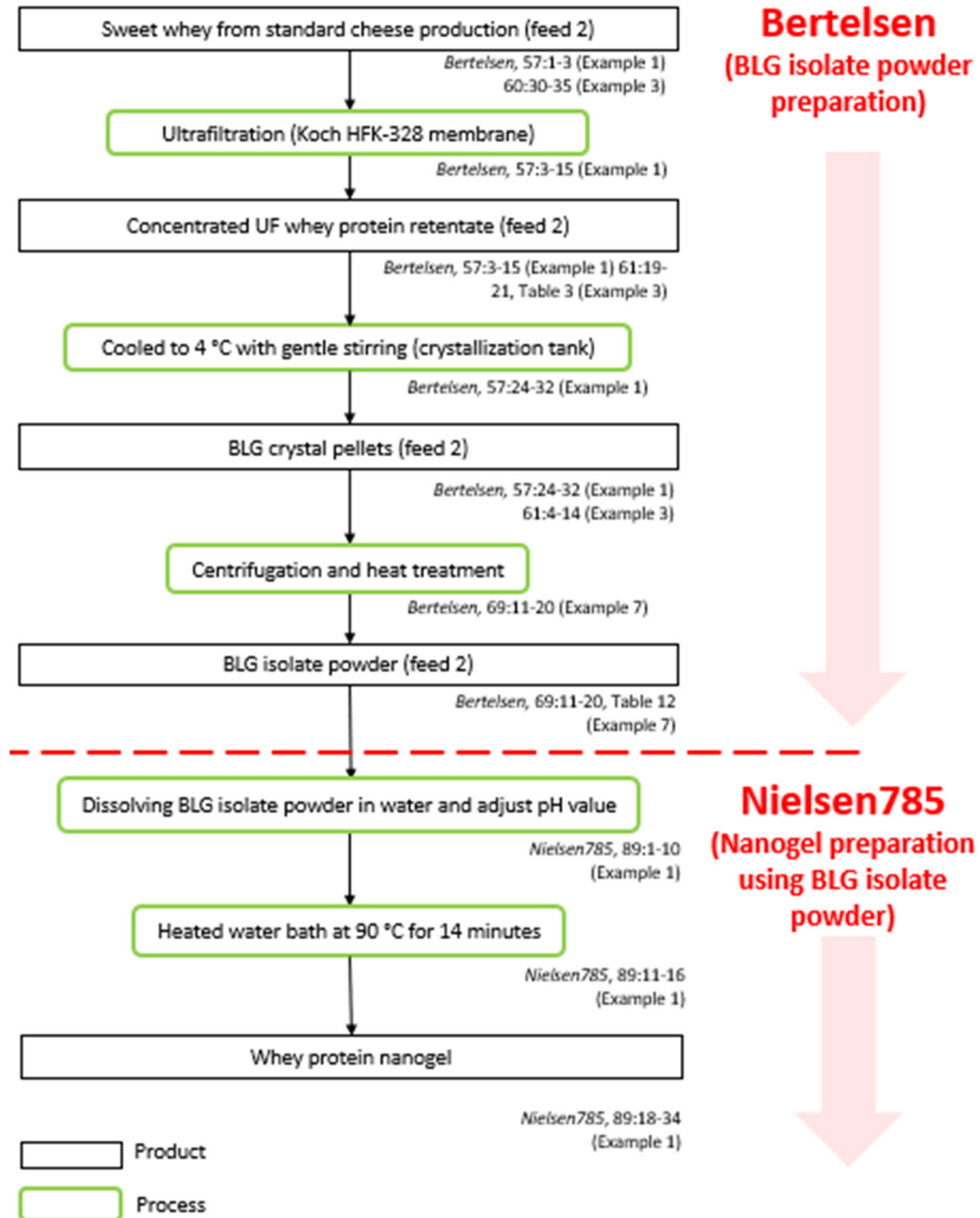
Fig. 12



72. Ex1006, Fig. 12 (annotated), 5:23-24, 63:19-21. According to Bertelsen, the BLG crystals were separated from the remaining protein solution to make “a dry product such as e.g. a powder.” *Id.*, 3:25-39. After separation, the resulting crystalline BLG powder had a GMP concentration below the detection limit, compared to 17.1% GMP in the retentate used for crystallization. Ex1006, 61:19-62:5 (Table 3), 70:1-5 (Table 12).

73. As I explained in Section VII.A.1, Nielsen⁷⁸⁵ used Bertelsen’s crystallized protein compositions and incorporated Bertelsen by reference. Ex1005, 89:1-3, 18:34-35. Based on the disclosures of Nielsen⁷⁸⁵ and Bertelsen, I created a flow chart illustrating the preparation processes of Nielsen⁷⁸⁵ (incorporating Bertelsen). *Id.* As visualized below, the preparation process began with performing ultrafiltration on sweet whey as taught by Bertelsen to produce a whey protein retentate. Ex1006, 57:1-35, 60:30-35, 61:4-21. The retentate was cooled and stirred overnight to activate a crystallization process for forming BLG crystals. *Id.* The BLG crystals were separated on a decanter centrifuge and subsequently dried on a pilot plant spray drier resulting in BLG crystals in a powder form. *Id.*, 69:11-20. The preparation process proceeded as taught by Nielsen⁷⁸⁵ by dissolving the BLG powder in milli-Q water and adjusting the solution’s pH value to 5.9 using NaOH. Ex1005, 89:1-10. Samples each containing 15mL of the BLG solution were placed into Duran GL18 screw thread tubes and thermally treated in a water bath at 90 °C

for 14 min. Ex1005, 89:11-16. If the samples contained 10% protein, a treatment duration of 10 minutes was performed. *Id.* The samples were subsequently cooled in an ice-water bath, resulting in the formation of whey protein nanogels. *Id.*



3. Independent Claim 8**a. 8.pre: “A method of making a denatured whey protein composition, the method comprising:”**

74. In my opinion, Nielsen785 (incorporating Bertelsen) taught claim limitation 8.pre. Nielsen785 taught methods for making denatured whey protein compositions as nanogels of denatured whey protein. *E.g.*, Ex1005, 1:30-2:29.

b. 8.1: “filtering cheese whey from enzymatically coagulated milk into a cheese whey retentate and a permeate; and”

In my opinion, Nielsen785 (incorporating Bertelsen) taught claim limitation 8.1.

75. Bertelsen, incorporated into Nielsen785, taught methods of producing “beta-lactoglobulin compositions...containing crystallised beta-lactoglobulin.” Ex1006, Abstract. Bertelsen’s “highly pure BLG crystals” were obtained from “crude whey protein solution,” Ex1006, 3:4-6, and produced using methods described in Bertelsen’s Examples 1, 3, and 7.

76. Bertelsen’s Example 1 described crystallizing BLG “from a crude whey protein concentrate.” *Id.*, 56:35-36. Whey protein concentrate is made by filtering cheese whey from enzymatically coagulated milk into a cheese whey retentate and a permeate. According to Bertelsen, “[t]he term ‘whey’ pertains to the liquid supernatant that is left after the casein of milk has been precipitated and removed. Casein precipitation may e.g. be accomplished by acidification of milk and/or by use of rennet enzyme.” Ex1006, 12:22-24. Casein precipitation is a form of coagulation.

See Ex1012, 13 (“Milk protein can thus be separated into a coagulum from the casein protein fraction, i.e. the cheese curd, and the whey.”). Cheese whey generally refers to the liquid remaining after casein precipitation during the cheesemaking process. If casein precipitation occurs by acidification of milk, the whey is referred to as acid whey, and if casein precipitation occurs using rennet enzyme, the whey is referred to as sweet whey. Therefore, sweet whey is a type of cheese whey. *Id.*, 13-14. Example 1’s sweet whey is made “from a standard cheese production process” and refers to “the whey product produced by rennet-based precipitation of casein.” Ex1006, 57:3-5, 12:26-27.

77. Bertelsen’s Example 1 described processing “sweet whey from a standard cheese production process” through “an ultrafiltration setup” to obtain a retentate for BLG crystallization. Ex1006, 57:1-32. a POSITA would have understood this meant a permeate was also produced containing materials that passed through the filter. *See Id.* Fig. 26 (showing UF resulted in a UF retentate and a UF permeate containing minerals, lactose, and water).

78. Bertelsen’s Example 3 used three different types of whey protein-containing raw materials “treatment as described in Example 1,” which included filtration, to prepare concentrates for BLG crystallization. Ex1006, 57:1-15, 60:30-35. The second whey protein solution discussed in Example 3 (feed 2) was “based on sweet whey.” *Id.*, 60:33-35. Using “the same experimental and analytical setup

as in Example 1,” all three feeds of Example 3 were subjected to crystallization. Ex1006, 60:28-61:14, 63:13-28.

79. Bertelsen’s Example 7 for preparing spray-dried BLG crystals used the crystals “produced in Example 3 (using feed 2).” *Id.*, 69:9-11. Nielsen⁷⁸⁵ described using the BLG powder of Bertelsen’s Example 7 to make denatured whey protein compositions. Ex1005, 89:1-38.

80. Accordingly, it is my opinion that Nielsen⁷⁸⁵ (incorporating Bertelsen) taught filtering cheese whey into a retentate and permeate.

c. 8.2: “reducing native glycomacropeptides (GMP) in the cheese whey retentate to form a reduced-GMP cheese whey retentate composition; and”

81. In my opinion, Nielsen⁷⁸⁵ (incorporating Bertelsen) taught claim limitation 8.2.

82. As an initial matter, in Nielsen⁷⁸⁵, “the term ‘caseinomacropeptide’ or ‘CMP’ pertains to the hydrophilic peptide, [amino acid] residue 106-169, originated from the hydrolysis of ‘κ-CN’ or ‘kappa-casein’ from mammal species, e.g. in native and/or glycosylated forms and includes the naturally occurring genetic variants, by an aspartic proteinase, e.g. chymosin.” Ex1005, 7:4-7. As I also explained in Section VI.B.2, the terms CMP and GMP refer to the same hydrophilic peptide released from kappa-casein. Indeed, the ’860 patent confirms that GMP is “sometimes referred to as cGMP or CMP.” Ex1001, 4:37-40.

83. As discussed in Section VII.A.3.b, Nielsen⁷⁸⁵ disclosed using crystalline BLG powder produced as described in Bertelsen's Examples 1, 3, and 7. The CMP/GMP identified in Bertelsen's whey protein solutions was native GMP. For example, Bertelsen described quantifying "*native* alpha-lactalbumin (C_{α}), beta-lactoglobulin (C_{β}), and caseinomacropeptide (C_{CMP})" in its analysis methods. *See* Ex1006, 72:6, 77:36-38 (emphasis added). Upon my review of Bertelsen and Nielsen, neither reference described using a protease to cleave GMP. Whereas the '860 patent used one or more enzymes to selectively reduce native GMP levels, Bertelsen did not. Bertelsen selectively reduced native GMP levels using an innovative method for the crystallization of BLG. Formation of the BLG crystal lattice excludes GMP. The result was that Nielsen⁷⁸⁵ (incorporating Bertelsen) disclosed features recited in claim 8 prior to the '860 patent, and used a method not considered in the Examiner's "Reasons for Allowance."

84. Bertelsen quantified the change of CMP/GMP levels during production of crystalline BLG powder, as I explain below. For example, Bertelsen's Table 3 (below) reported several whey protein concentrations contained in the second whey-protein source of Example 3 (feed 2). The CMP level relative to total protein was 17.1% w/w.

Feed 2 standardized to 95% TS Protein composition (% w/w relative to total protein)	
ALA	12.2
BLG	70.0
CMP	17.1
Other components (% w/w relative to the total weight of the standardized feed)	
Ca	0.387
K	0.204
Mg	0.066
Na	0.051
P	0.174
fat	BDL
protein concentration	89

Ex1006, 61:19-20, Table 3 (annotated).

85. Bertelsen's Example 7 for preparing spray-dried BLG crystals used crystallized BLG protein "produced in Example 3 (using feed 2)." *Id.*, 60:30-35, 69:11. The BLG crystals were separated "from the remaining whey protein solution" to make "a dry product such as e.g. a powder." *Id.*, 3:25-39, 69:9-20. During Bertelsen's process, the CMP level was reduced from over 17% to below the detection limit. Ex1006, 70:1-3, Table 12. This is because BLG crystallization is a highly selective separation process whereby the crystal lattice excludes other proteins such as CMP that cannot fit into the BLG crystal lattice. I have annotated Tables 3 and 12 from Bertelsen to demonstrate the reduction of CMP levels.

Table 3 The concentration of selected components of feed 2 (ALA-reduced whey protein concentrate based on sweet whey). BDL= below detection limit in wet, non-standardized sample.

Feed 2 standardized to 95% TS	
Protein composition (% w/w relative to total protein)	
ALA	12.2
BLG	70.0
CMP	17.1
Other components (% w/w relative to the total weight of the standardized feed)	
Ca	0.387
K	0.204
Mg	0.066
Na	0.051
P	0.174
fat	BDL
protein concentration	89

Example 3 (whey protein solution)

Table 12 The concentration of selected components of the spray-dried BLG crystal preparation of Example 7. BDL= below detection limit

Spray dried BLG crystal powder	
Protein composition (% w/w relative to total protein)	
ALA	0.7
BLG	97.4
CMP	BDL
Other components (% w/w relative to total weight of the BLG crystal powder)	
Ca	0.118
K	0.026
Mg	0.017
Na	BDL
P	BDL
water	3.8
protein concentration	94

Example 7 (BLG isolate powder)

CMP
Reduction

Although Bertelsen did not state the detection limit reflected in Table 12, Nielsen785 measured the CMP in BLG isolate powder produced as in Bertelsen's Example 7 and reported a concentration of 0.7%, as shown in annotated Nielsen785's Table 1 below.

Protein source	BLG isolate
pH	5.67
Total solids%	95.2
Protein/total solids %	98.7
Ash %	0.51
Fat %	0.11
Lactose %	<0.09
Pho % of TS	<0.025
Na % of TS	0.025
K % of TS	0.051
Ca % of TS	0.146
Mg % of TS	0.022
Native ALA %	0.2
Native BLG %	96.5
CMP %	0.7
Ca:BLG w/w ratio	0.0016

Example 1 (BLG isolate powder)

Ex1005, 88:15-20, Table 1 (annotated).

d. 8.3: “heating the reduced-GMP cheese whey retentate composition to form the denatured whey protein composition,”

86. In my opinion, Nielsen⁷⁸⁵ (incorporating Bertelsen) taught claim limitation 8.3.

87. Nielsen⁷⁸⁵ described dissolving BLG isolate powder produced according to Bertelsen’s Example 7 in water to form whey protein solutions. *See* Ex1005, 89:1-10. Those solutions were “thermally treated at 90 degrees C for 14 minutes...in a water bath.” *Id.*, 89:12-16. Nielsen⁷⁸⁵ reported that “thermal treatment at e.g. 90 degrees C for 10 minutes lead to 95-97% denaturation with only 3-5% non-denatured protein” remaining. *Id.*, 89:29-31. Nielsen⁷⁸⁵ also taught that “a high level of BLG denaturation gives a better heat-stability of the resulting whey

protein nanogels composition.” *Id.*, 20:25-26. Adjusting heat-treatment durations achieved denaturation of “most preferably at least 99% w/w of the native BLG.” *Id.*, 20:16-23.

e. 8.4: “wherein the denatured whey protein composition is characterized by at least 60 wt. % whey protein on a dry weight basis;”

88. In my opinion, Nielsen⁷⁸⁵ (incorporating Bertelsen) taught claim limitation 8.4.

89. As I explained in Section VII.A.3.d, Nielsen⁷⁸⁵’s Example 1 taught using heat to denature the BLG protein. Whey protein powders used for denaturation contained 98.7% protein/total solids and 96.5% BLG. Ex¹⁰⁰⁵, 88:15-20 (Table 1, reproduced below.)

Table 1 Characteristics of exemplary whey protein powder used for preparation of whey protein nano-gels.

Protein source	BLG isolate
pH	5.67
Total solids%	95.2
Protein/total solids %	98.7
Ash %	0.51
Fat %	0.11
Lactose %	<0.09
Pho % of TS	<0.025
Na % of TS	0.025
K % of TS	0.051
Ca % of TS	0.146
Mg % of TS	0.022
Native ALA %	0.2
Native BLG %	96.5
CMP %	0.7
Ca:BLG w/w ratio	0.0016

90. Nielsen⁷⁸⁵ described applying thermal treatment to a protein solution made from that powder without adding or removing any protein. *See* Ex1005, 89:1-16. The disclosed heat treatment was performed at the same temperature and for a longer duration than that yielding 95-97% denaturation, so a POSITA would have understood that at least 95% of the protein in the solutions of crystallized BLG powder was denatured after heat treatment. The solution of Nielsen⁷⁸⁵ had 98.7 % whey protein on a dry weight basis which is at least 60 wt. % whey protein on a dry weight basis as claimed (i.e., 98.7 % >> 60 %). Furthermore, the solution of Nielsen⁷⁸⁵ had 95 wt. % denatured whey protein relative to the total weight of

protein which is greater than 50 wt % denatured whey proteins relative to the total weight of protein as claimed in Leprino '860 (i.e. 95% >> 50%).

f. 8.5: “less than 11 wt. % native GMP relative to a total weight of protein in the denatured whey protein composition;”

91. In my opinion, Nielsen785 (incorporating Bertelsen) taught claim limitation 8.5.

92. As I explained in Section VII.A.3.c, Bertelsen's Example 7 and Nielsen785's Example 1 taught reducing the CMP weight percentage from a feed whey protein solution to a crystallized BLG powder. *See* Ex1006, Tables 3, 12, 60:30-35, 62:19-20, 69:11, 70:1-3; Ex1005, 88:15-89:3. The CMP content by total protein weight of the whey protein powder used in Nielsen785's denaturation step was 0.7%. Ex1005, 88:15-20. No protein was added or removed from the whey protein solution during the thermal treatment of Nielsen785's Example 1. Therefore, the CMP weight percentage remained approximately the same (0.7% w/w relative to the total protein) in the denatured whey protein nanogel. Nielsen785's GMP content is “native” because no enzymatic hydrolysis was involved in Nielsen785 and Bertelsen's processes, therefore, Nielsen785's GMP remained non-hydrolyzed and was 100% native GMP. Nielsen785 attained 0.7 wt. % native GMP relative to the total weight of protein which is less than 11 wt. % native GMP relative to the total weight of protein as claimed. Nielsen785 reduced the native GMP content of the

denatured whey protein composition using a novel BLG crystallization method that was different from methods described in the '860 patent, which did not mention BLG crystallization at all. In my opinion, the claims of the '860 patent were written in such a manner as to cover more than what was described in the specification of the '860 patent.

93. Accordingly, Nielsen785 (incorporating Bertelsen) described producing a denatured whey protein composition having GMP at 0.7% w/w relative to the total weight of protein. It is my opinion that Nielsen785 (incorporating Bertelsen) taught claim limitation 8.5 because a GMP level of 0.7% w/w is far less than 11%.

g. 8.6: “a proteolysis index of at least 8.0 wt. % or a beta-lactoglobulin to alpha lactalbumin ratio of greater than 5.00; and”

94. In my opinion, Nielsen785 (incorporating Bertelsen) taught claim limitation 8.6.

95. According to Nielsen785, crystallized “whey protein powder used for preparation of whey protein nanogels” contained 0.2% ALA and 96.5% BLG.

Protein source	BLG isolate
pH	5.67
Total solids%	95.2
Protein/total solids %	98.7
Ash %	0.51
Fat %	0.11
Lactose %	<0.09
Pho % of TS	<0.025
Na % of TS	0.025
K % of TS	0.051
Ca % of TS	0.146
Mg % of TS	0.022
Native ALA %	0.2
Native BLG %	96.5
CMP %	0.7
Ca:BLG w/w ratio	0.0016

Ex1005, 88:8-20, Table 1 (annotated). Those levels correspond to BLG-to-ALA ratio of about 482.5 (dividing 96.5 by 0.2). The disclosed heat-denaturation process would not affect the BLG-to-ALA ratio because claim limitation 8.6 does not differentiate between denatured and undenatured BLG, therefore, a POSITA would have understood that both denatured and undenatured BLG contents are considered in the calculation of the BLG-to-ALA ratio.

h. 8.7: “greater than 50 wt. % denatured whey proteins relative to the total weight of the protein in the denatured whey protein composition.”

96. In my opinion, Nielsen⁷⁸⁵ (incorporating Bertelsen) taught claim limitation 8.7.

97. Nielsen⁷⁸⁵ taught “a high level of BLG denaturation gives a better heat-stability of the resulting whey protein nanogels composition” and heat treatment “is performed for a duration sufficient to denature at least 50% w/w of the native BLG, more preferably at least 80% w/w of the native BLG, even more preferably at least 90% of the native BLG and most preferably at least 95% w/w of the native BLG.” Ex1005, 20:16-26. As I explained in Sections VII.A.3.d-VII.A.3.e, at least 95-97% of the whey protein relative to the total weight of protein in Nielsen’s whey protein nanogel preparations was denatured after heat treatment. Ex1005, 89:12-31 (“It was generally found that thermal treatment at e.g. 90 degrees C for 10 minutes lead to 95-97% denaturation with only 3-5% non-denatured protein (by Analysis 6) present after thermal treatment.”).

98. Denaturing at least 95% of the whey protein in the BLG powder composition relative to the total weight of protein corresponded to a denatured whey protein composition having well over 50 wt.% denatured whey proteins relative to the total weight of protein in the composition.

4. **Claim 9: “The method of claim 8, wherein the reduction of native GMP in the cheese whey retentate includes combining the cheese whey retentate with one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate to form the reduced-GMP cheese whey retentate composition, the one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate comprises at least one alkaline serine protease enzyme and at least one neutral protease enzyme, or wherein the reduction of GMP occurs through the microfiltration of the cheese whey retentate.”**

99. As I explained in Sections VII.A.2 and VII.A.3.b, Bertelsen’s Example 3 used three different types (i.e., feeds 1-3) of whey protein-containing raw materials, of which feed 2 was “derived from sweet whey.” Ex1006, 57:1-15, 60:30-35. All three feeds were subjected to crystallization. *Id.*, 60:28-61:14, 63:13-28. Feed 1 was centrifuged twice “on a Maxi-Spin filter with a 0.45 micron CA membrane.” *Id.*, 61:4-6. In my opinion, a POSITA would have known this was a microfiltration step because the 0.45µm cut off level—a common CA membrane cut-off level—was within known microfiltration membrane cut-off ranges. For example, Table 7 of Hinkova (Ex1013), annotated and reproduced below, listed membrane cut-off value of 500nm (0.5µm).

Table 7. Average protein rejection on ceramic membranes

Rejection factor $\pm$ SD/%				
Protein	Protein size ^a /kDa	Membrane cut-off		
		5 kDa	100 nm	500 nm
CMP	7	94.6 $\pm$ 7.6	70.2 $\pm$ 7.6	16.3 $\pm$ 2.3
α -La	14.2	96.7 $\pm$ 5.7	69.7 $\pm$ 1.5	16.3 $\pm$ 2.8
β -Lg B	18.4	97.5 $\pm$ 4.3	81.8 $\pm$ 2.7	17.8 $\pm$ 2.1
β -Lg A	18.4	96.3 $\pm$ 6.5	87.2 $\pm$ 3.1	26.3 $\pm$ 0.9

a) Maubois and Ollivier (1997); R_{CMP} – rejection of casein macropeptide, $R_{\alpha\text{-La}}$ – rejection of α -lactalbumin, $R_{\beta\text{-Lg A}}$ – rejection of β -lactoglobulin B, $R_{\beta\text{-Lg A}}$ – rejection of β -lactoglobulin A, SD – standard deviation.

100. Hinkova refers to filtration using 0.5 μ m membrane cut-off value as “microfiltration.” Ex1013, 331 (“Microfiltration using a 500 nm membrane was one of the fastest processes...”). Indeed, Nielsen⁴⁵⁰ also taught that filtrations using membrane pore size between 0.2 μ m and 1 μ m are considered “microfiltration.” See Ex1007, 48:7-11. A POSITA would have understood that a filtration process using membrane cut-off size of 0.45 μ m is microfiltration because 0.45 μ m is between 0.2 μ m and 1 μ m. Additionally, based on the teaching in Table 7 of Hinkova, a POSITA would also have understood that microfiltration with 0.45 μ m cut-off levels caused CMP reduction because filtration using 0.1 μ m and 0.5 μ m both resulted in CMP reduction. Ex1013, Table 7. A POSITA would also have understood that membranes with lower cut-off resulted in higher CMP rejection rate. See Ex1013, Table 7. For example, membranes with a 100nm cut-off resulted in CMP rejection rate of 70.2 $\pm$ 7.6%. *Id.*

101. According to Bertelsen, Feed 2 was also centrifuged twice with the same amount and type of water added as Feed 1. See Ex1006, 61:8-10. Specifically,

“[t]he pellet from feed 2 was washed with 2 volume MilliQ water and centrifuged again under standard conditions before the pellet was analyzed by HPLC.” *Id.* Bertelsen taught feed 2 was centrifuged twice because after water was added, feed 2 was “centrifuged **again**.” *Id.* (emphasis added).

102. It would have been obvious to a POSITA that feed 2 used the 0.45µm CA membrane because feed 2 also underwent a dual-centrifugation and water-adding process “under standard conditions.” *Id.* A POSITA would have understood that Bertelsen referred to “standard conditions” as the processing conditions of feed 1 because that disclosure related to feed 1 was the only disclosure in Example 3 regarding processing conditions prior to the discussion of processing feed 2. Similar to microfiltration process on feed 1, the microfiltration process on feed 2 would have also caused reduced CMP because Ex1013 taught that microfiltration using cut-offs between 0.1µm and 0.5µm causes CMP reduction. Bertelsen used microfiltration to separate BLG crystals from native CMP, which was not incorporated into the BLG crystal lattice.

5. Claim 11: “The method of claim 8, wherein the reduced-GMP cheese whey retentate composition is heated to a temperature of greater than or about 160° F.”

103. As I explained above in Section VII.A.3.d, Nielsen785’s whey protein solution produced from crystallized BLG powder was heated to “90 degrees C for 14 minutes...in a water bath.” Ex1005, 89:12-16. A POSITA would have recognized

that 90°C is 194°F¹, so Nielsen785 described heating to a temperature of at least about 160°F. POSITAs would have understood and reasonably expected that the 14-minute incubation in a 90°C (194°F) water bath would have raised temperatures of those beverage compositions to at least about 160°F because the heat-treatment step was included to denature BLG, BLG's denaturation temperature was well known to be about 70°C/158°F, and Nielsen785 disclosed that immersion in water baths at 90°C for even ten minutes did in fact result in 95-97% denaturation. Ex1005, 89:12-31, 19:11-16, 20:6-26; Ex1023, 40.

6. **Claim 13: “The method of claim 8, wherein the denatured whey protein composition is characterized by a weight ratio of native GMP to total whey protein of less than or about 0.15, and/or wherein the denatured whey protein composition is characterized by less than or about 11 wt. % GMP relative to the total weight of the protein in the denatured whey protein composition.”**

104. As I explained in Section VII.A.3.f, Nielsen785 (incorporating Bertelsen) taught a denatured whey protein composition having CMP at 0.7 wt% relative to the total protein, which is less than 11 wt% relative to the total weight of protein in the composition. In addition, the disclosed CMP concentration corresponds to 0.007 weight ratio of CMP relative to total protein (0.7 divided by 100).

¹ https://en.wikipedia.org/wiki/Conversion_of_scales_of_temperature (°F = °C × 1.8 + 32)

B. Ground 2: Obviousness over Bertelsen and Nielsen⁷⁸⁵ (Claims 8-9, 11-13)

1. Motivation to Combine

105. In Ground 1, I explained that Nielsen⁷⁸⁵ incorporated Bertelsen in its entirety, so their teachings formed a single reference. As I further explain below, even if considered separately, a POSITA would have been motivated to combine their teachings.

106. First, both were directed toward the same field of endeavor concerning protein compositions for food products. *Compare* Ex1006, Abstract (“The invention furthermore relates to new beta-lactoglobulin compositions, uses of these compositions and food products comprising these compositions”), *with* Ex1005, Abstract (“The present invention pertains to production of special whey protein nano gels by denaturation of whey protein and furthermore to the resulting whey protein nanogels, and their use in food products, such as beverages”). The two references both focused on protein compositions that are high in BLG. *Compare* Ex1006, 3:1-9, *with* Ex1005, 1:32-35. In addition, both references noted the substantial benefits of using BLG in food products. *See* Ex1006, 4:10-12 (“BLG is well-known to be a great source of essential amino acids, including e.g. leucine, and the edible BLG composition provided by the present invention therefore has several interesting nutritional uses”); Ex1005, 5:26-27 (“BLG is the most predominant protein in bovine whey and milk serum and exists in several genetic variants...”).

107. Second, Bertelsen and Nielsen785 were filed by the same applicant—Arla Foods AMBA, which is the Petitioner for this IPR. *Compare* Ex1005, (71), *with* Ex1006, (71). Bertelsen and Nielsen785 overlap in application, substantive content, and field of use. For example, both Bertelsen and Nielsen785 are in the field of the production of whey protein compositions for use in food products. *Compare* Ex1005, Abstract, *with* Ex1006, Abstract. The inventors listed in Bertelsen and Nielsen785 were colleagues working in the same building in the same city in Denmark and sharing the same sources of cheese whey and the same common analytical laboratory services.

108. Third, Bertelsen taught making BLG isolate powder with high BLG concentration, and Nielsen785 taught applications of such BLG isolate powders, such as using the powder to produce denatured protein compositions for beverages. For example, Nielsen785 taught ways to use crystallized BLG powders prepared as Bertelsen described to produce denatured BLG nanogel compositions for high-protein beverages that are “pleasant to drink.” Ex1005, 3:34-36. Bertelsen’s Examples 1, 3, and 7 collectively described a process for preparing “spray-dried BLG crystals.” Ex1006, 69:9-20. Bertelsen taught that the crystallized BLG preparations could have “several interesting nutritional uses” as a food ingredient. Ex1006, 4:10-23.

109. A POSITA would have looked to Nielsen785 because it described an apt use for Bertelsen's novel crystallized protein compositions—to make denatured whey protein nanogels for use as a food ingredient—and in fact Nielsen785 expressly called for using crystallized BLG isolate powder as produced in Bertelsen and even incorporated Bertelsen by reference. Ex1005, 89:1-3, 18:34-35 (“WO 2018/115520 A1 and PCT/EP2019/066998 are incorporated herein by reference for all purposes.”). In my opinion, it makes sense that after the discovery of how to make crystallized BLG, Arla Foods amba would launch a search for uses for the crystallized BLG.

110. Nielsen785's nanogels were “suitable for high protein beverages and enable[d] the production of high protein, heat-sterilised beverage products that have a low viscosity and therefore are pleasant to drink.” Ex1005, 3:34-36. This purpose aligned with Bertelsen's teaching. For example, Bertelsen expressly taught the importance of preparing high-protein beverages using BLG crystals. Ex1006, 55:13-14 (“The present inventors have realised that the preparation of acidic, high protein, low mineral, beverages or liquid from dry edible BLG composition comprising BLG crystals is not trivial.”). Therefore, a POSITA would have been motivated to combine Bertelsen's teachings with steps from Nielsen785 directed to making denatured whey protein nanogels from Bertelsen's BLG powder compositions for use in beverages.

111. In my opinion, a POSITA would have reasonably expected success in using the BLG powder from Bertelsen to produce Nielsen785's nanogels because Nielsen785 expressly taught using Bertelsen's BLG powders to successfully prepare denatured whey protein nanogel compositions for nutritional applications. Ex1005, 88:8-90:17 ("Exemplary whey protein solutions were prepared by dissolving BLG isolate powder produced as described in WO 2018/115520, Example 7"), 56:10-25. This combination was well within the skill of a POSITA and would have required nothing more than the application of known techniques (e.g., ultrafiltration, centrifugation, heating, heated/cooled water bath, etc.) and products (BLG isolate powders) as taught in Bertelsen to be used as described by Nielsen785. *See* Ex1006 57:1-32, 61:4-14, 69:11-20. The flow chart I provided in Section VII.A.2 illustrates the combined preparation processes of Bertelsen and Nielsen785. *Id.*

112. Thus, a POSITA would have understood Bertelsen and Nielsen785 were combinable and would have been motivated to combine them as set forth below with reasonable expectations of success.

2. Independent Claim 8

a. 8.pre: "A method of making a denatured whey protein composition, the method comprising:"

113. In my opinion, if limiting, the Bertelsen-Nielsen785 combination taught claim limitation 8.pre. For example, Bertelsen taught producing "beta-lactoglobulin compositions...containing crystallised beta-lactoglobulin." Ex1006,

Abstract (“The present invention relates to a new method of producing isolated beta-lactoglobulin compositions and/or compositions containing crystallised beta-lactoglobulin.”).

114. According to Bertelsen, its method of producing highly purified BLG composition “has the potential to change the way whey protein is handled” and “opens up for both efficient and gentle production of highly purified BLG which is safe to use as a food ingredient.” Ex1006, 3:11-13, 4:10 (“BLG is well-known to be a great source of essential amino acids...”).

115. Bertelsen’s BLG isolate powder with “highly pure BLG crystals” is produced using methods collectively described in Bertelsen’s Examples 1, 3, and 7, as I explain below.

116. Bertelsen’s Example 1 is titled “[c]rystallization of beta-lactoglobulin from a crude whey protein concentrate.” Ex1006, 56:35-36. “[S]weet whey from a standard cheese production process” is processed through “an ultrafiltration setup” to obtain ultrafiltered (UF) retentates. Ex1006, 57:3-18.

117. Bertelsen’s Example 3 used “the same experimental and analytical setup as in Example 1” to study three different types of whey protein-containing raw material for BLG crystallization. Ex1006, 60:30-35. The second type of whey protein solution prepared and studied in Example 3 (i.e., feed 2) is “based on sweet whey.” *Id.*, 60:33-35.

118. Bertelsen's Example 7 for preparing spray-dried BLG crystals used the sweet whey protein solution "produced in Example 3 (using feed 2)." Ex1006, 60:30-35, 69:11. In Example 7, sweet whey protein solution from feed 2 was "supersaturated with respect to BLG and has a pH in the range of 5-6," and the method proceeds to "crystallising BLG in the supersaturated whey protein solution." *Id.*, 3:19-23. The BLG crystals were separated "from the remaining whey protein solution" to make "a dry product such as e.g. a powder." *Id.*, 3:25-39

119. As I explained above in Section VII.B.1, the same BLG powder produced by Bertelsen's method was used in Nielsen785 to make BLG nanogels for high-protein beverages. Ex1005, 89:1-3 ("Exemplary whey protein solutions were prepared by dissolving BLG isolate powder produced as described in WO 2018/115520, Example 7."). Nielsen785 taught that BLG powder samples from Bertelsen were dissolved in water to form whey protein solutions. *See* Ex1005, 89:8-10. The whey protein solutions were "thermally treated at 90 degrees C for 14 minutes...in a water bath and subsequently cooled immediately in an ice-water bath." *Id.*, 89:12-16. Production of whey protein nanogel in the solution was confirmed using dynamic light scattering. *See id.*, 89:18-20.

120. After heat-treating the BLG solutions, Nielsen785 determined that "thermal treatment at e.g. 90 degrees C for 10 minutes lead to 95-97% denaturation with only 3-5% non-denatured protein" remaining. Ex1005, 89:29-31 ("It was

generally found that thermal treatment at e.g. 90 degrees C for 10 minutes lead to 95-97% denaturation with only 3-5% non-denatured protein (by Analysis 6) present after thermal treatment.”). Thermal treatments from the example above lasted longer than 10 minutes, which would have resulted in an even greater denaturation level because denaturation level generally increases with longer treatment time and higher treatment temperature.

b. 8.1-8.7

121. As I explained in Sections VII.A.3.b through VII.A.3.h Bertelsen and Nielsen taught 8.1-8.7, and as I also explained in Section VII.B.1, a POSITA would have been motivated to combine those references with a reasonable expectations of success.

- 3. Claim 9: “The method of claim 8, wherein the reduction of native GMP in the cheese whey retentate includes combining the cheese whey retentate with one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate to form the reduced-GMP cheese whey retentate composition, the one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate comprises at least one alkaline serine protease enzyme and at least one neutral protease enzyme, or wherein the reduction of GMP occurs through the microfiltration of the cheese whey retentate.”**

122. As I explained in Section VII.A.4, Bertelsen and Nielsen⁷⁸⁵ taught reducing GMP through microfiltration. Bertelsen used crystallization as a separation process to make pure BLG crystals, which are a solid, from cheese whey retentate,

and to leave behind spent supernatant solution, which is a liquid. Microfiltration was used to separate the solid BLG crystals—reduced in GMP content—from the liquid supernatant. Additionally, as I explained in Section VII.A.4, even if Bertelsen did not expressly teach using a 0.45 μ m CA membrane for feed 2, it would have been obvious for a POSITA to do so based Bertelsen’s express teaching on centrifuging feed 1 and that feed 2 was also centrifuged twice “under standard conditions.” Similarly, the microfiltration process would have also caused GMP reduction in feed 2.

4. Claim 11: “The method of claim 8, wherein the reduced-GMP cheese whey retentate composition is heated to a temperature of greater than or about 160° F.”

123. As I explained in Section VII.A.5, it is my opinion that Bertelsen and Nielsen⁷⁸⁵ taught the heating limitation of claim 11.

5. Claim 12: “The method of claim 8, wherein the heating of the reduced-GMP cheese whey retentate composition further comprises exposing the reduced-GMP cheese whey retentate composition to high shear conditions.”

124. It is my opinion that the combination of Bertelsen and Nielsen⁷⁸⁵ taught claim 12.

125. Nielsen⁷⁸⁵ taught that heat treatment to form whey protein nanogels may involve mechanical shearing: “mechanical shear is not excluded from the present invention” and in preferred embodiments heat-treatment step b) “does involve mechanical shearing.” Ex1005, 20:37-39. Step b) referred to “heating the

whey protein solution” to an elevated temperature (e.g., 68°C or higher) “for a duration sufficient to form a suspension of whey protein nanogels.” *Id.*, 2:22-23; *see also id.*, 3:6-7, 11:7-8, 11:31-32, 19:24-27, 27:31-34, 28:25-28, 29:29-32, 30:15-18, 32:1-4.

126. Although Nielsen⁷⁸⁵ did not identify a specific shear rate, it was well known to denature whey protein solutions under high-shear conditions while heating to achieve sufficient levels of denaturation, avoid aggregation of protein particles, and control particle-size distribution. Scraped surface heat exchangers are commonly used in the dairy industry to simultaneously heat and shear whey protein solutions. The rotator blade scrapes the walls of the heat exchanger to reduce particle sizes of the aggregated proteins and prevent buildup of deposits on the walls of the heat exchanger. Shear is essentially the rate of change of the velocity with distance and the short distance between the scraping blade and the heat exchanger wall, and the high rotation speed of the rotator causes high shear. For example, denaturing whey proteins at high temperature (e.g., 80-120°C) and “under very high shear forces” reduced processing time and avoided the formation of larger protein particles. *See* Ex1016, 16:19-17:13. Particularly, “very high” shear rates of “450,000

to 600,000 and usually about 500,000 reciprocal minutes”² were applied. *Id.*, 17:7-11.

127. A POSITA would have understood that shear rates such as $8,333\text{s}^{-1}$ is an example of high-shear conditions. Shear rates common to foods range from chewing (10 to 100 s^{-1}) to flow in pipes (100 to $1,000\text{ s}^{-1}$) to milk homogenizers having shear rates much greater than $1,000\text{ s}^{-1}$. Indeed, the '860 patent itself acknowledged that “[m]echanical shear conditions as used herein generally refer to high shear conditions in which at least about $1,000\text{s}^{-1}$ of shear is applied....” Ex1001, 8:66-9:1. As another example, heating performed simultaneously with high mechanical shearing denatured whey proteins (e.g., BLG) and converted whey protein gels to whey protein microparticles. *See* Ex1017, 1:14-19, 7:4-10, 13:31-36, 14:15-20, 18:14-36, 51:10-12. “Traditionally microparticulation of whey protein was performed in two steps employing heat denaturation followed by mechanical creation of microparticles,” but “heat denaturation and mechanical shear [could be combined] in one step” for greater efficiency. Ex1010, 3-4. Such mechanical shear

² $500,000\text{ reciprocal minutes shear rate equals about }8,333\text{s}^{-1}\text{ shear rate } (500,000\text{ min}^{-1}=500,000\text{ min}^{-1}/60\text{s/min}=8,333\text{s}^{-1})$.

could be “high-shear conditions” that enables “the formation of particles with a specific particle size similar to fat globules.”³ *Id.*

6. **Claim 13: “The method of claim 8, wherein the denatured whey protein composition is characterized by a weight ratio of native GMP to total whey protein of less than or about 0.15, and/or wherein the denatured whey protein composition is characterized by less than or about 11 wt. % GMP relative to the total weight of the protein in the denatured whey protein composition.”**

128. As I explained in Section VII.A.6, Bertelsen and Nielsen⁷⁸⁵ taught the alternative limitations of claim 13.

C. Ground 3: Obviousness Over Nielsen⁴⁵⁰ (Claims 8-9, 11-13, 15-20)

1. Overview of Nielsen⁴⁵⁰

129. In my opinion, Nielsen⁴⁵⁰ (Ex1007) is analogous art. Nielsen⁴⁵⁰ is directed to preparing beverages with high whey protein content (e.g., containing BLG that is at least 85% w/w of the protein). *Compare* Ex1007 3:1-32, 4:19-20, *with* Ex1001, Abstract, 9:38-47 (“the denatured whey protein composition may then be packaged or added directly to other ingredients for making a food or beverage composition”), 9:43-46, *see* 11:29-12:7.

³ Ex1010, Ex1016, and Ex1017 are cited herein to demonstrate POSITAs’ knowledge. *KSR*, 550 U.S. at 420.

130. Nielson⁴⁵⁰ recognized the “unique nutritional benefits for athletes” from incorporating whey protein into “beverages developed for sports nutrition.” Ex1007, 1:8-11. But whey products may have a yellow color, *id.*, 1:17-18, and beverage color played an important role in affecting “consumer’s perception of a beverage comprising whey proteins” because consumers disfavored yellowish colors. *Id.*, 3:2-5. Recognizing the importance of developing a colorless but still highly nutritious beverage, Nielsen⁴⁵⁰ described incorporating whey protein into a heat-treated beverage “which is more colour neutral than traditional whey containing beverages.” *Id.*, 3:7-10.

131. Nielsen⁴⁵⁰ described preparing exemplary whey powders and beverages. Ex1007, 95:11-113:12 (Examples 2-13). Those included BLG powders prepared through BLG crystallization (Examples 2-4) and beverage compositions made using such BLG powders (Examples 4-13). *Id.*, 95:11-113:12.

132. In Example 11, Nielsen⁴⁵⁰ described high-protein beverage compositions made using a BLG isolate powder containing 93.97% protein (w/w), of which 95.9% was BLG:

Table 9: Chemical composition of BLG isolate powder A.

Description	A - Dry BLG (w/w%)
BLG	95.9
Ash	0.51
Ca	0.1455
Cl	0.04
Lipid	0.11
K	0.0512
Mg	0.022
Na	0.025
NO ₃	2
NO ₂	0.07
PHO	0.025
Protein	93.97
Dry matter	95.19
pH	5.7

Ex1007, 109:29-31 (citing Table 9), 108:20-32 (Table 9).

133. According to Nielsen⁴⁵⁰, several different compositions were prepared, subjected to heat treatment in a water bath at 90°C, and tested for properties including viscosity, turbidity, and color. Ex1007, 109:28-110:24. The results showed production of “a stable colourless and transparent beverage at pH 7.0 even at a high protein concentration” and “a milky beverage with remarkably low viscosity.” Ex1007, 110:11-24.

134. In Nielsen⁴⁵⁰’s Example 12, high-protein beverages prepared using the same BLG powder from Example 11, but “[l]ipids were added...to evaluate the opportunity to prepare nutritional beverages also in the presence of fat.” Ex1007, 111:1-10 (citing Table 9). Solutions containing dissolved BLG powders and lipid

were heat-treated in a water bath at 90°C, optionally homogenized, and tested for properties including viscosity, turbidity, and color. *Id.*, 110:11-112:12. According to Nielsen450, “a stable colourless and transparent beverage” at high protein concentration was prepared using Powder A of Table 9. *Id.*, 110:13-16. Those results showed “it was possible to produce stable high protein BLG beverages even with a lipid content of 25% and 50% of the total energy content and still having a remarkably low viscosity.” Ex1007, 112:3-12.

2. Nielsen450 incorporated Bertelsen in its entirety and used BLG powders produced through Bertelsen’s methods

135. As I explained above, Nielsen450’s Examples 11 and 12 described high-protein beverage compositions prepared using crystalline BLG powder to form a liquid solution. *See* Ex1007, 108:14-20, 109:29-110:4, 111:3-5. The BLG powder composition used was shown in Table 9, denoted “BLG isolate powder A” in Examples 11 and 12. Ex1007, 108:20-32 (Table 9), 109:29-30, 111:3-5 (“Nutritional high protein beverages comprising 3w/w%, 6w/w%, 10w/w % and 12w/w % whey protein in which 95.9% w/w is BLG was prepared from BLG powder A (shown in Table 9). Lipids were added to a lipid content of 25% and 50% of the total energy content in order to evaluate the opportunity to prepare nutritional beverages also in the presence of fat.”).

136. Another example in Nielsen450—Example 9—involved the same crystalline BLG powder identified as “BLG powder A” in Table 9 and Examples 11 and 12 but there referred to it as “BLG powder B,” corresponding to its use in a preparation labeled “Beverage B.” Ex1007, 104:20-105:3 (Example 9 & Table 8). I have annotated Tables 8 and 9 to show the BLG powder composition data from those examples:

Table 9: Chemical composition of BLG isolate powder

Description	A - Dry BLG (w/w%)
BLG	95.9
Ash	0.51
Ca	0.1455
Cl	0.04
Lipid	0.11
K	0.0512
Mg	0.022
Na	0.025
NO ₃	2
NO ₂	0.07
PHO	0.025
Protein	93.97
Dry matter	95.19
pH	5.7

Table 8: Composition of protein ingredients (BDL=below detection limit)

Component	BLG powder A	BLG powder B	WPI powder
BLG	98.2	95.9	61
ALA	<0.5%	<0.5%	8
CMP	<1%	1.08	17
Ash	0.09	0.51	3.7
Ca	BDL	0.146	0.072
K	BDL	0.051	1.14
Na	BDL	0.025	0.484
Mg	BDL	0.022	0.007
pH	3.79	5.7	6.7

Ex1007, 108:20-32 (Table 9), 104:20-34 (Table 8). As shown in the above annotated tables, there are matching composition values in every overlapping parameter between them. For example, Table 9’s BLG, Ash, Mg, Na, and pH values are identical to those in Table 8, whereas Table 9’s Ca and K values are within rounding of those in Table 8. Therefore, those tables would have made clear to a POSITA that

the BLG powder identified as “BLG powder B” in Example 9 was the same powder used in Examples 11 and 12.

137. Although Examples 11 and 12 did not detail processes for preparing the BLG powder, Nielsen⁴⁵⁰ taught that BLG powder was preferably prepared using Bertelsen’s methods. Specifically, Nielsen⁴⁵⁰ taught BLG isolates were “preferably obtained according to WO 2018/115520.” Ex1007, 74:22-24 (citing Bertelsen). Example 9 confirmed the BLG powder with 95.9% BLG and 5.7 pH described in Tables 8 and 9 was produced according to Bertelsen’s methods. Example 9 specified its “beverages were produced according to example 4,” Nielsen⁴⁵⁰, 104:16, and Example 4 in turn explained that non-neutral BLG powders were “produced as outlined in example 7 of PCT/EP2017/084553,” Ex1007, 100:10-11. Application PCT/EP2017/084553 is Bertelsen. Ex1006, (21). And as I explained above in Sections VII.A.2, VII.A.3.a, and VII.A.3.b, Bertelsen’s Example 7 (through nested citations pointing to related Examples 1, 3) described the crystallization-based method for preparing BLG isolate powders from a cheese whey feedstock.

138. Upon review, I note that Nielsen⁴⁵⁰ incorporated Bertelsen in its entirety. Nielsen⁴⁵⁰ expressly stated that “[a]ll patent and non-patent references cited in the present application are hereby incorporated by reference in their entirety.” Ex1007, 79:19-20. Nielsen⁴⁵⁰ also specifically incorporated Bertelsen by reference, confirming that “in particularly preferred embodiments of the invention,

the BLG-enriched composition is prepared by crystallization at pH 5-6 under salting-in conditions as described in the PCT application PCT/EP2017/084553, which is incorporated herein by reference for all purposes.” *Id.*, 62:7-9. Therefore, it is my understanding that Bertelsen is effectively a part of Nielsen450. Because Bertelsen was directed to producing BLG products throughout, a POSITA would have understood Nielsen450 to incorporate with detailed particularity Bertelsen’s entire disclosure. At minimum, disclosures related to making crystalline BLG powders were expressly incorporated with particularity.

3. Denaturing exemplary high-protein beverages

139. I note that Nielsen450’s Examples 11-12 described preparing high-protein beverages with different protein by weight beverage solutions. Ex1007, 109:29-30, 111:3-4. For example, the various beverage solutions included 6-12% (Example 11) or 3-12% (Example 12) protein by weight. *Id.* Since the high-protein beverages were prepared using BLG powders of Table 9, I note that the main whey protein in those beverages was BLG—making up 95.9% w/w of the total protein. Ex1007, 108:20-32. Furthermore, compositions made with BLG powder “were heat treated in a water bath at 90°C for 5 min” in Examples 11-12. Ex1007, 109:32-110:1, 111:3-12.

140. I note that Nielsen450 did not teach specific degrees of denaturation achieved through heating in Examples 11-12. However, Nielsen450 did teach that

when a disclosed protein solution was heat-treated, especially at “85-95 degrees C” for “5-20 minutes,” the resulting degree of denaturation was “most preferably at least 80%.” Ex1007, 72:14-32; *see id.*, 39:23-27 (describing denatured, high-BLG compositions as “particularly advantageous to use for high protein beverages”). Furthermore, it was well known that heating whey-protein solutions, such as those in Examples 11-12, to a high temperature (e.g., 90°C) would have resulted in significant denaturation. For example, “it is known that whey protein is poor in heat stability and is therefore rapidly denatured by heating at 70 to 90°C.” Ex1019, [0003]. Accordingly, it would have been obvious to a POSITA that heating as described in Examples 11-12 would have resulted in rapid, significant denaturation because the heating temperatures in those examples (e.g., 85-95°C which is greater than the treatment temperature taught by Ex1019) and treatment durations were sufficient to cause significant whey protein denaturation.

141. I decided to replicate the beverage compositions described in Nielsen450’s Examples 11-12 to determine the degree of denaturation in heat-treated whey protein beverages using the same procedure used in the ’860 patent. As I explain below, I observed that the denaturation degrees of the samples in Nielsen450’s Examples 11-12 would have significantly exceeded 50% (e.g., 77%-85%).

142. I visited Arla Foods Ingredients Innovation Centre, located at Sønderupvej 2614, 6920 Videbæk, Denmark in person and directed experiments replicating beverage compositions described in Nielsen⁴⁵⁰ Examples 11-12—using the same “BLG powder A” material—and measuring the properties of those compositions.

143. At least based on my education credentials and scientific research experience in the field of biochemical engineering for dairy products, I am well-qualified to replicate Nielsen⁴⁵⁰’s Examples 11-12. As I further explain below, I had access to the original batch of crystalline BLG powder used in the Nielsen⁴⁵⁰ experiments as well as the same lab equipment setup. Ex1021 (“*Jæger*”), ¶¶1-14. Therefore, in my opinion, we faithfully reproduced the original experiments from Nielsen⁴⁵⁰ while adding the test for protein denaturation (using the denaturation determination method described in the ’860 patent) and measuring the particle size distribution of the denatured whey protein composition.

144. First, we performed the replicated experiments using BLG powder from the same batch used in Nielsen⁴⁵⁰’s original experiments for Examples 11-12: Table 9’s BLG powder composition used for preparing the high-protein beverages of Examples 11-12. *See* Ex1007, 109:29, 111:3-4. A named inventor from Nielsen⁴⁵⁰ identified and provided me a stored sample of the same batch of BLG powder that was used in the original experiments described in Examples 11-12. *Jæger*, ¶¶6-10.

That inventor was able to locate and identify a BLG powder sample from the same batch used to prepare the beverage compositions described in Examples 11-12. *Id.*

145. Upon my inspection, the stored sample provided to me had been labeled with a batch number and date (“Batch N11, 28-11-17, week 48”) that not only matched records documenting the original experiments reported as Examples 11-12 in Nielsen450, but also was consistent with the “N11” notations visible in Nielsen’s Figure 10 depicting beverage compositions from Example 11. *Jæger*, ¶¶6-10; see Ex1007, Fig. 10. The retrieved BLG powder sample was determined to contain 92.18% dry matter by weight and 89.25% protein by weight (92.03% of the total protein being BLG) using gravimetric analysis for dry matter and Kjeldahl analysis for protein. In my opinion, the slight (~3%) decrease in dry matter content compared to the earlier value reported in Nielsen450’s Table 9 most likely reflects limited moisture adsorption by the powder during storage.

146. Second, it is my understanding that the Petitioner of this IPR is the applicant of Nielsen450, and the original experiments described in Nielsen450 were performed in Arla’s laboratory facilities in Denmark. *See* Ex1007, Cover (71); *Jæger* ¶¶1-13. The replicated experiments were performed in the same facility using the same equipment. *Jæger* ¶¶1-13.

147. Third, as I explained in further details below for each claim limitation, Nielsen450 provided detailed, step-by-step narratives of sample preparation in Examples 11-12. *See* Ex1007, 109:28-112:12.

148. Fourth, I note that the '860 patent identified specific, well-known procedures for determining protein properties when assessing values recited in the challenged claims. For example, the '860 patent described the appropriate protocol for measuring denatured whey protein in a sample. Ex1001, 14:47-15:32, 13:3-36. The patent also identified equipment and parameters that can be used for measuring particle size distributions as recited in the claims. Ex1001, 15:33-40. I used those protocols to accurately assess whether the compositions prepared as described in Nielsen450's Examples 11-12 would have possessed the properties recited in the challenged claims.

4. Independent Claim 8

a. 8.pre: "A method of making a denatured whey protein composition, the method comprising:"

149. In my opinion, if limiting, Nielsen450 taught claim limitation 8.pre.

150. As I explained in Sections VII.C.1-VII.C.2, Nielsen450's Examples 11-12 described high-protein beverages made using BLG powder that was produced as described by Bertelsen. Nielsen450 described dissolving the BLG powder in water to form whey protein solutions, which were then treated "in a water bath at 90°C for 5 min." *See* Ex1007, 109:29-110:2, 111:3-13. As I explained above in

Section VI.B.3, heat treatment performed at high temperature (e.g., greater than 70 °C) can lead to significant denaturation, therefore, a POSITA would have understood and expected that the disclosed high-temperature treatments (e.g., 90 °C) would have denatured BLG in those whey protein solutions. In addition, as I more fully explain below in Section VII.C.4.g, I replicated Nielsen450's Examples 11-12 and demonstrated the processes described there made a denatured whey protein composition.

b. 8.1: “filtering cheese whey from enzymatically coagulated milk into a cheese whey retentate and a permeate; and”

8.2: “reducing native glycomacropeptides (GMP) in the cheese whey retentate to form a reduced-GMP cheese whey retentate composition; and”

151. In my opinion, Nielsen450 taught claim limitations 8.1 and 8.2.

152. As I explained in Section VII.C.2, Nielsen450 incorporated Bertelsen by reference in its entirety and specifically relied on Bertelsen's method for preparing crystalline BLG powder compositions. And as I explained in Sections VII.A.1-VII.A.2, that method included filtering cheese whey from enzymatically coagulated milk into a cheese whey retentate and a permeate and reducing GMP in the cheese whey retentate.

c. 8.3: “heating the reduced-GMP cheese whey retentate composition to form the denatured whey protein composition,”

153. In my opinion, Nielsen450 taught claim limitation 8.3.

154. I note that in both of Nielsen450’s Examples 11-12, high-protein beverages were prepared by dissolving BLG powder produced according to Bertelsen’s methods and heating the resulting liquid compositions at 90°C for five minutes. *See* Ex1007, 109:29-110:4; 111:11-13. As I explained in Section VII.C.3, a POSITA would have understood and expected those heat treatments to cause significant denaturation of the BLG protein in the beverage compositions. In addition, and as I explain below in Section VII.C.4.g, I confirmed that whey-protein compositions prepared and heated as described in Examples 11-12 demonstrated that vast majority of the whey proteins were denatured.

d. 8.4: “wherein the denatured whey protein composition is characterized by at least 60 wt. % whey protein on a dry weight basis;”

155. In my opinion, Nielsen450 taught claim limitation 8.4.

156. In Nielsen450’s Examples 11-12, high-protein beverages were prepared using the Table 9 BLG powder. Ex1007, 109:29-110:4, 111:11-13. That powder contained 93.97% protein by weight, 95.9% of which was BLG. Ex1007, 108:20-32 (Table 9). As I explained in Section VI.B.1, BLG is a whey protein present in cheese whey. Ex1007, 1:13-15; *see also*, Ex1010, Table 1.

157. In Example 11, Nielsen⁴⁵⁰ described beverage compositions made using the Table 9 BLG powder in solution at, among others, 6% protein by weight of the solution. Ex1007, 109:28-110:10. A POSITA would have understood that all protein in such beverage compositions was from the input BLG powder because neither the added water nor the NaOH or HCl (for adjusting pH value) contained any protein content. Therefore, the whey protein content of such beverage is determined solely by the input BLG powder, which contained 98.7% whey protein on a dry weight basis (93.97 % whey protein by total weight ÷ 95.2% dry matter by total weight). Ex1007, 108:20-32 (Table 9). Therefore, a POSITA would have understood that Example 11's beverage compositions contained at least 60% whey protein on a dry weight basis.

158. In Example 12, Nielsen⁴⁵⁰ described beverage compositions made using the Table 9 BLG powder in combination with added lipid. Ex1007, 111:1-112:2. For example, one disclosed beverage composition was made with 3% protein by weight of the solution and 0.45% lipid by weight of the solution. Ex1007, 111:20-30. As I explained above, a POSITA would have understood that (1) all protein in such beverage compositions was from the input BLG powder, and (2) the dry-matter content of such beverages would depend on the protein-powder and lipid inputs. As a POSITA would also have understood, 100g preparation of a beverage with 3% protein and 0.45% lipid as in Example 12 would have required 0.45g lipid (i.e.,

0.45% w/w) and 3g protein from the BLG powder (i.e., 3% w/w), calculated by using the total weight of the beverage and the weight-to-weight ratios of lipid and protein. The input protein powder contained 93.97% protein by weight, *see* Ex1007, 108:20-32 (Table 9), meaning that approximately 3.2g of the BLG powder would be required to provide 3g of protein. From that 3.2g of BLG powder, approximately:

- 3.04g would have been dry matter (i.e., 3.2g powder $\times$ 95.19% dry matter total weight basis); and
- 3g of the 3.04g of dry matter would have been protein (i.e., 3.2g powder $\times$ 93.97% protein total weight basis).

159. Accordingly, a POSITA would have understood that the total dry matter in an exemplary 100g sample of such a beverage composition to have been 3.49g (i.e., 3.04g from the BLG powder and 0.45g lipid), and that such compositions would have contained approximately 86.0% whey protein on a dry weight basis (i.e., $3 \div 3.49$) because essentially all the protein in the BLG powder is whey protein. Accordingly, a POSITA would have understood that such a composition contained at least 60% whey protein on a dry weight basis.

e. 8.5: “less than 11 wt. % native GMP relative to a total weight of protein in the denatured whey protein composition;”

160. In my opinion, Nielsen⁴⁵⁰ taught claim limitation 8.5.

161. As I explained in Section VII.C.4.d, a POSITA would have understood that the BLG powder used in Examples 11-12 was the only source of protein in the disclosed beverage compositions. Because Nielsen450 taught that GMP accounted for 1.08% by weight of the BLG powder used to make the beverage compositions, *see* Ex1007, 104:12-105:3 (Table 8), 108:20-32 (Table 9), a POSITA would have understood that GMP could have represented no more than 1.08 wt. % GMP relative to a total weight of protein in the disclosed denatured whey protein beverage composition. This is consistent with Nielsen450's disclosure indicating < 1% GMP in BLG powder A and 1.08% GMP in the BLG powder B, as shown below in Table 8 of Nielsen450. Conversely, the WPI powder of Table 8, made without the Bertelsen BLG crystallization process that separated native GMP from the BLG crystals, had 17 wt. % native GMP relative to a total weight of protein. This example illustrates that there are two different means to meet limitation 8.5: (1) to enzymatically hydrolyze native GMP as in the '860 patent and (2) to crystallize the BLG and separate native GMP from the BLG crystals as in Bertelsen and Nielsen785.

Table 8: Composition of protein ingredients (BDL=below detection limit).

Component	BLG powder A	BLG powder B	WPI powder
BLG	98.2	95.9	61
ALA	<0.5%	<0.5%	8
CMP	<1%	1.08	17
Ash	0.09	0.51	3.7
Ca	BDL	0.146	0.072
K	BDL	0.051	1.14
Na	BDL	0.025	0.484
Mg	BDL	0.022	0.007
pH	3.79	5.7	6.7

See Ex1007, 104:20-30; Section VII.C.2.

f. 8.6: “a proteolysis index of at least 8.0 wt. % or a beta-lactoglobulin to alpha lactalbumin ratio of greater than 5.00; and”

162. In my opinion, Nielsen450 taught claim limitation 8.6.

163. As I explained in Section VII.C.4.d, a POSITA would have understood that the BLG powder used in Examples 11-12 was the only source of protein in the disclosed beverage compositions. Because Nielsen450 taught that BLG accounted for 95.9% by weight of the total protein in the BLG powder used to make the compositions, see Ex1007, 108:20-32 (Table 9), a POSITA would have understood that ALA could have represented no more than 4.1% by weight of the protein (100% - 95.9%). Accordingly, a POSITA would have understood that the BLG-to-ALA ratio in the beverage compositions described in Examples 11-12 would have been at least 23.4 (95.9% ÷ 4.1%). Furthermore, that is consistent with the Nielsen450’s

disclosure indicating <0.5% ALA in the BLG powder, as shown in Table 8 of Nielsen450 below.

Table 8: Composition of protein ingredients (BDL=below detection limit).

Component	BLG powder A	BLG powder B	WPI powder
BLG	98.2	95.9	61
ALA	<0.5%	<0.5%	8
CMP	<1%	1.08	17
Ash	0.09	0.51	3.7
Ca	BDL	0.146	0.072
K	BDL	0.051	1.14
Na	BDL	0.025	0.484
Mg	BDL	0.022	0.007
pH	3.79	5.7	6.7

Ex1007, 104:20-30; Section VII.C.2. Less than 0.5% of ALA combined with 95.9% BLG provides a BLG-to-ALA ratio of at least 191.8 ($95.9\% \div 0.5\%$), exceeding the ratio of 5.00 as recited in claim limitation 8.6.

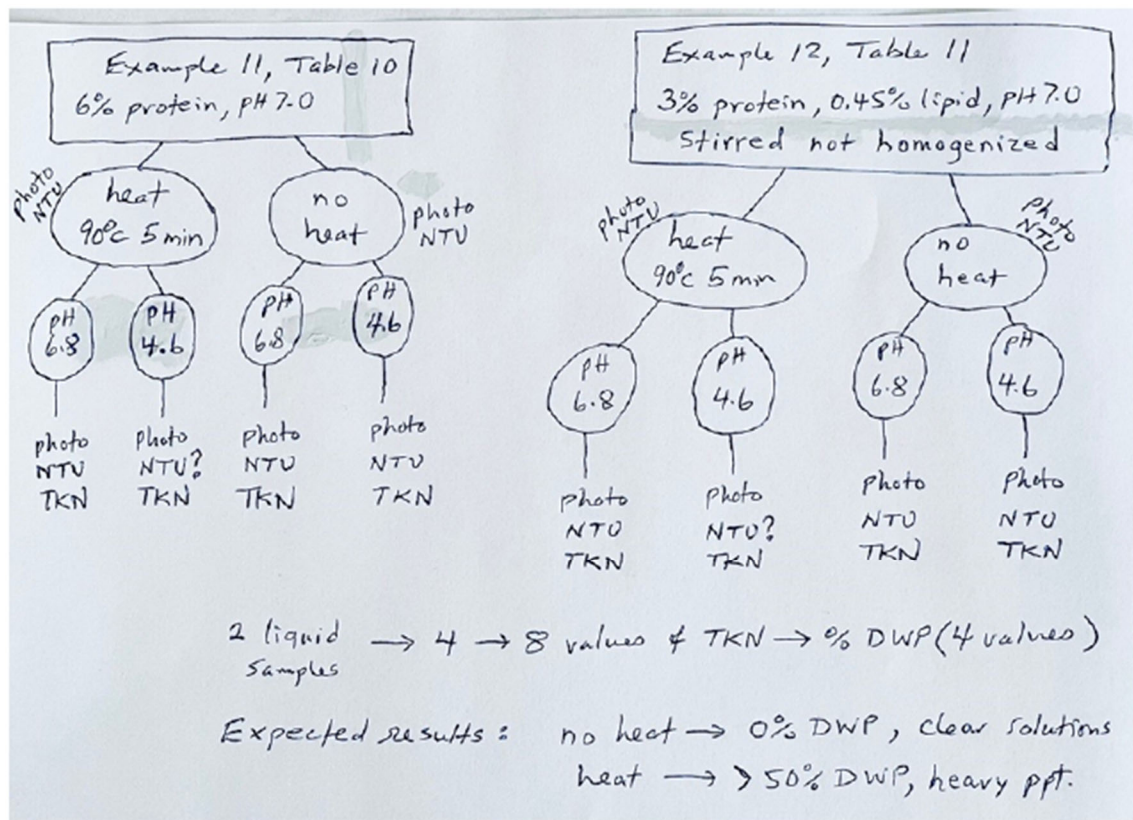
g. 8.7: “greater than 50 wt. % denatured whey proteins relative to the total weight of the protein in the denatured whey protein composition.”

164. In my opinion, Nielsen450 taught claim limitation 8.7.

165. As I explained in Section VII.C.4.c, Nielsen450 taught heating the beverage compositions described in its Examples 11-12 at 90°C for 5 min, and as I also explained in Sections VI.B.3 and VII.C.3, a POSITA would have understood that such high temperature and treatment duration would have caused rapid and significant denaturation of the BLG protein in those compositions. Furthermore,

Nielsen⁷⁸⁵ reported that “thermal treatment at e.g. 90 degrees C for 10 minutes lead to 95-97% denaturation with only 3-5% non-denatured protein” remaining. Ex1005, 89:29-31. As found by de Wit and Swinkels (1980) (Ex1023) using differential scanning calorimetry, BLG denatures at 70°C. Ex1023, 40 (“[I]t was concluded that 70°C is a critical temperature for the denaturation of β -lactoglobulin” at which aggregation process would start). Given the use of a water bath set to a temperature of 90°C, well above the known denaturation temperature of BLG, for a substantial time of 5 min before cooling, a POSITA would have understood and reasonably expected that denatured whey proteins would have made up at least 50% of the total weight of protein in the heat-treated compositions of Nielsen⁴⁵⁰’s Examples 11-12.

166. Moreover, as I explained in Section VII.C.3 and further below, I personally conducted experiments to confirm the denaturation levels by recreating one high-protein beverage composition from Example 11 and one from Example 12 according to the instructions provided in Nielsen⁴⁵⁰ and using the same BLG powder composition that was used during the original experiments reported in Examples 11-12. An excerpt from my lab notebook demonstrating the preparation of the experiments is provided below:



167. A list of raw ingredients is provided below, illustrating the batch number of the BLG powder used, which Arla's scientist informed me is the same batch of material used in Nielsen450:

Raw materials

Sample name	SAP no	Protein [%]
BLG powder A	batch N11, 28-11-17, week 48	Measured 2017=93.97% 2025 = 89.25 % (SAP no 696248)
3w/w% NaOH		
Rapeseed oil = canola oil		
Grinsted citrem LR10 (stabilisator)		

168. I also confirmed with Arla scientists that the lab equipment for performing those experiments were the same or functionally equivalent as those used in Nielsen450. An equipment list is provided below:

ID	Equipment Name	Location	Category	Responsible
E-0040	Homogenizer	Tech. & Func.	Training required	Lab. Technicians
E-0041	Malvern Mastersizer 3000	Tech. & Func.	Dedicated operator only	BIPI
E-0055	Turbiquant	Tech. & Func.	Training required	CKLJ
	Water bath			
	pH-meter			
	Magnet stirrer			
	Thin-walled glass tube (with red lids)			
E-0024	Sigma centrifuge	Centrifuges & Freezers	Training required	LDJEN

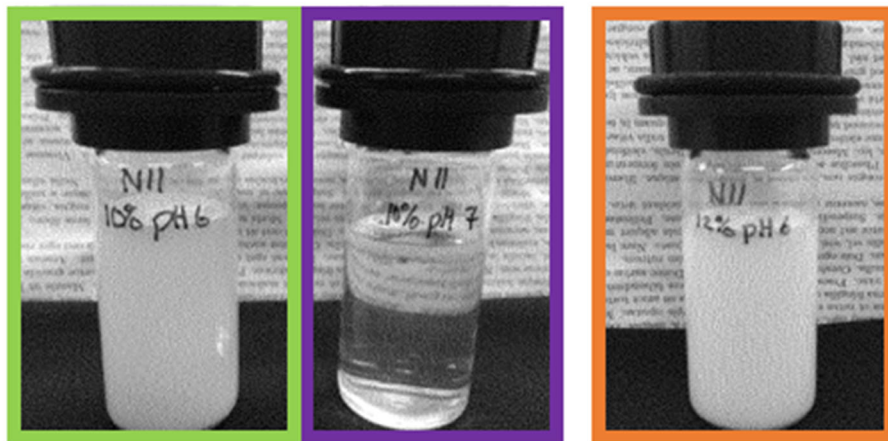
(a) Experiments confirmed Example 11 taught greater than 50% denatured whey proteins

169. In Example 11, Nielsen450 taught that the Table 9 BLG powder was solubilized to prepare whey protein beverages comprising 6, 10, or 12 w/w% protein. Ex1007, 109:29-110:6. The pH values of the solutions were “adjusted to pH 6.0 and 7.0 with 3 w/w% NaOH or HCL.” Ex1007, 109:31-32. Properties of the Example 11’s high-protein beverages were listed in Table 10 and some of the compositions were depicted in photographs in Figure 10:

Table 10. Properties of high protein BLG beverages at pH 6.0 and pH 7.0. Grey cells = not determined due to sample gelation.

Pow- der	Pro- tein w/ w%	pH	Vis- cosity cP	Turbid- ity NTU	De- script ion	L*	a*	b*	Δb^*	Insol- uble protein matter %
A	6	6.0								
			1.9	-	Milky	90.73	-1.96	1.76	-1.54	0
	10	7.0	4.1	14.6	Clear	39.87	-0.11	0.04	0.26	0
		6.0	2.8	>11000	Milky	90.47	-2.54	-2.4	-2.18	0
	12	7.0	57.7	11.1	Clear	39.74	-0.11	0.04	0.26	0
		6.0	4.5	-	Milky	90.38	-2.24	1.92	-1.70	0
		7.0	Gel							

Figure 10



Ex1007, 110:6-10, Fig. 10, Table 10 (both annotated).

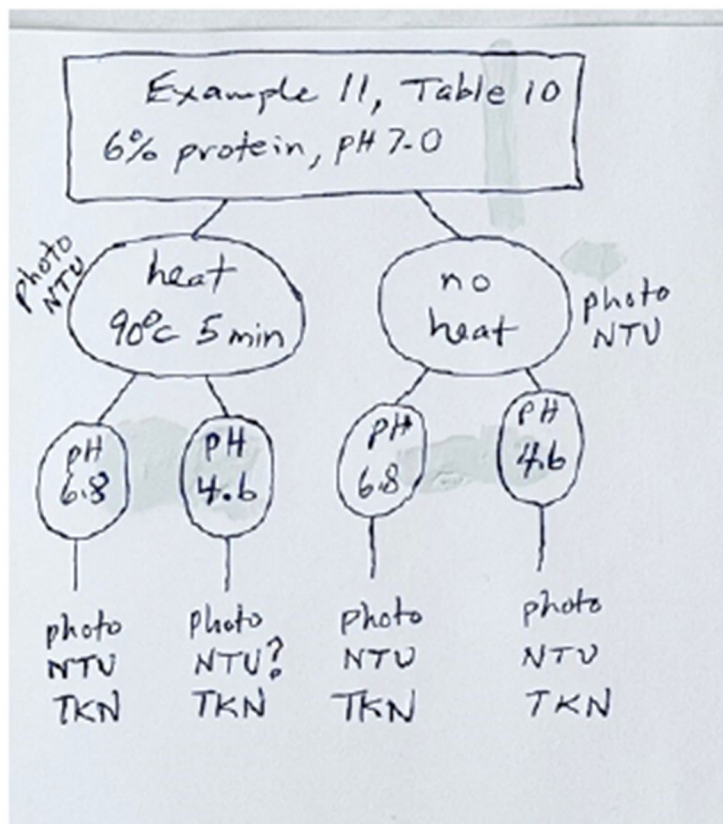
170. At Arla's laboratory facility in Denmark, I directed experiments to repeat the preparation of one of Example 11's high-protein BLG beverages—in particular, the beverage composition having 6% protein and pH 7.0, as indicated in the annotated version of Table 10 below:

Table 10. Properties of high protein BLG beverages at pH 6.0 and pH 7.0. Grey cells = not determined due to sample gelation.

Pow- der	Pro- tein w/ w%	pH	Vis- cosity cP	Turbid- ity NTU	De- script ion	L*	a*	b*	Δb^*	Insol- uble protein matter %
A	6	6.0						-		0
			1.9	-	Milky	90.73	-1.96	1.76	-1.54	
		7.0	4.1	14.6	Clear	39.87	-0.11	0.04	0.26	0
	10	6.0	2.8	>11000	Milky	90.47	-2.54	-2.4	-2.18	0
	12	7.0	57.7	11.1	Clear	39.74	-0.11	0.04	0.26	0
		6.0						-		0
			4.5	-	Milky	90.38	-2.24	1.92	-1.70	
		7.0	Gel							

As I explained above and in Section VII.C.3, I was able to prepare that composition using the same BLG powder, in the same laboratory facility, using the same equipment that was used in the original experiments described in Nielsen450's Example 11.

171. I directed preparation and processing steps matching those set forth in Example 11. Ex1007, 109:28-110:2, 100:24-33. The experiments were planned as below (excerpt from lab notebook):



172. In particular, a batch of the (6% protein, pH 7.0) Example 11 composition was prepared by mixing 16.8g of the retrieved BLG powder (containing 89.25% protein by weight) with water to a total mass of 250g and adjusting the pH to 7.0 with 3w/w% NaOH.

173. The resulting composition was split in two: one portion was maintained at ambient temperature with no heat treatment (Sample 1), and a second portion was subjected to heat treatment as described in Example 11 (Sample 2):

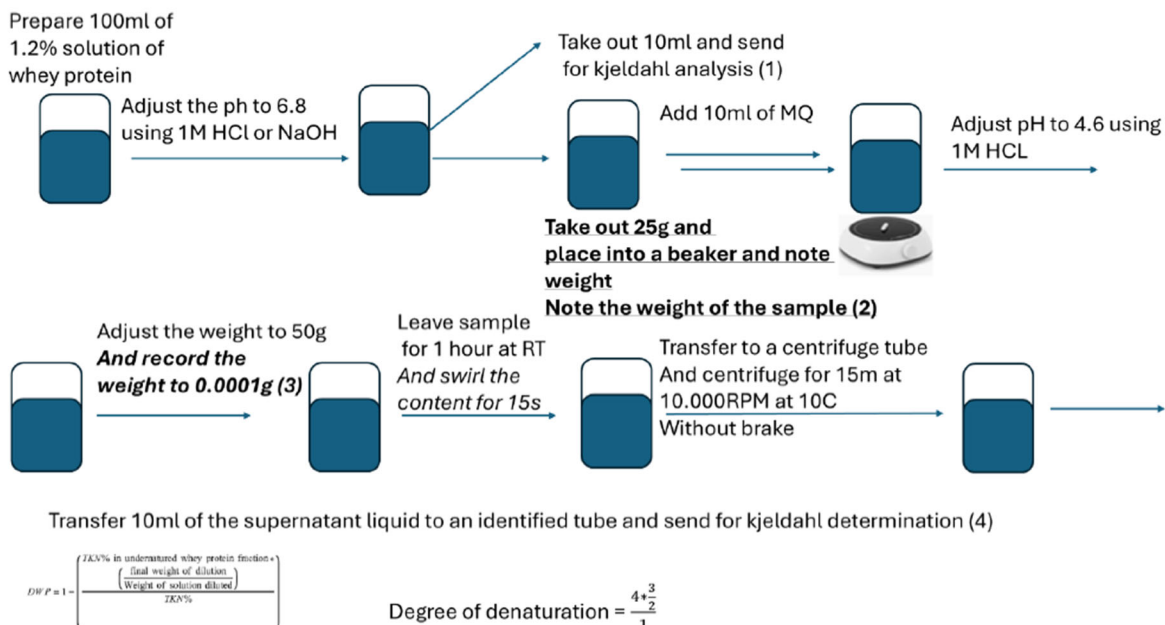
Sample No.	Protein w/w%	pH	Heat treatment
1	6	7	No
2	6	7	Yes

174. The portion designated for heat treatment as Sample 2 was used to fill five of the same “thin-walled glass vials” described and depicted in Nielsen450. *See* Ex1007, 100:30-33 (Example 5), 109:32-110:2 (Example 11, describing heat treatment “according to Example 5”), Fig. 10. Each vial received 20 ml of the beverage composition. The vials were then capped, except for one vial that was covered with aluminum foil to permit measuring the temperature of the beverage composition during the heating process. The Sample 2 vials were then immersed in a water bath preequilibrated to 90°C and incubated for five minutes, followed by cooling in an ice water bath and incubation at room temperature until the samples reached ambient temperature. A copy of relevant sections from my lab notebook is provided below:

For '860 claim 8 – WO'450 Example 11

- o Prepare 250 g of 6% w/w protein, pH 7.0 beverage (WO'450 at p.110, Table 10).
 - § Add 16.8 g powder and to total 250g with water. Stir for 30 min. with magnet stirrer. pH adjust to pH 7.0 (approx.. 20°C), with 3 w/w% NaOH.
- o Split solution into samples for heat treatment and no heat treatment.
- o Heat-treated samples.
 - § Fill (5 vials) of same "thin-walled glass vials" (WO'450 at p.100, Example 5) with 20 ml of 6% protein solution. Add on the lids. (30 ml will be too full)
 - § Heat treat the protein solution in those glass vials by immersing and incubating the vial in a 90°C water bath for 5 minutes, then cool in ice water (for approx. 15 min). Allow to reach room temperature as indicated in Example 11.
 - Record the temperature of the protein solution in the glass vials during the heating stage, before cooling in ice water. (See '860 patent, claim 11.). Use the temperature-logger, add to vial with sample and tinfoil as a lid. Take picture of the measurement at 5 min. incubation. Note down ____88.7____°C
- o Unheated samples – maintain at ambient temperature.
- o Take photos and measure NTU (add approx. 20 mL in glass) of the heat-treated and unheated samples.

175. The degree of denaturation in Sample 1 and Sample 2 was then determined according to the same standard procedure designated for that purpose in the '860 patent. Ex1001, 14:47-15:32. The denaturation level measurement is summarized in the flow chart I created below:



176. The procedure described in the '860 patent for measuring denaturation is substantially similar to the method for measuring protein denaturation described in Nielsen⁴⁵⁰'s Example 1.3; both methods depend on the selective precipitation of denatured whey protein at pH 4.6 that was well known in the art. *Compare* Ex1007, 80:28-81:10, *with* Ex1001, 14:47-15:40.

177. The results showed that the heat-treated Sample 2 composition contained 85% denatured protein relative to the total protein weight, while the Sample 1 portion that did not undergo heat treatment contained only 1% denatured protein:

Calculation of Degree of Denaturation

	6% protein pH 7 -HT	6% protein pH 7 +HT
Final weight of dilution	49,9483	50,0651
Weight of solution diluted	25,0072	24,9919
TKN%	1,23	1,2
DWP%	0,61	0,09
Degree of denaturation	1%	85%

Sample 1 Sample 2

Commas are used as the decimal separator in the table above. Those results showed that the retrieved BLG powder sample used in the experiments had remained almost entirely undenatured during storage. The results also confirmed a POSITA's reasonable expectation that the same heat-treated, 6% protein, pH 7.0 high-protein

beverage composition described in Nielsen450's Example 11—which was prepared and treated in the same way using the same BLG powder—would have contained greater than 50% denatured whey proteins relative to the total weight of protein in the composition just like Sample 2.

(b) Experiments confirmed Example 12 taught greater than 50% denatured whey proteins

178. In Example 12, Nielsen450 taught the same Table 9 BLG powder was solubilized to prepare whey protein beverages comprising 3, 6, 10, or 12w/w% protein. Ex1007, 111:1-112:2. The Example 12 compositions also contained lipid at concentrations ranging from 0.45 to 5.4w/w% “to evaluate the opportunity to prepare nutritional beverages also in the presence of fat.” Ex1007, 111:4-6. The pH was adjusted to 6.0 or 7.0, and the samples were heat-treated at 90°C, with an optional homogenization step. Ex1007, 111:7-16. Properties of the resulting high-protein beverages were reported in Nielsen450's Table 11:

Table 11. Properties of milky BLG beverages with added lipids.

Pro- tein w/w%	Lipid w/w% (%E)	pH	Viscos- ity cP	Turbid- ity NTU	De- scrip- tion	L*	a*	b*	Δb^*	Insolu- ble protein matter %
3	0.45 (25%E)	6.0	2.1	-	Milky	89.36	-0.78	-0.92	-0.70	0
		7.0	1.4	7652	Milky	58.35	-1.46	-6.76	-6.54	0
	1.35 (50%E)	6.0	1.9	-	Milky	88.76	-0.8	-1.13	-0.91	0
		7.0	2.0	>11000	Milky	69.07	-1.47	-4.97	-4.75	0
6	0.9 (25%E)	6.0	1.9	>11000	Milky	90.7	-2.34	-2.4	-2.18	0
		7.0	5.0	2122	Milky	33.87	-0.18	-2.23	-2.01	0
	2.7 (50%E)	6.0	1.9	>11000	Milky	90.71	-2.42	-2.49	-2.27	0
		7.0	4.7	2951	Milky	37.71	-0.32	-2.3	-2.08	0
10	1.5 (25%E)	6.0	3.8	>11000	Milky	90.96	-2.83	-2.46	-2.24	0
		7.0	178.3	3628	Milky	37.44	-0.41	-1.49	-1.27	0
	4.5 (50%E)	6.0	4.8	>11000	Milky	90.6	-2.66	-2.11	-1.89	0
		7.0	5.5	>11000	Milky	90	-2.94	-2.85	-2.63	0
12	1.8 (25%E)	6.0	5.7	>11000	Milky	90.7	-2.16	-2.2	-1.98	0
		7.0	Gel							
	5.4 (50%E)	6.0	7.8	>11000	Milky	89.09	-2.35	-2.9	-2.68	0
		7.0	Gel							

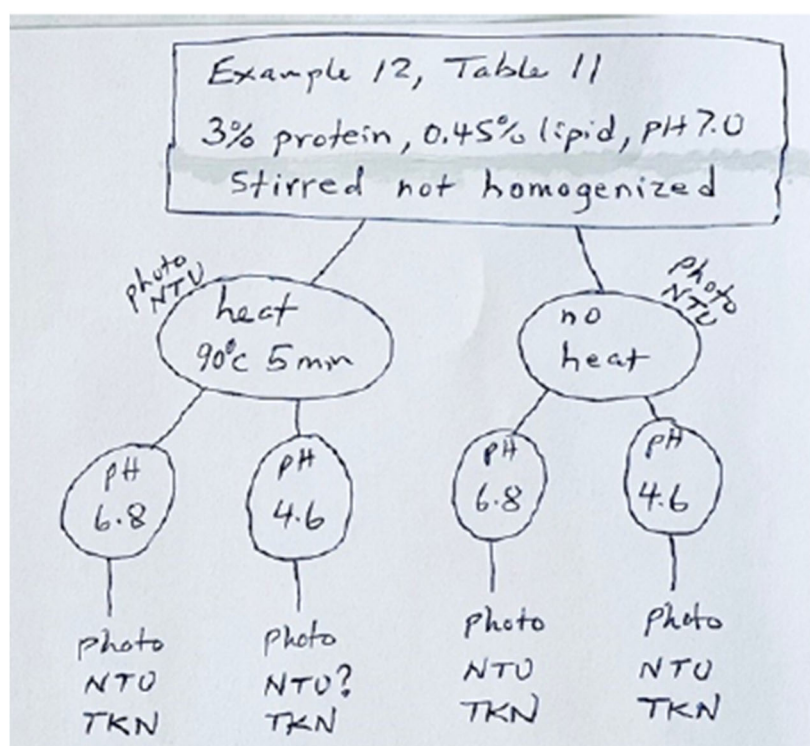
Ex1007, 111:24-112:2.

179. I directed experiments to repeat one preparation of a composition described in Nielsen450's Example 12—in particular, the one having 3% protein, 0.45% lipid, and pH 7.0, as emphasized in the annotated Table 11 below:

Table 11. Properties of milky BLG beverages with added lipids.

Protein w/w%	Lipid w/w% (%E)	pH	Viscosity cP	Turbidity NTU	Description	L*	a*	b*	Δb^*	Insoluble protein matter %
3	0.45 (25%E)	6.0	2.1	-	Milky	89.36	-0.78	-0.92	-0.70	0
		7.0	1.4	7652	Milky	58.35	-1.46	-6.76	-6.54	0
	1.35 (50%E)	6.0	1.9	-	Milky	88.76	-0.8	-1.13	-0.91	0
		7.0	2.0	>11000	Milky	69.07	-1.47	-4.97	-4.75	0
6	0.9 (25%E)	6.0	1.9	>11000	Milky	90.7	-2.34	-2.4	-2.18	0
		7.0	5.0	2122	Milky	33.87	-0.18	-2.23	-2.01	0
	2.7 (50%E)	6.0	1.9	>11000	Milky	90.71	-2.42	-2.49	-2.27	0
		7.0	4.7	2951	Milky	37.71	-0.32	-2.3	-2.08	0
10	1.5 (25%E)	6.0	3.8	>11000	Milky	90.96	-2.83	-2.46	-2.24	0
		7.0	178.3	3628	Milky	37.44	-0.41	-1.49	-1.27	0
	4.5 (50%E)	6.0	4.8	>11000	Milky	90.6	-2.66	-2.11	-1.89	0
		7.0	5.5	>11000	Milky	90	-2.94	-2.85	-2.63	0
12	1.8 (25%E)	6.0	5.7	>11000	Milky	90.7	-2.16	-2.2	-1.98	0
		7.0	Gel							
	5.4 (50%E)	6.0	7.8	>11000	Milky	89.09	-2.35	-2.9	-2.68	0
		7.0	Gel							

180. I directed preparation and processing steps matching Example 12. Ex1007, 111:1-112:12, 100:24-33. An excerpt from my lab notebook outlining the plans for replicating Example 12 is provided below:



181. The samples were prepared as outlined below (excerpt from my lab notebook). Specifically, samples without homogenization were prepared as follows:

- § Prepare 250 g of 3% w/w protein, 0.45% w/w lipid (canola oil), pH 7.0 beverage (WO'450 at 111, Table 11). (without homogenization) (approx. 13% wt. % fat on a dry weight basis)
- § Equilibrate oil and water (min. 240.48g) at 70°C in a water bath.
- § Dissolve 0.2% Grindsted Citrem LR10 in the heated oil (approx. 0.02 g LR10 to total 10g oil).
- § Then slowly mix (using magnet stirrer) 1.125 g of the oil with 240.48 g preheated water.
- § Cool solution to 60°C by set water bath temperature to 50°C. Check by measure temperature.
- § Add 8.4 g of Protein A BLG powder and stir with magnetic stirrer for 45 minutes.
- § Adjust the pH to 7.0 with 3%w/w NaOH.
- § Photograph and record NTU of the solution.
- o Split solution into samples for heat treatment and no heat treatment. (due to inhomogeneous sample split the sample while stirring)
- o Heat-treated samples.
- § Fill (5 vials) of the same "thin-walled glass vials" (WO'450 at p.100, Example 5) with 20 ml of the 3% protein / 0.45% lipid solution. Add on the lids.
- § Heat treat the vial containing the protein solution by immersing the vial in a 90°C water bath for 5 minutes, then cool in ice water. (for approx. 15 min). Allow to reach ambient temperature as indicated in Example 12.
- Record the temperature of the protein solution in the glass vials during the heating stage, before cooling in ice water (See '860 patent claim 11). Use the temperature-logger, add to vial with sample and tinfoil as a lid. Take picture of the measurement at 5 min. incubation. Note down ____ 88.3 ____ °C
- o Unheated samples – maintain at ambient temperature.
- o Take photos and measure NTU of the heat-treated and unheated samples.
- o Measure particle size distribution of heat-treated sample by Mastersizer (Leprino settings).

Samples prepared with homogenization were prepared as follows:

- o Prepare 500 g of 3% w/w protein, 0.45% w/w lipid, pH 7.0 beverage (WO'450 at 111, Table 11). (with homogenisation)
 - § Equilibrate oil and water at 70°C in a water bath.
 - § Dissolve 0.2% Grindsted Citrem LR10 in the heated oil (approx. 0.02 g LR10 to total 10g oil).
 - § Then slowly mix (using magnet stirrer) 2.25 g of the oil with 480.95 g preheated water.
 - § Cool solution to 60°C by set water bath temperature to 50°C. Check by measure temperature.
 - § Add 16.8 g of Protein A BLG powder and stir with magnetic stirrer for 45 minutes.
 - § Homogenized the solution at 200/50 bar (step 2 is regulated to 50 bar and step 1 is regulated to 250 bar according to the display) for 5min. recirculation.
 - § Adjust the pH to 7.0 with 3%w/w NaOH.
 - § Photograph and record NTU of the solution.
- o Split solution into samples for heat treatment and no heat treatment.
- o Heat-treated samples.
 - § Fill (5 vials) of the same "thin-walled glass vials" (WO'450 at p.100, Example 5) with 20 ml of the 3% protein / 0.45% lipid solution. Add on the lids.
 - § Heat treat the vial containing the protein solution by immersing the vial in a 90°C water bath for 5 minutes, then cool in ice water. (for approx. 15 min). Allow to reach ambient temperature as indicated in Example 12.
 - Record the temperature of the protein solution in the glass vials during the heating stage, before cooling in ice water (See '860 patent claim 11).). Use the temperature-logger, add to vial with sample and tinfoil as a lid. Take picture of the measurement at 5 min. incubation. Note down ____88.4____ °C
- o Unheated samples – maintain at ambient temperature.
- o Take photos and measure NTU of the heat-treated and unheated samples.
- o Measure particle size distribution of heat-treated sample by Mastersizer (Leprino settings).

182. As shown above, a 500g batch of the (6% protein, 0.45% lipid, pH 7.0) Example 12 composition was prepared. Separate vessels containing water and canola oil were equilibrated at 70°C in a water bath. Ex1007, 111:6, 33:28-30. Approximately 0.02g of Grindsted Citrem LR10 emulsifier was dissolved in heated oil to a total mass of 10g (0.02% LR10 in oil), and 2.25g of the LR10/oil was slowly mixed with 480.95g of the heated water. Ex1007, 111:7-8. The resulting oil/water solution was then immersed in a water bath set to 50°C, and its temperature was monitored until the solution reached 60°C. Ex1007, 111:8-9. At that point, 16.8g of the retrieved BLG powder (containing 89.25% whey protein by weight) was added

and stirred for 45 minutes. The solution was then adjusted to a pH of 7.0 using 3%w/w NaOH. Ex1007, 111:8-9.

183. The solution was then split in half. The first half was split again into portions denoted Samples 3 and 4 both without homogenization, but without and with heat treatment, respectively. The second half of the solution was then split into portions denoted Samples 5 and 6, both with homogenization at 200/50 bar, but without and with heat treatment, respectively. Samples 3 and 5 were maintained at ambient temperature, while Samples 4 and 6 were subjected to heat treatment as described in Example 12. Specifically, Samples 4 and 6 were each used to fill five of the same “thin-walled glass vials” described and depicted in Nielsen450. *See* Ex1007, 100:30-33 (Example 5), 111:12-13 (Example 12, describing heat treatment “according to example 5”), Fig. 10. Each vial received 20 ml. Four vials were capped, and one vial was covered with aluminum foil to permit measuring the temperature of the beverage composition during the heating process. The vials were then immersed in a water bath preequilibrated to 90°C and incubated for 5 minutes, cooled in an ice water for approximately 15 minutes, and incubated at room temperature until the samples reached ambient temperature. Ex1007, 111:13. Samples 3-6 are summarized below:

Sample No.	Protein w/w%	Fat%	pH	Heat treatment	Homogenization
3	3	0.45	7	No	No
4	3	0.45	7	Yes	No
5	3	0.45	7	No	Yes
6	3	0.45	7	Yes	Yes

184. I note that when Samples 3 and 4 were first prepared for denaturation testing, I immediately realized that the labelling of Samples 3 and 4 was switched and that the samples were pipetted into to the opposite beaker. After all six samples were adjusted to pH 4.6 it was immediately obvious that Samples 3 and 4 were accidentally switched because the sample without heat treatment had more precipitated protein than the sample with heat treatment. This did not make sense. The next day, the remaining excess material for Samples 3 and 4 were correctly pipetted into new beakers and sent for re-testing, yielding the correct data shown above for Samples 3 and 4.

185. As I explained in Section VII.C.4.g(a), the degree of denaturation in the heat-treated and untreated beverage samples were then determined according to the same standard procedure designated for that purpose in the '860 patent. Ex1001, 14:47-15:32. The results showed that the heat-treated compositions made according to Example 12 (Samples 4 and 6) contained over 70% denatured protein relative to the total protein weight, while the portions that did not undergo heat treatment

(Samples 3 and 5) contained minimal denatured protein (comma is used as decimal separator):

	3%0,45%oil PH 7 - homo - HT	3%0,45%oil PH 7 - homo + HT
Final weight of dilution	49,816	50,004
Weight of solution diluted	24,977	24,998
TKN%	1,26	1,29
DWP%	0,61	0,17
Degree of denaturation	3,4%	73,6%

Sample 3

Sample 4

	3%0,45%oil PH 7 + homo - HT	3%0,45%oil PH 7+ homo + HT
Final weight of dilution	49,9891	50,0803
Weight of solution diluted	25,004	25,0042
TKN%	1,23	1,22
DWP%	0,59	0,14
Degree of denaturation	4%	77%

Sample 5

Sample 6

186. Those results confirmed a POSITA's reasonable expectation that the same heat-treated, 3% protein, 0.45% lipid, pH 7.0 high-protein beverage composition described in Nielsen⁴⁵⁰'s Example 12—which was prepared and treated in the same way using the same BLG powder—would have contained greater than 50% denatured whey proteins relative to the total weight of protein in the composition, just like Samples 4 and 6.

5. **Claim 9: “The method of claim 8, wherein the reduction of native GMP in the cheese whey retentate includes combining the cheese whey retentate with one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate to form the reduced-GMP cheese whey retentate composition, the one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate comprises at least one alkaline serine protease enzyme and at least one neutral protease enzyme, or wherein the reduction of GMP occurs through the microfiltration of the cheese whey retentate.”**

187. As I explained in Section VII.C.2, Nielsen⁴⁵⁰ incorporated Bertelsen by reference in its entirety and specifically relied on Bertelsen’s method for preparing BLG powder compositions. And as I also explained in Section VII.A.2, that method included filtering cheese whey from enzymatically coagulated milk into a cheese whey retentate and a permeate and reducing GMP in the cheese whey retentate. As I further explained in Section VII.A.4, Bertelsen taught reducing GMP through microfiltration. Therefore, it is my opinion that Nielsen⁴⁵⁰ incorporating Bertelsen taught claim 9.

6. **Claim 11: “The method of claim 8, wherein the reduced-GMP cheese whey retentate composition is heated to a temperature of greater than or about 160° F.”**

188. As I explained in Section VII.C.4.g, Examples 11-12 involved heating solutions produced from BLG isolate powder to “90°C for 5 min.” Ex1007, 109:32-110:1, 111:11-13. As a POSITA would have known, 90°C equals 194°F, well above

160°F⁴. A POSITA would have understood and reasonably expected that the five-minute incubation in a 194°F water bath of small-volume samples in thin-walled glass tubes described by Nielsen⁴⁵⁰ would have raised the beverage compositions in those tubes from ambient temperature to at least about 160°F because the heat-treatment step was included to denature BLG protein in the beverage compositions, and BLG's denaturation temperature was well known to be about 70°C/158°F. Ex1007, 72:14-32.

189. Furthermore, our experiments replicating sample-production steps in Examples 11-12 confirmed that understanding by measuring the temperature of the beverage compositions during heat treatment. Our experiments confirmed that the samples produced according to Example 11 reached temperatures of 88.7°C and Example 12 reached temperatures of 88.3°C and 88.4°C, during heat treatment—over 190°F in each case. Original recordings of the measured temperature during our experiment are provided in annotated excerpts of the lab notebook below:

⁴ https://en.wikipedia.org/wiki/Conversion_of_scales_of_temperature ($^{\circ}\text{F} = ^{\circ}\text{C} \times 1.8 + 32$)

WO'450 Example 11

Record the temperature of the protein solution in the glass vials during the heating stage, before cooling in ice water. (See '860 patent, claim 11.). Use the temperature-logger, add to vial with sample and tinfoil as a lid. Take picture of the measurement at 5 min. incubation. Note down ____88.7____°C

WO'450 Example 12 (without homogenization)

Record the temperature of the protein solution in the glass vials during the heating stage, before cooling in ice water (See '860 patent claim 11).). Use the temperature-logger, add to vial with sample and tinfoil as a lid. Take picture of the measurement at 5 min. incubation. Note down ____88.3____°C

WO'450 Example 12 (with homogenisation)

Record the temperature of the protein solution in the glass vials during the heating stage, before cooling in ice water (See '860 patent claim 11).). Use the temperature-logger, add to vial with sample and tinfoil as a lid. Take picture of the measurement at 5 min. incubation. Note down ____88.4____°C

7. Claim 12: “The method of claim 8, wherein the heating of the reduced-GMP cheese whey retentate composition further comprises exposing the reduced-GMP cheese whey retentate composition to high shear conditions.”

190. In my opinion, Nielsen450 taught claim 12.

191. As I explained in Sections VII.C.4.c-VII.C.4.d regarding Examples 11-12 of Nielsen450, Nielsen450 taught heating liquid BLG compositions in a water bath at 90°C for 5 min. Ex1007, 109:31-110:1, 111:11-13. Nielsen450 further taught applying high shear simultaneously with the type of heat treatment described in Examples 11-12, as I explain below.

192. Nielsen450 taught that a “first heat treatment” of liquid protein compositions involved heating the solution to “a temperature in the range of 70-145 degrees C” *Id.*, 72:14-17. Heating the liquid BLG composition to 90°C (between 70-145°C) is an example of such first heat treatment. Nielsen450’s first heat treatment can be “the only heat-treatment” of the method of the packaged, heat-treated

beverage preparation. In this case, the first heat-treatment is applied to the liquid solution, either prior to packaging or after packaging.” *Id.*, 72:34-36.

193. Nielsen450’s further taught that the “first heat treatments” of BLG liquid solutions “may take place under *high shear conditions*, e.g. using scraped surface heat exchangers or similar high shear equipment.” Ex1007, 72:19-20 (emphasis added). It was well known to a POSITA that “[t]he most common process [for microparticulating whey protein] is a scraped surface heat exchanger (SSHE), a proven solution with a successful track record in applications such as soft cheese, semi hard cheese and ice cream.” Ex1010, 4. A POSITA would also have known that SSHE provided “controlled high shear” conditions. *Id.*, 3.

194. Therefore, Nielsen450 taught simultaneously heating the liquid BLG composition while exposing it to high shear conditions.

8. **Claim 13: “The method of claim 8, wherein the denatured whey protein composition is characterized by a weight ratio of native GMP to total whey protein of less than or about 0.15, and/or wherein the denatured whey protein composition is characterized by less than or about 11 wt. % GMP relative to the total weight of the protein in the denatured whey protein composition.”**

195. As discussed in Section VII.C.4.e, Nielsen450 taught denatured whey-protein compositions produced using a BLG powder in which the native GMP accounted for 1.08% by weight of the total protein in the BLG powder, so a POSITA would have understood that native GMP could have represented no more than 1.08%

by weight relative to the total protein in those disclosed compositions. Ex1007, 108:20-32 (Table 9).

9. Independent Claim 15

196. Upon my review, I note that claim 15 recites a whey-protein composition with limitations mirroring limitations 8.4-8.7. Claim 15 further recites “greater than 7 wt. % fat.” Ex1001, 24:31.

a. 15.pre: “A denatured whey protein composition comprising:”

197. In my opinion, if limiting, Nielsen450’s Example 12 described claim limitation 15.pre for the same reasons as I explained in Section VII.C.4.a regarding claim limitation 8.pre.

b. 15.1: “at least 60 wt. % protein on a dry weight basis;”

198. In my opinion, Nielsen450’s Example 12 described claim limitation 15.1 for the same reasons as I explained in Section VII.C.4.d regarding claim limitation 8.4.

c. 15.2: “less than 11 wt. % native glycomacropeptide (GMP) relative to total weight of the protein;”

199. In my opinion, Nielsen450’s Example 12 described claim limitation 15.2 for the same reasons as I explained in Section VII.C.4.e regarding claim limitation 8.5.

d. 15.3: “greater than 7 wt. % fat on a dry basis;”

200. As I explained in Section VII.C.4.g(b), Nielsen450’s Example 12 taught high-protein beverage compositions prepared using a BLG powder. Ex1007, 111:1-112:2. Those included one comprising 3% protein and 0.45% lipid, at pH 7.0. Ex1007, 111:21-112:2 (Table 11). The 0.45w/w% lipid specified the weight percentage of lipid in that beverage composition because Table 11 expressly uses weight-to-weight percentage. As a POSITA would have understood, the disclosed beverage composition’s fat content on a dry weight basis could be determined using information Nielsen450 provided because other added content (e.g., water and NaOH or HCl) did not alter the protein content. Example 12 confirmed the BLG powder used to make the composition was provided in Table 9:

Table 9: Chemical composition of BLG isolate powder A.

Description	A - Dry BLG (w/w%)
BLG	95.9
Ash	0.51
Ca	0.1455
Cl	0.04
Lipid	0.11
K	0.0512
Mg	0.022
Na	0.025
NO ₃	2
NO ₂	0.07
PHO	0.025
Protein	93.97
Dry matter	95.19
pH	5.7

Ex1007, 111:3-6, 108:20-32 (Table 9, annotated). According to Table 9 above, BLG powder contained 93.97w/w% protein and had a dry matter content of 95.19w/w%. To produce BLG solutions containing 3w/w% of protein, the total wt.% of BLG powder included in the solution requires dividing 3w/w% by the percentage of protein in the powder (i.e., 93.97w/w%), which equals 3.19w/w%. Of that 3.19w/w%, 3.04% would be dry matter (i.e., 3.19 multiplied by 0.9519, the proportion of total dry matter in the powder). In other words, a POSITA would have recognized that the disclosed BLG solution of 3w/w% protein in Example 12 contained about 3.04w/w% of dry matter from the BLG powder in Table 9. Lipid was added to 0.45w/w% of the solution, resulting in total dry content of 3.49w/w% (i.e., 3.04w/w% + 0.45w/w%).

201. Therefore, a POSITA would have understood that the fat content of the high-protein beverage composition (3% protein, 0.45% lipid, pH 7.0) described in Example 12 was approximately 12.9w/w% fat on a dry basis (i.e., dividing 0.45w/w% by 3.49w/w%), exceeding the 7w/w% recited in 15.3.

e. 15.4: “a beta-lactoglobulin to alpha lactalbumin ratio of greater than 5.00; and”

202. In my opinion, Nielsen450’s Example 12 taught claim limitation 15.4 for the same reasons as I explained in Section VII.C.4.f regarding claim limitation 8.6.

f. 15.5: “greater than 50 wt. % denatured whey proteins relative to the total weight of the protein.”

203. In my opinion, Nielsen450’s Example 12 taught claim limitation 15.5 for the same reasons as I explained in Section VII.C.4.g regarding claim limitation 8.7.

10. Claim 16: “The denatured whey protein composition of claim 15, wherein the denatured whey protein composition contains at least 60 wt. % beta lactoglobulin relative to a total weight of protein and/or wherein the denatured whey protein composition contains at most 12 wt. % alpha lactalbumin relative to the total weight of protein.”

204. As I explained in Section VII.C.4.d, a POSITA would have recognized that the high-protein compositions in Nielsen450’s Example 12 were prepared using BLG powder of Table 9 as the protein source, and that the disclosed compositions containing 3% protein and 0.45% lipid would have had about 95.9% BLG and less than 0.5% ALA relative to a total weight of protein. This BLG value exceeded 60 wt.% BLG relative to the total weight of protein in the composition as recited in claim 16.

205. In addition, a POSITA would have understood that the same composition from Example 12 met claim 16’s alternative limitation requiring at most about 12 wt.% ALA relative to the total weight of the protein. Because the input BLG powder was the sole source of protein in the composition, and because that

BLG powder contained less than 0.5% wt. % ALA relative to the weight of the total protein as shown in Table 8 of Nielsen450 below:

Table 8: Composition of protein ingredients (BDL=below detection limit).

Component	BLG powder A	BLG powder B	WPI powder
BLG	98.2	95.9	61
ALA	<0.5%	<0.5%	8
CMP	<1%	1.08	17
Ash	0.09	0.51	3.7
Ca	BDL	0.146	0.072
K	BDL	0.051	1.14
Na	BDL	0.025	0.484
Mg	BDL	0.022	0.007
pH	3.79	5.7	6.7

See Ex1007, 104:20-30, Table 8; Section VII.C.2.

11. Claim 17: “The denatured whey protein composition of claim 15, wherein the denatured whey protein composition comprises a weight ratio of beta lactoglobulin to alpha lactalbumin of greater than or about 5.”

206. In my opinion, Nielsen450 taught claim 17.

207. As I explained in Section VII.C.10, a POSITA would have recognized that the composition containing 3% protein, 0.45% lipid described in Nielsen450’s Example 12 contained 95.9% BLG and no more than 0.5% ALA by weight of the protein. A POSITA would have also understood that meant that the weight ratio of BLG to ALA in that composition was at least 192 (i.e., 95.9% divided by 0.5%).

12. Claims 18-20

208. In my opinion, Nielsen⁴⁵⁰ taught claims 18-20 which recite particle-size distribution values for the compositions of claim 15, summarized below.

209. Claim 18 recites a D50 particle size-distribution value of less than or about 0.3 μm , which a POSITA would have known as 50% of particles in a sample being less than or about 0.3 μm in size. Ex1007, 11:8-18.

210. Claim 19 recites a D10 particle size-distribution value of less than or about 0.1 μm , which a POSITA would have known as 10% of particles in a sample being less than or about 0.1 μm in size. Ex1007, 11:19-28.

211. Claim 20 recites a D90 particle size-distribution value of less than or about 1.0 μm , which a POSITA would have known as 90% of particles in a sample being less than or about 1.0 μm in size. Ex1007, 10:65-11:7.

212. Claims 18-20 would have been obvious over Nielsen⁴⁵⁰'s Example 12. It was well known that particle size could be easily controlled in denatured whey-protein compositions by applying different levels of shear force using known equipment such as a homogenizer. *See* Ex1010, 4 (heating WPC "under controlled high-shear conditions" enabled "the formation of fine particles with a specific particle size.")

213. As taught by Nielsen⁴⁵⁰, minimizing particle size in denatured whey-protein compositions also had known benefits, such as reducing satiety, improving

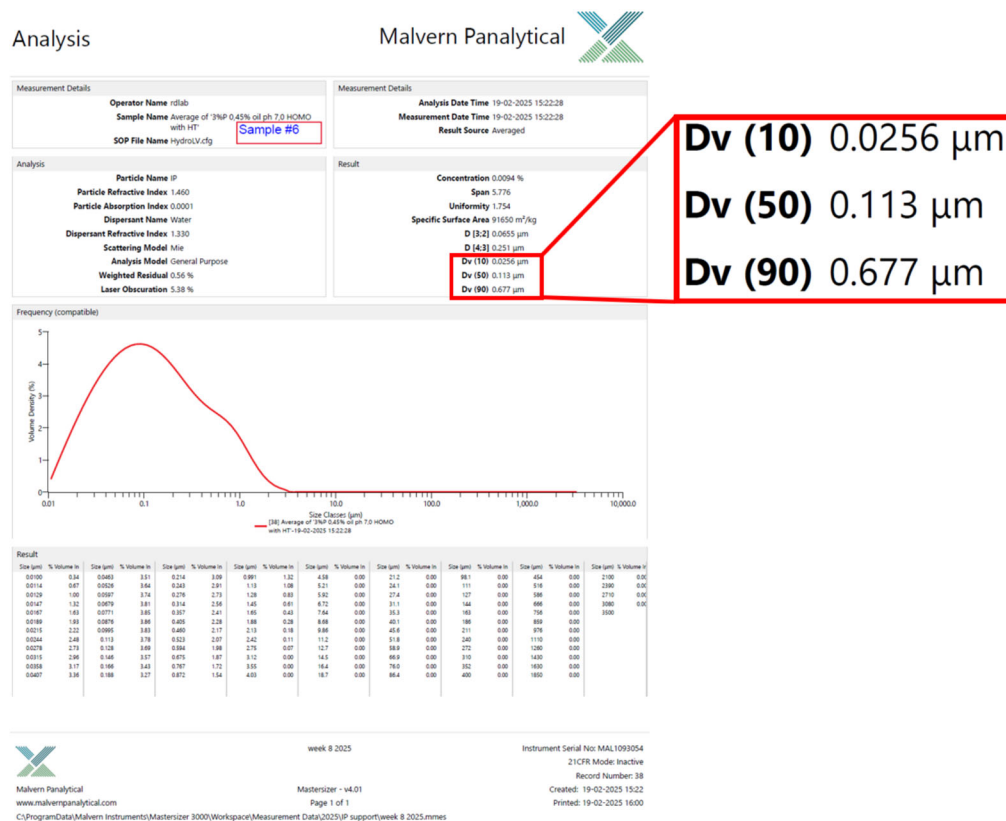
suitability for opaque beverages, improving drinkability, facilitating higher protein content in beverages, and improving mouthfeel. *See* Ex1007, 37:27-39 (“high content of protein nanogels therefore invoke less satiety upon ingestion than a comparable beverage containing soluble whey protein aggregates”), 38:1-7 (“the term ‘protein protein nanogels’ or ‘protein nanogels’ pertains to submicron sized particles of denatured whey protein, typically spherical or nearly spherical in shape”), 39:18-27 (“it is believed that the high BLG protein nanogel offers a more compact protein nanogel structure than protein nanogel based on normal WPI, and that this difference makes it possible to include more protein into a beverage without affecting its drinkability”).

214. Nielsen⁴⁵⁰ linked such benefits to the presence of “submicron sized particles” identified as “nanogels.” Ex1007, 38:1-3 (“In context of the present invention the term ‘protein protein nanogels’ or ‘protein nanogels’ pertains to submicron sized particles of denatured whey protein, typically spherical or nearly spherical in shape.”). A POSITA reading Nielsen⁴⁵⁰ thus would have been motivated to prepare beverage compositions with submicron-sized particles to reap the benefits of nanogel particles taught by Nielsen⁴⁵⁰. I also note that the terms “submicron” and “nano” overlap because 0.1 μm equals 100 nm, and in some instances those terms were used interchangeably.

215. A POSITA reading Nielsen450 also would have reasonably expected to succeed in preparing compositions according to Example 12 that met the particle-size limitations of claims 18-20 for at least the reasons below. First, Nielsen450 taught that submicron nanogel particles could be prepared using the 95.9% BLG powder that was used in Example 12. Ex1007, 104:10-105:22, 108:14-109:24. Second, Nielsen450's Example 12 expressly suggested incorporating a homogenization step during production of the disclosed high-protein beverage compositions, Ex1007, 111:15-16, which a POSITA would have known could be used and customized to yield a composition characterized by particles of desired size, such as submicron particles as recited in claims 18-20.

216. In addition, our replication of Example 12 bore out that understanding. Our testing included measuring particle-size distributions in heat-treated Samples 4 and 6 using conventional equipment and techniques. Milk homogenization is common throughout the world. Homogenization of milk is used so that the cream does not rise to the top in a bottle of milk. Milk homogenization uses conventional equipment available in dairy plants and dairy research laboratories such as Arla's in Denmark. In particular, Sample 6 was homogenized using equipment and techniques that were known and available by the time of Nielsen450, and Sample 4 was included for comparison of an analogous composition prepared without homogenization. The particle-size distributions in Samples 4 and 6 were determined using well-known

methods in the art. The observed particle-size values in Sample 4 were relatively large, likely indicating detection of coalescing lipid droplets in the non-homogenized sample. But with conventional dairy homogenization, Sample 6 had a D10 value was 0.0256 μm , the D50 value was 0.113 μm , and the D90 value was 0.677 μm , as shown below:



Those values met the limitations of claims 18-20. Specifically, a D10 value of 0.0256 μm met the value of 0.3 μm recited by claim 19; a D50 value of 0.113 μm met the value of 0.3 μm recited by claim 18; and a D90 value of 0.677 μm met the value of 1.0 μm recited by claim 20. These values further support the obviousness of those claims in view of the motivation to prepare nanogel-sized particles and Nielsen450's

express suggestion to incorporate homogenization when preparing the beverage compositions described in Example 12.

D. Ground 4: Obvious Over Ozturk, Kawasaki, and LeanCreme (Claims 8-9, 11-13, 15-17)

1. Overview of Ozturk

217. In my opinion, Ozturk (Ex1008) is analogous art. Ozturk was directed to investigating the composition and properties of whey protein products, including whey protein concentrate (WPC), whey protein phospholipid concentrate (WPPC) to evaluate their use as food products preparing beverages with high whey protein content Ex1008, Abstract, 290 (“The discovery of such a large quantity of lactoferrin in WPPC is promising for the translation of this bioactive molecule into functional foods, given its role in iron transfer and immunity”), 293 (“This is an important finding that could have potential implications for developing functional foods or nutraceuticals from WPPC.”) *Compare* Ex1008, Abstract, 290, *with* Ex1001, Abstract, 4:43-45 (“Depending on the purification process and the extent of purification, a whey protein concentrate (WPC) may be formed through concentration of the whey protein...”), 15:44-60 (“The process begins with WPC retentate...that is concentrated using ultrafiltration (UF) of pasteurized sweet whey separated from cheese curd.”)

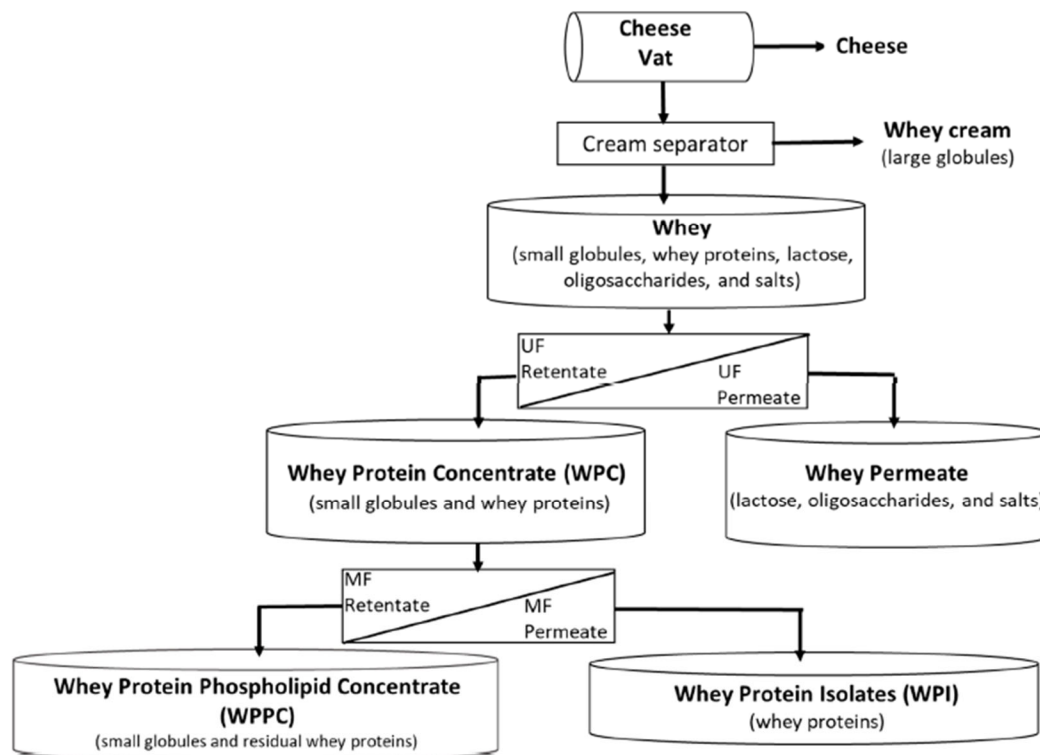
218. Ozturk was an article published on April 20, 2022, in *Dairy*—an international, peer-reviewed, open-access journal on dairy science published

bimonthly online by Multidisciplinary Digital Publishing Institute (MDPI).⁵

Ex1008, 277; Ex1009, 194, 196.

219. Ozturk described filtration-based processing steps applied to cheese whey to derive several types of concentrated whey-protein compositions. Ex1008, 278-79, Fig. 1. Ozturk confirmed that applying ultrafiltration to cheese whey was “a widely-adopted process used commercially to recover whey protein concentrate (WPC).” Ex1008, 278. To produce higher-purity protein products such as whey protein isolate (WPI), WPC undergoes a subsequent microfiltration process “separat[ing] the majority of the whey proteins from the residual fat.” *Id.* That microfiltration process results in a “co-product known as whey protein phospholipid concentrate (WPPC).” *Id.* Figure 1 showed process steps for manufacturing WPC, WPI, and WPPC from cheese whey.

⁵ <https://www.mdpi.com/journal/dairy>



Ex1008, Fig. 1, 278-79.

220. According to Ozturk, WPPC should contain a minimum of 50% protein (dry basis) that consists primarily of whey protein and at least 12% fat (dry basis), and Ozturk aimed to characterize the composition of WPPC. Ex1008, 279. Ozturk assessed commercially available WPPCs by measuring the “total protein, fat, solids as well as protein profile.” Ex1008, 280. The results showed those products contained BLG and ALA among numerous other proteins from the input cheese whey, as shown in Figures 2 and 3. I note that Figure 3 showed data from only one of the WPPC samples (6B), as explained in the methods section of Ozturk at pp.

280-81. As shown in Fig. 3, BLG is the most dominant whey protein of WPPC and substantially greater than other whey proteins, such as ALA.

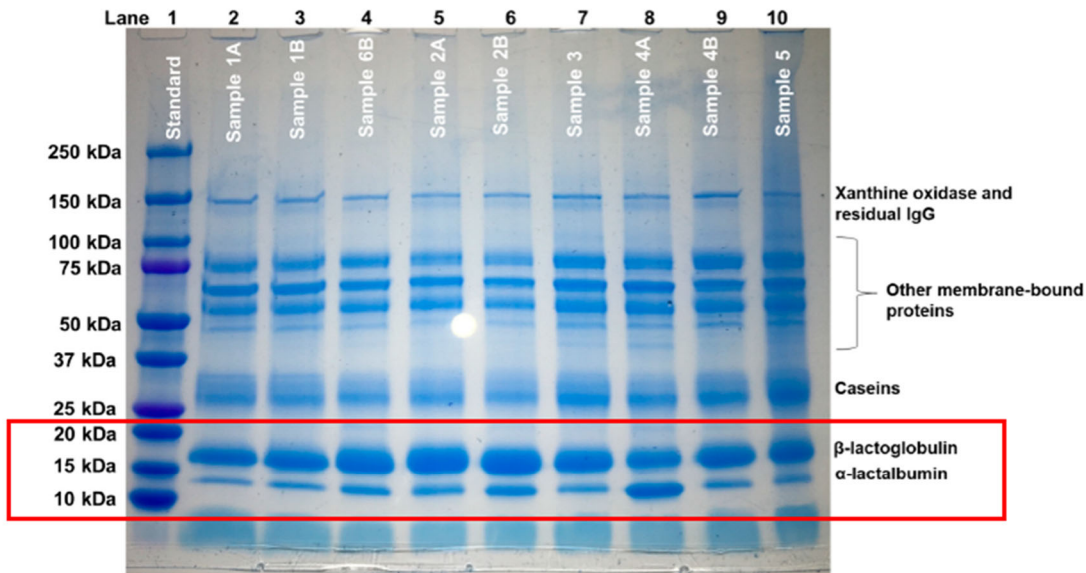


Figure 2 SDS-PAGE profile of whey protein phospholipid concentrate (WPPC) from different manufacturers. Lane 1: standard; Lane 2: sample 1A; Lane 3: sample 1B; Lane 4: sample 6B; Lane 5: sample 2A; Lane 6: sample 2B; Lane 7: sample 3; Lane 8: sample 4A; Lane 9: sample 4B; and Lane 10: sample 5. Annotation based on [57] with the exception of xanthine oxidase and IgG.

Ex1008, Fig. 2 (annotated), 287.

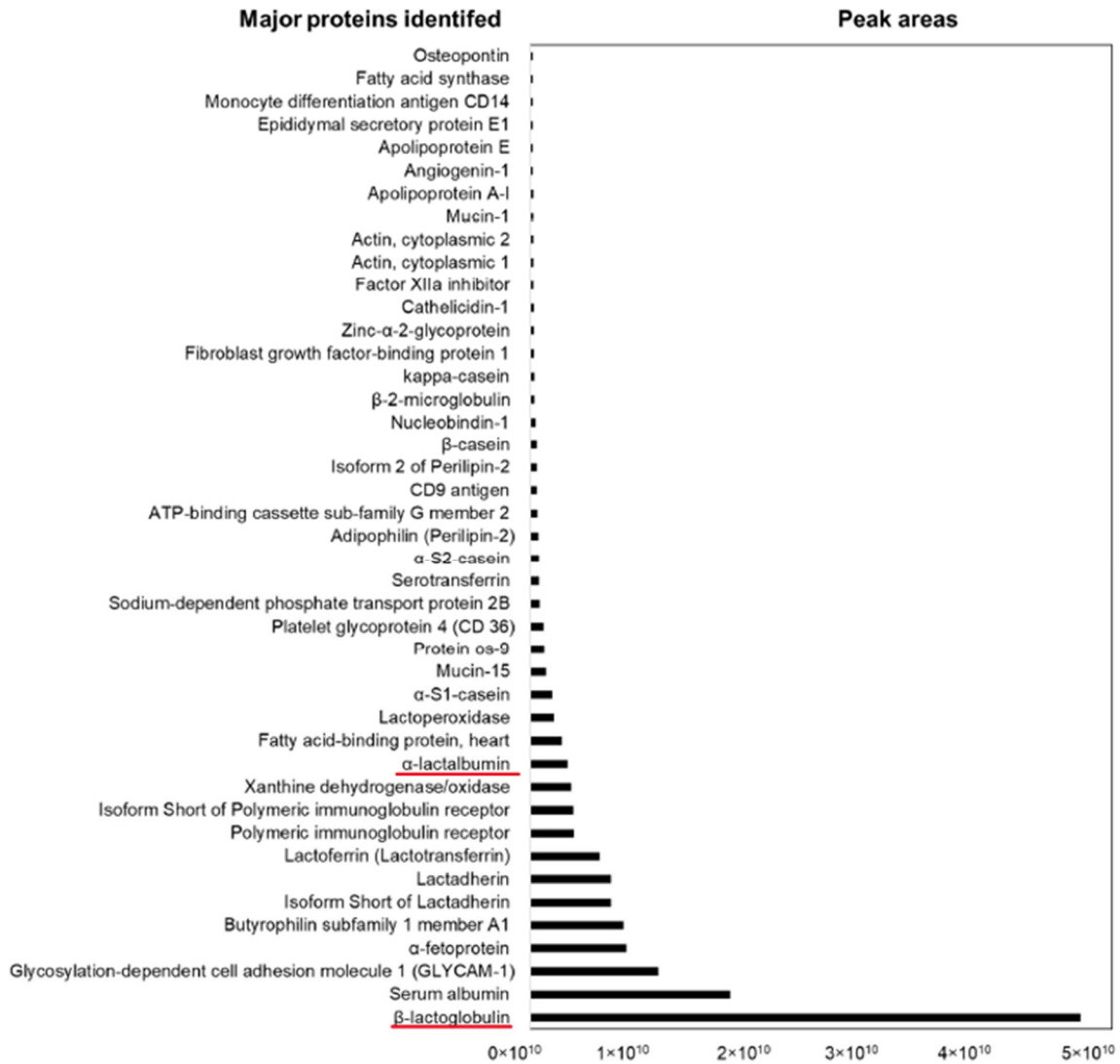


Figure 3. Relative abundance of major proteins identified in WPPC by proteomics.

Ex1008, Fig. 3 (annotated), 289. Sample 6B also contained 20.20% fat.

Table 1. Comparison between %solids, %protein, and %fat of the fat globule population measured from all WPPC samples.

Sample Description	Total Solids (%)	Protein (%)	Fat (%)
Sample 1A (liquid)	20.47	65.46 *	27.25 *
Sample 1B (liquid)	21.56	62.15 *	28.10 *
Sample 1 (powder)	-	62.7	24.4
Sample 2A (powder)	-	>72	-
Sample 2B (powder)	-	>73	-
Sample 3 (powder)	-	75.09	18.11
Sample 4A (powder)	-	76.19	13.08
Sample 4B (powder)	-	69.39	16.45
Sample 5 (powder)	-	67.61	-
Sample 6A (powder)	-	52.63	13.08
Sample 6B (liquid)	13.40	63.43	20.20
Bovine milk (liquid)	13	24.92 *	26.92 *

* % Fat and protein values were converted to dry basis values.

Id., Table 1 (annotated).

2. Overview of Kawasaki

221. In my opinion, Kawasaki (Ex1009) is analogous art.

222. Kawasaki was an article published in 1993 in *Milk Science International - Milchwissenschaft*—a peer-reviewed, open access journal.⁶ Ex1009, 192-94. I’m familiar with the Kawasaki reference and its teachings since the late 1990s. In fact, I have cited it a few times in my own publications, a few of which listed below:

- “Effect of Conductivity, pH, and Elution Buffer Salinity on Glycomacropeptide Recovery from Whey Using Anion Exchange

⁶ <https://openjournals.hs-hannover.de/milkscience/about>

Chromatography,” *Journal of Food Science*, May 31, 2006, by Tek, et al.;

- “Fractionation of Glycomacropeptide from Whey Using Positively Charged Ultrafiltration Membranes,” *Foods*, October 9, by Arunkumar, et al.

223. Kawasaki taught benefits of using GMP “as an ingredient in dietetic foods and pharmaceuticals” and recognized that cheese whey “is more suitable for the production of GMP on an industrial scale.” Ex1009, 191. Several studies had isolated GMP from whey proteins (e.g., BLG) by heat coagulation, but those compositions were “inferior to those of whey protein concentrates (WPC) produced by ultrafiltration.” *Id.*, 192. As such, Kawasaki developed a filtration method to isolate GMP from whey protein. Ex1009, 192-93.

224. Kawasaki’s “simple procedure for isolating GMP from WPC by UF” took advantage of GMP’s pH-dependent change of molecular weight. *See* Ex1009, 192-93. Kawasaki found that GMP’s molecular weight was lower at pH 3.5 and higher at pH 7.0. *Id.*, 193, Fig. 2. According to Kawasaki, the change in molecular weight was “completely reversible.” Ex1009, 193.

225. Figure 3 depicted Kawasaki’s multi-stage ultrafiltration “[p]rocedure to isolate GMP by UF.” Ex1009, 193, Fig. 3. WPC solution was acidified to reduce GMP molecular weight to between 10-30 kDa. Ex1009, 192-93, Figs. 1, 3. WPC

solution was then filtered through a first ultrafiltration membrane stage (“UF#1”) resulting in retentate (“Retentate #1”) and permeate (“Permeate #1”). *See* Ex1009, 193, Fig. 3. GMP with decreased molecular weight was small enough to pass through the ultrafiltration membrane, but “the majority of whey proteins such as β -lactoglobulin, α -lactalbumin, immunoglobulin and bovine serum albumin were rejected by the membrane.” *See id.*, 192-93, Figs. 1, 3. Retentate #1 proceeded through additional ultrafiltration steps (red path in annotated Figure 3 below) to produce WPC with reduced GMP, whereas Permeate #1 proceeded through separate ultrafiltration steps (green path) to produce isolated GMP. *See id.*

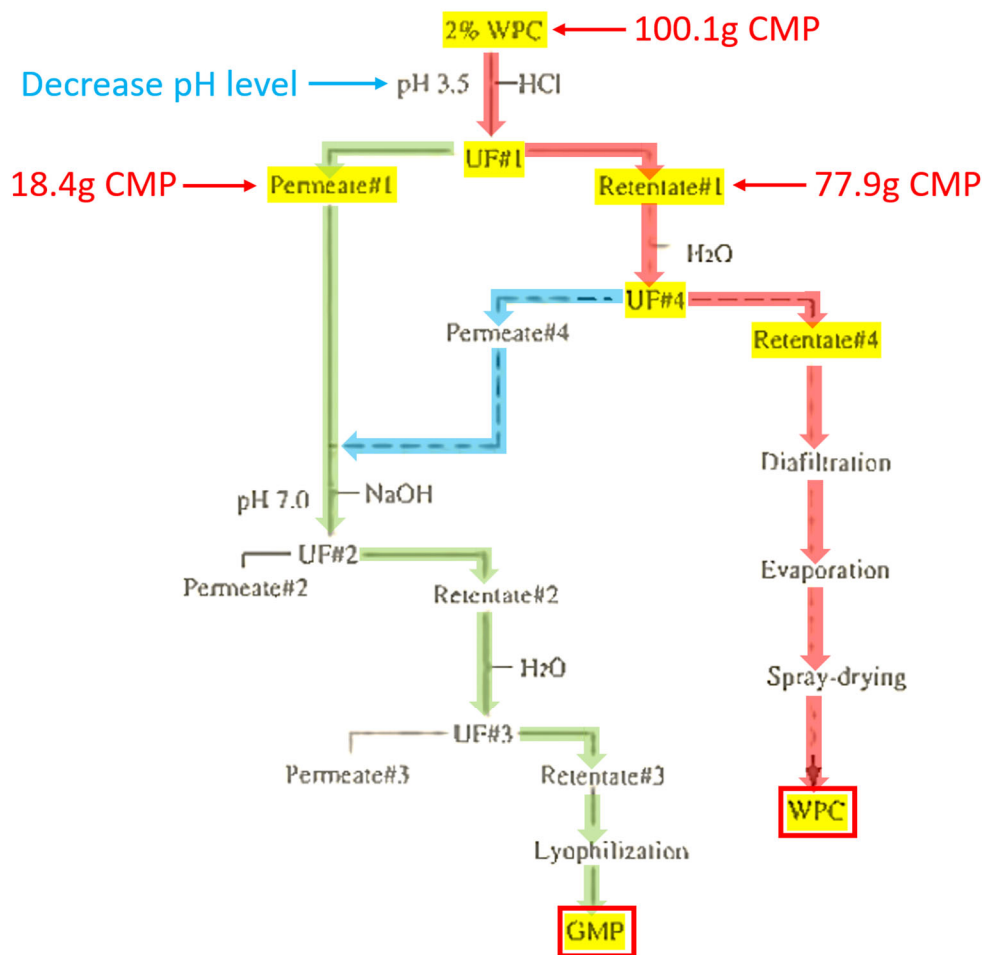


Fig. 3 Procedure to isolate GMP by UF

Ex1009, 192-93, Fig. 3 (annotated).

226. Kawasaki taught that a single ultrafiltration step at UF#1 using a membrane with 20 kDa cutoff (e.g., UF-membrane GR61pp) removed about 22.2% ($1 - 77.9/100.1 = 22.2\%$) of GMP from the initial WPC solution. See Ex1009, 193, Fig. 3, Table 1. Additional ultrafiltration could be performed on Retentate#1 (e.g., UF#4) to remove further GMP. Again, GMP passed through the membrane into the

permeate (e.g., Permeate #4) which could be mixed with Permeate #1 (blue path in annotated Figure 3) to increase CMP recovery. Ex1009, 193-94.

3. Overview of LeanCreme

227. In my opinion, LeanCreme (Ex1010) is analogous art. LeanCreme is in the same field of endeavor as the '860 patent, both developing whey protein concentrates as highly nutritious food ingredients. *Compare* Ex1010, 3 (“the process uses whey protein concentrate to make a creamy liquid that can be talored [sic] to a long line of different products.”), 21 (“LeanCreme as a powdered ingredient constitutes the ideal starting ingredient for a wide range of markets and applications such as slimming milk products with delicious taste, cheeses, food, chocolate, confectionary, ice cream etc”), *with* Ex1001, 3:28-29 (“Embodiments of the present technology include a protein fortified food product”), 4:43-44 (“Depending on the purification process and the extent of purification, a whey protein concentrate (WPC) may be formed....”).

228. LeanCreme was a white paper published by SPX FLOW, a food-plant manufacturing company.⁷ LeanCreme was published on SPX FLOW’s official website by June 26, 2016. *See* Ex1011, 1-3. LeanCreme described methods and manufacturing plants for using whey-protein concentrate to produce APV

⁷ SPX FLOW spun off from SPX in 2015. *See* <https://www.spxflow.com/about/our-company/>

LeanCreme—a creamy liquid containing microparticulated whey proteins. Ex1010, 3-4. APV LeanCreme could be tailored to “a long line of different products,” such as drinking yogurts. *See* Ex1010, 3, 22.

229. According to LeanCreme, WPC was used as the raw material for producing APV LeanCreme. Ex1010, 5. LeanCreme also taught that other raw materials can be used. For example, WPC with added dairy fat could also be used. *Id.*, 8 (“WPC can be mixed with cream prior to the APV LeanCreme™ process”). BLG was the most prominent and important protein in WPC that “determines the overall denaturation kinetics.” *Id.*, 5, Table 1 (BLG representing 48-58% of the total whey protein). LeanCreme’s Figure 2 showed the typical protein composition in sweet whey.

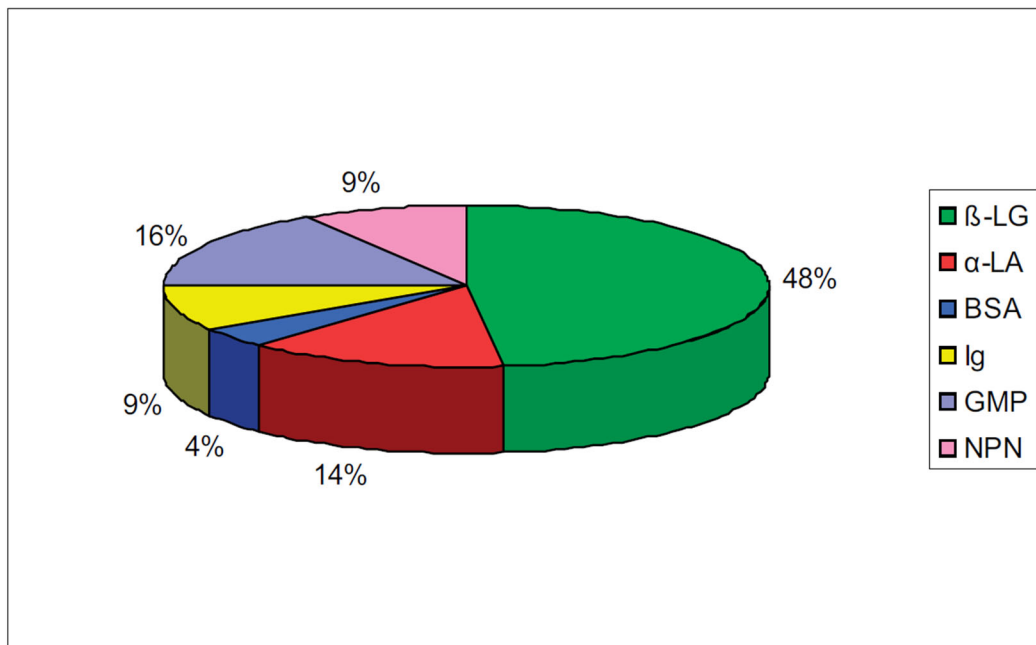


Fig. 2: Typical composition of whey proteins in sweet whey

Ex1010, Fig. 2.

230. LeanCreme taught it was well known to microparticulate whey protein either by separately employing heat denaturation and mechanical shear, or by performing them together in a one-step process using a scraped surface heat exchanger (SSHE) common in the dairy industry. Ex1010, 4. “[S]imultaneous heat denaturation of the protein” and “controlled high shear” ensured “production of denatured whey protein particles with the desired smooth mouthfeel instead of a sandy or gritty mouthfeel.” *Id.*, 3-5. “The ASA (APV Shear Agglomerator) is the name of the specially designed SSHE. It is designed specifically to create microparticulated whey proteins with unmatched functionality that can only be achieved using the one-step solution.” *Id.*, 14. According to LeanCreme, whey proteins were known to denature at 60-85°C. Ex1010, 6. Obtaining small particles “normally requires a high denaturation degree” and LeanCreme recommended using a denaturation temperature of 85°C. *Id.*, 7, 15.

231. LeanCreme also taught that particle-size distribution could be “easily” controlled. Ex1010, 7. For example, mean particle size was increased from 2.5µm to 4µm by reducing from 65% to 35% of the maximum speed of the dashers in the SSHE (“Scrape Surface Heat Exchanger”).

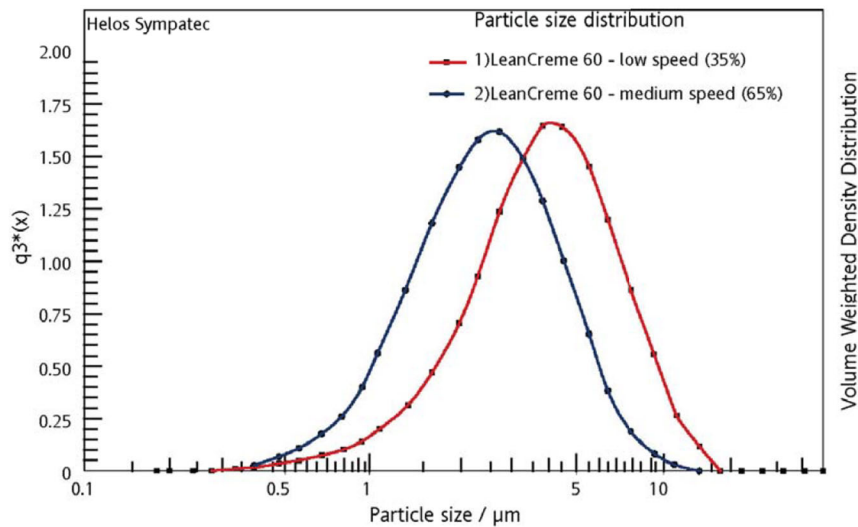


Fig. 3: Particle size distribution of APV LeanCreme™ based on WPC60 with 35% and 65% of max speed respectively

Ex1010, Fig. 3, 13.

4. Motivations to Combine

232. In my opinion, a POSITA would have been motivated to combine the teachings of Ozturk, Kawasaki, and LeanCreme, as I explain below.

a. Motivations to Combine Ozturk with Kawasaki

233. First, both references were directed toward the same field of endeavor concerning preparation of protein compositions for food products. *Compare* Ex1008, Abstract (“[I]nvestigat[ing] the composition of whey protein phospholipid (WPPC)” and “reveal[ing] that it is a source of many bioactive compound that can benefit the immune system and gut health”), *with* Ex1009, 191 (“These functions [of GMP] encouraged us to utilize GMP as an ingredient in dietetic foods and pharmaceuticals.”)

234. Second, Kawasaki taught that GMP⁸ from whey could be useful in certain food products and pharmaceuticals. *See* Ex1009, 191. In my opinion, a POSITA would have been motivated to separate GMP from Ozturk's WPPC products. As I explain below, purified GMP can be used as a separate ingredient while products containing GMP were not suitable for certain infants.

235. It was well known to a POSITA that purified GMP had certain uses, such as inhibiting the adhesion of streptococcus bacteria to red blood cells and inhibiting "the binding of cholera toxin to its receptor." Ex1009, 191. It was also well known that products containing GMP were not suitable for certain infants because the "high content of the amino acid threonine" in GMP causes infant hyperthreoninemia. *See* Ex1012, 14. Ozturk investigated suitability of whey products for use as functional foods or nutraceuticals, and particularly infant food products. *See* Ex1008, 293 ("This is an important finding that could have potential implications for developing functional foods or nutraceuticals from WPPC"), 288 (examining proteins in WPPC for preventing "symptomatic rotavirus infection in breast-fed infants"); *see id.*, 289, 290-93. Indeed, a known primary use of WPPC was in producing infant formulas. *Id.*, 288-89.

⁸ As I explained in Sections VI.B.2 and VII.A.3.c, CMP and GMP refer to the same hydrophilic peptide released from kappa-casein.

236. Additionally, it was known that GMP could contain an undesirable flavor. In particular, I was aware that GMP imparts an “off-flavor...described as ‘stale’ or ‘chemical’” on food. Ex1018, 8-9. Indeed, the ’860 patent admitted that it was well known that GMP suffers from several disadvantages, including being an inferior source of protein for muscle building and imparting an “undesirable flavor” to food products. *See* Ex1001, 1:36-40. For all of those reasons, a POSITA would have been motivated to separate GMP from Ozturk’s WPPC products. Implementing Kawasaki’s teachings of filtration techniques in WPPC to remove GMP would have provided benefits to Ozturk’s products, such as rendering WPPC more suitable for infant food, and in turn, GMP isolated from WPPC could have been used as an ingredient for adult dietetic foods. In my opinion, the combination would have used a known technique (Kawasaki’s GMP isolation process) to improve Ozturk’s known product (WPPC) in the same way (removing GMP for use as a separate ingredient for food products).

237. To the extent that PO argues Ozturk did not explicitly teach GMP levels in its WPPC compositions, it is my opinion that a POSITA would have known Ozturk’s process for producing WPPC started with raw materials containing GMP because Ozturk uses cheese whey as its raw material. According to Ozturk, it was directed to “investigat[ing] the composition” of WPPC, which is made from cheese whey. *See* Ex1008, Abstract, 278, Fig.1 (showing whey is produced from cheese

vat). It was well known to a POSITA that sweet or rennet-whey contains CMP (i.e., GMP). *See* Ex1012, Abstract, 13 (“Whey, therefore, consists of...caseinomacropeptide (CMP)”); Ex1013, 325 (“Whey proteins represent approximately 90% of all present milk proteins, the remaining 10% is represented by casein or caseinomacropeptide (CMP), respectively”)⁹.

238. In addition, as I explain below, a POSITA would have had a reasonable expectation of success with predictable results in combining Ozturk with Kawasaki.

239. First, Kawasaki is evidence that a POSITA would have known the benefits of separating GMP from the other whey proteins. *See* Ex1009, 191 (utilizing “GMP as an ingredient in dietetic foods and pharmaceuticals”). Kawasaki is also evidence that a POSITA would have known how to implement ultrafiltration processes for isolating GMP—indeed, Ozturk already used ultrafiltration. *See* Ex1008, 278, 293 (steps (ii) and (iii)), Figure 1 (“UF”); *see* Ex1009, 192-93, Fig. 3; *see also* Ex1012, 14; *see also* Ex1013, Abstract, Table 7, 330-31.

240. Second, because Kawasaki’s filtration was performed on a whey-protein composition (e.g., WPC), a POSITA would have similarly implemented Kawasaki’s filtration step on the whey-protein phospholipid concentrate (WPPC) in

⁹ Ex1012 (Tolkach) and Ex1013 (Hinkova) are cited in this petition to demonstrate POSITAs’ knowledge and/or as evidence supporting motivation to modify Ozturk. *KSR*, 550 U.S. at 420. These exhibits are not part of the unpatentability grounds.

Ozturk because the WPPC is a product of WPC. Removing GMP from WPC makes the resulting WPPC more valuable for infant formula. *Compare* Ex1008, Fig. 1, *with* Ex1009 Fig. 3. A POSITA would have had a reasonable expectation of success because the fat and whey proteins in Ozturk's WPPC had already been retained during an earlier ultrafiltration step and had also been retained during a coarser microfiltration step, so a POSITA would have expected the proteins and fat in Ozturk's WPPC to be retained during ultrafiltration according to Kawasaki's method while allowing the reduced-size GMP to pass through the filter.

241. Third, implementing Kawasaki would have called for Kawasaki's filtration process depicted in Kawasaki's Figure 3, which produced retentate having reduced GMP. According to Kawasaki, whey proteins (e.g., BLG) were retained in the retentate. Ex1009, 192-93, Fig. 3.

b. Motivations to Combine Ozturk and Kawasaki with LeanCreme

242. First, all three references were directed toward the same field of endeavor concerning preparation of protein composition for use in food products. *Compare* Ex1008, Abstract (“[I]nvestigat[ing] the composition of whey protein phospholipid concentrate (WPPC)...” and “reveal[ing] that it is a source of many bioactive compounds that can benefit the immune system and gut health”), *with* Ex1009, 191 (“These functions encouraged us to utilize GMP as an ingredient in

dietetic foods and pharmaceuticals”), *with* Ex1010, 4 (“Whey proteins...are now becoming increasingly popular in their ability to improve health whilst also being highly functional ingredients in dairy and food formulations”).

243. Second, Ozturk taught that whey-protein compositions such as WPPC were readily available as sources of functional compounds and further encouraged using WPPC to “pursue innovations beyond the traditional vision of dairy components used for nutritional purposes.” Ex1008, 298. LeanCreme developed “an innovative microparticulation process” that heated whey-protein concentrate under high-shear conditions in a scraped surface heat exchanger that denatured the whey proteins while forming microparticulated protein aggregates. Ex1010, 4. According to LeanCreme, heating produced stable particles, “partly due to a high degree of denaturation.” *Id.*, 18. A POSITA would have been motivated to modify the reduced-GMP version of WPPC from Ozturk/Kawasaki by further processing it to produce denatured protein microparticulates as taught by LeanCreme. That would have involved heating the Ozturk/Kawasaki WPPC to between 60-85°C as taught by LeanCreme to achieve “a high degree of denaturation.” *See* Ex1010, 6, 20. The heating process would have been performed simultaneously under high-shear conditions to form “fine particles with a specific particle size similar to fat globules.” *See* Ex1010, 3-4, 19.

244. Third, a POSITA would have reasonably expected success with predictable results in combining LeanCreme with the Ozturk/Kawasaki process because Ozturk/Kawasaki's WPPC and LeanCreme's cream-added WPC both had BLG as the dominant whey protein. *Compare* Ex1008 Table 2 (BLG at 30.11%), *with* Ex1010, Table 1 (BLG at 48-58%); According to LeanCreme, BLG was "the most important protein influencing the properties" of protein aggregation and "determines the overall denaturation kinetics." Ex1010, 5. Although APV LeanCreme™ contained GMP, GMP does not denature through heat nor affect the denaturation of whey proteins such as BLG. *See* Ex1010, 6 ("GMP cannot be unfolded and denatured."); Ex1012, 14 (heat treatment of "rennet whey or WPC at 90°C for 1h leads to a complete denaturation and aggregation of whey proteins." Denatured proteins can be removed by centrifugation and "CMP can be concentrated by ultrafiltration.").

5. Independent Claim 8

a. 8.pre: "A method of making a denatured whey protein composition, the method comprising:"

245. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 8.pre.

246. As I explained in Sections VII.D.1 and VII.D.3, Ozturk taught methods for making WPPC, and LeanCreme taught heat-treating whey-protein compositions to form denatured whey-protein compositions. *See* Ex1008, Abstract, 279-81, 287,

290-91, Figs. 1-3, Table 2; Ex1010, 3-8. As I explained in Section VII.D.4, a POSITA would have motivated to combine these teachings.

b. 8.1: “filtering cheese whey from enzymatically coagulated milk into a cheese whey retentate and a permeate; and”

247. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 8.1.

248. Ozturk taught producing whey protein compositions such as WPPC. Ex1008, Fig. 1, 278-79, 293, Abstract (“This work investigates the composition of whey protein phospholipid concentrate (WPPC), an underutilized dairy stream, and reveals that it is a source of many bioactive compounds that can benefit the immune system and gut health”).

249. Ozturk’s processes began with cheese whey. *Id.*, Fig. 1, 278-79. Ozturk taught that cheese whey was a “co-product of cheesemaking” using milk. *Id.*, 277-78. It was well known to a POSITA that cheese whey is produced from enzymatically coagulated milk. For example, “[s]weet whey is produced in large amounts worldwide from milk using the enzymatic action of chymosin (also called rennet enzyme) on the casein fraction. Casein represents about 80% of the total milk protein. It loses its colloidal solubility following chymosin treatment. Milk protein can thus be separated into a coagulum from the casein protein fraction, i.e. the cheese curd, and the whey.” Ex1012, 13.

250. Ozturk's Figure 1 depicted a process for producing WPPC. As shown in annotated Figure 1 below, Ozturk's first processing step involved ultrafiltration of cheese whey to produce (1) a retentate, whey protein concentrate (WPC) ("*cheese whey retentate*") containing fat and whey proteins; and (2) a whey permeate ("*permeate*") containing lactose, oligosaccharides, and salts. Ex1008, 278-79, 293, Fig. 1.

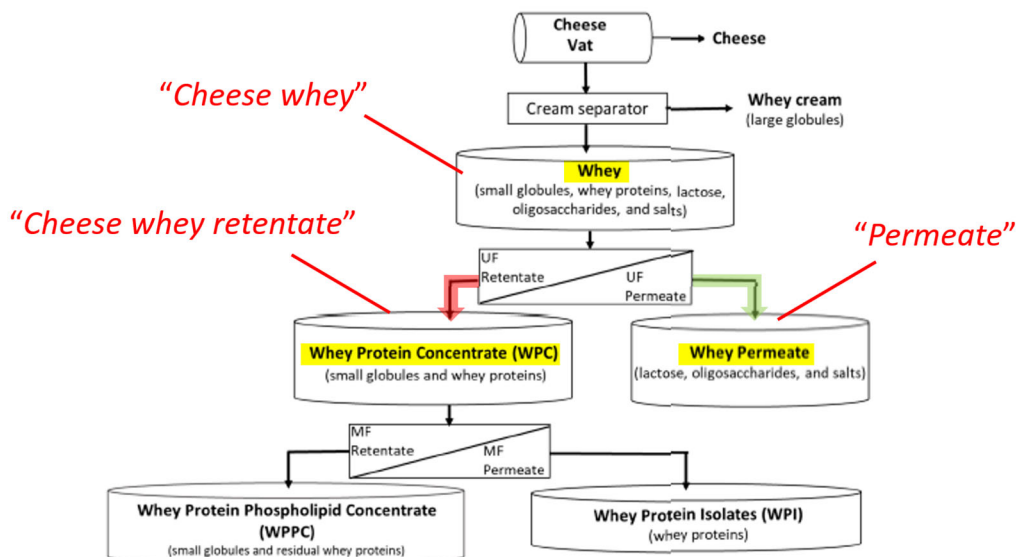


Figure 1. Manufacture of whey protein concentrate and isolate, which results in the accumulation of whey protein phospholipid concentrate (WPPC). Figure adapted from [40].

Ex1008, Fig. 1 (annotated).

251. Ozturk's ultrafiltration of cheese whey into a retentate and a permeate is consistent with the '860 patent's description of filtering step 102 to obtain a cheese whey retentate as resulting in the whey feedstock being "filtered 102 from lactose and minerals." Ex1001, 6:24-28, Fig. 1, 15:44-50.

c. **8.2: “reducing native glycomacropeptides (GMP) in the cheese whey retentate to form a reduced-GMP cheese whey retentate composition; and”**

252. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 8.2.

253. As I explained in Section VII.D.5.b, Ozturk taught performing ultrafiltration on cheese whey to form a retentate of WPC. Ex1008, Fig. 1, 278-79, 293. As shown in annotated Figure 1 of Ozturk below, WPC was further processed by microfiltration to produce (1) a retentate containing fat and whey proteins (WPPC); and (2) a permeate containing whey proteins (WPI). *Id.*

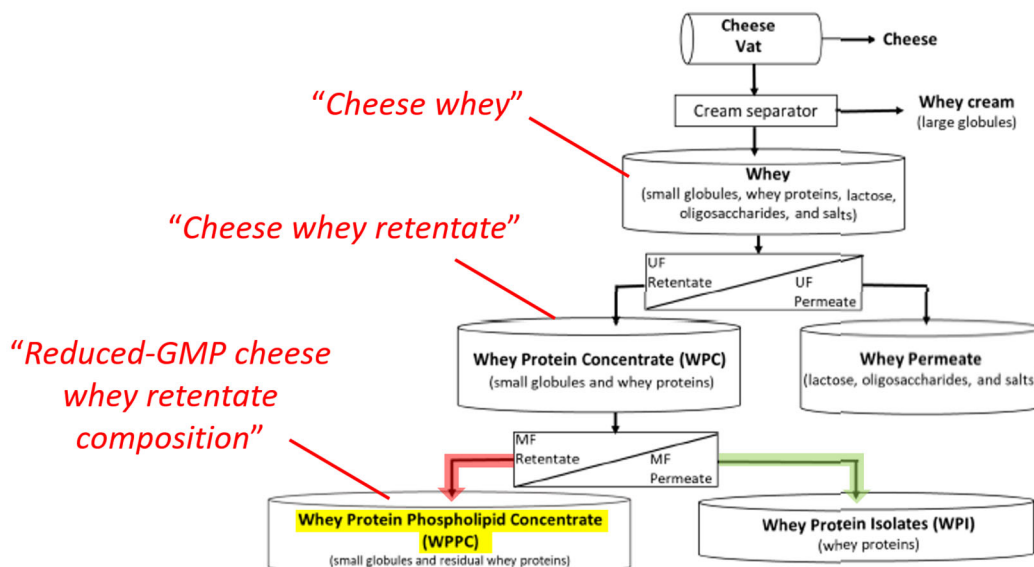


Figure 1. Manufacture of whey protein concentrate and isolate, which results in the accumulation of whey protein phospholipid concentrate (WPPC). Figure adapted from [40].

Ex1008, Fig. 1 (annotated).

254. As I explain below, a POSITA would have understood that Ozturk's microfiltration step removed GMP from the WPC retentate resulting in a WPPC composition having reduced GMP.

255. First, it was known that cheese whey as used for input into Ozturk's process typically included 12-20% GMP of total whey protein. For example, LeanCreme taught that a "[t]ypical composition of sweet whey proteins" included about 12-20% of GMP. Ex1010, 5, Table 1.

PROTEIN	% OF TOTAL WHEY PROTEIN
B-LACTOGLOBULIN	48-58
A-LACTALBUMIN	13-25
GLYCOMACROPEPTIDES (GMP)	12-20
IMMUNOGLOBULINS	08-12
BOVINE SERUM ALBUMIN	6
LACTOFERRIN	2
LACTOPEROXIDASE	0.05

Table 1: Typical composition of sweet whey proteins (Belitz and Grosch 1999)

256. Second, undenatured proteins mostly pass through microfiltration membranes while denatured proteins aggregate, especially denatured BLG, are preferentially retained. For example, "higher amounts of denatured proteins were found in WPPC, probably due to the size of these large aggregates they were retained

(concentrated) in the MF retentate). Ex1014, 12255, *see also id.*, 12253, 12249, Fig. 5).

257. Third, as I explained in Section VII.D.4, GMP cannot be denatured and thus would have passed through the microfiltration membrane into the permeate. Ex1010, 5-7 (“Denaturation during heat treatment means that the structure of whey proteins with the exception of GMP can change.”). Ozturk taught that its microfiltration step used “a 0.1 μm pore size” resulting in accumulation of “residual whey proteins in the microfiltration retentate.” Ex1008, 293. A POSITA would have understood that membranes with “0.1 μm pore size” would have allowed substantial GMP removal. I note that a pore size of 0.1 μm is the same as a pore size of 100 nm. For example, Ex1013 showed that CMP rejection rate is 70.2 ± 7.6 for membranes with 100 nm¹⁰ cut off. *See* Ex1013, Table 7 (annotated and reproduced below).

Table 7. Average protein rejection on ceramic membranes

Rejection factor $\pm$ SD/%				
Protein	Protein size ^a /kDa	Membrane cut-off		
		5 kDa	100 nm	500 nm
CMP	7	94.6 ± 7.6	70.2 ± 7.6	16.3 ± 2.3
α -La	14.2	96.7 ± 5.7	69.7 ± 1.5	16.3 ± 2.8
β -Lg B	18.4	97.5 ± 4.3	81.8 ± 2.7	17.8 ± 2.1
β -Lg A	18.4	96.3 ± 6.5	87.2 ± 3.1	26.3 ± 0.9

a) Maubois and Ollivier (1997); R_{CMP} – rejection of casein macropeptide, $R_{\alpha\text{-La}}$ – rejection of α -lactalbumin, $R_{\beta\text{-Lg B}}$ – rejection of β -lactoglobulin B, $R_{\beta\text{-Lg A}}$ – rejection of β -lactoglobulin A, SD – standard deviation.

¹⁰ 0.1 μm equals 100 nm (1 μm =1000nm).

258. To the extent that PO argues Ozturk did not expressly teach reducing GMP levels, as I explained below, a POSITA would have been motivated to modify Ozturk using the GMP-removing filtration techniques taught by Kawasaki to reap the well-known benefits of low-GMP infant foods and to isolate GMP as a separate ingredient for novel adult food products.

259. As I explained in Sections VII.D.2 and VII.D.4, Kawasaki described a technique for removing GMP from WPC. Ex1009, 193-94. Kawasaki's method involved acidifying the composition and performing ultrafiltration, which removed GMP by rendering its molecular weight small enough to pass through ultrafiltration membranes. *Id.*, 192-93. Kawasaki taught that ultrafiltration with a 20 kDa cutoff (GR61pp) resulted in the majority of whey proteins being rejected by the membrane, "whereas GMP, lactose, and minerals permeated." *Id.*, 193. It was well known to a POSITA that WPC contained fat globules and whey proteins. For example, Figure 1 of Ozturk annotated and reproduced below shown that WPC contained small globules and whey proteins.

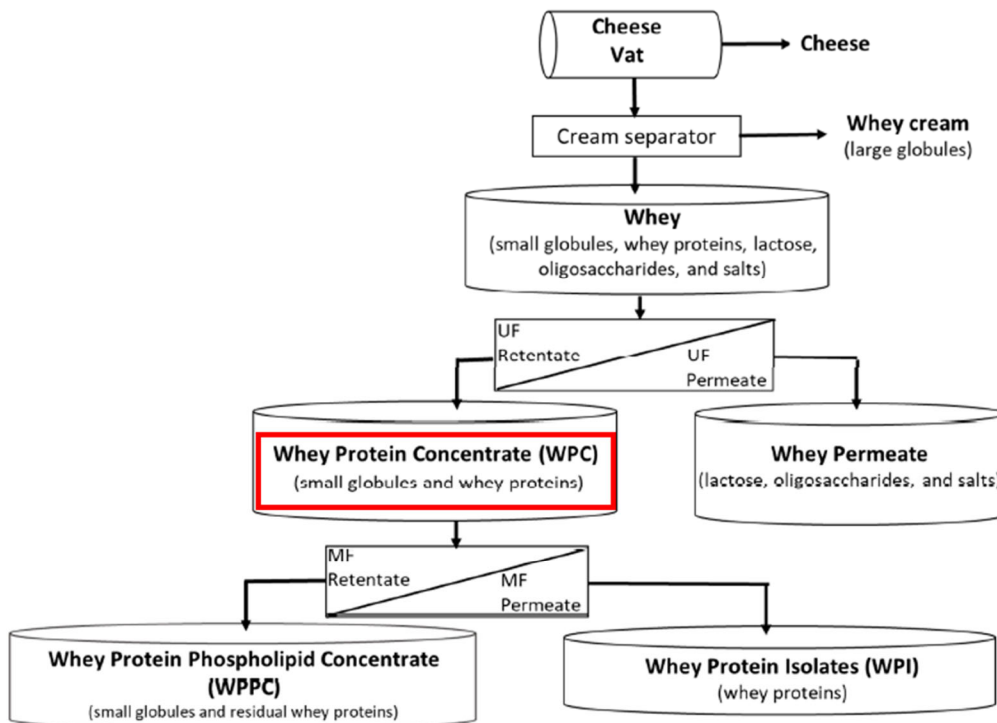


Figure 1. Manufacture of whey protein concentrate and isolate, which results in the accumulation of whey protein phospholipid concentrate (WPPC). Figure adapted from [40].

Ex1008, Figure 1 (annotated).

260. A POSITA would also have known that WPPC contained similar complements of whey proteins, and both WPC and WPPC contained fat. For example, Figure 1 of Ozturk above also shown that WPPC contained “small globules and residual whey proteins.” Ex1008, Fig. 1. If anything, a POSITA would have expected non-GMP proteins (e.g., BLG) to be more effectively retained in WPPC relative to WPC because WPPC is more enriched for large proteins and denatured proteins than WPC. For example, a separate study on microfiltration of whey proteins showed that a microfiltration (MF) feed containing predominantly whey

proteins (e.g., BLG) with minor amounts of MFGM proteins retained the whey proteins after microfiltration. *See* Ex1014, Fig. 5 (compare lanes 2 and 3), 12249, 12253, 12255.

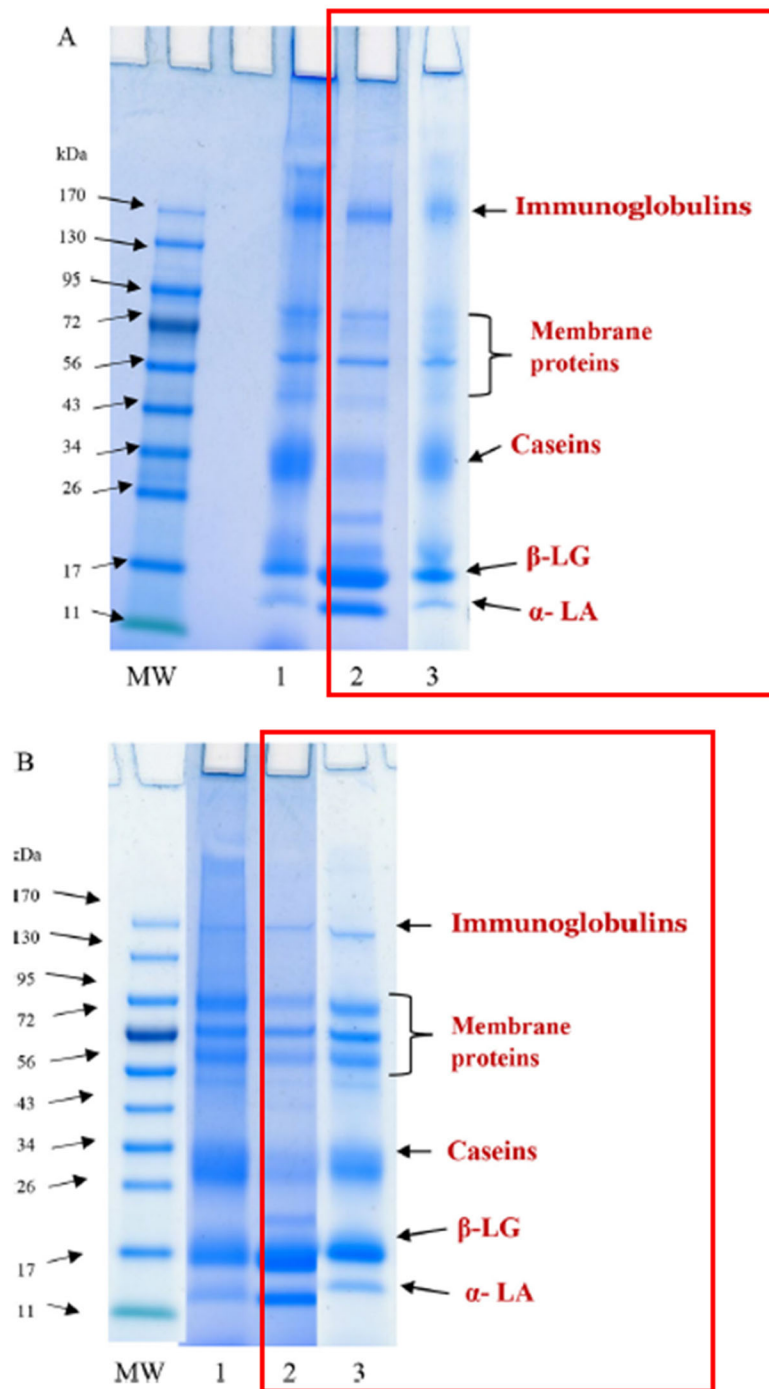


Figure 5. Sodium dodecyl sulfate-PAGE profiles of rehydrated whey protein phospholipid concentrate (WPPC) solution, liquid WPPC, and microfiltration (MF) feed for whey protein isolate production. Lane MW = molecular weight marker; lane 1 = rehydrated WPPC solution; lane 2 = MF feed; lane 3 = liquid WPPC under (A) nonreducing, and (B) reducing conditions.

Ex1014, Figure 5 (annotated).

261. Therefore, performing ultrafiltration on Ozturk's WPPC using Kawasaki's ultrafiltration techniques would have been expected to remove GMP but retain non-GMP proteins and fat.

262. As I further explained below, a POSITA would have implemented Kawasaki's ultrafiltration procedure into the process depicted in Ozturk's Figure 3. Ex1009, 192-93, Fig. 3. Kawasaki taught that acidification to pH 3.5 decreased GMP's molecular weight to between 10 and 30 kDa. *Id.* GMP with decreased molecular weight was small enough to pass through the ultrafiltration membrane, but "the majority of whey proteins such as β -lactoglobulin, α -lactalbumin, immunoglobulin and bovine serum albumin were rejected by the membrane." Ex1009, 192-93, Figs. 1, 3. I have annotated and reproduced Figure 3 of Kawasaki to show that Retentate #1 proceeded through an additional ultrafiltration step (red path in annotated Figure 3 below) to produce WPC having reduced GMP, whereas Permeate #1 proceeded through a separate set of processing steps (green path) to produce GMP isolated from WPC. *See id.*

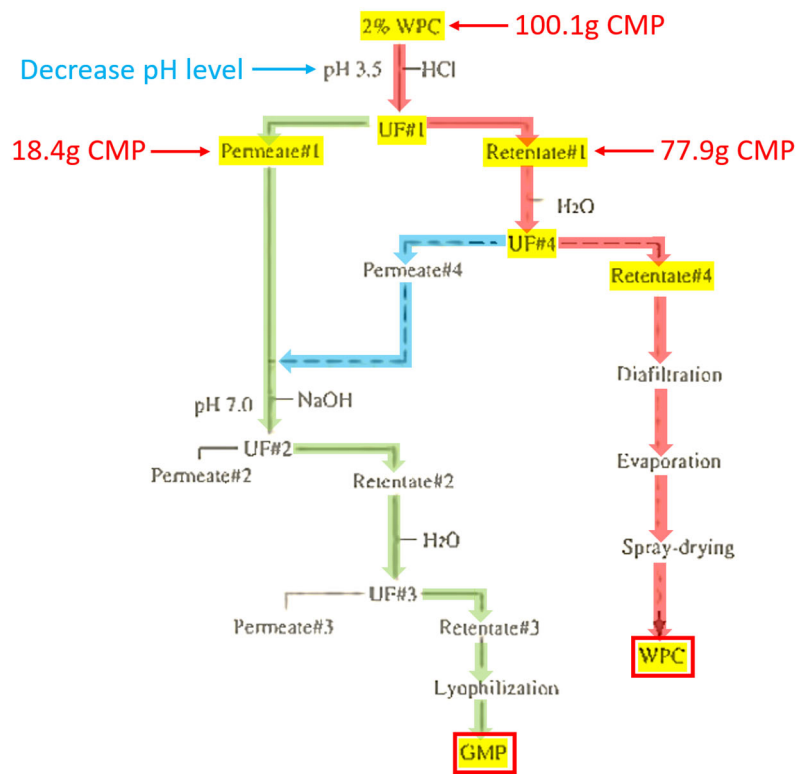


Fig. 3 Procedure to isolate GMP by UF

Ex1009, 192-93, Fig. 3 (annotated). In my opinion, a POSITA would have modified Ozturk by performing Kawasaki's ultrafiltration step on WPPC to obtain reduced-GMP WPPC while retaining the non-GMP proteins and fat in WPPC, as shown in modified and annotated Ozturk Figure 1 below.

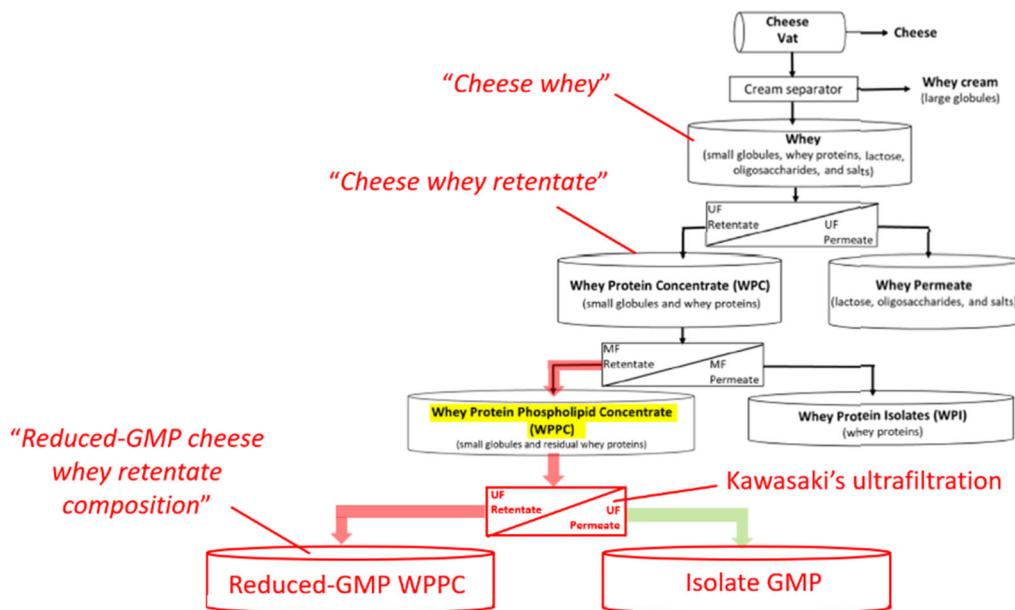


Figure 1. Manufacture of whey protein concentrate and isolate, which results in the accumulation of whey protein phospholipid concentrate (WPPC). Figure adapted from [40].

263. A POSITA would have expected Kawasaki's technique to work similarly on Ozturk's WPPC because WPPC and WPC contain similar complements of proteins, and both contain fat. Ex1008, 278-79, 293, Fig. 1; Ex1014, Fig. 5. For example, WPPC and WPC both contained whey proteins (e.g., BLG and ALA) as well as globules. If anything, a POSITA would have expected non-GMP proteins to be more effectively retained in WPPC relative to WPC because as I explained above, WPPC is more enriched for large proteins and denatured proteins than WPC. Ex1014, Fig. 5 (compare lanes 2 and 3), 12249, 12253, 12255.

264. In my opinion, a POSITA would also have had a reasonable expectation of success when modifying Ozturk with Kawasaki. This is because fat and proteins (other than GMP) in Ozturk's WPPC would be retained by Kawasaki's 20-kDa

membrane. Ex1009, 193 (“the majority of whey proteins such as β -lactoglobulin, α -lactalbumin, immunoglobulin and bovine serum albumin were rejected by the membrane”). In addition, those components had already been retained during Ozturk’s much coarser (0.1 μ m) microfiltration step. Ex1008, 293 (“Microfiltration with a 0.1 μ m pore size...” resulted in “a significant accumulation of small MFG and residual whey proteins in the microfiltration retentate”). In contrast, a POSITA would have expected that the GMP in Ozturk’s WPPC would convert to smaller effective size after acidification and preferentially pass through the Kawasaki filter. Ex1009, 192-93, Fig. 3, Table 1.

d. 8.3: “heating the reduced-GMP cheese whey retentate composition to form the denatured whey protein composition,”

265. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 8.3.

266. As I explained in Sections VII.D.3 and VII.D.4, LeanCreme taught denaturing whey protein compositions by applying heat with mechanical shearing. *See* Ex1010, 4-5. LeanCreme disclosed that the raw material used for denaturation can be WPC made from sweet whey, but other options can also be used, including WPC mixed with cream (i.e., whey protein compositions with high fat content). *Id.*, 8.

267. LeanCreme taught that it was well known to microparticulate whey protein either by separately employing heat denaturation and mechanical shear, or by performing those two steps together. *See* Ex1010, 3-6. “[S]imultaneous heat denaturation of the protein” and “controlled high shear” ensured “production of denatured whey protein particles with the desired smooth mouthfeel instead of a sandy or gritty mouthfeel.”

268. According to LeanCreme, whey proteins were known to denature at 60-85°C. Ex1010, 6 (“In general whey proteins denature between 60°C and 85°C (140-185°F) at natural pH”). Obtaining desired small particles “normally requires a high denaturation degree” and LeanCreme recommended using a temperature of 85°C. *Id.*, 7, 15. Whey-protein composition affected denaturation degree, and “up to 75% of the protein can be microparticulated” for the composition shown in Figure 2. Ex1010, 7, Fig. 2.

269. As I explained above in Section VII.D.4, a POSITA would have been motivated to modify Ozturk/Kawasaki’s WPPC by further processing to produce “novel products” such as APV LeanCreme™ taught by LeanCreme. Such modification would have involved heating the Ozturk/Kawasaki reduced-GMP WPPC to between 60-85°C as taught by LeanCreme to achieve “a high degree of denaturation.” *See* Ex1010, 6, 20. The heating process would have been performed simultaneously under high-shear conditions to form “fine particles with a specific

particle size similar to fat globules.” *See* Ex1010, 3-4, 19. The heat treatment provided “very stable particles” as a result of “high degree of denaturation.” *Id.*, 20. Additionally, the heating and shearing treatments “ensure[d] production of denatured whey protein particles with the desired smooth mouthfeel instead of a sandy or gritty mouthfeel.” Ex1010, 4, 9, 11.

e. 8.4: “wherein the denatured whey protein composition is characterized by at least 60 wt. % whey protein on a dry weight basis;”

270. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 8.4.

271. As I explained in Sections VII.D.1, VII.D.5.a-VII.D.5.b, Ozturk taught ultrafiltration on cheese whey to form a retentate of WPC. *See* Ex1008, Fig. 1, 278-79, 293. The WPC retentate was further processed through microfiltration to yield a retentate (WPPC) and a permeate (WPI). *Id.*

272. Ozturk performed detailed testing to determine gross compositions of WPPC, comparing solids, protein, and fat percentages across samples. *See* Ex1008, Table 1, 280 (“We first screened the gross composition of WPPC by measuring its total protein, fat, solids as well as protein profile by SDS PAGE and the milk fat globules’ size, to obtain a general understanding of the dataset.”). In particular, WPPC Sample 6B was a liquid WPPC containing 63.43% protein. *Id.*, Table 1. The “protein values were converted to dry basis values.” *Id.*

Table 1. Comparison between %solids, %protein, and %fat of the fat globule population measured from all WPPC samples.

Sample Description	Total Solids (%)	Protein (%)	Fat (%)
Sample 1A (liquid)	20.47	65.46 *	27.25 *
Sample 1B (liquid)	21.56	62.15 *	28.10 *
Sample 1 (powder)	-	62.7	24.4
Sample 2A (powder)	-	>72	-
Sample 2B (powder)	-	>73	-
Sample 3 (powder)	-	75.09	18.11
Sample 4A (powder)	-	76.19	13.08
Sample 4B (powder)	-	69.39	16.45
Sample 5 (powder)	-	67.61	-
Sample 6A (powder)	-	52.63	13.08
Sample 6B (liquid)	13.40	63.43	20.20
Bovine milk (liquid)	13	24.92 *	26.92 *

* % Fat and protein values were converted to dry basis values.

Ex1008, Table 1 (annotated); *see also* Ex1001, 4:36-53, 12:35-50, 14:47--15:32, 16:41-47 (discussing whey protein and calculating whey protein content).

273. I note that Sample 6B is the only liquid sample in Table 1 without the asterisk marked at the protein and fat percentages. However, a POSITA would have understood that to be a clerical oversight, for at least the reasons I provide below. First, the comparison with other samples in Table 1 is nonsensical if Sample 6B was the only one that was not reported on a dry weight basis. Second, the protein and fat content reported for Sample 6B would have been unreasonably high if its water weight had also factored into the reported values. Third, Ozturk expressly stated that all of the samples in Table 1 met the American Dairy Products Institute (ADPI) proposed standard which stated that the ADPI standard was based on dry basis measurements. Ex1008, 279 (stating “that WPPC should contain a minimum of 50%

protein (dry basis), consisting primarily of whey protein, and 12% fat [(dry basis) (ADPI, 2020)”), 286. Therefore, it is my opinion that Ozturk taught that its WPPC contained whey protein of 63.43% on a dry weight basis, exceeding 60% as recited in the claim.

274. As I explained below, performing Kawasaki’s GMP-reduction process would have lowered GMP in Ozturk’s WPPC, with the resulting whey protein level remaining above 60%. Additionally, heating whey compositions causes protein denaturation but does not alter protein content because heating processes would not have added or removed protein from the whey compositions and the whey protein level determination took into account both undenatured and denatured proteins.

275. Although Ozturk did not explicitly teach the amount of GMP in the initial whey input prior to ultrafiltration, a POSITA would have known that typical levels of GMP in sweet whey ranged from 12% to 20% of the total whey protein. *See* Ex1010, Table 1 (showing that “[t]ypical composition of sweet whey proteins” contained about 12-20% GMP content on a total whey protein basis). A POSITA would also have known that Ozturk’s WPPC contained GMP concentrations below such level due to its microfiltration step as explained above. If Ozturk’s WPPC had a GMP content within such range (e.g., 13%) of the total whey protein, the GMP content would constitute 8.24% of the WPPC on a dry weight basis ($63.43\% \times 0.13 = 8.24\%$ dry basis). According to Kawasaki, a single filtration step removed

22.1% of the GMP ($1 - \frac{77.9}{100.1} = 0.221$). *See* Ex1009, 193, Table 1 (retentate #1 maintaining 77.9% of the original GMP content).

Table 1: Recovery of GMP in each fraction during processing from WPC*	
Fraction	Content of GMP (g)
2 % WPC	100.1
Retentate #1	77.9
Permeate #1	18.4
Permeate #2	17.8
Permeate #2	0.1
Retentate #3	17.8
GMP powder	18.0
* GR61pp was employed.	

276. Performing Kawasaki's UF#1 step on Ozturk's WPPC would have removed 22.1% of GMP from the WPPC, corresponding to 1.82% of the WPPC's dry matter ($8.24\% \times 0.221 = 1.82\%$). This process would have resulted in a GMP level at 6.42% of dry matter ($8.24\% - 1.82\% = 6.42\%$) and protein at about 61.61% of dry matter ($63.43\% - 1.82\% = 61.61\%$), for a final GMP level of about 10.42% of total protein ($\frac{6.42}{61.61}\% = 10.45\%$). Additionally, Kawasaki's Table 2 also taught that diafiltration (UF#4) process resulted in removal of 63% of the GMP content. *See* Ex1009, Table 2.

277. Therefore, in my opinion, performing Kawasaki's GMP-reduction process lowers GMP content in Ozturk's WPPC (e.g., from 13% to 10.42%) and the resulting whey protein level remained above 60% (e.g., 61.61%).

f. 8.5: “less than 11 wt. % native GMP relative to a total weight of protein in the denatured whey protein composition;”

278. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 8.5.

279. As I explained in Section VII.D.5.e, the Ozturk-Kawasaki-LeanCreme combination taught this claim limitation because performing Kawasaki’s GMP-reduction process lowers GMP content in Ozturk’s WPPC to a level below 11% (e.g., from 13% to 10.42%). Additionally, a POSITA would have known to reduce GMP levels to any suitable levels because Kawasaki taught that reiterative filtration steps could be performed to remove additional GMP, and a POSITA would have been motivated to perform any number of cycles to remove further GMP as needed. For example, a POSITA would have depleted GMP from WPC using additional ultrafiltration cycles to make the resulting product suitable for infant food. A POSITA would have known how to do so by using well-known filtration techniques. *See* Ex1009, 193-94 (ultrafiltration techniques for removing GMP); Ex1012, Abstract (“pretreatment of whey protein concentrate with the enzyme transglutaminase followed by microfiltration”); Ex1013, 326 (removing GMP using “inorganic tubular membranes” with different cut-offs”).

280. A POSITA would also have been motivated to monitor GMP levels at each stage of the process to ensure proper functioning of the filtration system and

would have known how to do so based on Kawasaki's teachings. For example, Kawasaki taught that Retentate #1 can undergo ultrafiltration UF#4 (blue path) to further reduce GMP. *See* Ex1009, 193-94, Fig. 3. Indeed, a POSITA would have understood that extra filtration steps and adding diafiltration to any step all using the same membrane would have resulted in additional GMP removal. Indeed, U.S. Pat. No. 5,280,107 filed by Yoshihiro Kawasaki—the same individual who authored Kawasaki—taught that ultrafiltration processes can be conducted repeatedly with water added in each ultrafiltration step. Ex1015, 4:61-5:14.

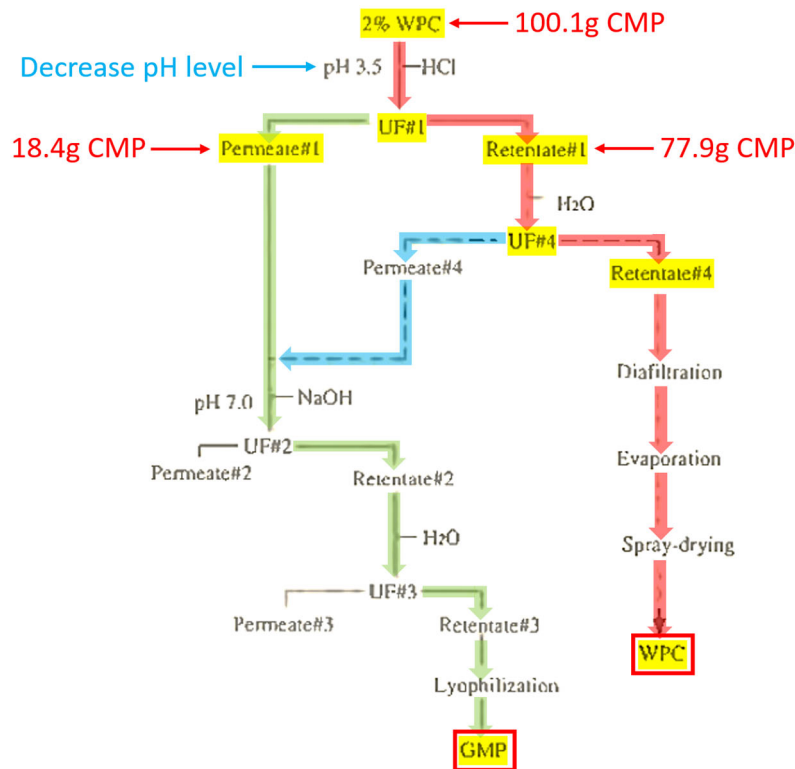


Fig. 3 Procedure to isolate GMP by UF

Ex1009, 192-93, Fig. 3 (annotated).

g. 8.6: “a proteolysis index of at least 8.0 wt. % or a beta-lactoglobulin to alpha lactalbumin ratio of greater than 5.00; and”

281. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 8.6.

282. Ozturk taught that the WPPC composition had a BLG/ALA ratio of greater than 5. The testing of WPPC sample 6B revealed BLG as 30.11% of total protein and ALA as 2.07% of total protein, resulting in a BLG to ALA ratio of 14.5, exceeding 5.00. *See* Ex1008, 291, Table 2.

Table 2. Comparative protein results in each sample expressed as the relative percentage of total and relative percentages of the milk fat globule membrane (MFGM), milk, other protein results.

	This Study		Brink et al. (2020)							
	Whey Based		Formula				Cream Based			
	WPPC	MFGM-10	PF	SF	PL-20	BPC-50	BSP2	PLC1	SM2	
MFGM proteins	22.81	10.71	5.06	2.85	24	25.73	23.33	23.93	26.39	
Butyrophilin	5.11	1.65	1.14	0.1	4.99	5.7	5.42	5.44	5.2	
Fatty acid-binding protein	1.75	2.35	1.35	1.03	2.60	4.26	4	4.54	3.18	
GLYCAM-1	7.00	3.94	2.17	1.32	7.16	3.88	3.64	4.52	7.74	
Lactadherin	4.45	1.36	0.1	0.1	5.42	4.93	4.21	4.24	4.26	
Adipophilin (Perilipin-2)	0.44	0.1	0.1	0.1	2.3	3.63	2.94	3.11	3.13	
Platelet glycoprotein 4 (CD36)	0.74	1.21	0.1	0.1	0.1	1.05	1.15	0.1	1.09	
Xanthine oxidase	2.25	0.1	0.1	0.1	1.43	2.28	1.97	1.98	1.79	
Mucin-15	0.90	-	-	-	-	-	-	-	-	
Mucin-1	0.18	-	-	-	-	-	-	-	-	
Milk proteins	45.42	55.64	61.64	68.5	56.5	50.58	51.39	52.4	52.34	
α-lactalbumin	2.07	0.1	1.4	2.65	1.05	1.12	1.2	0.1	1.4	
α-S1-casein	1.22	0.1	8.20	12.23	9.80	9.45	9.90	10.45	9.07	
α-S2-casein	0.48	0.1	8.24	11.92	11.60	10.64	11.24	14.5	10.22	
β-lactoglobulin	30.11	46.29	13.62	14.14	15.30	10.07	13.64	10.69	10.91	
Serum albumin	10.95	7.10	4.58	4.17	1.97	1.70	2.23	1.51	2.03	
β-casein	0.36	0.1	15.05	24.27	16.58	17.5	12.98	13.79	18.51	
Kappa-casein	0.24	0.1	0.1	0.1	0.1	0.1	0.1	1.26	0.1	
Lactoferrin (Lactotransferrin)	3.80	1.75	10.45	1.81	0.1	0.1	1.1	0.1	0.1	
Other proteins	31.32	33.65	33.3	28.65	19.5	76.31	25.28	23.67	21.27	

Milk fat globule membrane. Mucin-15, Mucin-1, and serum albumin values were not reported in the reference paper [70]. GLYCAM-1: glycosylation-dependent cell adhesion molecule 1; WPPC: whey protein phospholipid concentrate; MFGM-10: lactoprotein MFGM-10; PF: premium formula; SF: standard formula; PL-20: lactoprotein PL-20; BPC-50: bovine serum concentrate; BSP2: bovine serum product; PLC1: phospholipid concentrate; and SM2: sweet buttermilk powder.

Ex1008, Table 2 (annotated.)

283. Further, adding Kawasaki’s acid ultrafiltration step would not have been expected to materially alter the BLG/ALA ratio because Kawasaki taught that both ALA and BLG were rejected by the UF membrane. Ex1009, 193 (“When WPC solution was concentrated through UF membrane GR61pp at pH 3.5, the majority of whey proteins such as β-lactoglobulin, α-lactalbumin, immunoglobulin and bovine

serum albumin were rejected by the membrane, whereas GMP, lactose and minerals permeated (Permeate #1).”). Therefore, it is my opinion that a POSITA would not have expected any material change in Ozturk’s BLG/ALA ratio, much less a change anywhere near enough to reduce the ratio from 14.5 to less than 5.

h. 8.7: “greater than 50 wt. % denatured whey proteins relative to the total weight of the protein in the denatured whey protein composition.”

284. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 8.7.

285. As explained in Section VII.D.5.d, LeanCreme taught denaturing whey protein compositions by simultaneously applying heat with mechanical shearing. *See* Ex1010, 4-5.

286. Whey proteins were known to denature at 60-85°C. *See* Ex1010, 6 (“In general whey proteins denature between 60°C and 85°C (140–185°F) at natural pH.”); *see also* Ex1023, 40. Obtaining the desired small particles “normally requires a high denaturation degree” and LeanCreme recommended a denaturation temperature of 85°C to achieve this goal. Ex1010 7, 15. Whey-protein composition affects the denaturation degree, and “up to 75% of the protein can be microparticulated” for the composition shown in Figure 2. Ex1010, 7, 20, Fig. 2. A POSITA would also have understood that the percentage of 75% was calculated on a weight-ratio basis. *See* Ex1008, 10, 17. As LeanCreme explained, whey-protein

microparticulation resulted directly from heat and shear applied simultaneously. *See* Ex1010, 4. “[S]imultaneous heat denaturation of the protein” and “controlled high shear” ensured “production of denatured whey protein particles with the desired smooth mouthfeel instead of a sandy or gritty mouthfeel.” Ex1010, 3-6.

287. Accordingly, a POSITA would have found it obvious to apply the LeanCreme denaturation step to the GMP-depleted WPPC to achieve at least 75% wt. % denatured whey proteins relative to the total weight of the protein in the denatured whey protein composition such that the resulting product has “the desired smooth mouthfeel instead of a sandy or gritty mouthfeel.”

- 6. Claim 9: “The method of claim 8, wherein the reduction of native GMP in the cheese whey retentate includes combining the cheese whey retentate with one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate to form the reduced-GMP cheese whey retentate composition, the one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate comprises at least one alkaline serine protease enzyme and at least one neutral protease enzyme, or wherein the reduction of GMP occurs through the microfiltration of the cheese whey retentate.”**

288. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim 9.

289. As I explained in Section VII.D.5.c, a POSITA would have understood that Ozturk’s microfiltration step would have removed GMP from the WPC retentate resulting in a WPPC composition having reduced GMP level (“*wherein the*

reduction of GMP occurs through the microfiltration of the cheese whey retentate”).

See Ex1010, 5-7, Table 1; Ex1014, 12249, 12253, 12255, Fig. 5; Ex1008, 293; Ex1013, Table 7 (showing CMP rejection rate is 70.2 ± 7.6 for membranes with 100 nm cut off). As I also explained in in Section VII.D.5.c, Ozturk as modified by Kawasaki also taught reducing GMP from WPPC through microfiltration processes. Therefore, it is my opinion that Ozturk along or combined with Kawasaki taught claim 9.

7. Claim 11: “The method of claim 8, wherein the reduced-GMP cheese whey retentate composition is heated to a temperature of greater than or about 160° F.”

290. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim 11.

291. As I explained in Section VII.D.5.d, the Ozturk-Kawasaki-LeanCreme combination taught this limitation. In particular, LeanCreme taught that “whey proteins denature between 60°C and 85°C (140-185°F) at natural pH.” Ex1010, 6. Accordingly, LeanCreme’s heat treatment was performed at temperatures between 60°C and 85°C, and particularly at 85°C to achieve the smallest particle size. See *id.*, 7 (“The smallest particles are, typically produced around 85°C (185°F), depending on other factors.”) 85°C equals 185°F¹¹ and exceeds 160°F.

¹¹ https://en.wikipedia.org/wiki/Conversion_of_scales_of_temperature (°F = °C × 1.8 + 32)

8. Claim 12: “The method of claim 8, wherein the heating of the reduced-GMP cheese whey retentate composition further comprises exposing the reduced-GMP cheese whey retentate composition to high shear conditions.”

292. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim 12.

293. As I explained in Section VII.D.5.c, Ozturk alone or in combination with Kawasaki taught “*reduced-GMP cheese whey retentate composition*.” It is my opinion that LeanCreme further taught claim 12’s remaining limitations.

294. LeanCreme’s whey protein microparticulation resulted directly from heat and shear applied simultaneously. *See* Ex1010, 4. “[S]imultaneous heat denaturation of the protein” and “controlled high shear” ensured “production of denatured whey protein particles with the desired smooth mouthfeel instead of a sandy or gritty mouthfeel.” Ex1010, 3, 5, 6. Although LeanCreme did not expressly teach a specific shear rate for its “controlled high shear,” a POSITA would have known to denature whey protein solutions using shear rates exceeding $1,000\text{s}^{-1}$. For example, a POSITA knew that denaturing whey proteins under high temperature (e.g., $80\text{-}120^{\circ}\text{C}$) and high shear could include “450,000 to 600,000 and usually about 500,000 reciprocal minutes.”¹² Ex1016, 17:7-11. A POSITA would have understood that shear rates such as $8,333\text{s}^{-1}$ were an example of high-shear conditions because

¹² 500,000 reciprocal minutes shear rate equals about $8,333\text{s}^{-1}$ shear rate.

Ex1016 expressly referred such shear rates as “very high...shear.” Ex1016, 17:8-11. Indeed, the ’860 patent itself acknowledged that “[m]echanical shear conditions as used herein generally refer to high shear conditions in which at least about $1,000\text{s}^{-1}$ of shear is applied...” Ex1001, 8:66-9:1. As another example, heating performed simultaneously with high mechanical shearing denatured whey proteins (e.g., BLG) and converted whey protein gels to whey protein microparticles. *See* Ex1017, 1:14-19, 7:4-10, 13:31-36, 14:15-20, 18:14-36, 51:10-12.

9. **Claim 13: “The method of claim 8, wherein the denatured whey protein composition is characterized by a weight ratio of native GMP to total whey protein of less than or about 0.15, and/or wherein the denatured whey protein composition is characterized by less than or about 11 wt. % GMP relative to the total weight of the protein in the denatured whey protein composition.”**

295. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim 13.

296. As I explained in Section VII.D.5.f, the Ozturk-Kawasaki combination taught claim 13’s additional limitations.

10. Independent Claim 15

297. Claim 15 recites a whey protein composition with limitations mirroring those recited in 8.4-8.7 with the exception that claim 15 further requires the composition to comprise “greater than 7 wt. % fat.” Ex1001, 24:31. As I explain

below, the combination of Ozturk-Kawasaki-LeanCreme taught each limitation of claim 15.

a. 15.pre: “A denatured whey protein composition comprising:”

298. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 15.pre. If limiting, the Ozturk-Kawasaki-LeanCreme combination taught 15.pre for the same reasons as I explained in Section VII.D.5.a regarding claim limitation 8.pre.

b. 15.1: “at least 60 wt. % protein on a dry weight basis;”

299. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 15.1. The Ozturk-Kawasaki-LeanCreme combination taught claim limitation 15.1 for the same reasons as I explained in Section VII.D.5.e regarding claim limitation 8.4.

c. 15.2: “less than 11 wt. % native glycomacropeptide (GMP) relative to total weight of the protein;”

300. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 15.2. The Ozturk-Kawasaki-LeanCreme combination taught claim limitation 15.2 for the same reasons I explained in Section VII.D.5.f regarding claim limitation 8.5.

d. 15.3: “greater than 7 wt. % fat on a dry basis;”

301. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 15.3.

302. Ozturk described testing WPPC samples to determine their compositions and compared solids, protein, and fat percentages across samples. *See* Ex1008, Table 1, 280. WPPC Sample 6B was a liquid WPPC containing 20.20% fat, which exceeded 7%. *Id.*, Table 1. The “%[f]at and protein values were converted to dry basis values.” *Id.*

Table 1. Comparison between %solids, %protein, and %fat of the fat globule population measured from all WPPC samples.

Sample Description	Total Solids (%)	Protein (%)	Fat (%)
Sample 1A (liquid)	20.47	65.46 *	27.25 *
Sample 1B (liquid)	21.56	62.15 *	28.10 *
Sample 1 (powder)	-	62.7	24.4
Sample 2A (powder)	-	>72	-
Sample 2B (powder)	-	>73	-
Sample 3 (powder)	-	75.09	18.11
Sample 4A (powder)	-	76.19	13.08
Sample 4B (powder)	-	69.39	16.45
Sample 5 (powder)	-	67.61	-
Sample 6A (powder)	-	52.63	13.08
Sample 6B (liquid)	13.40	63.43	20.20
Bovine milk (liquid)	13	24.92 *	26.92 *

* % Fat and protein values were converted to dry basis values.

Ex1008, Table 1 (annotated). The composition percentages of solid, protein, and fat are calculated based on weight percentages. As I explained above in Section VII.D.5.e, I note that a POSITA would have understood that the missing

asterisk in Sample 6B was a clerical oversight and that the protein and fat values of Sample 6B in Table 1 are to dry basis values.

e. 15.4: “a beta-lactoglobulin to alpha lactalbumin ratio of greater than 5.00; and”

303. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 15.4. The Ozturk-Kawasaki-LeanCreme combination described 15.4 for the same reasons as I explained in Section VII.D.5.g regarding claim limitation 8.6.

f. 15.5: “greater than 50 wt. % denatured whey proteins relative to the total weight of the protein.”

304. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim limitation 15.5. The Ozturk-Kawasaki-LeanCreme combination described 15.5 for the same reasons as I explained in Section VII.D.5.h regarding claim limitation 8.7.

11. Claim 16: “The denatured whey protein composition of claim 15, wherein the denatured whey protein composition contains at least 60 wt. % beta lactoglobulin relative to a total weight of protein and/or wherein the denatured whey protein composition contains at most 12 wt. % alpha lactalbumin relative to the total weight of protein.”

305. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim 16.

306. Ozturk taught that ALA content of the WPPC samples were less than 12 wt.% of the total weight of the protein. The testing of Ozturk’s WPPC revealed

ALA as 2.07% of total protein, lower than 12%. *See* Ex1008, 291, Table 2. In my opinion, the comparative protein results listed in Table 2 of Ozturk are based on weight percentages.

Table 2. Comparative protein results in each sample expressed as the relative percentage of total and relative percentages of the milk fat globule membrane (MFGM), milk, other protein results.

	This Study	Brink et al. (2020)								
		Whey Based		Formula		Cream Based				
		WPPC	MFGM-10	PF	SF	PL-20	BPC-50	BSP2	PLC1	SM2
MFGM proteins	22.81	10.71	5.06	2.85	24	25.73	23.33	23.93	26.39	
Butyrophilin	5.11	1.65	1.14	0.1	4.99	5.7	5.42	5.44	5.2	
Fatty acid-binding protein	1.75	2.35	1.35	1.03	2.60	4.26	4	4.54	3.18	
GLYCAM-1	7.00	3.94	2.17	1.32	7.16	3.88	3.64	4.52	7.74	
Lactadherin	4.45	1.36	0.1	0.1	5.42	4.93	4.21	4.24	4.26	
Adipophilin (Perilipin-2)	0.44	0.1	0.1	0.1	2.3	3.63	2.94	3.11	3.13	
Platelet glycoprotein 4 (CD36)	0.74	1.21	0.1	0.1	0.1	1.05	1.15	0.1	1.09	
Xanthine oxidase	2.25	0.1	0.1	0.1	1.43	2.28	1.97	1.98	1.79	
Mucin-15	0.90	-	-	-	-	-	-	-	-	
Mucin-1	0.18	-	-	-	-	-	-	-	-	
Milk proteins	45.42	55.64	61.64	68.5	56.5	50.58	51.39	52.4	52.34	
α-lactalbumin	2.07	0.1	1.4	2.65	1.05	1.12	1.2	0.1	1.4	
α-S1-casein	1.22	0.1	8.20	12.23	9.80	9.45	9.90	10.45	9.07	
α-S2-casein	0.48	0.1	8.24	11.92	11.60	10.64	11.24	14.5	10.22	
β-lactoglobulin	30.11	46.29	13.62	14.14	15.30	10.07	13.64	10.69	10.91	
Serum albumin	10.95	7.10	4.58	4.17	1.97	1.70	2.23	1.51	2.03	
β-casein	0.36	0.1	15.05	24.27	16.58	17.5	12.98	13.79	18.51	
Kappa-casein	0.24	0.1	0.1	0.1	0.1	0.1	0.1	1.26	0.1	
Lactoferrin (Lactotransferrin)	3.80	1.75	10.45	1.81	0.1	0.1	1.1	0.1	0.1	
Other proteins	31.32	33.65	33.3	28.65	19.5	76.31	25.28	23.67	21.27	

Milk fat globule membrane. Mucin-15, Mucin-1, and serum albumin values were not reported in the reference paper [70]. GLYCAM-1: glycosylation-dependent cell adhesion molecule 1; WPPC: whey protein phospholipid concentrate; MFGM-10: lactoprotein MFGM-10; PF: premium formula; SF: standard formula; PL-20: lactoprotein PL-20; BPC-50: bovine serum concentrate; BSP2: bovine serum product; PLC1: phospholipid concentrate; and SM2: sweet buttermilk powder.

Ex1008, Table 2 (annotated).

12. Claim 17: “The denatured whey protein composition of claim 15, wherein the denatured whey protein composition comprises a weight ratio of beta lactoglobulin to alpha lactalbumin of greater than or about 5.”

307. In my opinion, the combination of Ozturk-Kawasaki-LeanCreme taught claim 17.

308. Ozturk taught that the WPPC had a BLG/ALA ratio of greater than 5. Ozturk’s testing revealed BLG as 30.11% of total protein and ALA as 2.07% of total protein, resulting in a BLG to ALA ratio of 14.5, exceeding 5. *See* Ex1008, 291, Table 2. As I explained in Section VII.D.11, the comparative protein results listed in Table 2 of Ozturk were based on weight percentages.

Table 2. Comparative protein results in each sample expressed as the relative percentage of total and relative percentages of the milk fat globule membrane (MFGM), milk, other protein results.

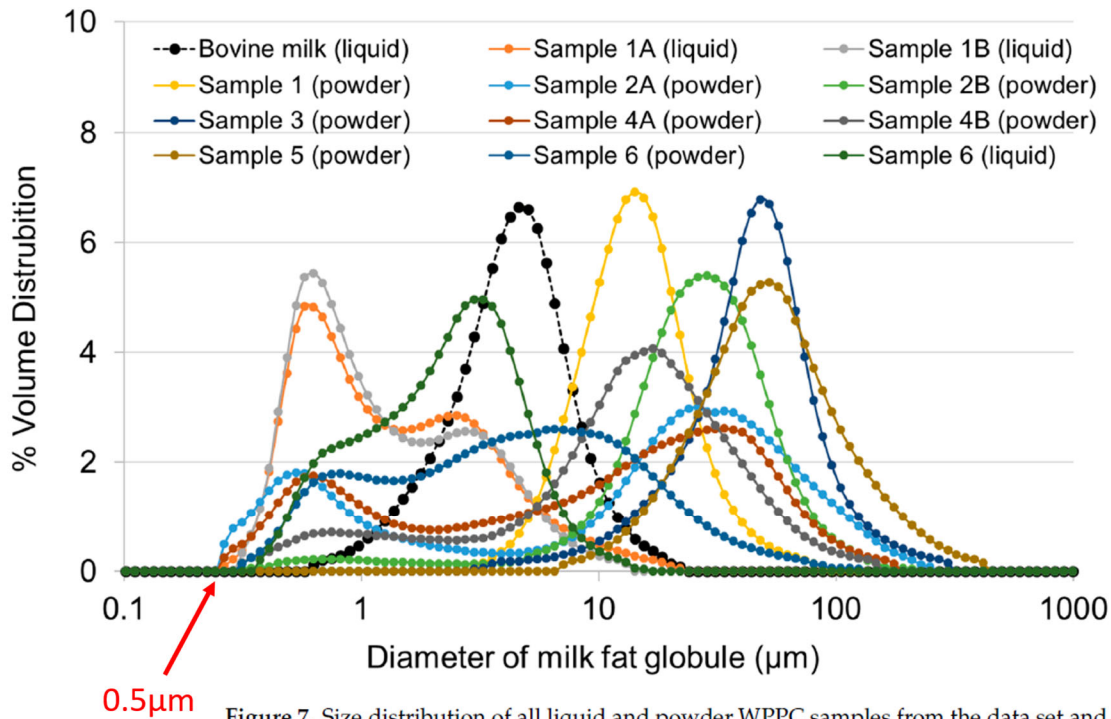
	This Study	Brink et al. (2020)							
	WPPC	Whey Based		Formula		Cream Based			
		MFGM-10	PF	SF	PL-20	BPC-50	BSP2	PLC1	SM2
MFGM proteins	22.81	10.71	5.06	2.85	24	25.73	23.33	23.93	26.39
Butyrophilin	5.11	1.65	1.14	0.1	4.99	5.7	5.42	5.44	5.2
Fatty acid-binding protein	1.75	2.35	1.35	1.03	2.60	4.26	4	4.54	3.18
GLYCAM-1	7.00	3.94	2.17	1.32	7.16	3.88	3.64	4.52	7.74
Lactadherin	4.45	1.36	0.1	0.1	5.42	4.93	4.21	4.24	4.26
Adipophilin (Perilipin-2)	0.44	0.1	0.1	0.1	2.3	3.63	2.94	3.11	3.13
Platelet glycoprotein 4 (CD36)	0.74	1.21	0.1	0.1	0.1	1.05	1.15	0.1	1.09
Xanthine oxidase	2.25	0.1	0.1	0.1	1.43	2.28	1.97	1.98	1.79
Mucin-15	0.90	-	-	-	-	-	-	-	-
Mucin-1	0.18	-	-	-	-	-	-	-	-
Milk proteins	45.42	55.64	61.64	68.5	56.5	50.58	51.39	52.4	52.34
α-lactalbumin	2.07	0.1	1.4	2.65	1.05	1.12	1.2	0.1	1.4
α -S1-casein	1.22	0.1	8.20	12.23	9.80	9.45	9.90	10.45	9.07
α -S2-casein	0.48	0.1	8.24	11.92	11.60	10.64	11.24	14.5	10.22
β-lactoglobulin	30.11	46.29	13.62	14.14	15.30	10.07	13.64	10.69	10.91
Serum albumin	10.95	7.10	4.58	4.17	1.97	1.70	2.23	1.51	2.03
β -casein	0.36	0.1	15.05	24.27	16.58	17.5	12.98	13.79	18.51
Kappa-casein	0.24	0.1	0.1	0.1	0.1	0.1	0.1	1.26	0.1
Lactoferrin (Lactotransferrin)	3.80	1.75	10.45	1.81	0.1	0.1	1.1	0.1	0.1
Other proteins	31.32	33.65	33.3	28.65	19.5	76.31	25.28	23.67	21.27

Milk fat globule membrane. Mucin-15, Mucin-1, and serum albumin values were not reported in the reference paper [70]. GLYCAM-1: glycosylation-dependent cell adhesion molecule 1; WPPC: whey protein phospholipid concentrate; MFGM-10: lactoprotein MFGM-10; PF: premium formula; SF: standard formula; PL-20: lactoprotein PL-20; BPC-50: bovine serum concentrate; BSP2: bovine serum product; PLC1: phospholipid concentrate; and SM2: sweet buttermilk powder.

Ex1008, Table 2 (annotated).

13. Claim 20: “The denatured whey protein composition of claim 15, wherein the denatured whey proteins are further characterized by a D90 particle size distribution value of less than or about 1.0 μm .”

309. As I explained in Section VII.D.5.d, LeanCreme taught heating to form “fine particles with a specific particle size similar to fat globules,” and “[o]ptimal particle size depends on the application and can be varied.” *See* Ex1010, 3-4, 9, 19. LeanCreme’s “mean particle size must be minimum 0.5-1 micron and maximum 7-10 micron,” preferably combined with a “narrow distribution.” *Id.*, 9. LeanCreme’s particle sizes were within the size range of fresh raw bovine milk and WPPC which ranged from smaller (e.g., about 0.5 μm) to larger fat globules. It was known that particle sizes of fat globules in bovine milk ranged from less than 1 μm to more than hundreds of microns. For example, I have annotated and reproduced Figure 7 of Ozturk below which shown diameter of milk fat globule as small as about 0.5 μm .



See Ex1008, Fig. 7 (annotated).

310. As I explain below, a POSITA would have been motivated to keep most particles (e.g., D90) under $1\mu\text{m}$ for several reasons.

311. First, LeanCreme's mean particle size must be at minimum $0.5\text{-}1\mu\text{m}$ and kept at "a narrow distribution" with a bell-shaped curve. Ex1010, 9. A POSITA would have understood such distribution for a mean particle size such as $0.5\mu\text{m}$ would have resulted in D90 under $1\mu\text{m}$ or less.

312. Second, "particle size similar to fat globules" led to customers' perception of "creaminess," and fat globules can be as small as $0.5\mu\text{m}$ as taught by Ozturk.

313. Third, smaller particle sizes were beneficial for preventing poor mouthfeel when consuming the dairy products. For example, it was known that dairy products with larger particle sizes led to undesirable “gritty and mealy mouthfeel.” Ex1010, 5, 9.

314. Additionally, LeanCreme taught ways to decrease particle sizes, and a POSITA would have relied upon LeanCreme’s teaching to reduce particle sizes to a nominal level. For example, LeanCreme taught that “viscosity increases by increasing particle size and protein content.” Ex1010, 11. LeanCreme’s Figure 13 showed that higher dasher speed resulted in smaller particle size. *Id.*, Fig. 13, Table 5 (Table 5 showing increasing dasher speed decreased mean particle size); *see also id.*, Fig. 9 (showing higher shear rate led to lower viscosity in both LeanCreme and WPC).

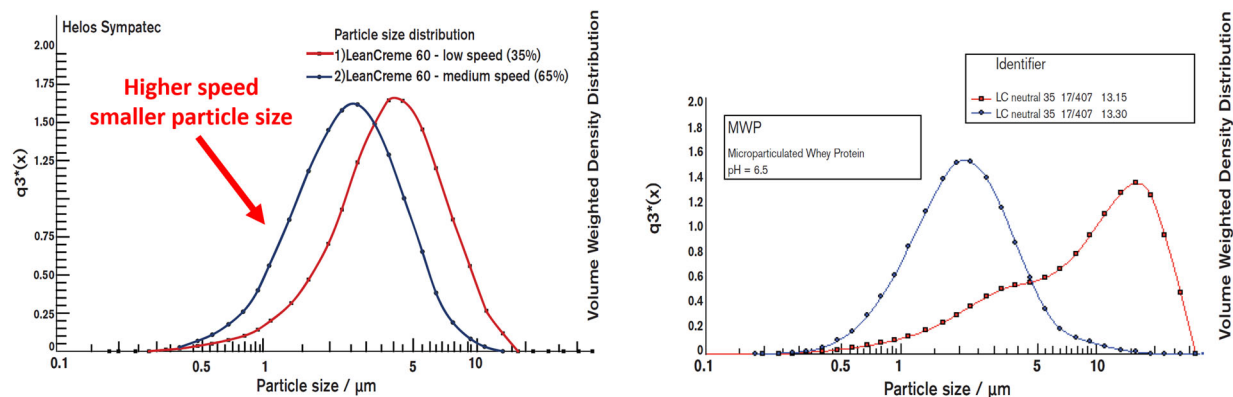


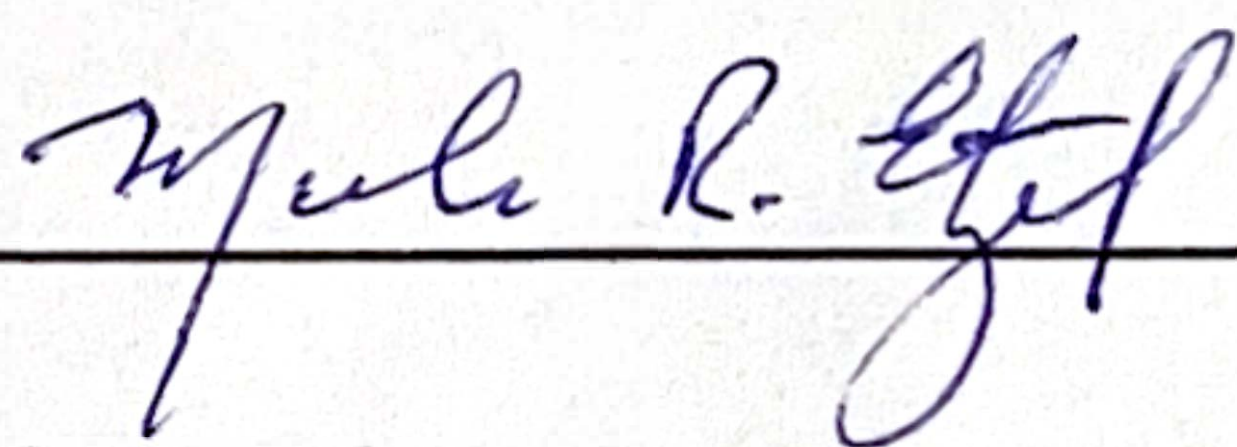
Fig.13: Control of particle size (left) and particle size distribution (right) by changing dasher speed

Ex1010, Fig. 13 (annotated).

VIII. CONCLUSION

This declaration and my opinions herein are made to the best of my knowledge and understanding, and based on the material available to me, at the time of signing this declaration. I declare that all statements made herein on my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 or Title 18 of the United States Code.

Date: June 27, 2025



Mark Etzel

APPENDIX A – MATERIALS CONSIDERED

No.	Exhibit
Ex1001	U.S. Patent No. 11,825,860 (“’860 patent”)
Ex1002	File History of the ’860 patent
Ex1005	PCT Application Publication No. WO2021/136785 (“Nielsen785”)
Ex1006	PCT Application Publication No. WO2018/115520 (“Bertelsen”)
Ex1007	PCT Application Publication No. WO2020/002450 (“Nielsen450”)
Ex1008	Gulustan Ozturk, et al., “Glycoproteomic and Lipidomic Characterization of Industrially Produced Whey Protein Phospholipid Concentrate with Emphasis on Antimicrobial Xanthine Oxidase, Oxylipins and Small Milk Fat Globules,” Dairy, Vol. 3, Issue 2, April 20, 2022, (“Ozturk”)
Ex1009	Y. Kawasaki, et al., “pH-Dependent Molecular Weight Changes of κ -casein Glyco-macropeptide and Its Preparation by Ultrafiltration,” Milchwissenschaft, Vol. 48, Issue 4, 191-196, April 1993 (“Kawasaki”)
Ex1010	“APV LeanCreme™ Microparticulation of Whey Protein with SPX Flow Technology, White Paper,” November 2012, (“LeanCreme”), Wayback Machine Capture, June 24, 2016, at https://web.archive.org/web/20160624161613/https://www.spxflow.com/en/assets/pdf/LeanCreme_22008_04_11_2012_GB_tcm11-7662.pdf
Ex1011	Affidavit of Tanya Zeif
Ex1012	Alexander Tolkach and Ulrich Kulozik, “Fractionation of Whey Proteins and Caseinomacropeptide by Means of Enzymatic Crosslinking and Membrane Separation Techniques,” Journal of Food Engineering, Vol. 67, Issues 1-2, 13-20, March 2005

Ex1013	Andrea Hinkova, et al., “Cheese Whey Tangential Filtration Using Tubular Mineral Membranes,” Chemical Papers, Vol. 70 (3), 325-32, December 28, 2016
Ex1014	A. V. Swaminathan, et al., “A Study of Various Chemical Pretreatments to Fractionate Lipids from Whey Protein Phospholipid Concentrate,” Journal of Dairy Sci., Vol. 104, Issue 12, 12249-12262, December 2021
Ex1015	U.S. Pat. No. 5,280,107 to Kawasaki et al., issued January 18, 1994
Ex1016	U.S. Pat. No. 4,734,287 to Singer et al., issued March 29, 1988
Ex1017	PCT Application Publication No. WO2015059245
Ex1018	Mark Johnson, “Cheese pH—What’s Behind the Rise and Fall?” Dairy Pipeline, Vol. 14, No. 4, 1-11, December 2002
Ex1019	U.S. Pat. Appl. Pub. No. US2011/0003975, published January 6, 2011 to Arase et al.
Ex1020	U.S. Pat. Appl. Pub. No. US2016/0058025, published March 3, 2016 to Christensen et al.
Ex1021	Declaration of Tanja Christine Jæger (“Jæger”)
Ex1022	Declaration of June Ann Munford
Ex1023	J.N. De Wit and G.A.M. Swinkels, “A Differential Scanning Calorimetric Study of the Thermal Denaturation of Bovine β -lactoglobulin Thermal Behaviour at Temperatures Up to 100°C,” Biochimica et Biophysica Acta, Vol. 624, 40-50, July 24, 1980

APPENDIX B – LISTING OF CHALLENGED CLAIMS

Reference	Limitation
Claim 8	
8[pre]	A method of making a denatured whey protein composition, the method comprising:
8[a]	filtering cheese whey from enzymatically coagulated milk into a cheese whey retentate and a permeate; and
8[b]	reducing native glycomacropeptides (GMP) in the cheese whey retentate to form a reduced-GMP cheese whey retentate composition; and
8[c]	heating the reduced-GMP cheese whey retentate composition to form the denatured whey protein composition,
8[d]	wherein the denatured whey protein composition is characterized by
8[e]	at least 60 wt. % whey protein on a dry weight basis;
8[f]	less than 11 wt. % native GMP relative to a total weight of protein in the denatured whey protein composition;
8[g]	a proteolysis index of at least 8.0 wt. % or a beta-lactoglobulin to alpha lactalbumin ratio of greater than 5.00; and
8[h]	greater than 50 wt. % denatured whey proteins relative to the total weight of the protein in the denatured whey protein composition.
Claim 9	
9	The method of claim 8, wherein the reduction of native GMP in the cheese whey retentate includes combining the cheese whey retentate with one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate to form the reduced-GMP cheese whey retentate composition, the one or more enzymes that selectively hydrolyze GMP in the cheese whey retentate comprises at least one alkaline serine protease enzyme and at least one neutral

	protease enzyme, or wherein the reduction of GMP occurs through the microfiltration of the cheese whey retentate.
Claim 11	
11	The method of claim 8, wherein the reduced-GMP cheese whey retentate composition is heated to a temperature of greater than or about 160° F.
Claim 12	
12	The method of claim 8, wherein the heating of the reduced-GMP cheese whey retentate composition further comprises exposing the reduced-GMP cheese whey retentate composition to high shear conditions.
Claim 13	
13	The method of claim 8, wherein the denatured whey protein composition is characterized by a weight ratio of native GMP to total whey protein of less than or about 0.15, and/or wherein the denatured whey protein composition is characterized by less than or about 11 wt. % GMP relative to the total weight of the protein in the denatured whey protein composition.
Claim 15	
15[pre]	A denatured whey protein composition comprising:
15[a]	at least 60 wt. % protein on a dry weight basis;
15[b]	less than 11 wt. % native glycomacropeptide (GMP) relative to total weight of the protein;
15[c]	greater than 7 wt. % fat on a dry basis;
15[d]	a beta-lactoglobulin to alpha lactalbumin ratio of greater than 5.00; and
15[e]	greater than 50 wt. % denatured whey proteins relative to the total weight of the protein.

Claim 16	
16	The denatured whey protein composition of claim 15, wherein the denatured whey protein composition contains at least 60 wt. % beta lactoglobulin relative to a total weight of protein and/or wherein the denatured whey protein composition contains at most 12 wt. % alpha lactalbumin relative to the total weight of protein.
Claim 17	
17	The denatured whey protein composition of claim 15, wherein the denatured whey protein composition comprises a weight ratio of beta lactoglobulin to alpha lactalbumin of greater than or about 5.
Claim 18	
18	The denatured whey protein composition of claim 15, wherein the denatured whey proteins are characterized by a D50 particle size distribution value of less than or about 0.3 μm .
Claim 19	
19	The denatured whey protein composition of claim 15, wherein the denatured whey proteins are further characterized by a D10 particle size distribution value of less than or about 0.1 μm .
Claim 20	
20	The denatured whey protein composition of claim 15, wherein the denatured whey proteins are further characterized by a D90 particle size distribution value of less than or about 1.0 μm .