

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MOTIF FOODWORKS, INC.,

Petitioner,

v.

IMPOSSIBLE FOODS INC.,
Patent Owner.

Case No.: IPR2023-00206
U.S. Patent No. 9,943,096

**DECLARATION OF DR. TARTÉ
IN SUPPORT OF PETITION FOR *INTER PARTES* REVIEW**

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I, Rodrigo Tarté, Ph.D., declare as follows:

I. INTRODUCTION

1. I have been retained by Quinn Emanuel Urquhart & Sullivan LLP on behalf of Motif FoodWorks, Inc. (“Petitioner” or “Motif”) as an independent expert in this *inter partes* review (“IPR”) proceeding which is pending before the Patent Trial and Appeal Board (“the Board”) of the United States Patent and Trademark Office (the “Proceeding”). I understand that, in this Proceeding, Motif is challenging the validity of claims 1-12 and 14-24 (the “Challenged Claims”) of U.S. Patent No. 9,943,096 (the “’096 patent”). Based on the first page of the ’096 patent, I understand it to be assigned to Impossible Foods Inc. (“Patent Owner”).

2. I have been asked by Motif to provide my opinions regarding the validity of the ’096 patent claims in this declaration (“Declaration”).

3. I am informed that the ’096 patent has been asserted by Patent Owner against Motif in the co-pending litigation *Impossible Foods Inc. v. Motif FoodWorks, Inc.*, Case No. 22-cv-311 (D. Del.) (“Litigation”). I understand that the Litigation is proceeding in the District Court for the District of Delaware (“District Court”).

4. I understand that, in the Litigation, neither party has exchanged any contentions relating to infringement (or non-infringement) or invalidity (or validity), and that neither party has yet proposed any claim constructions. I further understand that the District Court has not been yet asked to construe any claims of the ’096

patent and that no claim construction order has been issued. I also understand that Patent Owner has not filed any motions seeking injunctive relief and the District Court likely will not order claim construction briefing or a hearing until a later point in the Litigation. Lastly, I understand that the '096 patent has not been previously asserted in any litigation nor subject to any prior post-grant proceeding to review its validity against the prior art. I reserve the right to amend or supplement my opinions in this Declaration in response to any positions that Patent Owner may take in the Litigation, or in response to any order of the District Court.

II. QUALIFICATIONS

5. Exhibit 1004 accompanying this Declaration is a true and correct copy of my current CV. It describes in greater detail my education, publications, employment and research history, and professional activities and awards.

6. I received a Bachelor of Science degree in Food Science and Technology in 1987, a Master of Science degree in Food Science and Technology in 1990, and a Ph.D. in 1996 in Food Science & Technology and Meat Science, all from Iowa State University.

7. I am presently an Associate Professor of Meat Science and Technology, in the Department of Animal Science at Iowa State University, USA. At Iowa State, I teach courses in “Foods of Animal Origin,” “Science and Technology of Value-

Added Meat Products,” and “Advanced Meat Processing,” and serve as Director of the Online Graduate Certificate in Meat Science program.

8. I joined the Iowa State faculty in 2015 after nineteen years in the meat processing industry, during which I held key research & development posts in major meat and food processing companies, primarily Kraft Foods/Oscar Mayer and John Morrell Food Group (a division of Smithfield Foods).

9. I have contributed numerous research articles, and several book chapters and trade articles relating to food science and meat processing, including oil structuring for animal fat replacement and fatty acid profile modification. *See, e.g., Kibler et al., Novel biphasic gels can mimic and replace animal fat in fully-cooked coarse-ground sausage*, 194 Meat Sci. 108984 (2022); *Tarté et al., High-oleic and conventional soybean oil oleogels structured with rice bran wax as alternatives to pork fat in mechanically separated chicken-based bologna sausage*, 131 LWT – Food Sci. & Tech. 109659 (2020); *Wolfer et al., Replacement of pork fat in frankfurter-type sausages by soybean oil oleogels structured with rice bran wax*, 145 Meat Sci. 352-362 (2018); *see also Tarté, Leveraging meat flavor understanding for product success*, 5(3):7 Meat Musc Biol. 1–6 (2022); *Ruther et al., Effects of processing method and non-meat binding ingredients on batter stability, yield and texture of frankfurters*, 44 J. Food Process Preserv. 14626 (2020);

Lee, Tarté, et al., *Synergistic effects of starch nanoparticles and chitin nanofibers on the stability of oil-in-water Pickering emulsions*, 363 Food Chem. 130301 (2021).

10. Among my honors, I have served as President of Phi Tau Sigma, The Honor Society of Food Science and Technology, past Chair of the Institute of Food Technologists (IFT) Muscle Foods Division and Board Member of the American Meat Science Association. In recognition of my longtime work and contributions in this industry, I have been awarded the Meat Processing Award from the American Meat Science Association.

11. I am a regular invited speaker at national and international conferences, symposia, workshops and webinars, and have presented my work at national and international meetings and conferences, such as the Reciprocal Meat Conference, the American Meat Science Association, the American Oil Chemists' Society Annual Meeting of the International Congress of Meat Science and Technology, and the Institute of Food Technologists Annual Meeting.

12. My primary areas of expertise and research are meat further processing, meat product formulation, non-meat ingredient technology and food safety microbiology. During the course of my work at Kraft Foods and Oscar Mayer, I worked on a variety of meat products in support of the Oscar Mayer, Louis Rich, and Lunchables brands. I also led a team of researchers in developing new food

technologies to enable the development of new products, improve utilization of raw materials, and cost, formula, and process improvements.

13. In the course of my work at Kraft Foods, I also worked on the development and improvement of meat substitute products. As an example of my work on meat substitutes: in 2000, Kraft purchased Boca Burger, Inc., a manufacturer and marketer of soy-based meat alternative products. I personally worked on the development and improvement of the texture, appearance, flavor, and meat-like characteristics of various Boca brand products. These products included beef burger and chicken analog products (patties and nuggets).

III. SCOPE OF ASSIGNMENT

14. In forming my opinions regarding the validity of the '096 patent, I have considered the '096 patent's specification, including the Abstract and the figures. I have also considered the language of the patent's claims, as those terms would have been understood by a person having ordinary skill in the relevant field at least at the time of the '096 patent's earliest possible priority date. I have also reviewed the prosecution (the "file history") of the '096 patent.

15. In forming my opinions, I have also considered the Exhibits that are listed in the Petition and any additional materials and information cited in this Declaration. I have also searched for and reviewed technical literature relevant to the field of the '096 patent.

16. I have also relied on my personal knowledge, education, training, and professional experience in order to form my opinions concerning the '096 patent, including my experience in researching, studying, developing, or using meat substitutes and meat replica technology.

17. This Declaration explains, based on facts and information currently available to me, the subject matter and opinions related to this Proceeding. As such, I am prepared to provide expert testimony regarding opinions formed resulting from my analysis of the issues and materials considered in this Declaration, if asked to do so by the Board or by the parties' attorneys.

18. Additionally, I may discuss my own work, teachings, and knowledge of the state of the art in the relevant time period. I may rely on handbooks, textbooks, technical literature, and the like to demonstrate the state of the art in the relevant time period and the evolution of relevant technologies.

19. Furthermore, I reserve the right to consider and respond to any arguments or technical literature that Patent Owner or its counsel may identify or assert in this Proceeding. I reserve the right to amend or supplement the opinions set forth in this Declaration as additional information becomes available to me and/or in response to positions asserted by Patent Owner.

20. Throughout this Declaration, I refer to specific pages of the '096 patent and other documents. These citations are intended to be exemplary and are not

intended to convey that the citations are the only source of evidence to support the propositions for which they are cited.

21. I am being compensated for my time preparing this declaration for this matter at a rate of \$300 per hour. My compensation is in no way contingent upon the outcome of this matter or on the opinions I offer. All of the opinions expressed in this Declaration are my own.

IV. LEGAL UNDERSTANDING

22. In this section I describe my understanding of certain legal principles that I have relied upon in forming my opinions set forth in this Declaration.

23. I have been informed of these legal standards by counsel for Motif. I am not an attorney and I have not researched the law on patent invalidity. I am relying only on Motif's attorneys relating to these legal standards.

A. Person of Ordinary Skill in the Art

24. I am informed that patent validity is determined from the perspective of a person of ordinary skill in the pertinent art at the time of the invention ("POSITA"). I understand that a POSITA is a hypothetical person who is presumed to be aware of all pertinent art, conventional wisdom in the art, and is a person of ordinary creativity—not an automaton.

25. In deciding the level of ordinary skill in the art, I am informed that the following factors may be considered:

- the levels of education and experience of persons working in the field;
- the types of problems encountered in the field;
- the sophistication of the technology.

B. Claim Construction

26. I am informed that a patent may include two types of claims, independent claims and dependent claims. An independent claim stands alone and includes only the limitations it recites. A dependent claim can depend from an independent claim or another dependent claim. I am informed that a dependent claim includes all the limitations that it recites, in addition to the limitations recited in the claim from which it depends.

27. I understand that patent claim terms can be interpreted, or “construed.” I understand that, in construing a claim, the words of a patent claim are given their plain meaning, as a POSITA would understand them at the time of the invention, in view of the patent and file history (which I understand is considered “intrinsic” evidence), unless their meaning is defined or disclaimed. I am informed that dictionaries, treatises, and other “extrinsic” sources of evidence may assist in determining the plain meaning of a term, but they cannot override a meaning that is otherwise unambiguous based on the intrinsic evidence.

28. I understand that in construing claims in an IPR proceeding, words in a claim are given their plain meaning, which is the meaning understood by a person

of ordinary skill in the art in view of the patent and file history, unless specifically defined in the patent or prosecution history. I also understand that dictionaries or other extrinsic sources may assist in determining the plain and ordinary meaning but cannot override a meaning that is unambiguous from the intrinsic evidence.

29. I have been informed by Motif's counsel that claim construction is a matter of law for the arbiter of law to decide. I am informed that, in an *inter partes* review, the Patent Trial and Appeal Board interprets claims in the same way as a district court would. Likewise, I understand that a POSITA interprets claims in the same way in both types of proceedings.

30. I reserve my right to amend or alter my analysis and opinions in view of any claim constructions adopted by the arbiter of law.

C. **Anticipation**

31. I am informed that a patent claim is anticipated when a single piece of prior art describes every element of the claimed invention, either expressly or inherently, arranged in the same way as in the claim. For inherent anticipation to be found, it is required that the missing descriptive material is necessarily present in the prior art. I am informed that, for the purpose of an *inter partes* review, prior art that anticipates a claim can include both patents and printed publications from anywhere in the world.

32. I am further informed that when a patent claims a range, that range is anticipated by a prior art reference if the reference discloses a point within the range. I understand that, if the prior art discloses its own range, rather than a specific point, then the prior art is only anticipatory if it describes the claimed range with sufficient specificity such that a reasonable fact finder could conclude that there is no reasonable difference in how the invention operates over the ranges.

D. Obviousness

33. I am informed that a patent claim is unpatentable and invalid if the subject matter of the claim as a whole would have been obvious to a person of ordinary skill in the art of the claimed subject matter as of the time of the invention at issue. I am informed that the following factors must be evaluated to determine whether the claimed subject matter is obvious: (1) the scope and content of the prior art; (2) the difference or differences, if any, between each claim of the patent and the prior art; and (3) the level of ordinary skill in the art at the time the patent was filed. Unlike anticipation, which allows consideration of only one item of prior art, I am informed that obviousness may be shown by considering more than one item of prior art. Moreover, I understand that when the prior art discloses a range, rather than a point, the court must evaluate whether the patentee has established that the claimed range is critical to the operability of the claimed invention.

34. Moreover, I understand that objective indicia of non-obviousness, also known as “secondary considerations,” like the following are also to be considered when assessing obviousness: (1) commercial success; (2) long-felt but unresolved needs; (3) copying of the invention by others in the field; (4) initial expressions of disbelief by experts in the field; (5) failure of others to solve the problem that the inventor solved; and (6) unexpected results. I also understand that evidence of objective indicia of non-obviousness must have a nexus with the claimed subject matter.

E. Product-by-process Claims

35. I have been informed by counsel that claim 10 is a product-by-process claim. I have been further informed by counsel that although a product-by-process claim is limited by and defined by the process recited in the claim, determination of *patentability* is based on the product itself. Moreover, the patentability of a product does not depend on its *method* of production. Thus, I understand that if the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. However, I have also been informed that if the process by which a product is made imparts structural and functional differences distinguishing the claimed product from the prior art, then those differences are relevant as evidence of no

anticipation of the patent's product-by-process claim, although they are not explicitly part of the claim.

F. Written Description

36. I understand that a patent's specification is required to contain a written description of the invention. I am informed that the test for whether the written description is adequate is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had "possession" of the claimed subject matter as of the filing date. I am informed and understand that this inquiry is a factual question and requires an objective inquiry into the specification from the perspective of a POSITA. I further understand that demonstrating adequate written description requires a precise definition of the invention. Relatedly, I understand it is not enough for purposes of the written description support that the disclosure, when combined with the knowledge in the art, would lead one to speculate as to the modifications that the inventor might have envisioned, but did not disclose. Moreover, when a range of values is claimed in a patent claim, I understand that a skilled artisan must be able to reasonably discern a disclosure of that range in the specification to satisfy the written description requirement.

V. THE '096 PATENT

A. Level of Ordinary Skill In The Art

37. The '096 patent is directed to the art of food science and recombinant protein expression arts. A POSITA would have a Bachelor of Science degree in food science, biology, chemistry, microbiology, or a related discipline. A POSITA would also have a Master of Science degree or Ph.D. in food science or at least three years of experience working as a food scientist. A POSITA could also be part of a team of food scientists, including flavor chemists. As explained above I exceed all of these requirements. My opinions expressed herein are from the perspective of a POSITA working in the field before January 11, 2013.

B. Claims

38. The '096 patent contains 24 claims, 3 independent and 21 dependent claims. I understand that the dependent claims contain all of the elements of the claims from which they depend, in addition to the elements recited in the dependent claims.

39. Independent claims 1 and 10 are directed to a food flavor additive composition. Specifically, claim 1 is a product claim and claim 10 is a product-by-process claim. Independent claim 23 is directed at a process for imparting a meaty flavor/aroma to a food whereby the food flavor additive composition of claim 1 is added to the food and heated.

C. Specification

40. The '096 patent is directed to food flavor additive compositions and methods of preparing and using the same. The '096 patent states that “[c]urrent plant-based meat substitutes have largely failed to cause a shift to a vegetarian diet” because these substitutes “fail to replicate the aromas, flavors, and other key features, such as texture and mouth-feel, associated with cooking or cooked meat.” EX1001, 1:46-55. With respect to flavor and aroma, the '096 patent describes combining a “heme-containing protein” with “one or more flavor precursor molecules” to “provide a range of savory and meaty aromas and tastes ... in a cooked consumable food product.” *Id.*, 2:43-50.

41. Table 1 in the specification identifies a long list of such “flavor precursor molecules,” which include, *inter alia*, sugars, such as glucose and ribose, and sulfur compounds, such as cysteine and thiamine. As for “heme-containing protein,” the '096 patent explains that it “includes any polypeptide that can covalently or noncovalently bind a heme moiety,” such as hemoglobin, myoglobin, cytochrome, peroxidase, and leghemoglobin. *Id.*, 8:66-9:9, 9:23-30.

D. Prosecution History for the '096 Patent

42. The '096 patent issued from U.S. Application No. 15/398,479 (“’479 application”). During its Track One prioritized examination, the '479 application received a single substantive office action (“’479 Office Action”) that rejected

original “composition” claim 31 (corresponding to issued claim 1 ’096 patent) as anticipated by “Tong” (in view of “Shimbayashi”) and separately by “Koutsidis” (in view of “Field”). EX1002, 180-84. Tong/Shimbayashi disclose the composition of beef blood, while Koutsidis/Field disclose the contents of beef muscle tissue. Original product-by-process claim 42 (corresponding to issued claim 10) was similarly rejected over “Jamieson,” which disclosed a recipe for a stew containing beef, in view of Koutsidis and “Griffiths.” *Id.* Griffiths was used to show that beef contains globulin. *Id.*, 183.

43. The Examiner argued that Tong and Koutsidis disclosed that beef blood and beef muscle tissue, respectively, included the claimed “isolated heme-containing protein” (*e.g.*, hemoglobin), “a sugar ... selected from glucose, ribose” (*e.g.*, glucose), and “a compound selected from cysteine, ... thiamine, [or] methionine.” Notably, the Examiner did not give the term “isolated” patentable weight, reasoning that because claims 31 and 42 were both directed to a composition,¹ the term “isolated” could be ignored because “[t]he patentability of a product does not depend on its method of production.” *Id.*, 180-83 (citing *In re Thorpe*, 777 F.d 695, 698 (Fed. Cir. 1985) (internal quotations omitted)). Accordingly, the Examiner held that the hemoglobin found in beef *prima facie* satisfied the “isolated heme-containing

¹ Claim 31 (issued claim 1) claims a “food flavor additive *composition*.” Claim 42 (issued claim 10) claims a product-by-process: “food flavor additive *composition prepared by a process of*.”

protein” limitation even though “**the heme-containing protein is not isolated.**”²

Id., 180-84. The Examiner stated that “the burden shifts [to the Applicant] to establish an unobvious difference between the claimed product and the prior art product.” *Id.*

44. Unsurprisingly, Applicant did not rebut the Examiner’s contention that the term “isolated” imparted no patentable weight, nor did Applicant attempt to explain whether there was an unobvious difference between the claimed product and prior art product (*i.e.*, beef) on account of the heme-containing protein being “isolated.” *See id.*, 231-38, 955-62. Rather, Applicant amended the claims to recite “wherein the flavor additive composition contains no animal products” (*id.*, 949 (Claim 31), 1178-79 (Claim 42)), and argued that the prior art references asserted in the ’479 Office Action, which included real beef (or beef blood), failed to satisfy this limitation (*id.*, 959-61).

45. Following this amendment, the Examiner allowed the claims. *Id.*, 1172-82. The Examiner stated that “[w]hile the various pieces of applied prior art disclose compositions comprising **animal derived** heme-containing protein, sugars and amino acids, **the references do not disclose food flavor additive compositions that contain no animal products as presently claimed.**” *Id.*, 1180.

² All emphasis added herein unless otherwise stated.

46. The prosecution history also makes reference to a printed publication, *Iron Bioavailability of Hemoglobin from Soy Root Nodules Using a Caco-2 Cell Culture Model*, published by Amy K. Proulx and Manju B. Reddy on Jan. 31, 2006 (“Proulx”). Proulx was not the basis of a rejection of the ’479 Application. However, the Examiner noted in the Notice of Allowance that “while **Proulx** ... [disclosed] that hemoglobin from soy root nodules ... is a good source of bioavailable iron and can be used as a food fortificant, there is no motivation to include the fortificant, in combination with the claimed sugars and amino acids to produce meat associated flavors.” *Id.*³

47. The Examiner appears to have reconsidered this conclusion in subsequent office actions issued for a child application 15/916,090 (’090 Application) to the ’096 patent having substantially similar claims.⁴ There, the same Examiner argued that “since Proulx ... teach[es] that bioavailability is higher from heme iron sources including, leghemoglobin from soy root nodules, it would have been obvious to one of ordinary skill in the art to have fortified the structured plant protein product of Hsieh ... with leghemoglobin from soy root nodules, to obtain a product with improved nutritional status, i.e. bioavailable source of iron.”

³ A POSITA would understand that the issued claims do not require any particular compound(s), including the heme-containing protein, to be responsible for the production of the claimed “meat-associated aroma”/“meaty flavor.”

⁴ The ’090 Application issued as U.S. Patent No. 11,224,241 (’241 Patent), which is also the subject of co-pending IPR2023-00207.

EX1150('241 PH), 1124. Ultimately, the Examiner withdrew this rejection and allowed the claims of the '090 Application only after Applicant amended the claims to specify that the “meat-like food product is free of animal heme-containing protein.” *Id.*, 1270-71. This amendment overcame the primary reference, “Hsieh,” of the §103 combination (that included Proulx) because Hsieh’s consumable included real meat, not because the amendment defeated a motivation to include Proulx’s heme-containing protein as an iron fortificant. *See id.* (“The closest prior art, Hsieh ... in combination with Proulx ... teach the concept of adding leghemoglobin to a structured plant protein product to fortify with iron. While Hsieh ... disclose[s] that the plant protein product can comprise beef, and beef is known to comprise (a) ... amino acids ... and (b) ... reducing sugars ... , the reference does not disclose a similar product free of animal heme-containing protein or animal products.”) (emphasis in original).

E. Priority Date of the '096 Claims

48. I understand that Motif’s expert Dr. Robert McGorin is offering an opinion that U.S. Provisional Application No. 61/751,816 (the “’816 Provisional”) fails to provide adequate support for the Challenged Claims. EX1005 (McGorin), Section VI.C. I have reviewed the McGorin Declaration and rely on Dr. McGorin’s opinions that the '096 patent claims are not entitled to the January 11, 2013 priority date of the '816 Provisional.

VI. CHALLENGED CLAIMS

49. I understand Motif is challenging the validity of claims 1-12 and 14-24 of the '096 patent ("Challenged Claims"). I have analyzed the Challenged Claims in connection with Motif's Petition for *inter partes* review that accompanies this Declaration. The Challenged Claims are reproduced below for reference.

Claim 1	
Element No.	Claim Limitation
1[pre]	A food flavor additive composition comprising:
1[a]	a) an isolated heme-containing protein;
1[b]	b) a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, maltodextrin, and galactose, and mixtures of two or more thereof; and
1[c]	c) a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof;
1[d]	wherein the flavor additive composition contains no animal products; and
1[e]	wherein cooking the food flavor additive composition results in the production of at least two volatile compounds which have a meat-associated aroma.
Claim 2	
The food flavor additive composition of claim 1, wherein the heme-containing protein is selected from the group consisting of a androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, a leghemoglobin, an erythrocrurin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histaglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3.	
Claim 3	

The food flavor additive composition of claim 1, wherein the heme-containing protein comprises amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.
Claim 4
The food flavor additive composition of claim 1, wherein the food flavor additive composition is a powder or a liquid composition.
Claim 5
The food flavor additive composition of claim 1, wherein the heme-containing protein is a plant, a yeast or filamentous fungi, or bacterial heme-containing protein.
Claim 6
The food flavor additive composition of claim 1, further comprising one or more of an extract or hydrolysate selected from a vegetable protein hydrolysate, a soy protein hydrolysate, a yeast extract, a yeast protein hydrolysate, and an algal protein hydrolysate.
Claim 7
The food flavor additive composition of claim 1, further comprising one or more of a compound selected from alanine, arginine, asparagine, aspartate, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine, maltodextrin, thiamine, IMP, GMP, lactic acid, and creatine.
Claim 8
The food flavor additive composition of claim 1, further comprising one or more of an oil selected from coconut oil, mango oil, sunflower oil, cottonseed oil, safflower oil, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, com oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, and oil from bacteria or fungi.
Claim 9
The food flavor additive composition of claim 1, further comprising one or more of albumin or a globulin.

Claim 10	
10[pre]	A food flavor additive composition prepared by a process of:
10[a]	a) combining an isolated heme-containing protein;
10[b]	a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose and galactose, and mixtures of two or more thereof; and
10[c]	a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof, to form a heme flavor reaction mixture, and
10[d]	b) heating the heme flavor reaction mixture to at least 150° C. for at least 1 minute to result in the food flavor additive composition;
10[e]	wherein the food flavoring additive composition contains no animal products; and
10[f]	wherein the heme flavor reaction mixture has a meaty flavor and/or meaty aroma during the heating of step b) and the food flavoring additive composition has a meaty flavor and/or meaty aroma after the heating of step b).
Claim 11	
A food flavor additive composition of claim 10, wherein the food flavoring additive composition further comprises a compound selected from the group consisting of 2-methyl-furan, bis(2-methyl-3-furyl)disulfide, 2-pentyl-furan, 3,3'-dithiobis-2-methyl-furan, 2,5-dimethyl-pyrazine, 2-methyl-3-furanthiol, bis(2-methyl-4,5-dihydro-3-furyl) disulfide, dihydro-3-(2H)thiophenone, 5-methyl-2-thiophenecarboxaldehyde, 3-methyl-2-thiophenecarboxaldehyde, 2-methyl-1-thiazole, dimethyl sulfide, decanal, 5-ethyl-2(3H)-furanone, dihydro-5-pentyl-2(3H)-furanone, 2-octanone, 3,5-octadien-2-one, p-Cresol, and hexanoic acid.	
Claim 12	
The food flavor additive composition of claim 11, wherein the compound is detectable in the headspace above the heme flavor reaction mixture during the	

heating of step b) or in the headspace above the food flavoring additive composition after the heating of step b).
Claim 14
The food flavor additive composition of claim 10, wherein the heme-containing protein is present in an amount between about 0.01 % and about 5% by weight in the heme flavor reaction mixture.
Claim 15
The food flavor additive composition of claim 10, wherein the heme-containing protein is selected from the group consisting of an androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, a leghemoglobin, an erythrocrurin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histaglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3.
Claim 16
The food flavor additive composition of claim 10, wherein the heme-containing protein comprises an amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.
Claim 17
The food flavor additive composition of claim 10, wherein the heme flavor reaction mixture further comprises one or more oils selected from coconut oil, mango oil, sunflower oil, cottonseed oil, safflower oil, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, corn oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, and oil from bacteria or fungi.
Claim 18
The food flavor additive composition of claim 10, further comprising an ingredient selected from an emulsifier and a gelling agent.
Claim 19

The food flavor additive composition of claim 10, the process further comprising adding an emulsifier and a gelling agent to the heme flavor reaction mixture prior to the heating of step b).

Claim 20

The food flavor additive composition of claim 10, wherein the heme flavor reaction mixture is an aqueous solution.

Claim 21

The food flavor additive composition of claim 10, wherein the heme flavor reaction mixture is an oil-based mixture.

Claim 22

The food flavor additive composition of claim 10, further comprising one or more of an extract or hydrolysate selected from a vegetable protein hydrolysate, a soy protein hydrolysate, a yeast extract, a yeast protein hydrolysate, and an algal protein hydrolysate, and/or a globulin.

Claim 23

A process for imparting a meaty flavor and/or meaty aroma to a consumable food product, comprising: adding to the consumable food product a food flavor additive composition of claim 1; and heating the consumable food product after the adding step.

Claim 24

The food flavor additive composition of claim 1, in the form of a soup, stew base, a bouillon powder, bouillon cube, flavor packets or seasoning packet.

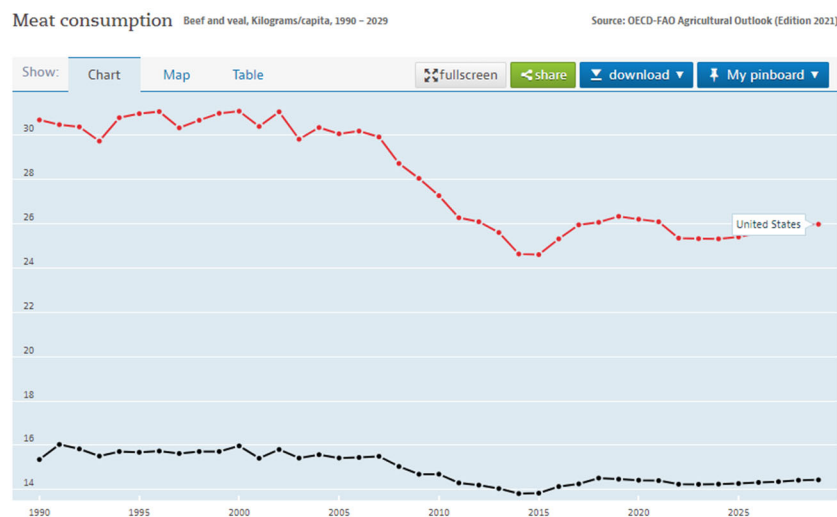
VII. STATE OF THE ART

A. Benefits of Artificial Meat Flavor Additives and Meat Substitutes

1. Meat Consumption

50. Meat has long been an extremely popular food, particularly in the United States. In fact, “[t]he majority of the population in most developed countries consume meat” obtained from conventional practices of animal husbandry and slaughter. EX1029(Williamson), 350.

51. As shown in meat consumption data collected by the Organisation for Economic Co-operation and Development (OECD) below, consumption of beef and veal in the United States far exceeds consumption worldwide.



EX1123(OECD), <https://data.oecd.org/agroutput/meat-consumption.htm>. Despite a decline in meat consumption in the 2000s, inhabitants of the United States continue to consume large quantities of meat, and this trend is projected to continue.

Consequently, a POSITA would recognize that many consumers desire meat, whether for its taste, texture, aroma, nutritive benefits, or other advantages.

52. But despite the popularity of meat, there is still a significant number of consumers that avoid meat and meat products in their diets for various reasons, including ethical, environmental, health, personal, and/or religious reasons.

2. Health

53. There is a consumer segment in the market that believes that the husbandry and consumption of animals may affect human health negatively. For example, a significant number of individuals abstain from eating meat because they believe the saturated fat and cholesterol certain types of meat contain may cause heart disease and other health problems.

Consumer concerns about food-related hazards, food safety risks, and the impact of food consumption on human health have continuously increased during the last decade.

EX1035(Verbeke), 141 (citations omitted).

Survey results ... confirmed product safety concerns to be paramount to concern about animal welfare. A major part of the recent decreases in beef and pork consumption appeared to be associated with growing consumer concerns about product safety. Also this finding is not surprising, given the large number of safety-crises that hit the meat image during recent years in Belgium (hormones, BSE, antibiotics, tranquilizers, dioxin).

EX1035(Verbeke), 149 (citations omitted).

3. Environment

54. The huge scale of the worldwide enterprise required to raise animals for food in the modern era has triggered concerns among some consumers about these activities' impacts on the environment. These concerns include the amount of land that is dedicated to raise the animals, and the amount of water necessary to sustain the animals themselves and grow their feed, particularly for large animals such as beef cattle.

55. For example, the husbandry of beef cattle requires significant amounts of farmland and water, although estimates vary.

Producing 1 kg of animal protein requires about 100 times more water than producing 1 kg of grain protein. Livestock directly uses only 1.3% of the total water used in agriculture. However, when the water required for forage and grain production is included, the water requirements for livestock production dramatically increase. For example, producing 1 kg of fresh beef may require about 13 kg of grain and 30 kg of hay. This much forage and grain requires about 100 000 L of water to produce the 100 kg of hay, and 5400 L for the 4 kg of grain. On rangeland for forage production, more than 200 000 L of water are needed to produce 1 kg of beef.

EX1036(Pimentel), 662S.

4. Animal Welfare

56. I am aware that certain consumers avoid meat because they are concerned about causing harm or death to animals, and researchers have remarked on this concern increasing in prominence as a factor in the decision of whether to consume meat.

[I]t should be noticed that the welfare issue appears to be associated with consumption decisions that were unfavorable for beef and pork in the past.... [I]t was expected that the ethical issue of animal welfare concern would gain importance in the near future.

EX1035(Verbeke), 149.

57. In light of these varied health and societal concerns among certain consumers, a POSITA would have been motivated to create substitutes for meat products and artificial meat flavoring compositions in order to appeal to this consumer base.

58. Alternatives to animal meat consumption are available for these consumers. One solution is a purely vegetarian diet; however, this may not appeal to consumers who enjoy consuming conventionally sourced meat. These individuals may be more inclined to consume meat substitute products or other foods containing artificial meat flavoring compositions that replicate desirable features of meat, such as meat's characteristic flavor and aroma.

B. Attributes of Meat

59. In recent years, in order to appeal to certain vegetarians, or to encourage meat consumers to change their eating habits, workers in the food technology industry have endeavored to create food products that can successfully substitute for, or mimic, meat products that are obtained directly through conventional practices of animal husbandry and slaughter (*i.e.*, “conventionally obtained” or “conventionally sourced” meat). Use of simulated meat flavoring compositions that can be added to meat substitutes addresses the health, environmental and animal welfare concerns that some consumers may have about producing and consuming meat, while still providing consumers an option that tastes like real meat.

60. To encourage the consumption of meat “replicas”—also called “analogs” or “substitutes”—that contain meat-flavoring compositions, and thereby mitigate these harms, the art taught replicating meat’s natural properties in replica products, including its taste, texture, aroma, appearance, and nutritional profile.

1. Nutritional Content of Meat

61. One desirable feature of conventionally obtained meat is its nutritional profile. Lean red meat, which includes beef, is an excellent source of protein, vitamins, and other nutritive materials, such as iron.

Red meat contains high biological value protein and important micronutrients that are needed for good health throughout life. It also contains a range of fats, including essential omega-3 polyunsaturated

fats.... While the nutritional composition will vary somewhat according to breed, feeding regimen, season and meat cut, in general lean red meat has a low fat content, is moderate in cholesterol and rich in protein and many essential vitamins and minerals.

EX1087(Williams), S113.

[I]n general lean red meat is a particularly good source of protein, niacin, vitamin B6, vitamin B12, phosphorus, zinc and iron, with 100g providing more than 25% RDI of these nutrients. It also provides more than 10% RDI of riboflavin, pantothenic acid, and selenium.

Id., S113-14.

Raw red muscle meat contains around 20-25g protein/100g. Cooked red meat contains 28-36g/100g, because the water content decreases and nutrients become more concentrated during cooking.... Protein from meat provides all essential amino acids (lysine, threonine, methionine, phenylalanine, tryptophan, leucine, isoleucine, valine) and has no limiting amino acids.

Id., S114.

Beef and lamb meat are among the richest sources of the minerals iron and zinc, with 100g providing at least one quarter of daily adult requirements ... The iron in meat is mostly haem-iron which is well absorbed, and meat protein also appears to enhance the absorption of iron from meat. Similarly, absorption of zinc from a diet high in animal protein is greater than from plant foods, and the requirements for zinc may be as much as 50% higher for vegetarians ... Red meats are also good sources of selenium, providing over 20% RDI per 100g serve.

Id., S117.

62. Heme-containing proteins (“heme-proteins”) contribute multiple properties characteristic of meat. Meat naturally contains the heme-containing proteins myoglobin and hemoglobin. Myoglobin is an important source of dietary iron.

Meat is an important dietary source of bioavailable minerals and trace elements, in particular iron and zinc. Iron plays a major role as an oxygen carrier in haemoglobin in blood, or myoglobin in muscle, and it is also required for many metabolic processes. Dietary iron exists in two forms, haem and non-haem iron, with haem iron being more readily absorbed and utilised by the body. Most of the iron present in meat is in the haem form. Approximately 20–30% of haem iron is absorbed in the intestine, compared with only 7% of non-haem iron.

EX1029(Williamson), 329.

63. A POSITA would be aware of the relative levels of myoglobin in different meat tissues. Notably, bovine skeletal muscle contains “4 to 10 mg/g” myoglobin and, in “old beef animals, 16 to 20 mg/g.”

In regard to age, the young animal has less myoglobin and relatively more hemoglobin than older animals of the same species. This is shown by the following values for myoglobin for fresh bovine skeletal muscle: veal, 1 to 3 mg/ g; beef, 4 to 10 mg/g; and old beef animals, 16 to 20 mg/g. Pork contains 1 to 3 mg/g for young animals of slaughter weight,

but may reach 8 to 12 mg/g in old animals. Lamb may vary from 3 to 8 mg/g, but old ewes and rams may reach levels from 12 to 18 mg/g.

EX1027(Pearson), 65.

2. Color of Meat

64. Heme iron in myoglobin and hemoglobin also serves as a natural pigment, which produces the reddish colors characteristic of blood and meat.

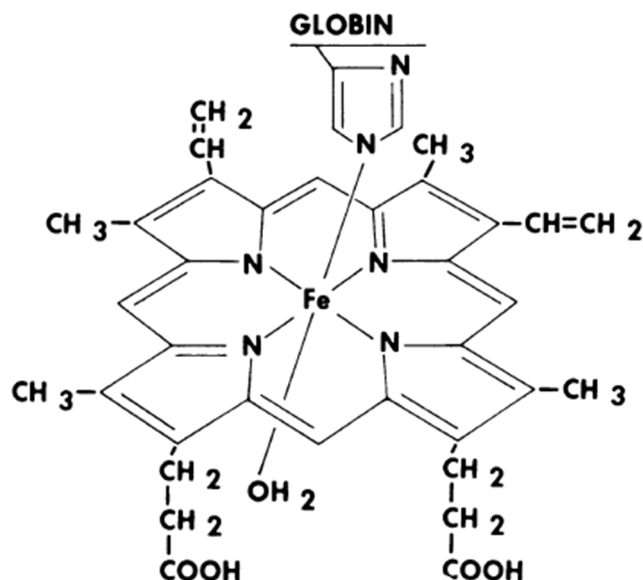
Although hemoglobin is the predominant pigment in the living animal, after slaughter by bleeding, myoglobin becomes the major pigment. Myoglobin accounts for only 10% of the total iron in the live animal, but after bleeding, may account for as much as 95% of the iron in beef skeletal muscle. Nevertheless, hemoglobin is still present in appreciable quantities and may play an important part in meat color.

EX1027(Pearson), 64-65.

Color of the Pigments: In living tissue, myoglobin and hemoglobin exist in equilibrium between the reduced dull purple-red form, myoglobin and hemoglobin, and the bright red oxygenated form, oxymyoglobin and oxyhemoglobin. Upon death, the oxygen in the tissues is rapidly depleted, leaving the pigment in the dull purple-red form of myoglobin or hemoglobin.

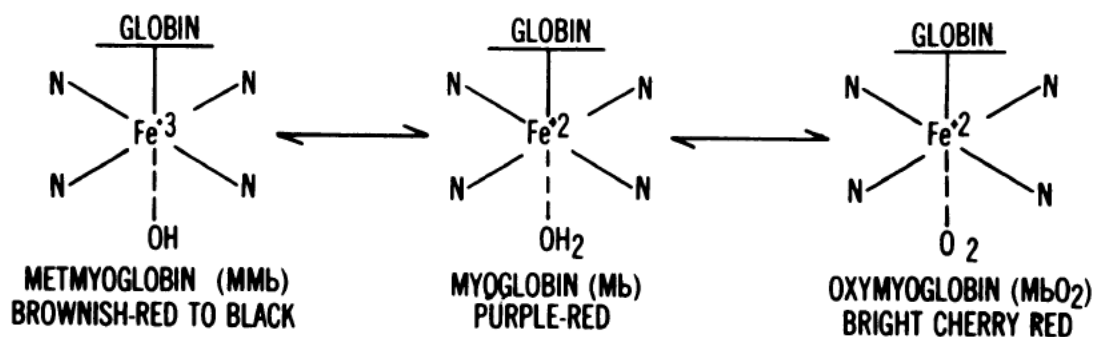
Id., 66.

65. The following is an exemplary structure for the iron-binding subunit of heme in the myoglobin complex:



Id., 66. The heme iron serves as a source or sink of electrons during electron transfer, or redox, reactions.

66. As exemplified below, the coloration of myoglobin is affected by the oxidation state of the bound heme iron and the chemical ligand bound to it.



Id., 67.

67. When heme-containing proteins such as hemoglobin or myoglobin are heated, or cooked, the globin portion is denatured and the heme is converted primarily to a denatured globin hemochrome, which gives the pigment an

irreversible brown hue. EX1107(Science of Cooking) (“Above 140° F, myoglobin loses its ability to bind oxygen, and the iron atom at the center of its molecular structure loses an electron. This process forms a tan-colored compound called hemichrome, which gives medium-done meat its color.”).

68. It was well-known in the art that this color-changing feature (from red to brown) could be implemented into food products. For example, Rolan describes the use of “thermally unstable pigments” and “browning agents” that serve to change from a red color to a brown color when the meat substitute is cooked. EX1021(Rolan), [0081]-[0083]. Conrad teaches the use of hemoglobin to impart a “meat colour.” EX1013(Conrad), 4:3-10.

3. Non-animal Heme-Containing Proteins

69. Non-animal heme-proteins are known to have structural similarities to hemoglobin and myoglobin found in animals.

Leghaemoglobins are plant haemoproteins which resemble animal myoglobins with respect to their molecular weight, monomeric state and their ligand-binding (especially oxygen-binding) properties.

EX1135(Nicola), 133.

There is a high degree of structural homology between myoglobin and leghaemoglobin revealed by sequence alignments

Id., 139.

The tertiary folding patterns of lupin and soybean Lb are very similar to those of mammalian myoglobins, and the α and β subunits of human hemoglobin.

EX1133(Hargrove), 1032.

70. Also like animal hemoglobin and myoglobin, plant hemoglobins such as leghemoglobin were known to contain heme-iron and have red pigmentation. A POSITA would recognize that these heme-proteins have similar reddish coloration properties as the heme-proteins found in meat.

Plant Hbs were first identified by Kubo (1939). *This author analyzed the red pigment of soybean root nodules* From this evidence Kubo concluded that *the red pigment isolated from soybean root nodules was a hemeprotein....* Biochemical, biophysical and molecular biology analyses have shown that Kubo's hemeprotein is a plant Hb with similar (i.e. structural) properties to animal Hbs (Fig. 1). *Kubo's plant Hb was named as leghemoglobin* (Lb) by Virtanen and Laine (1946) and is also known as plant symbiotic Hb.

EX1030(Garrocho-Villegas), 79.

71. Plant heme-proteins also have similar nutritional benefits as the heme-proteins found in meat. Recognizing that “iron deficiency is a major nutritional problem, affecting over 2 billion people,” (EX1019(Proulx), 1518), Proulx and colleagues used plant heme-proteins to fortify foodstuffs. They studied “the effectiveness of soy root nodule (SRN) and purified soy hemoglobin (LHb) in improving iron bioavailability using an in vitro Caco-2 cell model” and concluded

that “heme iron from plant sources may be a novel value added product that can provide highly bioavailable iron as a food fortificant.” *Id.* This is due to the fact that plant hemoglobin is characterized by “minimal inhibition of heme iron, unlike nonheme iron, by dietary factors and because of the high heat stability of this iron.” *Id.*, 1522. Proulx demonstrated that “the bioavailability of hemoglobin from soy root nodules is similar to that of heme iron from animal sources when added with tortillas.” *Id.*, 1521. Thus, it “provide[s] a unique alternative fortificant...to improve the iron status of the population.” *Id.*

72. Based on their extensive experiments, these researchers assessed that “[g]iven optimal nodulation conditions, 2-3 plants would provide sufficient LHb to meet 25% of the recommended daily requirement of iron, assuming 25% of heme iron absorption.” *Id.*, 1522. Thus, soy root nodule can be a “novel value-added product for soy producers.” *Id.*

C. Recombinant Technology

73. Scientists and researchers have long recognized the feasibility and the value of using recombinant technologies to engineer proteins for use in food products. For instance, scientists had engineered plants fortified with high levels of iron-containing proteins using transgenic expression systems. One early example of using recombinant technology to achieve this goal was a late-1990s study of the fortification of rice using genetic engineering. *See generally* EX1046(Goto). Goto

and colleagues recognized that “[i]ron deficiency is a serious nutritional problem that afflicts an estimated 30% of the world population[], especially where vegetable-based diets are the primary food source.” *Id.*, 282. To address this problem, they expressed the soybean ferritin gene in transgenic rice (*Oryza sativa*) using familiar genetic engineering techniques. They observed that “ferritin is used by both plants and animals as the storage form of iron[] and that, orally administrated, it can provide a source of iron for treatment of rat anemia.” *Id.*

74. These researchers observed that “soybean ferritin could be highly expressed and accumulated in the endosperm tissue of heterogeneous rice plants,” and that “transgenic seeds stored up to three times more iron than the normal seeds.” *Id.*, 282, 285 (“[T]he seeds from the transgenic rice accumulated up to threefold more iron ... than normal seeds This achievement suggests that it may be feasible to produce ‘ferritin rice’ as an iron supplement in the human diet.”). They recognized that “increasing the ferritin content of cereals by genetic engineering may help to solve the problem of dietary iron deficiency.” *Id.*, 282.

75. It was also well-known in the art that heme-containing proteins, such as hemoglobin, myoglobin, and soy leghemoglobin, could be produced using recombinant technology, such as using recombinant yeast or bacterial expression systems. *See generally* EX1014(Crane).

D. Meat Flavor Chemistry

76. It has long been known in the art that the products of what are known as Maillard reactions—chemical reactions between sulfur-containing amino acids and sugars—are in large part what give browned meats, in particular beef, their distinctive flavor.

77. I am familiar with the Maillard reaction and other principles of flavor chemistry. I understand that Motif’s expert Dr. Robert McGorrin has provided a review and analysis of meat flavor chemistry in this Proceeding. I have reviewed the McGorrin Declaration, EX1005. Dr. McGorrin’s analysis of meat flavor chemistry principles is consistent with my understanding and I rely on his analysis in forming my opinions in this Declaration.

VIII. SUMMARY OF THE PRIOR ART

A. “Brown” – EX1012

78. I have reviewed International Patent Application No. WO 2013/010042 to Brown et al. (“Brown”). Brown was filed on July 12, 2012 and claims priority to a U.S. provisional application dated July 12, 2011. Brown was published on January 17, 2013. Brown only shares a single inventor listed on the ’096 patent, and thus I have been informed was invented by “another.” Hence, I understand that Brown is considered prior art under pre-AIA 35 U.S.C. § 102(e), or, in the alternative under AIA 35 U.S.C. § 102(a)(2).

79. I understand that Brown is also prior art under 35 U.S.C. § 102(a)(1) because the '096 patent is not entitled to the '816 Provisional's January 11, 2013 priority date. *See supra* Section V.E.

80. Brown is generally directed to a “meat substitute composition” that “accurately mimics the taste, texture, or color of a meat product derived from animal sources.” EX1012(Brown), [0006]. The meat substitute “may be made entirely from plant based sources.” *Id.*, [00273], [00296]. Notably, Brown discloses that the meat substitute includes a heme-containing protein, *e.g.*, soy leghemoglobin, that “contributes favorably to aroma of meat replicas.” *Id.*, [00364].

81. Brown discloses one exemplary formula for a “muscle replica” that together with fat and connective tissue replicas, forms a “meat replica.” *See, e.g., id.*, [00364] (muscle replica formula), [00189] (describing “a meat substitute product” having “a muscle replica; a fat tissue replica; and a connective tissue replica” that “assembled in a manner that approximates the physical organization of meat”), [00191] (exemplary percentages of muscle, fat, and connective tissue replicas), [00305]-[00311] (muscle replicas), [00312]-[00322] (fat replicas), [00323]-[00359] (connective tissue replicas). The muscle replica comprises “pea flour, sunflower oil, and glucose” and is “heated for 10 minutes at 140C in the presence of ... leghemoglobin (LHb)” to provide volatile compounds that “are often associated with the aroma of cooked meat.” *Id.*, [00364].

82. Generally, Brown also teaches that “flavor and fragrance components ... produced during the cooking process by chemical reactions including amino acids, fats and sugars which are found in plants as well as meat,” can be used to produce a meaty aroma and flavor. *Id.*, [00295]. Mixtures of these components “enable these compounds to undergo chemical reactions during cooking to produce odorants and flavor-producing compounds.” *Id.*, [00361]. “Odorants released during cooking of meat are generated by reactions that can involve as reactants fats, protein, amino acids, peptides, nucleotides, organic acids, sulfur compounds, sugars, and other carbohydrates.” *Id.*, [00362].

83. Brown also explains that “[s]ome reactions that generate odorants released during cooking of meat can be catalyzed by iron, in particular the heme iron of myoglobin.” *Id.* [00363]. Thus, Brown states that “some of the characteristic flavor and fragrance components are produced during the cooking process by chemical reactions catalyzed by heme.” *Id.* In some embodiments, “the meat replica ... comprises an iron-carrying protein” that “has been isolated and purified from a source” by various percentages. *Id.* [00367]. Indeed, Brown teaches methods for isolating leghemoglobin for use in its muscle replicas. *See, e.g., id.*, [0089]-[0090], [00376]-[00380].

B. “MacLeod” – EX1024

84. I have also reviewed “*Natural and Simulated Meat Flavors (With Particular Reference to Beef)*,” by Glesni MacLeod and M. Seyyedain-Ardebili, published in Volume 14, Issue 4 of the journal *Critical Reviews in Food Science and Nutrition* on August 1981 (“MacLeod”).⁵ MacLeod was published in 1981, well before the ’096 patent’s earliest alleged priority date, and is thus prior art under 35 U.S.C. §102(a)(1) or pre-AIA §102(b). MacLeod describes in detail the science behind meat flavors and aroma including the various chemical reactions that select compounds can undergo to produce volatile compounds that are associated with a meaty aroma. MacLeod also describes the state of the art (as of 1981), providing a

⁵ As a person of ordinary skill in the art, I am familiar with the journal *Critical Reviews in Food Science and Nutrition*, as well as its publisher, the Taylor & Francis Group. The journal was actually published by the CRC Press in 1981, which was acquired in the early 2000s by Taylor & Francis. CRC Press was founded in 1903 and by 1981 was a reputable publisher of several journals in the chemistry arts. By the time of its acquisition, Taylor & Francis was (and still is) a leading source of scientific information within the field of food science and publishes thousands of peer-reviewed scientific journals every year—indeed, it is known as one of the “Big Four” STEM publishers. In particular, the journal *Critical Reviews in Food Science and Nutrition* has, for decades, been a highly-reputable scientific journal within the field of food science. In 1981, and certainly by the time of the claimed invention, a POSITA would have considered the publication dates provided on Taylor & Francis’s website, the face of the journal, and the face of the paper itself to all be reliable indicators of its publication date. Thus, it is my opinion that Proulx was available to a POSITA exercising reasonable diligence in 1981, and certainly by the time of the invention of the ’096 patent.

comprehensive overview of research and patents that describe the preparation of simulated meat flavoring compositions.

C. “Giacino” – EX1015

85. I have also reviewed U.S. Patent No. 3,519,437 (“Giacino”), titled “Meat Flavor Compositions.” Giacino issued on July 7, 1970, more than four decades before the ’096 patent, and is thus prior art under 35 U.S.C. §102(a)(1) or pre-AIA §102(b). Giacino discloses “artificial meaty flavoring compositions and ... processes for preparing them.” EX1015(Giacino), 1:19-20. The compositions have “meaty flavor characteristics such as beef, pork, and poultry flavor” and can be used for “novel food compositions containing them.” *Id.*, 1:21-25. Giacino acknowledges the ubiquity of cysteine in prior art meat flavoring compositions: “[I]t has been regarded as being highly desirable if not essential, to include cysteine in food flavor compositions.” *Id.*, 4:47-49. Giacino also discloses that “the compositions of the invention are amenable to the inclusion of cysteine as seen fit by the individual processors.” *Id.*, 4:49-53. Indeed, many of Giacino’s exemplary meat flavoring compositions include cysteine and thiamine. *See, e.g., id.*, 4:63-5:20 (cysteine, thiamine), 7:40-58 (L-cysteine hydrochloride, thiamine hydrochloride), 8:37-60 (same).

D. “Conrad” – EX1013

86. I have reviewed U.S. Patent No. 4,818,557 issued to Conrad, titled “Bran-Gluten Meat Replacement Product and Meat Products Comprising Same,” which bears a “date of patent” of April 4, 1989 (“Conrad”). I understand that Conrad is considered prior art under AIA 35 U.S.C. § 102(a)(1) or, in the alternative, under pre-AIA 35 U.S.C. § 102(b) because it is a printed publication published more than one year before the effective filing date of the ’096 patent.

87. Conrad teaches “a meat replacement product to be used in mixed minced meat products, process for its preparation, and meat products comprising same, whereby the meat replacement product comprises the gluten protein and the bran fractions of whole cereal grain,” and to which “a blood hemoglobin fraction can be added.” EX1013(Conrad), Abstract. Conrad discloses that “[t]he addition of blood/hemoglobin further gives a desired taste improvement as it improves the meat flavour of the final product.” *Id.*, 4:14-16. Conrad teaches that the hemoglobin can be isolated from blood before being added to the product. *Id.*, 4:7-9 (“[P]referably the hemoglobin part separated off from blood, the protein content of which is about 90% by weight”).

E. “Crane” – EX1014

88. I have also reviewed U.S. Patent Publication 2011/0287467 (“Crane”). Crane was published on November 24, 2011. Hence, Crane is prior art under pre-

AIA §102(b) (or alternatively under AIA 35 U.S.C. § 102(a)(1)) because it was published more than a year before the '096 patent's effective filing date.

89. Crane teaches “methods of producing recombinant functional heme-binding proteins with complete heme incorporation and purified preparations” thereof. EX1014(Crane), Abstract. Crane discloses that “the methods of the present invention generate recombinant heme-binding proteins that have complete heme incorporation,” and, “[t]herefore, these proteins are completely functional and are more suitable for research, clinical, and commercial applications.” *Id.*, [0024].

F. “Perret” – EX1020

90. I have reviewed U.S. Patent No. 3,365,306 (“Perret”), titled “Meat Flavoring Compositions.” Like Giacino, Perret issued more than four decades before the '096 patent, and is thus prior art under 35 U.S.C. §102(a)(1) or pre-AIA §102(b).

91. Perret discloses “beef-flavored compositions” that include a “beef-flavored substance” made of cysteine/cystine and a reducing sugar (*e.g.*, glucose, arabinose, etc.) along with other flavoring compounds (*e.g.*, vegetable protein hydrolysate, glutamic acid, etc.). EX1020(Perret), 1:11-16, 2:1-3:2. Perret teaches that its compositions produce a “roast meat flavor and odor.” *See, e.g., id.*, 4:6-8, 12-13. “The beef-flavored substance [is] formed by heating a compound selected from a group consisting of hexose and pentose monosaccharides with cysteine and

cystine in the presence of water.” *Id.*, 2:4-10. These compositions allow for “meatless beef-flavored foods.” *Id.*, 1:66-68.

G. “Proulx” – EX1019

92. I have reviewed “*Iron Bioavailability of Hemoglobin from Soy Root Nodules Using a Caco-2 Cell Culture Model*,” by Dr. Amy K. Proulx and Dr. Manju B Reddy, published in Volume 54, Issue 4 of the *Journal of Agricultural and Food Chemistry* on January 31, 2006 (“Proulx”).⁶ I understand that Proulx is considered prior art under AIA 35 U.S.C. § 102(a)(1) or, in the alternative, under pre-AIA 35 U.S.C. § 102(b) because it is a printed publication published more than one year before the effective filing date of the ’096 patent.

93. The Proulx article generally relates to the use of plant-derived soy leghemoglobin to fortify non-animal food products. *See* EX1019(Proulx), Abstract. Proulx explains that “[i]ron deficiency is a major nutritional problem, affecting 2 billion people.” *Id.*, 1518. “Heme iron in the human diet is generally present in

⁶ As I am at least a person of ordinary skill in the art, I am familiar with the *Journal of Agricultural and Food Chemistry*, as well as its publisher, the American Chemical Society (“ACS”). ACS is a well-known and world-renowned non-profit scientific society that was founded in 1876. In 2006, ACS was (and still is) a leading source of scientific information within the field of food science and publishes dozens of peer-reviewed scientific journals. In particular, the *Journal of Agricultural and Food Chemistry* has, for decades, been a highly-reputable scientific journal within the field of food science. In 2006, a POSITA would have considered the publication dates printed on the face of the journal and the paper itself to be a reliable indicator of its publication date. Thus, it is my opinion that the Proulx reference was available to a POSITA exercising reasonable diligence in 2006.

animal sources as a part of hemoglobin and myoglobin,” but is also “widely distributed in the plant kingdom.” *Id.* For example, “[l]eghemoglobin (LHb), a symbiotic hemoglobin, is a monomeric heme protein originally identified in soybean root nodules.” *Id.* Proulx focuses on “the use of plant hemoglobins for improving iron bioavailability of human diet” (*id.*), because “the incorporation of animal-sourced heme iron is often unfeasible because of economic costs or because [of] cultural and religious barriers.” *Id.*, 1521.

94. The objective of Proulx’s study “was to determine the iron bioavailability of crude soy root nodule extract (SRN) and two purified soy leghemoglobins” and “compare their bioavailability of bovine hemoglobin (BHb).” *Id.*, 1521. Proulx’s underlying objective “is to introduce the concept of using plant hemoglobin as a heme iron source in diets that are consumed by humans.” *Id.* The results of the study showed that “the bioavailability of hemoglobin from soy root nodules [is] similar to that of heme iron from animal sources” and can “provide a unique alternative fortificant” and “improve the iron status of the population.” *Id.*, 1521.

IX. SUMMARY OF OPINIONS

95. In my opinion:

- Brown anticipates claims 1-5, 7-9, 23, and 24. Brown discloses muscle replicas that are added to meat substitutes to impart a cooked meat aroma. The muscle replicas include glucose, pea flour, leghemoglobin,

and sunflower oil. Pea flour is a known source of sulfur compounds, such as cystine, thiamine, and methionine. Brown teaches that heating this mixture of compounds produces the aroma of cooked meat.

- The combination of Giacino and Brown renders obvious claims 1-12, 14-17, and 20-24 of the '096 patent. Relevant to the '096 patent's claims, Giacino discloses meaty flavoring compositions that include various sulfur compounds, such as cysteine and thiamine, and reducing sugars, such as ribose. These compounds produce a number of volatiles having a meat-associated aroma when heated. Brown teaches the use of heme-containing proteins, such as leghemoglobin, in artificial meat compositions. A POSITA would have been motivated to add leghemoglobin to Giacino's meaty flavoring compositions to better mimic the true flavor of meat. The combination of Giacino, Brown, and MacLeod renders obvious claims 18-19 as MacLeod teaches the use of gelling agents and emulsifiers in meat-flavored compositions.
- The combination of Giacino, Conrad, and Crane renders obvious claims 1-2, 4-7, 9-12, 14-15, and 20-24 of the '096 patent. Conrad teaches the use of hemoglobin in meat-replacement products to improve meaty flavor. Crane teaches that heme-containing proteins, such as hemoglobin and leghemoglobin, can be efficiently produced using recombinant expression systems that would obviate the need to source such proteins from previously live animals or plants. A POSITA would have been motivated to add recombinant hemoglobin/leghemoglobin to Giacino's meaty flavoring compositions to enhance their meat flavor (as taught by Conrad). Similarly, the combination of Giacino, Conrad, Crane, and Proulx renders obvious claims 3 and 16 as Proulx teaches

the use of soy leghemoglobin as an additive to foods to fortify the foods with heme iron. The combination of Giacino, Conrad, Crane, and Perret renders obvious claims 8 and 17 because Perret teaches the use of safflower oil in its meat-flavored composition. The combination of Giacino, Conrad, Crane, and MacLeod renders obvious claims 18-19 as MacLeod teaches the use of gelling agents and emulsifiers in meat-flavored compositions.

- The combination of Giacino, Proulx, and Conrad renders obvious claims 1-7, 9-12, 14-16, and 20-24 of the '096 patent. Giacino discloses meaty flavoring compositions that include sulfur compounds, such as thiamine and cysteine, and reducing sugars, such as ribose. These compounds produce a number of volatiles having a meat-associated aroma when heated. Proulx teaches the use of soy leghemoglobin as a heme iron fortificant in foods. A POSITA would have been motivated to add soy leghemoglobin to Giacino's meaty flavoring compositions to fortify them with heme iron (as taught by Proulx), which was known to have higher bioavailability than non-heme iron. Conrad teaches the use of hemoglobin in meat-replacement products to improve meaty flavor. Based on Conrad's teachings, a POSITA would have been further motivated to add a heme-containing protein, such as Proulx's soy leghemoglobin, for the added reason that it would enhance meat flavor of the compositions. Similarly, the combination of Giacino, Proulx, Conrad, and Perret renders obvious claims 8 and 17 because Perret teaches the use of safflower oil in its meat-flavored composition. The combination of Giacino, Proulx, Conrad, and MacLeod renders

obvious claims 18-19 as MacLeod teaches the use of gelling agents and emulsifiers in meat-flavored compositions.

X. CLAIM CONSTRUCTION

96. I have been asked to review the '096 patent claims to determine how a POSITA would interpret the claims at the time of the invention in view of the patent and file history.

A. “contains no animal products”

97. The challenged claims require that the food-flavor additive composition “contains no animal products.” As discussed below, I understand Patent Owner has taken the position that the term “contains no animal products” should be interpreted to allow the use of proteins that are native to an animal species, *Bos taurus* (the domesticated cow) but are not obtained from a previously live animal.

98. I have reviewed Patent Owner’s Second Amended Complaint (“SAC”) which I understand to have been filed in the co-pending Litigation. *See* EX1116. From my review of the SAC, I understand that Patent Owner has alleged that certain Motif products, which contain “myoglobin produced by fermentation from a modified strain of *Pichia pastoris* expressing the myoglobin gene from *Bos taurus*,” practice claim 1 of the '096 patent. *Id.*, ¶32. I am further informed and understand that a claim term such as “contains no animal products” should be given the same interpretation when determining a patent’s validity, as in this present *inter partes*

review proceeding, as when determining whether the patent is infringed (as in a district court litigation).

99. Thus, based on Patent Owner's interpretation, Grounds 3A-3D below (*see infra* Section XIII) map "heme-containing protein" to bovine hemoglobin produced recombinantly (*i.e.*, from a non-animal source). I note that even if Patent Owner's interpretation of this term is not adopted, Grounds 3A-3D are unaffected because they also alternatively map "heme-containing protein" to leghemoglobin, which is a heme-containing protein native to plants.

B. "food flavor additive composition"

100. It is my opinion that a POSITA would interpret the term "food flavor additive composition" according to the plain and ordinary meaning of these words, namely, a composition that, when added to a food product, modulates the food product's flavor and/or aroma.

101. In my opinion, the '096 patent's specification is consistent with this understanding. The specification explains that "[c]onsumable food products for use in the present disclosure can be flavor additive compositions, e.g., for addition to another consumable food product before, during, or after its cooking process." EX1001, 3:32-35. The patent also discloses that the composition "can be used to **modulate the flavor and/or aroma profile of a consumable food product.**" *Id.*, 3:38-48. Notably, the specification does not place limitations as to the *form* of the

food flavor additive. *Id.*, 3:49-51 (“A flavor additive composition can be in the form, of ***but not limited to***, soup or stew bases, bouillon, e.g., powder or cubes, flavor packets, or seasoning packets or shakers.”).

102. In my opinion, the Challenged Claims are also consistent with the above interpretation. For instance, claims 4 and 24 narrow independent claim 1 to specify the form of the food flavor additive composition (*e.g.*, powder, liquid, soup, stew base, etc.), which supports a POSITA’s understanding that claim 1 does not require any specific form.

103. Generally, a composition that is added to a food product and modulates that food product’s flavor and/or aroma satisfies the term. This includes “muscle replicas” (as taught by Brown, *see infra*) that are added to impart a meaty aroma/flavor to meat substitutes.

104. I further understand that Patent Owner has taken the broader position in the parallel district court litigation that Petitioner’s “***meat replica*** products (including but not limited to its ***burgers*** and ***sausage*** products” infringe the claimed “food flavor additive composition.” EX1116, ¶¶35-36, 51. Hence, Patent Owner’s interpretation of the term covers meat substitutes that are end products *directly* consumed by the consumer.

C. **“a compound”**

105. I understand that the independent claims recite “*a compound* selected from glucose” and “*a compound* selected from cysteine.” Dependent claim 7 similarly recites “*a compound* selected from alanine.” In my opinion, the term “a compound” has a plain meaning and does not require construction for the purposes of this proceeding. I understand that Patent Owner has implicitly taken the position in the Litigation that this term is not limited to free compounds of the claimed sugars and sulfur compounds (*i.e.*, compounds not chemically bound to the structure of another compound) because Patent Owner alleges that Petitioner’s meat substitute products infringe the Challenged Claims even though Motif’s products are not made using free cysteine, cystine, methionine, or thiamine. *See* EX1116, ¶¶36, 51. Thus, based on Patent Owner’s interpretation of the term, Ground 1 maps “*a compound* selected from cysteine” and “*a compound* selected from alanine” to pea flour, which contains proteins having the claimed amino acids and sulfur compounds. Even if Patent Owner’s interpretation is not adopted, Grounds 2-4 are unaffected because they map these terms to free amino acids and sulfur compounds.

XI. GROUND 1: BROWN (ANTICIPATION)

106. As I explain below, Brown anticipates claims 1-5, 7-9, 23, and 24.

A. **Claim 1**

107. In my opinion, Brown discloses all limitations of claim 1 of the ’096 patent.

1. 1[pre]: A food flavor additive composition comprising:

108. Brown discloses a food flavor additive composition.

109. Brown provides exemplary compositions for “muscle replicas.” For example, Brown describes a muscle replica that comprises “pea flour, sunflower oil, and glucose” and that is “heated for 10 minutes at 140C in the presence of ... leghemoglobin (LHb)” to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. Brown further teaches that this muscle replica is added to “a meat substitute product,” which contains fat and connective tissue replicas, and modulates the aroma/flavor of the meat substitute product by imparting an aroma of cooked meat. *Id.*, [00189] (describing “a meat substitute product” having “a muscle replica; a fat tissue replica; and a connective tissue replica” that “assembled in a manner that approximates the physical organization of meat”), [00191] (exemplary percentages of muscle, fat, and connective tissue replicas), [00305]-[00311] (muscle replicas), [00312]-[00322] (fat replicas), [00323]-[00359] (connective tissue replicas), [00364] (muscle replica produces “aroma of cooked meat”).

110. As I explained above, the term “food flavor additive composition” in view of the ’096 patent specification does not require any specific form and is, per its plain and ordinary meaning, a composition that, when added to a food product, modulates the food product’s flavor and/or aroma. *See supra* Section X.B.

111. The '096 patent's specification is consistent with this understanding. The specification explains that “[c]onsumable food products for use in the present disclosure can be flavor additive compositions, e.g., for addition to another consumable food product before, during, or after its cooking process.” EX1001, 3:32-35. The patent also discloses that the composition “can be used to **modulate the flavor and/or aroma profile of a consumable food product.**” *Id.*, 3:38-48. Notably, the specification does not place limitations as to the *form* of the food flavor additive. *Id.*, 3:49-51 (“A flavor additive composition can be in the form, of ***but not limited to***, soup or stew bases, bouillon, e.g., powder or cubes, flavor packets, or seasoning packets or shakers.”).

112. The Challenged Claims are also consistent with the above interpretation. For instance, claims 4 and 24 narrow independent claim 1 to specify the form of the food flavor additive composition (*e.g.*, powder, liquid, soup, stew base, etc.), which supports a POSITA's understanding that claim 1 does not require any specific form.

113. Based on this understanding, Brown's muscle replica is a “food flavor additive composition” because it is added to a food product (*e.g.*, “a meat substitute product”), and modulates the aroma/flavor of the meat substitute product by imparting an aroma of cooked meat.

114. Hence, Brown discloses “[a] food flavor additive composition.”

2. 1[a]: a) an isolated heme-containing protein

115. In my opinion, Brown discloses “an isolated heme-containing protein.”

116. Brown discloses an exemplary muscle replica that is prepared by mixing pea flour, sunflower oil, and glucose and then heating the mixture in the presence of leghemoglobin to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. In my opinion, a POSITA would have understood that the leghemoglobin is “isolated” (to the extent that term has patentable weight) because Brown expressly teaches extracting soy leghemoglobin from plants and isolating it to different purity levels.

Sources of leghemoglobin

In some embodiments the present invention provides methods for obtaining leghemoglobin from plants. **Leghemoglobin can be obtained from a variety of plants.** Various legumes species and their varieties, for example, Soybean, Fava bean **Figure 3 shows 100 mls of leghemoglobin solution isolated from 30 grams of pea root nodules.** Leghemoglobins from different species are homologs and have similar color properties (Figure 4)....**We purified leghemoglobin** from fava bean (green curve) and Soybean (red curve) root nodules using the protocol described elsewhere in the specification.

Id., [00376].

We purified soybean leghemoglobin from soybean root-nodules using here described protocol. Purified equine myoglobin was purchased from SigmaAldrich.

Id., [00377].

Leghemoglobin can be purified from legume root nodules, such as the root nodules of peas or soybeans (Figure 1 shows pea root nodules, **Figure 2 shows Leghemoglobin isolated from same**).... In some instances this was the **last purification step, while in other instances leghemoglobin was further purified using anion exchange chromatography** (FFQ GE Healthcare), which was sometimes followed by size-exclusion chromatography (Sephacryl S-100, GE Healthcare).... Leghemoglobin content at different purification steps was determined by determining the fraction of leghemoglobin band on SDS-PAGE gel in a respective sample using ImageDoc analysis software (BioRad). **Purity (partial abundance) of leghemoglobin at respective steps in the purification steps was: lysate: 32.7% (lane 1), 60/90 % (wt/v) ammonium sulfate fractionation 78% (lane 2), anion-exchange chromatography ~ 83% (lane 3), and size-exclusion chromatography to ~ 95% (lane 4).**

Id., [00380]. Brown also discloses that isolated soy leghemoglobin can be obtained in recombinant expression systems:

Leghemoglobin can also be produced by genetically engineering a bacterium or fungus to produce it. One illustrative example is shown in Figure 8. Figure 8 shows stained SDS-PAGE gel analysis of (A) **soybean leghemoglobin expressed and purified using recombinant protein technology** and (B) soybean leghemoglobin purified from soybean root nodules.

Id., [00381]. Brown also expressly discloses use of such isolated leghemoglobin in muscle replicas:

In some embodiments, the **muscle tissue replica** further comprises one or more **isolated and purified iron-containing proteins**. In some embodiments, said one or more isolated and purified iron-containing proteins is selected from the group consisting of hemoglobin, myoglobin, [and] **leghemoglobin***Id.*, [0089]-[0090].

117. Hence, Brown discloses that the leghemoglobin used in its muscle replica preparations are isolated.

3. **1[b]: b) a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, maltodextrin, and galactose, and mixtures of two or more thereof; and**

118. In my opinion, Brown discloses this limitation.

119. Brown expressly discloses that the exemplary “muscle replica” includes glucose. EX1012(Brown), [00364] (“A **muscle replica comprising** pea flour, sunflower oil, and **glucose** was heated for 10 minutes at 140C in the presence of ... leghemoglobin.”).

4. **1[c]: c) a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof;⁷**

120. In my opinion, Brown discloses this limitation.

⁷ As I discuss above, to the extent “a compound” is interpreted to not be limited to free compounds, Brown’s muscle replica satisfies this limitation because it contains pea flour. *See supra* Section X.C.

121. Brown discloses an exemplary muscle replica that is prepared by mixing **pea flour**, sunflower oil, and glucose and then heating the mixture in the presence of leghemoglobin to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. A POSITA would have understood that pea flour includes cystine, methionine, and thiamine.

122. For example, peer-reviewed, scientific publications reveal that, like other legume flours, pea flour contains a host of amino acids, including specifically cystine and methionine:

	Soya	Chickpea	Lupin	Green pea
Cystine	1.5 ± 0.1	1.7 ± 0.1	1.4 ± 0.2	1.4
Methionine	1.4 ± 0.1	1.6 ± 0.1	0.7 ± 0.1	0.9
Threonine	4.1 ± 0.1	3.9 ± 0.2	4.2 ± 0.6	4.2
Valine	4.4 ± 0.4	4.2 ± 0.2	3.8 ± 0.3	4.4
Isoleucine	4.2 ± 0.2	4.1 ± 0.2	4.0 ± 0.4	3.9
Leucine	7.7 ± 0.4	7.7 ± 0.3	7.3 ± 0.7	7.1
Tyrosine	4.0 ± 0.5	2.7 ± 0.2	4.3 ± 0.9	3.6
Phenylalanine	5.0 ± 0.2	5.9 ± 0.4	4.0 ± 0.4	4.9
Lysine	6.0 ± 0.1	7.0 ± 0.3	4.9 ± 0.4	7.2
Tryptophan	1.5 ± 0.1	1.4 ± 0.1	1.0 ± 0.3	0.7
Asparaginic acid/ Asparagine	11.8 ± 0.1	12.1 ± 0.4	10.7 ± 0.7	12.2
Serine	5.5 ± 0.2	5.6 ± 0.2	5.6 ± 0.4	5.6
Glutaminic acid/ Glutamine	18.2 ± 0.4	17.1 ± 0.4	21.5 ± 1.6	19.7
Glycine	4.4 ± 0.2	4.3 ± 0.1	4.4 ± 0.5	4.8
Alanine	4.7 ± 0.2	4.5 ± 0.1	3.8 ± 0.5	4.4
Histidine	2.7 ± 0.2	2.7 ± 0.1	2.8 ± 0.5	2.5
Arginine	7.8 ± 0.2	9.2 ± 0.5	11.2 ± 1.1	8.6
Proline	5.3 ± 0.8	4.4 ± 0.4	4.4 ± 0.5	3.9

Tab. 2: Amino acid content of the examined legume flours
(% total protein)

See EX1050/EX1059(Jahreis), 39, Table 2. The same paper also recognizes that legumes, such as peas, are also a rich source of thiamine (*i.e.*, vitamin B₁). See *id.*, 41 (“[L]egumes are rich in **vitamin B₁** (ca. **0.5 mg/100 g**), vitamin B₂ (0.3–0.5 mg/100 g), and folate (200–400 µg/100 g).”).

123. Another study that set out to “investigate amino acid content, biological value and dietary fibre content of conventional and organic pea (*Pisum sativum* L.) ... flours” similarly revealed that pea flour contains methionine. EX1057(Krumina-Zemture), 84-86 & Table 2 (indicating that conventional pea flour (CPF) contains 0.16 g methionine per 100 g, and organic pea flour (OPF) contains 0.15 g per 100 g).

124. These findings are consistent with the U.S. Department of Agriculture nutritional information on raw peas, which reveals that raw peas contain cystine, thiamine, and methionine. EX1106(USDA), 3, 7. A POSITA would understand that pea flour is made by grinding dried peas until a fine powder is obtained. A POSITA would recognize that this process does not remove the amino acids and vitamins present in the raw peas, including cystine, methionine, and thiamine because this is simply a mechanical process that breaks up the peas into very small pieces. There is no chemical process employed in making pea flour from peas that removes or destroys the amino acids/vitamins therein.

125. Thus, Brown’s muscle replica satisfies this claim limitation because at least the pea flour in the disclosed composition includes cystine, methionine, and thiamine.

5. 1[d]: wherein the flavor additive composition contains no animal products; and

126. In my opinion, Brown discloses this limitation.

127. Brown discloses that there are health and environmental drawbacks to a meat-eating diet. EX1012(Brown), [0001]-[0003]. To promote the adoption of meat-free products as an alternative to meat, Brown discloses a “meat substitute composition [that] accurately mimics the taste, texture, or color of a meat product derived from animal sources.” *Id.*, [0006]. Brown explains that different tissue replicas comprise the meat substitute composition, including a “muscle replica.” *Id.*, [00189]. The muscle replica can include proteins that are from non-animal sources, including plants and genetically modified yeast or bacteria engineered to produce non-animal proteins. *Id.*, [00192]-[00195].

128. One exemplary “muscle replica” described in Brown (*id.*, [00364]) includes pea flour, sunflower oil, glucose, and leghemoglobin. Brown does not disclose that any of these compounds are directly sourced from previously live animals. And, as I explain below, nor do any of these compounds have to be sourced from previously live animals. Hence, Brown’s muscle replica satisfies this claim limitation.

129. A POSITA would understand that pea flour and sunflower oil are produced from non-animal sources (peas and sunflower seeds, respectively). Leghemoglobin is also not from an animal as it is an oxygen-carrying phytoglobin found in the nitrogen-fixing root nodules of leguminous plants, such as soy. *See* EX1073(Santana), 1259 (discussing how leghemoglobin present in the root nodules of leguminous plants facilitates oxygen diffusion to bacteroids responsible for expressing nitrogenase). Indeed, Brown describes (at length) methods for obtaining leghemoglobin from plants and genetically modified yeast or bacteria engineered to produce such non-animal proteins. *See* EX1012(Brown), [00376]-[00383].

130. Glucose is a simple sugar. A POSITA would have understood that glucose is conventionally derived from plant starches, such as from corn, wheat, and potato. EX1089(Yebra-Biurrun), 479 (“Glucose ... is the major product from starch hydrolyzed by acid and/or enzymes. The major starch source in the USA and Japan is corn (*Zea mays*) and in Europe, wheat and potato.”).

131. In view of the foregoing, a POSITA would understand that the muscle replica described in Brown at [00364] does not contain animal products.

6. 1[e]: wherein cooking the food flavor additive composition results in the production of at least two volatile compounds which have a meat-associated aroma.

132. In my opinion, Brown discloses this limitation.

133. Brown discloses an exemplary muscle replica that is prepared by mixing pea flour, sunflower oil, and glucose and then heating the mixture in the presence of leghemoglobin to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. Brown expressly teaches that upon heating this muscle replica composition, various compounds associated with the aroma of cooked meat were detected during testing, including 2-octanone and 2-methyl furan. *Id.* Hence, Brown discloses “wherein cooking the food flavor additive composition results in the production of at least two volatile compounds which have a meat-associated aroma.”

134. Moreover, it was well-known in the art that heating a flavoring composition containing cystine and glucose produces a number of volatile compounds that are known to be associated with a meaty aroma/flavor. *See supra* Section VII.D; EX1005(McGorin), Sections V.B, V.D; EX1024(MacLeod), 384, Table 14 (listing volatiles produced by reacting glucose and cystine), 313-56, Table 1 (listing volatile compounds of natural beef aroma). Hence, Brown’s muscle replica, which contains glucose and cystine, would produce at least two volatile compounds having a meat-associated aroma when heated.

B. Claim 2

135. In my opinion, Brown discloses “[t]he food flavor additive composition of claim 1, wherein the heme-containing protein is selected from the group

consisting of a[n] androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, **a leghemoglobin**, an erythrocrucorin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histoglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3.”

136. Brown discloses an exemplary muscle replica that is prepared by mixing pea flour, sunflower oil, and glucose and then heating the mixture in the presence of **leghemoglobin** to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. Hence, Brown satisfies claim 2.

C. Claim 3

137. In my opinion, Brown discloses “[t]he food flavor additive composition of claim 1, wherein the heme-containing protein comprises amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.”

138. The '096 patent identifies SEQ ID NO:4 as a leghemoglobin from *Glycine max* (i.e., soybean). EX1001, 10:23-24. Brown discloses that the leghemoglobin added to its compositions is derived from soy. See EX1012(Brown), [00376]-[00377], [00380]-[00381]. Hence, a POSITA would understand that

Brown's soy leghemoglobin would have at least an 80% sequence identity to claimed SEQ ID NO 4.

139. Moreover, the '096 patent identifies the specific amino acid sequence for SEQ ID NO:4 (*Glycine max*) as follows:

```

<210> SEQ ID NO 4
<211> LENGTH: 145
<212> TYPE: PRT
<213> ORGANISM: Glycine max

<400> SEQUENCE: 4

Met Gly Ala Phe Thr Glu Lys Gln Glu Ala Leu Val Ser Ser Ser Phe
 1             5             10             15

Glu Ala Phe Lys Ala Asn Ile Pro Gln Tyr Ser Val Val Phe Tyr Thr
      20             25             30

Ser Ile Leu Glu Lys Ala Pro Ala Ala Lys Asp Leu Phe Ser Phe Leu
      35             40             45

Ser Asn Gly Val Asp Pro Ser Asn Pro Lys Leu Thr Gly His Ala Glu
      50             55             60

Lys Leu Phe Gly Leu Val Arg Asp Ser Ala Gly Gln Leu Lys Ala Asn
      65             70             75             80

Gly Thr Val Val Ala Asp Ala Ala Leu Gly Ser Ile His Ala Gln Lys
      85             90             95

Ala Ile Thr Asp Pro Gln Phe Val Val Val Lys Glu Ala Leu Leu Lys
      100            105            110

Thr Ile Lys Glu Ala Val Gly Asp Lys Trp Ser Asp Glu Leu Ser Ser
      115            120            125

Ala Trp Glu Val Ala Tyr Asp Glu Leu Ala Ala Ala Ile Lys Lys Ala
      130            135            140

Phe
145

```

EX1001, cols. 43-44.

140. Converting the above three-letter amino acid abbreviations to single-letter designations results in the following sequence:

MGAFTEKQEA LVSSSF EAFK ANIPQYSVVF YTSILEKAPA
AKDLFSFLSN GVDPSNP KLT GHAEKLFGLV RDSAGQLKAN
GTVVADAALG SIHAQKAITD PQFVVVKEAL LKTIKEAVGD
KWSDELSSAW EVAYDELA AAA IKKAF

141. Brown discloses an exemplary muscle replica that is prepared by mixing pea flour, sunflower oil, and glucose and then heating the mixture in the presence of **leghemoglobin** to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. Brown also discloses that the muscle replicas may comprise “iron-containing protein,” such as “leghemoglobin,” having “at least 98% homology to SEQ ID NO 1.” *Id.*, [0089]-[0091]. Brown defines SEQ ID NO 1 as having the following amino acid sequence:

comprises an amino acid sequence with at least 70% homology to SEQ ID NO 1. **SEQ ID NO 1:**

**MVAFTEKQDALVSSSF EAFKANIPQYSVVFYTSILEKAPAAKDLFSFLANGVDPTNP KLTGHAEK
LFALVRDSAGQLKASGTVVADAALG SVHAQKAVTDPQFVVVKEALLKTIKAAVGD KWSDELS
RAWEVAYDELA AAAIKKA.** In a particular embodiment, said one or more isolated and purified iron-

Id., [0091].

142. A POSITA would recognize that the SEQ ID NO 1 identified in Brown is substantially similar to SEQ ID NO 4 (leghemoglobin of *glycine max*) identified in the '096 patent. Indeed, the minor differences between these two amino acid

sequences are shown below with the highlighted amino acid residue designations in parentheses corresponding to the amino acid residue replacements found in Brown.⁸

MG(V)AFTEKQE(D)A LVSSSF EAFK ANIPQYSVVF YTSILEKAPA
 AKDLFSFLS(A)N GVDPS(T)NPKLT GHAEKLFG(A)LV
 RDSAGQLKAN(S) GTVVADAALG SI(V)HAQKAI(delete)TD
 PQFVVVKEAL LKTIKE(A)AVGD KWSDELSS(R)AW EVAYDELAAA
 IKKAF(delete)

143. Hence, a POSITA would recognize that 11 amino acid residues are different out of the 145 amino acid residues making up SEQ ID NO 4 (*glycine max*) identified in the '096 patent. This means that the amino acid sequence identified in Brown (*i.e.*, SEQ ID NO 1) has about 92% homology with SEQ ID NO 4 (*glycine max*) in the '096 patent.

144. This result was substantially confirmed using the National Library of Medicine's BLAST® tool where a comparison of these two amino acid sequences reveals that they have 93% homology. *See* EX1101.

145. This value (92-93% homology) is greater than the minimum 80% homology required by claim 3. Accordingly, a POSITA would understand that Brown discloses that the leghemoglobin used in its muscle replicas can have at least 80% sequence identity to the leghemoglobin protein found in *glycine max* (*i.e.*, SEQ ID NO 4 of '096 patent).

⁸ "Delete" means the preceding amino acid is not present in Brown.

146. Hence, Brown discloses “wherein the heme-containing protein comprises amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.”

D. Claims 4 and 24

147. In my opinion, Brown discloses the limitation “[t]he food flavor additive composition of claim 1, wherein the food flavor additive composition is a powder or a liquid composition” (claim 4), and “[t]he food flavor additive composition of claim 1, in the form of a soup, stew base, a **bouillon powder**, bouillon cube, flavor packets or seasoning packet” (claim 24).

148. Brown discloses an exemplary muscle replica that is prepared by mixing pea flour, sunflower oil, and glucose and then heating the mixture in the presence of leghemoglobin to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. Brown also discloses that the muscle replicas may be formed into fibers using extrusion techniques that are well known in the art. *Id.*, [00310]. Brown teaches the resulting extrusion “can be optionally dried at room temperature overnight, then ground to a **fine powder** (<60 mesh) using a Braun food grinder.” *Id.*, [00311]. Accordingly, a POSITA would understand that Brown discloses that its muscle replicas (*i.e.*, food flavor additive composition) may be dried and turned into a powder. A POSITA would

understand that such a powder is a bouillon powder since it provides a cooked meat aroma. *See id.*, [00364].

E. **Claim 5**

149. In my opinion, Brown discloses the limitation “[t]he food flavor additive composition of claim 1, wherein the heme-containing protein is a plant, a yeast or filamentous fungi, or bacterial heme-containing protein.”

150. Brown discloses an exemplary muscle replica that is prepared by mixing pea flour, sunflower oil, and glucose and then heating the mixture in the presence of **leghemoglobin** to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. Leghemoglobin is a plant heme-containing protein. *See id.*, [00376]-[00383] (describing methods for obtaining leghemoglobin from plants); EX1001, 2:43-46 (“Combining one or more iron complexes such as a hemecofactor (e.g., a heme-containing protein, including, for example a **plant-derived heme protein such as a plant leghemoglobin** (legH))”).

151. Hence, Brown discloses that the heme-containing protein in the muscle replica (e.g., food flavor additive composition) is a plant heme-containing protein.

F. **Claim 7**

152. In my opinion, Brown discloses the limitation “[t]he food flavor additive composition of claim 1, further comprising one or more of a compound

selected from **alanine, arginine, asparagine, aspartate, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine**, maltodextrin, **thiamine**, IMP, GMP, lactic acid, and creatine.”⁹

153. Brown discloses an exemplary muscle replica that is prepared by mixing **pea flour**, sunflower oil, and glucose and then heating the mixture in the presence of leghemoglobin to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. A POSITA would understand that pea flour includes alanine, arginine, asparagine, aspartate, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine, and thiamine.

154. For example, a peer-reviewed, scientific publication reveals that, like other legume flours, pea flour contains a host of amino acids, including specifically threonine, valine, isoleucine, leucine, tyrosine, phenylalanine, lysine, tryptophan, asparagine, glutamic acid, glutamine, glycine, alanine, histidine, arginine, and proline:

⁹ See *supra* n.5.

	Soya	Chickpea	Lupin	Green pea
Cystine	1.5 ± 0.1	1.7 ± 0.1	1.4 ± 0.2	1.4
Methionine	1.4 ± 0.1	1.6 ± 0.1	0.7 ± 0.1	0.9
Threonine	4.1 ± 0.1	3.9 ± 0.2	4.2 ± 0.6	4.2
Valine	4.4 ± 0.4	4.2 ± 0.2	3.8 ± 0.3	4.4
Isoleucine	4.2 ± 0.2	4.1 ± 0.2	4.0 ± 0.4	3.9
Leucine	7.7 ± 0.4	7.7 ± 0.3	7.3 ± 0.7	7.1
Tyrosine	4.0 ± 0.5	2.7 ± 0.2	4.3 ± 0.9	3.6
Phenylalanine	5.0 ± 0.2	5.9 ± 0.4	4.0 ± 0.4	4.9
Lysine	6.0 ± 0.1	7.0 ± 0.3	4.9 ± 0.4	7.2
Tryptophan	1.5 ± 0.1	1.4 ± 0.1	1.0 ± 0.3	0.7
Asparaginic acid/ Asparagine	11.8 ± 0.1	12.1 ± 0.4	10.7 ± 0.7	12.2
Serine	5.5 ± 0.2	5.6 ± 0.2	5.6 ± 0.4	5.6
Glutaminic acid/ Glutamine	18.2 ± 0.4	17.1 ± 0.4	21.5 ± 1.6	19.7
Glycine	4.4 ± 0.2	4.3 ± 0.1	4.4 ± 0.5	4.8
Alanine	4.7 ± 0.2	4.5 ± 0.1	3.8 ± 0.5	4.4
Histidine	2.7 ± 0.2	2.7 ± 0.1	2.8 ± 0.5	2.5
Arginine	7.8 ± 0.2	9.2 ± 0.5	11.2 ± 1.1	8.6
Proline	5.3 ± 0.8	4.4 ± 0.4	4.4 ± 0.5	3.9

Tab. 2: Amino acid content of the examined legume flours
(% total protein)

EX1050/EX1059(Jahreis), 39, Table 2. The same paper also recognizes that legumes, such as peas, are also a rich source of thiamine (*i.e.*, vitamin B₁). *See id.*, 41 (“[L]egumes are rich in **vitamin B₁** (ca. **0.5 mg/100 g**), vitamin B₂ (0.3–0.5 mg/100 g), and folate (200–400 µg/100 g).”).

155. Another study that set out to “investigate amino acid content, biological value and dietary fibre content of conventional and organic pea (*Pisum sativum* L.) ... flours” similarly revealed that pea flour contains a variety of different amino acids, as shown below.

Table 2

Amino acids content of pea and buckwheat flours, g 100 g⁻¹

Amino acids	WF	CPF	OPF	OBF	OSBF	CSBF
Essential amino acids						
Histidine	0.38	0.83	0.78	0.64	0.62	0.52
Isoleucine	0.14	0.41	0.43	0.14	0.17	0.30
Leucine	0.61	1.53	1.51	0.66	0.86	0.64
Lysine	0.33	1.48	1.58	0.68	0.56	0.65
Methionine	0.12	0.16	0.15	0.16	0.12	0.19
Phenylalanine	0.50	1.01	1.14	0.52	0.35	0.70
Threonine	0.19	0.73	0.75	0.34	0.43	0.43
Tryptophan	0.19	0.23	0.17	0.16	0.11	0.20
Valine	0.23	0.42	0.53	0.42	0.33	0.33
Unessential amino acids						
Alanine	0.19	0.81	0.82	0.66	0.52	0.34
Arginine	0.14	1.67	1.67	0.72	0.38	1.03
Aspartic acid	0.61	2.60	2.83	1.31	1.24	1.27
Glutamic acid	3.28	2.99	3.09	2.43	2.30	2.02
Glycine	0.30	0.90	0.92	0.68	0.56	0.70
Prolamin	1.22	1.25	1.04	0.20	0.16	0.56
Serine	0.38	0.99	1.09	0.53	0.58	0.69
Tyrosine	0.37	0.81	0.80	0.36	0.33	0.52
Total	9.18	18.82	19.30	10.61	9.62	11.09

EX1057(Krumina-Zemture), 86, Table 2; 85 (defining “CPF” as conventional pea flour and “OPF” as organic pea flour).

156. These findings are consistent with the U.S. Department of Agriculture nutritional information on raw peas, which reveals that raw peas contain a host of different amino acids and thiamine. See EX1106. A POSITA would understand that

pea flour is made by grinding dried peas until a fine powder is obtained. A POSITA would recognize that this process does not remove the amino acids and vitamins present in the raw peas, including cystine, methionine, and thiamine because turning peas into pea flour is simply a mechanical process that breaks up the peas into very small pieces. There is no chemical process employed in making pea flour from peas that removes or destroys the amino acids/vitamins therein.

157. Thus, Brown's muscle replica satisfies this claim limitation because the pea flour it contains includes **alanine, arginine, asparagine, aspartate, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine, and thiamine.**

G. Claim 8

158. In my opinion, Brown discloses the limitation "[t]he food flavor additive composition of claim 1, further comprising one or more of an oil selected from coconut oil, mango oil, **sunflower oil**, cottonseed oil, safflower oil, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, corn oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, and oil from bacteria or fungi."

159. Brown discloses an exemplary muscle replica that is prepared by mixing pea flour, **sunflower oil**, and glucose and then heating the mixture in the presence of leghemoglobin to provide volatile compounds that "are often associated

with the aroma of cooked meat.” EX1012(Brown), [00364]. Hence, the food flavor additive composition contains one of the claimed oils, namely, sunflower oil.

H. **Claim 9**

160. In my opinion, Brown discloses the limitation “[t]he food flavor additive composition of claim 1, further comprising one or more of **albumin** or a **globulin**.”

161. Brown discloses an exemplary muscle replica that is prepared by mixing **pea flour**, sunflower oil, and glucose and then heating the mixture in the presence of leghemoglobin to provide volatile compounds that “are often associated with the aroma of cooked meat.” EX1012(Brown), [00364]. A POSITA would understand that pea flour contains globulin proteins and albumin proteins. *See, e.g.*, EX1067(Meng), 235 (“Like other legume seeds, pea seeds contain high amounts of protein (20–30%). Pea proteins mainly exist as **globulins** (65–80%).”); EX1083(Buffo), 293 (“Pea protein consists primarily of **globulins** (>80% of total protein) and a small fraction of **albumins**. The **globulins** are storage proteins located in the cotyledons, whereas **albumins** are cytoplasmic proteins consisting of many different subunits (Boulter, 1983; Mosse and Pernollet, 1983).”); EX1070(Karaca), 196 (“Proteins in pea seeds are composed of main **globulins** (65%–80%), **albumins**, and glutelins.”).

162. Hence, a POSITA would understand that the food flavor additive composition (*e.g.*, muscle replica) taught in Brown includes globulins and albumins.

I. Claim 23

163. In my opinion, Brown discloses “[a] process for imparting a meaty flavor and/or meaty aroma to a consumable food product, comprising: adding to the consumable food product a food flavor additive composition of claim 1; and heating the consumable food product after the adding step.”

164. As discussed above, Brown discloses the food flavor additive composition of claim 1 in the form of a muscle replica. *See supra* Section XI.A. Brown expressly teaches that the muscle replica can be added to other tissue replicas, including a fat tissue replica and a connective tissue replica to form a meat replica (*i.e.*, claimed “consumable food product”). *See, e.g.*, EX1012(Brown), [00189] (describing “a meat substitute product” having “a muscle replica; a fat tissue replica; and a connective tissue replica” that “assembled in a manner that approximates the physical organization of meat”), [00191] (exemplary percentages of muscle, fat, and connective tissue replicas). A POSITA would understand that the resulting meat replica (*i.e.*, “consumable food product”) would then be heated before consumption. For example, Brown expressly teaches cooking “ground beef replica” patties made of muscle analog, fat tissue analog, and connective tissue analog for about 2 minutes to obtain a “distinctly ‘beef’” aroma. *Id.*, [00270], [00412], Fig. 17; *see also id.*, [0035]-[0042] (describing the cooking of a meat substitute), [00272] (“[A] consumable may be produced which is larger than a traditional cut of beef but which,

after the consumable is sliced and cooked appears the same as a traditional cooked meet [sic].”).

165. Hence, Brown discloses claim 23.

XII. GROUNDS 2A, 2B: GIACINO, BROWN, MACLEOD

166. As I explain below, the combination of Giacino and Brown renders obvious claims 1-12, 14-17, and 20-24 (Ground 2A). The combination of Giacino, Brown, and MacLeod renders obvious claims 18-19 (Ground 2B).

A. Giacino and Brown Are Analogous Art

167. Giacino and Brown are analogous art to the '096 patent. For example, a POSITA would have understood that these references are in the same field of endeavor as the claimed invention. Like the '096 patent, Giacino discloses various meaty flavoring compositions that are added to other consumable food products. *See, e.g.*, EX1015(Giacino), 1:19-25, 1:65-68, 5:1-10, 7:15-26. Similarly, Brown strives to create compositions that more accurately mimic the flavor of conventionally obtained meat. In particular, as in the '096 patent, Brown teaches the use of heme-containing proteins, such as soy leghemoglobin, to enhance the meaty flavor and aroma of its compositions. *See, e.g.*, EX1012(Brown), [00364].

168. Additionally, like the '096 patent, both Giacino and Brown describe formulations for flavoring compositions that contain flavor precursors that when

heated undergo reactions that produce meaty flavors and aromas. Also, the compositions described therein do not contain conventionally obtained meat.

169. Hence, a POSITA would understand that Giacino and Brown are analogous art to the '096 patent.

B. A POSITA Would Have Been Motivated to Combine Giacino and Brown

170. A POSITA would have been motivated to combine Giacino and Brown to achieve the subject matter of the challenged claims.

171. Giacino teaches that there is a market for meat-flavored products that do not contain actual meat. *See* EX1015(Giacino), 1:26-31. Giacino states that prior art artificial meat flavor compositions, however, are not satisfactory because they lack the “true flavor” of meat. *Id.*, 1:51-59. Accordingly, a POSITA would have understood that Giacino’s goal is to create meaty flavoring compositions that address this need and provide the closest approximation to the flavor and aroma of real meat as possible.

172. A POSITA would have also recognized that Giacino was receptive to modifications that would enhance the meaty flavors and aromas of its flavoring compositions. For instance, Giacino expressly discloses that “[v]arious other materials and ingredients can be incorporated into the compositions to provide a variety of flavor characteristics” that build upon the basic flavor of its flavoring compositions. *Id.*, 2:38-41.

173. Brown discloses that heme iron found in meat catalyzes reactions that produce volatiles associated with a meaty aroma and flavor during the cooking of meat. EX1012(Brown), [00363]. Brown further discloses that this property of heme iron is harnessed by using other heme-containing proteins, such as soy leghemoglobin, in reactions to produce the same “characteristic flavor and fragrance components” of cooked meat. *See id.* To leverage this fact, Brown teaches that “leghemoglobin solution” may be added to a consumable to better mimic meat. *See id.*, [00375]. Notably, Brown discloses adding leghemoglobin to a composition that already comprises well-known flavor precursors (including reducing sugars, amino acids, and proteins) because “the presence of leghemoglobin contributes favorably to [the] aroma of” the composition. *Id.*, [00364].

174. Brown teaches a POSITA how heating a composition containing leghemoglobin and flavor precursors (*e.g.*, pea flour, oil, and glucose) produces volatile compounds having “the aroma of cooked meat” that are “consistent[ly] differen[t]” than the volatiles produced by the same composition *lacking* leghemoglobin. *Id.* Brown further describes how gas chromatography mass spectrometry (GC-MS) revealed that the composition containing leghemoglobin produced a number of volatile compounds, including 2-octanone, 2-methyl furan, and “many other ... compounds,” that were “found exclusively or more abundantly” in the leghemoglobin-containing composition versus the composition without

leghemoglobin. *Id.* Brown discloses that these compounds are material because they “are often associated with the aroma of cooked meat.” *Id.*

175. In view of Brown’s teachings, a POSITA would have understood that adding a heme-containing protein, such as leghemoglobin, to a flavoring composition that includes well-known flavor precursors (*e.g.*, amino acids, proteins, oil, and/or reducing sugars) would provide an improved meaty aroma and flavor. This would also further Giacino’s goal of providing the “true flavor” of meat. As I mentioned above, Giacino also expressly contemplates adding additional ingredients to its compositions to modulate the compositions’ flavor. EX1015(Giacino), 2:38-41.

176. In view of the foregoing, a POSITA would have been motivated to combine the teachings of Giacino and Brown.

1. Lipid Oxidation

177. I understand that Patent Owner submitted declarations during the prosecution of the ’096 patent that opined that the relationship between heme-containing proteins, such as leghemoglobin, hemoglobin and myoglobin, and lipid oxidation would discourage a POSITA from including a heme-containing protein in a meat substitute or food flavor composition because the resulting flavor and/or aroma might be undesirable. For several reasons, I disagree.

178. **First**, a POSITA would understand that heme-containing proteins such as hemoglobin and myoglobin are naturally present in conventionally obtained meat, yet cooking conventionally obtained meat, which inevitably undergoes some amount of lipid oxidation, does not produce off-flavors. Quite the contrary, many consumers associate cooked meat with a pleasant aroma. Hence, heme-containing proteins already naturally play a part in the flavor and aroma of conventionally obtained meat. *See* EX1005(McGorin), Sections V.C, VIII.B.

179. **Second**, although heme-containing proteins can lead to lipid oxidation *over time*, this does not teach away from a method of generating a meaty flavor and/or aroma at the time of cooking the product. A POSITA would understand that the food product is likely to be consumed shortly after cooking, before any undesirable lipid oxidation has had a chance to develop. *See id.*

180. **Third**, it was well-known in the art that oxidized lipids can contribute positively to meat flavor. *See id.*

181. **Fourth**, a POSITA would understand that potential lipid oxidation can be mitigated with the use of antioxidants. *See id.*

182. Accordingly, a POSITA would understand that, although lipid oxidation could in some cases affect the flavor of food products such as heme-containing meat or meat flavorings, it would be inaccurate and an oversimplification

to say that there is an expectation that lipid oxidation would negatively, or in all instances, affect the flavor of such products.

C. A POSITA Would Have Had a Reasonable Expectation of Success When Combining Giacino and Brown

183. A POSITA would have had a reasonable expectation of success in combining the teachings of Giacino and Brown.

184. Brown discloses that adding leghemoglobin to a preparation comprising a reducing sugar (*e.g.*, glucose) and amino acids/sulfur compounds (*e.g.*, cystine, thiamine, and methionine) catalyzes chemical reactions that provide the aroma of cooked meat. Giacino's meaty flavoring compositions *also* include reducing sugars (ribose, etc.) and sulfur compounds (*e.g.*, cysteine, thiamine, or "other sulfur containing amino acids"). *See infra* ¶¶196, 198-99; EX1015(Giacino), 3:43-45, 3:68-73, 4:21-24, 5:75-6:7. Hence, a POSITA would reasonably expect the same catalyzation to take place when adding leghemoglobin to Giacino's compositions to produce volatiles associated with cooked meat. Moreover, nothing more than ordinary skill would have been required to obtain the soy leghemoglobin (which Brown describes in detail, *e.g.*, *see supra* Section XI.A.2), and mix it into Giacino's composition prior to heating.

185. Additionally, the chemistry of the Maillard reaction was long known, including the identity of specific precursor compounds that, when reacted using heat, would produce a desirable meaty flavor and aroma. *See supra* Section VII.D;

EX1005(McGorin), Sections V.B, V.D. As such, a POSITA would have known how to combine such flavor precursors, such as those taught in Giacino and Brown, to induce a Maillard reaction when heated and produce meat-associated volatiles.

D. Claim 1

186. In my opinion, Giacino and Brown render obvious claim 1 of the '096 patent.

1. 1[pre]: A food flavor additive composition comprising:

187. Giacino discloses food flavor additive compositions. Giacino discloses various “artificial meaty flavoring compositions” (*e.g.*, food flavor additive compositions) “having meaty flavor characteristics such as beef, pork and poultry flavor.” EX1015(Giacino), 1:19-25. Giacino explains that these compositions “can be used per se in a wide range of food stuffs, either as the dominant flavoring agent or as an aid in improving and enhancing existing flavor.” *Id.*, 1:65-68. Giacino relevantly also discloses:

The flavor compositions of this invention can be used to flavor various foods, liquid or dry.... For example, they can be incorporated into gravies, sauces, soups, dressings, salads, aspics, purees and other liquid preparations...they can be admixed with carrier materials or with other flavoring ingredients or foodstuffs for incorporation into finished products, illustrative of which are the dry foods such as snacks, chips, synthetic meat fibres and the like.

Id., 7:15-26.

188. Hence, Giacino discloses a food flavor additive composition.

2. 1[a]: a) an isolated heme-containing protein

189. In my opinion, Giacino in view of Brown renders obvious a food flavor additive composition comprising an isolated heme-containing protein.

190. Giacino explains that “[t]here is considerable demand for meat-flavored products in which the actual meat such as beef, pork, chicken, turkey, duck and the like is not needed or is actually undesirable.” EX1015(Giacino), 1:26-31. Giacino provides a number of reasons and examples as to when the use of real meat would be undesirable, including: cost; convenience (*e.g.*, preparing foods such as sauces, bouillons, broths, etc. that require a meaty flavor but cannot have actual pieces of meat in them); and weight and space/storage considerations where the inclusion of meat might cause spoilage. *Id.*, 1:31-48. Giacino further explains that “[p]rior attempts at preparing artificial meat flavor compositions...have not been entirely satisfactory, in **that true flavor is generally not achieved** in the case of spice formulations.” *Id.*, 1:51-59.

191. Giacino also teaches that its disclosed compositions are not fixed in stone, and instead “[v]arious other materials and ingredients can be incorporated into the compositions to provide a variety of flavor characteristics built upon the basic flavor of the taurine-thiamine reaction product.” *Id.*, 2:38-41. Hence, Giacino explicitly considers adding additional materials and ingredients to help develop the

meaty flavor of its compositions. In view of the foregoing and Giacino's goal of providing meaty flavoring compositions that achieve "true flavor reproduction" of meat (*id.*, 1:48-51), a POSITA would have understood that modifications to Giacino's compositions that would better mimic the true flavor of meat would be desirable and welcome by Giacino.

192. Brown teaches that "reactions that generate odorants released during the cooking of meat can be catalyzed by iron, in particular heme iron of myoglobin." EX1012(Brown), [00363]. Brown explains that this same "characteristic flavor and fragrance components [of meat] are produced during the cooking process by chemical reactions catalyzed by the heme iron in leghemoglobin" (*id.*), which is a heme-containing protein found in the root nodules of legumes. Taking advantage of this effect, Brown teaches that "leghemoglobin solution" may be added to a consumable to better replicate meat. *Id.*, [00375]. Notably, Brown discloses adding leghemoglobin to a composition that already comprises well-known flavor precursors (including reducing sugars, amino acids, and proteins) because "the presence of leghemoglobin contributes favorably to [the] aroma of" the composition. *Id.*, [00364].

193. Brown teaches a POSITA how heating a composition containing leghemoglobin and flavor precursors (*e.g.*, pea flour, oil, and glucose) produces volatile compounds having "the aroma of cooked meat" that are "consistent[ly]

differen[t]” than the volatiles produced by the same composition *lacking* leghemoglobin. *Id.* Brown further describes how gas chromatography mass spectrometry (GC-MS) revealed that the composition containing leghemoglobin produced a number of volatile compounds, including 2-octanone, 2-methyl furan, and “many other ... compounds,” that were “found exclusively or more abundantly” in the leghemoglobin-containing composition versus the composition without leghemoglobin. *Id.* Brown teaches that these compounds are relevant because they “are often associated with the aroma of cooked meat.” *Id.*

194. Brown’s soy leghemoglobin is an “isolated” (to the extent that term has patentable weight) heme-containing protein because Brown teaches processes for extracting the soy leghemoglobin from soy root nodules or obtained using recombinant expression systems.

Sources of leghemoglobin

In some embodiments the present invention provides methods for obtaining leghemoglobin from plants. **Leghemoglobin can be obtained from a variety of plants.** Various legumes species and their varieties, for example, **Soybean**, Fava bean.... **Figure 3 shows 100 mls of leghemoglobin solution isolated from 30 grams of pea root nodules.** Leghemoglobins from different species are homologs and have similar color properties (Figure 4)....**We purified leghemoglobin from fava bean (green curve) and Soybean (red curve) root nodules** using the protocol described elsewhere in the specification.

Id., [00376].

We purified soybean leghemoglobin from soybean root-nodules using here described protocol. Purified equine myoglobin was purchased from SigmaAldrich.

Id., [00377].

Leghemoglobin can be purified from legume root nodules, such as the root nodules of peas or **soybeans** (Figure 1 shows pea root nodules, **Figure 2 shows Leghemoglobin isolated from same**)....In some instances this was the **last purification step, while in other instances leghemoglobin was further purified using anion exchange chromatography** (FFQ GE Healthcare), which was sometimes followed by size-exclusion chromatography (Sephacryl S-100, GE Healthcare)....Leghemoglobin content at different purification steps was determined by determining the fraction of leghemoglobin band on SDS-PAGE gel in a respective sample using ImageDoc analysis software (BioRad). **Purity (partial abundance) of leghemoglobin at respective steps in the purification steps was:** lysate: **32.7% (lane 1)**, 60/90 % (wt/v) ammonium sulfate fractionation **78% (lane 2)**, anion-exchange chromatography ~ **83% (lane 3)**, and size-exclusion chromatography to ~ **95% (lane 4)**.

Id., [00380].

Leghemoglobin can also be produced by genetically engineering a bacterium or fungus to produce it. One illustrative example is shown in Figure 8. Figure 8 shows stained SDS-PAGE gel analysis of (A) **soybean leghemoglobin expressed and purified using recombinant**

protein technology and (B) soybean leghemoglobin purified from soybean root nodules.

Id., [00381].

195. In view of Brown’s teachings, a POSITA would have recognized that adding an isolated heme-containing protein, such as soy leghemoglobin, to a flavoring composition that includes well-known flavor precursors (*e.g.*, amino acids, proteins, oil, and/or reducing sugars) would provide an improved meaty aroma and flavor. This would have motivated a POSITA to add leghemoglobin to Giacino’s flavoring compositions to enhance those compositions’ meaty flavor and aroma and achieve the enhanced volatile profile touted by Brown. This would also further Giacino’s goal of providing the “true flavor” of meat. As I mention above, Giacino also expressly invites additional ingredients to be added to its compositions to adjust their flavor. EX1015(Giacino), 2:38-41.

196. A POSITA would have had a reasonable expectation of success because Brown specifically teaches adding the leghemoglobin to a preparation comprising a reducing sugar (*e.g.*, glucose) and sulfur compounds (*e.g.*, cystine, thiamine, and methionine found in pea flour¹⁰) to catalyze chemical reactions that provide the aroma of cooked meat. Giacino’s meaty flavoring compositions *also* include reducing sugars (glucose, ribose, xylose, etc.) and sulfur compounds (*e.g.*, cysteine,

¹⁰ *See supra* Section XI.A.4.

thiamine, or “other sulfur containing amino acids”). EX1015(Giacino), 3:43-45, 3:68-73, 4:21-24, 5:75-6:7. Hence, a POSITA would reasonably expect the same or similar catalyzation to take place when adding leghemoglobin to Giacino’s compositions. Moreover, nothing more than ordinary skill would have been required to isolate soy leghemoglobin (which Brown describes in detail, *e.g.*, *see supra* Section XI.A.2), and mix it in with the composition prior to heating.

197. Accordingly, the combination of Giacino and Brown renders obvious a food flavor additive composition comprising an isolated heme-containing protein.

3. 1[b]: b) a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, maltodextrin, and galactose, and mixtures of two or more thereof; and

1[c]: c) a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof;

198. In my opinion, Giacino discloses a food flavor additive composition that comprises “a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose, maltodextrin, and galactose, and mixtures of two or more thereof;” and “a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof.”

199. For example, Giacino teaches that a “saccharide material such as a mono saccharide [sic],” including “[r]ibose, sucrose [sic], dextrose, and xylose,” is added to Giacino’s flavoring compositions to provide “somewhat more intense

flavor characteristics.” EX1015(Giacino), 6:1-7. Giacino also teaches that its flavoring compositions include thiamine, cysteine, and/or cystine. *See, e.g.*, 2:5-8 (thiamine), 2:14-16 (same), 3:43-46 (cysteine), 3:75-4:3 (same), 4:21-23 (cystine), 5:1-10 (thiamine and cysteine).

200. Hence, Giacino discloses limitations 1[b] and 1[c].

4. 1[d]: wherein the flavor additive composition contains no animal products; and

201. Giacino’s artificial meaty flavoring compositions do not contain animal products. A POSITA would understand that Giacino teaches, as one example, a meaty flavoring composition that includes thiamine, taurine, vegetable protein hydrolysate, cysteine, and a monosaccharide, such as ribose. *See* EX1015(Giacino), 2:5-8 (“[T]he invention, in its broad aspect involves heating a mix composition comprising **taurine and thiamine** at an elevated temperature for a period of time whereby a meaty flavor is developed.”), 2:53-60 (“[D]evelopment of a variety of flavors is achieved in separate compositions by providing in the pre-mix ... a quantity of a source of one or more amino acids such as ... **hydrolysates**”), 3:23-25 (“**Vegetable hydrolysates**, such as those obtained from corn, wheat, yeast and the like are preferred.”), 3:43-46 (“There may be additionally present in the pre-mix composition small quantities of a sulfur containing amino acid such as **cysteine**”), 6:1-4 (“[T]here may be added to the pre-mix a quantity of a saccharide

material such as **[r]ibose**"); *see also id.*, 5:1-10 (disclosing the use of **thiamine** and **taurine** and optionally **hydrolyzed protein** and **cysteine**).

202. Giacino expressly discloses that for the hydrolyzed protein ingredient, non-animal, plant-based hydrolysates are preferred. *See id.*, 3:23-25 (“**Vegetable hydrolysates**, such as those obtained from corn, wheat, yeast and the like are preferred.”). With respect to thiamine, Giacino expressly teaches that it is sourced from yeast. *Id.*, 5:68-70.

203. As to cysteine, ribose, and taurine, Giacino does not disclose that these compounds are directly sourced from previously live animals. Hence, a POSITA would understand that Giacino allows for the use of cysteine, ribose, and taurine from non-animal sources.

204. Nor do these compounds have to be obtained from a previously live animal. A POSITA would have understood that it would have been obvious to use cysteine, ribose, and taurine that were obtained from non-animal sources. For example, it was well-known in the art that cysteine could be obtained from non-animal sources, including synthetic cysteine made in recombinant microorganisms. *See generally* EX1085(Wacker); EX1078(Reutter-Maier); EX1079(Leinfelder). Similarly, it was well-known that taurine is derived synthetically from, for example, ethylene oxide or monoethanolamine. *See generally* EX1081(Hu); *see also id.*, 1:5-29 (“Many chemical synthetic methods have been known in the prior arts for the

preparation of taurine and related derivatives. The following two methods have been used in industry to manufacture over 50,000 tons of taurine per year, starting from ethylene oxide (the EO process) and monoethanolamine (the MEA process).”). Ribose too is derived synthetically from, for example, xylose. *See generally* EX1080(Feniou); *see also id.*, 1:46-49 (“D-ribose can be synthesized from D-xylose, a monosaccharide which is widely distributed in the vegetable kingdom in the form of xylans.”).¹¹

205. A POSITA would have been motivated to use non-animal sourced cysteine, taurine, and ribose to keep the meaty flavoring composition (and thus the food product to which it is ultimately added) free of animal products for those individuals that refrain from consuming animal products in their diet for health, environmental, ethical, or religious reasons. Using non-animal sourced cysteine, taurine, and ribose is also consistent with Giacino’s teachings that “[t]here is considerable demand for meat-flavored products in which the actual meat such as beef, pork, chicken, turkey, duck and the like ... is actually undesirable.” EX1015(Giacino), 1:27-30.

206. Finally, adding leghemoglobin to Giacino’s meaty flavoring composition would also still satisfy this claim limitation because leghemoglobin is

¹¹ A POSITA would understand that “D-ribose” refers to the D configuration of ribose, which is its naturally occurring form.

an oxygen-carrying phytohemoglobin found in the nitrogen-fixing root nodules of leguminous plants, such as soy. *See* EX1073(Santana), 1259 (discussing how leghemoglobin present in the root nodules of leguminous plants facilitates oxygen diffusion to bacteroids responsible for expressing nitrogenase). Indeed, Brown describes (at length) methods for obtaining leghemoglobin from plants and genetically modified yeast or bacteria engineered to produce such non-animal proteins. *See* Brown, [00376]-[00383].

207. Hence, Giacino's meaty flavoring composition, as modified by Brown, contains no animal products.

5. 1[e]: wherein cooking the food flavor additive composition results in the production of at least two volatile compounds which have a meat-associated aroma.

208. Giacino and Brown renders this limitation obvious. A POSITA would have understood that heating Giacino's meaty flavoring composition produces at least two volatile compounds having a meat-associated aroma.

209. Giacino discloses that "[t]he meat flavor of the compositions of the present invention is developed by **heating** the pre-mix compositions at an elevated temperature for a period of time." EX1015(Giacino), 6:15-17. The heating step causes a "reaction" that produces the meaty flavor. *Id.*, 6:20-23, 2:5-8. A POSITA would understand that "flavor" involves the body's physiological response to ***aroma***

and taste. *See* EX1005(McGorin), ¶27 (explaining that flavor and aroma are highly linked).

210. That heating Giacino's flavoring composition produces a meaty flavor (and hence meaty aroma) is not surprising because Giacino's flavoring composition includes well-known flavor precursors, including thiamine, cysteine, ribose, and protein hydrolysate. A POSITA would understand that heating a reaction mixture that includes amino acids and sulfur compounds, such as thiamine and cysteine, in the presence of reducing sugars, such as ribose, would induce different reactions including, among other things, a Maillard reaction. *See supra* VII.D; EX1005(McGorin), Sections V.B, V.D; EX1017(Mottram), 417 ("The Maillard reaction, which occurs between amino compounds and reducing sugars, is one of the most important routes to flavour compounds in cooked foods, including meat. This reaction is complex and provides a large number of compounds which contribute to flavour."); EX1026(Dwivedi), 501 ("The use of thiamine as one of the ingredients used in the preparation of synthetic meat flavors is not surprising. Thiamine, like cystine and cysteine, on heating produces a number of sulfur compounds that contribute significantly in meat like synthetic flavor formulations."); EX1024(MacLeod), 399-407 (noting that "a large number of 'reaction product' patents [were] granted," in which meat flavor precursors, such as cysteine, thiamine, methionine, glucose, ribose, and vegetable protein hydrolysates, among others, react

with each other to produce meaty aromas and flavors). As explained below, a POSITA would have understood that these reactions, including the Maillard reaction, would produce at least two volatile compounds having a meat-associated aroma.

211. For example, it was well-known in the art that heating ribose and cysteine induces reactions that produce a number of volatile compounds that have been associated with a meaty aroma. *Compare* EX1024(MacLeod), 385, Table 15 (identifying a list of volatiles produced by reacting cysteine and ribose, including carbon disulfide, hydrogen sulfide, methanethiol, furfural, pyrrole, 2,5-dimethylpyrazine, 2-methylthiazole, among many others), *with id.*, 313-56 & Table 1 (identifying volatile compounds “of Natural Beef Aroma,” including the same carbon disulfide, hydrogen sulfide, methanethiol, furfural, pyrrole, 2,5-dimethylpyrazine, 2-methylthiazole compounds, as well as many others found in Table 15). Heating thiamine was also known to cause degradation of the thiamine compound and the production of many volatiles associated with a meaty aroma. *See id.*, 394 (identifying a list of thiamine degradation compounds, including many associated with a “cooked beef aroma,” such as 2-methylthiophen, 2-methylfuran, hydrogen sulfide, formic acid, and others).

212. A POSITA would understand that adding leghemoglobin to Giacino’s flavoring compositions would only further contribute to the meaty aroma and

volatiles produced since Brown teaches that reacting leghemoglobin in the presence of vegetable proteins/amino acids (*e.g.*, via pea flour) and glucose results in a “cooked meat” aroma. Notwithstanding the beneficial contributions of the heme-containing protein, however, as I explained above a POSITA would have understood that at the very least the reactions between the sulfur compounds (thiamine, cysteine) and reducing sugars (ribose) present in Giacino’s compositions would have produced at least two volatile compounds having a meaty aroma. *See supra* ¶¶209-11.

213. Hence, Giacino and Brown render obvious limitation 1[e].

E. Claims 2 and 15

214. In my opinion, Giacino and Brown render obvious the limitation “[t]he food flavor additive composition of claim [1/10], wherein the heme-containing protein is selected from the group consisting of a[n] androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, a **leghemoglobin**, an erythrocrurin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histaglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3.”

215. As discussed above, a POSITA would have added soy leghemoglobin to Giacino’s meaty flavoring compositions as taught by Brown. *See supra* Section

XII.D.2. Leghemoglobin is one of the elements identified in the group of heme-containing proteins for claims 2 and 15.

216. Hence, Giacino and Brown render obvious claims 2 and 15.

F. Claims 3 and 16

217. In my opinion, Giacino and Brown render obvious the limitation “[t]he food flavor additive composition of claim [1/10], wherein the heme-containing protein comprises amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.”

218. As I discussed above, a POSITA would have added soy leghemoglobin to Giacino’s meaty flavoring compositions as taught by Brown. *See supra* Section XII.D.2. The polypeptide set forth in SEQ ID NO 4 in the ’096 patent is for soy leghemoglobin (*Glycine max*). As I explain elsewhere in my declaration, Brown’s soy leghemoglobin has at least 80% sequence identity to SEQ ID NO 4 disclosed in the ’096 patent. *See supra* Section XI.C. Hence, Giacino and Brown render obvious claims 3 and 16.

G. Claims 4 and 24

219. In my opinion, Giacino discloses the limitation “[t]he food flavor additive composition of claim 1, wherein the food flavor additive composition is a powder or a liquid composition” (claim 4) and the limitation “[t]he food flavor

additive composition of claim 1, in the form of a soup, stew base, a bouillon powder, bouillon cube, flavor packets or seasoning packet” (claim 24).

220. Giacino discloses that its meaty flavoring compositions are a liquid. *See, e.g.*, EX1015(Giacino), 2:23-28 (“In practice, it is usually preferred to incorporate within the pre-mix composition a vehicle which includes materials such as **water, edible oils** or fats or the like to provide a medium for the reaction.”), 6:36-39 (“The preferred process of this invention relative to producing beef flavor compositions involves refluxing an **aqueous pre-mix**. It is most convenient to reflux the **aqueous mixture** for a period of from one to six hours.”), claim 12 (“A composition as defined in claim 11 wherein the heating is carried out at a temperature of from about 200° - 420° F. in an **aqueous or fat vehicle**.”).

221. Giacino also discloses that its meaty flavoring composition can be in the form of a powder since it discloses that the composition is spray dried. *Id.*, 9:70-10:2. That Giacino’s meaty flavoring composition may be a dry powder is also consistent with its teaching that the composition can be applied to dry foods such as snacks and chips. *See id.*, 7:15-26. A POSITA would understand that such a powder is a “bouillon powder” because it has a meaty flavor. *Id.*, 2:5-8. A POSITA would also understand that such a powder, when placed in a packet, is a “seasoning packet” and “flavoring packet.” It would have been obvious to place the powdered meaty flavoring composition into a packet for ease of use and to preserve freshness when

storing the flavoring composition. Doing so would have required no more than ordinary skill in the art.

222. Giacino also discloses that its meaty flavoring composition can be used to prepare a “bouillon mix.” *Id.*, 10:60-11:2. A POSITA would understand that the bouillon mix is a dry powder because all of the ingredients in the mixture are dry ingredients (*e.g.*, salt, celery powder, etc.) and Giacino teaches adding 40 parts water to it to make a bouillon. *Id.*, 11:3-6.

223. In view of the foregoing disclosures, Giacino and Brown render obvious claims 4 and 24.

H. **Claim 5**

224. In my opinion, Giacino and Brown render obvious the limitation “[t]he food flavor additive composition of claim 1, wherein the heme-containing protein is a plant, a yeast or filamentous fungi, or bacterial heme-containing protein.”

225. As discussed above, a POSITA would have been motivated to add soy leghemoglobin to Giacino’s meaty flavoring compositions. *See supra* Section XII.D.2. Soy leghemoglobin is a plant heme-containing protein.

I. **Claims 6 and 22**

226. In my opinion, Giacino discloses the limitation “[t]he food flavor additive composition of claim [1/10], further comprising one or more of an extract or hydrolysate selected from a **vegetable protein hydrolysate**, a soy protein

hydrolysate, a yeast extract, a yeast protein hydrolysate, and an algal protein hydrolysate[, and/or a globulin].” Giacino discloses that its meaty flavoring compositions include a “proteinaceous material,” such as “edible protein hydrolysate.” EX1015(Giacino), 3:3-5. Giacino further discloses that such edible protein hydrolysates are preferably vegetable protein hydrolysates. *See id.*, 3:18-25.

227. Hence, Giacino and Brown render obvious claims 6 and 22.

J. Claim 7

228. In my opinion, Giacino discloses the limitation “[t]he food flavor additive composition of claim 1, further comprising one or more of a compound selected from alanine, arginine, asparagine, aspartate, **glutamic acid**, glutamine, **glycine**, histidine, isoleucine, leucine, lysine, phenylalanine, proline, threonine, tryptophan, tyrosine, valine, maltodextrin, **thiamine**, IMP, GMP, lactic acid, and creatine.”

229. Giacino discloses that its meaty flavoring compositions include thiamine. *See, e.g.*, EX1015(Giacino), 2:5-8, 5:1-10. Giacino also discloses that the compositions may include glutamic acid and/or glycine. *See id.*, 4:18-21, 5:1-10. Giacino does not disclose that the glutamic acid and glycine are sourced from animals.

230. Hence, the proposed combinations render claim 7 obvious.

K. **Claims 8 and 17**

231. In my opinion, the combination of Giacino and Brown renders obvious the limitation “[t]he food flavor additive composition of claim [1/10], further comprising one or more of an oil selected from coconut oil, mango oil, **sunflower oil**, cottonseed oil, safflower oil, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, corn oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, and oil from bacteria or fungi.” Perret is analogous art to the ’096 patent because it too is directed to simulated meat flavoring compositions that provide a meaty aroma and flavor, but do not include meat. *See, e.g.*, EX1020(Perret), 1:10-12, 1:63-69, 2:1-38, 4:36-48.

232. Giacino discloses that its meaty flavoring compositions can include “edible oils” as a medium. EX1015(Giacino), 2:23-28, 5:22-25 (“vegetable fat”). While Giacino does not specify the type of edible oil that can be used, a POSITA would understand based on the teachings of Perret that safflower oil can be used in meat flavoring compositions. Safflower oil is derived from the safflower plant. Like Giacino, Perret discloses various meat flavoring compositions that include “edible fat,” including “vegetable fats,” such as “safflower oil.” EX1020(Perret), 4:6-11, 4:22-29. Perret teaches incorporating such fat leads to a “roast meat flavor and odor” that is “a very pleasing product.” *See id.*, 4:22-29. In view of Giacino’s teaching that edible oils serve as a medium for its meaty flavoring compositions, and Perret’s

teaching that using safflower oil leads to a “roast meat flavor and odor,” a POSITA would have been motivated to use safflower oil in Giacino’s meaty flavoring compositions. It would have also been obvious to try given the finite number of edible oils available.

233. A POSITA would have had a reasonable expectation of success given it would have required no more than routine skill in the art (*e.g.*, measuring, mixing) to add safflower oil to Giacino’s meaty flavoring compositions. Moreover, using safflower oil (as taught by Perret) would have been a simple substitution of the non-specific edible oil described in Giacino with safflower oil disclosed in Perret. This would have led to the predictable result of having meaty flavoring compositions in a medium of safflower oil.

234. Hence, Giacino, Brown, and Perret render claims 8 and 17 obvious.

L. Claims 9 and 22

235. In my opinion, Giacino discloses “[t]he food flavor additive composition of claim 1, further comprising one or more of albumin or a globulin” (claim 1), and “one or more of an extract or hydrolysate ... and/or a **globulin**” (claim 22).

236. Giacino discloses that its meaty flavoring compositions include “proteinaceous materials,” including, in particular, albumins and globulins. EX1015(Giacino), 3:3-10. Giacino elaborates by teaching that these proteins may

be sourced from meat, but “[v]egetable derived” versions are “preferred.” *Id.*, 3:1-14. Hence, a POSITA would understand that Giacino discloses using albumins and globulins (and other proteins) sourced from plants (*i.e.*, non-animal sources). Accordingly, Giacino’s teaching that albumins and globulins are added to the meaty flavoring compositions still satisfies the claims’ “no animal products”-requirement.

237. Moreover, Giacino and Brown together disclose these claims. Brown teaches using pea flour in a reaction with soy leghemoglobin and a reducing sugar (*e.g.*, glucose). EX1012(Brown), [00364]. A POSITA would have known that pea flour is an excellent source of albumins and globulins. *See, e.g.*, EX1067(Meng), 235 (“Like other legume seeds, pea seeds contain high amounts of protein (20–30%). Pea proteins mainly exist as **globulins** (65–80%) ...”); EX1083(Buffo), 293 (“Pea protein consists primarily of **globulins** (>80% of total protein) and a small fraction of **albumins**. The **globulins** are storage proteins located in the cotyledons, whereas **albumins** are cytoplasmic proteins consisting of many different subunits (Boulter, 1983; Mosse and Pernollet, 1983).”); EX1070(Karaca), 196 (“Proteins in pea seeds are composed of main **globulins** (65%–80%), **albumins**, and glutelins.”). In view of Giacino’s teaching that its meaty flavoring compositions preferably include a “vegetable derived” protein source, including in particular albumins and globulins, a POSITA would have been motivated to add Brown’s pea flour to Giacino’s meaty flavoring compositions, which a POSITA would have known contains albumins and

globulins. Adding this material would further Giacino's goal of developing "a variety of flavors." EX1015(Giacino), 2:52-3:2. A POSITA would have had a reasonable expectation of success because nothing more than conventional practices (measuring, mixing, etc.) and ordinary skill is required to add the pea flour to Giacino's compositions.

238. For the foregoing reasons, Giacino and Brown render obvious claims 9 and 22.

M. Claim 10

239. In my opinion, the combination of Giacino and Brown render obvious claim 10.

1. 10[pre]: A food flavor additive composition prepared by a process of:

240. As discussed above, Giacino discloses a food flavor additive composition. *See supra* Section XII.D.1.

2. 10[a]: a) combining an isolated heme-containing protein;

241. As discussed above, the combination of Giacino and Brown render obvious a food flavor additive composition comprising an isolated heme-containing protein (*e.g.*, soy leghemoglobin). *See supra* Section XII.D.2.

3. **10[b]: a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose and galactose, and mixtures of two or more thereof; and**

10[c]: a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof, to form a heme flavor reaction mixture, and

242. As discussed above, Giacino discloses a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose and galactose and a compound selected from cysteine, cystine, thiamine, and methionine. *See supra* Section XII.D.3. The mixture of Brown's leghemoglobin and Giacino's cysteine, thiamine, ribose, among other compounds in Giacino's flavoring composition, is a "heme flavor reaction mixture."

4. **10[d]: b) heating the heme flavor reaction mixture to at least 150° C. for at least 1 minute to result in the food flavor additive composition;**

243. Giacino discloses "heating the heme flavor reaction mixture to at least 150° C. for at least 1 minute to result in the food flavor additive composition."

244. Giacino teaches that its flavoring compositions develop a "meat flavor" "by heating the pre-mix compositions at an elevated temperature for a period of time." EX1015(Giacino), 6:15-17. Giacino explains that the compositions are preferably heated to a temperature between 200° F (93° C) and 420° F (216° C) for between 15 seconds and 6 hours to induce the required reactions that produce the meaty flavor. *Id.*, 6:26-31. Giacino further explains that when heat exchangers are used, "the reaction mixture can quickly be brought to the reaction temperature and

then quickly cooled in a second exchanger to a lower temperature at which no further reaction will take place.” *Id.*, 6:48-52. Giacino teaches that when heat exchangers are used, temperatures between 250° F (121° C) and 400° F (204° C) and heating times between 15 seconds and 3 minutes are preferred. *Id.*, 6:68-71.

245. A POSITA would have understood based on Giacino’s disclosed temperature and timing ranges that, for example, a meaty flavoring composition would be heated to a temperature of 160° C using a heat exchanger (which is within Giacino’s disclosed preferred range of 250° F (121° C) and 400° F (204° C)) for 2 minutes (which is within Giacino’s disclosed preferred range of 15 seconds to 3 minutes). Hence, a POSITA would have understood that Giacino teaches heating its meaty flavoring compositions to at least 150° C for at least 1 minute.

246. Accordingly, Giacino discloses limitation 10[d].

5. 10[e]: wherein the food flavoring additive composition contains no animal products; and

247. As discussed above, Giacino’s meaty flavoring compositions modified to include soy leghemoglobin (as taught by Brown) do not contain any animal products. *See supra* Section XII.D.4.

6. 10[f]: wherein the heme flavor reaction mixture has a meaty flavor and/or meaty aroma during the heating of step b) and the food flavoring additive composition has a meaty flavor and/or meaty aroma after the heating of step b).

248. Giacino and Brown render these limitations obvious.

249. As I explained above for limitation 1[e], a POSITA would have understood that heating Giacino's modified meaty flavoring compositions, which include, *inter alia*, sulfur compounds (*e.g.*, thiamine and cysteine), reducing sugars (*e.g.*, ribose), and leghemoglobin, would induce different reactions including, a Maillard reaction, that would produce many different volatiles associated with a meaty aroma and flavor. *See supra* Section XII.D.5.

250. A POSITA would recognize that these volatiles are produced during the heating step. *See* EX1015(Giacino), 2:5-8. Moreover, a POSITA would understand that the volatiles that were produced during the heating step remain present after the heating step completes. For example, it is common knowledge that foods, such as a freshly cooked piece of meat, give off aromas after the cooking process completes.

251. Hence, Giacino and Brown render obvious these limitations.

N. **Claim 11**

252. In my opinion, Giacino and Brown render claim 11 obvious: "[t]he food flavor additive composition of claim 10, wherein the food flavoring additive composition further comprises a compound selected from the group consisting of 2-methyl-furan, bis(2-methyl-3-furyl)disulfide, 2-pentyl-furan, 3,3'-dithiobis-2-methyl-furan, **2,5-dimethyl-pyrazine**, 2-methyl-3-furanthiol, bis(2-methyl-4,5-dihydro-3-furyl) disulfide, dihydro-3-(2H)-thiophenone, 5-methyl-2-

thiophenecarboxaldehyde, 3-methyl-2-thiophenecarboxaldehyde, **2-methyl-thiazole**, dimethyl sulfide, decanal, 5-ethyl-2(3H)-furanone, dihydro-5-pentyl-2(3H)-furanone, 2-octanone, 3,5-octadien-2-one, p-Cresol, and hexanoic acid.”

253. As I discussed above, a POSITA would have understood that heating Giacino’s modified meaty flavoring compositions, which include, thiamine, cysteine, ribose, and soy leghemoglobin, would produce a number of volatile compounds having a meaty flavor and aroma. *See supra* Sections XII.D.5, XII.M.6. In particular, a POSITA would have recognized that at the very least when the cysteine and ribose compounds are heated in Giacino’s modified composition, a Maillard reaction would occur causing the production of at least, among other volatile compounds, 2,5-dimethylpyrazine and 2-methyl-thiazole, which are both recited in claim 11. *See, e.g.*, EX1024(MacLeod), 385, Table 15 (identifying 2-methyl-thiazole and 2,5-dimethylpyrazine as volatile compounds when cysteine and ribose react). A POSITA would have understood that these two compounds are known to be associated with a meaty aroma/flavor. *See, e.g., id.*, 344, Table 1 (identifying 2,5-dimethylpyrazine as contributing to “natural beef aroma”), 351 Table 1 cont. (identifying 2-methyl-thiazole as contributing to “natural beef aroma”); EX1026(Dwivedi), 492, Table 1 (2-methylthiazole), 493, Table 1 cont. (2,5-dimethylpyrazine).

254. Hence, Giacino and Brown render claim 11 obvious.

O. Claim 12

255. In my opinion, Giacino and Brown render claim 12 obvious: “[t]he food flavor additive composition of claim 11, wherein the compound is detectable in the headspace above the heme flavor reaction mixture during the heating of step b) or in the headspace above the food flavoring additive composition after the heating of step b).”¹²

256. As I discussed above, a POSITA would have understood that heating Giacino’s modified meaty flavoring composition would release a variety of volatile compounds associated with a meaty flavor and/or aroma. *See supra* Sections XII.D.5, XII.M.6, XII.N. A POSITA would have understood that these volatiles are released in the volume of air above the composition (*e.g.*, headspace), and therefore would be detectable during and after the heating process.

257. Hence, a POSITA would understand that Giacino and Brown render claim 12 obvious.

P. Claim 14

258. In my opinion, Giacino and Brown render obvious the limitation “[t]he food flavor additive composition of claim 10, wherein the heme-containing protein

¹² A POSITA would understand that “headspace” refers to “the volume of vapor or gas above a sample.” *See* EX1072(Green), 229.

is present in an amount between about 0.01% and about 5% by weight in the heme flavor reaction mixture.”

259. As I explained above, a POSITA would have modified Giacino’s meaty flavoring composition by adding leghemoglobin as taught by Brown. *See supra* Section XII.D.2. A POSITA would have been informed on the amount of such leghemoglobin to add to Giacino’s compositions based on Brown’s express teaching that its meat replica compositions “contain[] between 0.01% and 5% by weight of leghemoglobin.” EX1012(Brown), [00354]; *see also id.*, [00367] (disclosing various percentages between 0.01% and 5%). In view of this teaching, a POSITA adding leghemoglobin to Giacino’s meaty flavoring compositions would have added an amount expressly taught by Brown, namely, between 0.01% and 5% by weight of the meaty flavoring composition. A POSITA would have had a reasonable expectation of success because Giacino teaches that the amounts of the ingredients in its composition can vary widely depending on the desired characteristics of the composition, and, hence, the proportion of other existing ingredients would have been reduced to make room for the 0.01% to 5% by weight leghemoglobin that is added. *See, e.g.*, EX1015(Giacino), 5:1-10 (0.1% to 15% by weight thiamine, 0.1% to 25% by weight taurine, 0% to 40% by weight hydrolyzed protein, 0 to 5% by weight cysteine), 5:22-31 (disclosing the presence of a “vehicle,” such as water or fat, at amounts varying from 10% to 95% by weight); 8:6-11 (teaching that the

amount of fat vehicle may be reduced to accommodate additional taurine added); 2:72-3:2 (“The actual amounts employed will generally vary depending upon the type of flavor desired.”).

260. Hence, Giacino and Brown render obvious claim 14.

Q. Claim 18

261. The combination of Giacino, Brown, and MacLeod renders claim 18 obvious: “The food flavor additive composition of claim 10, further comprising an ingredient selected from an emulsifier and a gelling agent.”

262. Giacino discloses that “[t]he pre-mix [composition] can also contain other ingredients normally used in the art ... such as **gum arabic**” to “stabilize the compositions.” EX1015(Giacino), 5:40-44, 9:21-27. A POSITA would have understood that gum arabic is well-known in the art as a plant-based emulsifier. *See* EX1074(dos Santos), 233 (“Arabic gum is also known as Acacia gum and is obtained from the exudates of Acacia trees.... Arabic gum has wide industrial uses as a stabilizer, thickening agent, and **emulsifier**, mainly in the food industry.”); EX1122(Saha), 590 (“Gum arabic (Acacia gum) is widely used in the food industry mainly to impart desirable qualities because of its influence over viscosity, body and texture. Mainly it is used as an **emulsifier**”). Hence, Giacino satisfies claim 18.

263. Additionally, the combination of Giacino, Brown, and MacLeod render claim 18 obvious. MacLeod discloses that artificial meat flavoring compositions

commonly include “agar, carageenan, cellulose, carboxymethylcellulose, gum arabic, gum tragacanth, gelatin, **pectin, and starch.**” EX1024(MacLeod), 414. Pectin and starch are well-known in the art as gelling agents and thickeners that are derived from non-animal sources (*e.g.*, apples, apricots, citrus peels, wheat, potatoes, corn, etc.). EX1071(Flutto), 4442, 4449 (pectin is derived from various fruits); EX1074(dos Santos), 231 (“Pectin mainly finds applications as **gelling** and thickening **agent** in food industry”); EX1122(Saha), 595 (“The frequently used gelling agents include modified **starch**, agar, carrageenans, [and] **pectins**”), Table 2 (listing pectin and modified starch as gelling agents).

264. A POSITA would have understood that adding pectin or starch to Giacino’s meaty flavoring composition would thicken and/or promote gelling of the mixture. Given Giacino’s teaching that its beef-flavored compositions can serve as a base for gravies and sauces (EX1015(Giacino), 7:15-22), a POSITA would have been motivated to thicken the composition. Similarly, given Giacino’s teaching that its beef-flavored compositions can be added to “synthetic meat fibres” (*id.*, 7:22-26), a POSITA would have been motivated to promote gelling to improve its texture as part of the “synthetic meat fibre” (*i.e.*, meat substitute). Moreover, Giacino invites such a modification because it teaches that many different “food additives” can be added to the meaty flavoring compositions including “carriers,” “thickeners,” and even starches (*e.g.*, cornstarch). *Id.*, 9:5-19, 11:13. A POSITA would have known

to do so by adding pectin or starch (as taught by MacLeod), which are known gelling agents and thickeners.

265. Separately, Brown teaches the use of transglutaminase in its compositions as a gelling agent because the transglutaminase stabilizes the emulsion present in the composition “into a gel” to improve its texture. *See* EX1012(Brown), [00319], [00322], [00400], [00402], Fig. 11. Transglutaminase is known as a gelling agent. *See* EX1131(Nio), Abstract (“Transglutaminase catalyzes the formation of ϵ -(γ -glutamyl)lysyl cross-links within and between protein molecules.... This paper presents unambiguous evidence that α_{S1} -casein solution is **gelled** by the formation of ϵ -(γ -glutamyl)lysyl cross-links.”); EX1130(Kang), Abstract (“**Gelation** of glycinins as catalyzed by transglutaminase was investigated.”). A POSITA would find this teaching relevant to certain applications of Giacino’s meaty flavoring composition expressly considered by Giacino including “synthetic meat fibres.” EX1015(Giacino), 7:22-26.

266. In view of these teachings, a POSITA would have been motivated to add transglutaminase, a gelling agent, to Giacino’s meaty flavoring composition to stabilize the emulsion of vegetable fat and proteins therein into a gel to improve its texture for “synthetic meat fibre” (*i.e.*, meat substitute) applications. *See* EX1015(Giacino), 3:3-25 (compositions include “proteinaceous materials” such as protein hydrolysates), 5:22-31 (compositions include “vegetable fat”). A POSITA

would have had a reasonable expectation of success because only conventional techniques (measuring, mixing) would have been needed to add transglutaminase to the meaty flavoring compositions.

267. Hence, Giacino, Brown, and MacLeod render claim 18 obvious.

R. Claim 19

268. The combination of Giacino, Brown, and MacLeod renders claim 19 obvious: “The food flavor additive composition of claim 10, the process further comprising adding an emulsifier and a gelling agent to the heme flavor reaction mixture prior to the heating of step b).”

269. As I discussed above for claim 18, Giacino’s compositions include gum arabic (an emulsifier), and based on Brown’s and MacLeod’s teachings, a POSITA would have added a gelling agent (*e.g.*, pectin/starch or transglutaminase) to the compositions. *See supra* Section XII.Q. As I explain below, these components would have been added *before* heating the composition according to step b).

270. Giacino expressly discloses that “[v]arious other materials and ingredients can be incorporated into the compositions **At any time**, that is, ***before*** ... **heat treatment**.” EX1015(Giacino), 2:38-43. A POSITA would understand that with respect to gelling agents, such as starch and pectin, heat activates the desired gelling/thickening properties of these compounds. *See, e.g.*, EX1134(Lund), 249 (“Starch granules are insoluble in cold water but swell when heated in an aqueous

medium. Initially, the swelling is reversible and the optical properties of the granule are retained (e.g., birefringence). But when a certain temperature is reached, the swelling becomes irreversible and the structure of the granule is altered significantly. The process is called ‘gelatinization’ and the temperature at which gelatinization occurs is called the ‘gelatinization temperature.’”); EX1136(Whistler), 114 (identifying gelatinization temperatures of various starches, which are all well above room temperature and would require heating), 124 (“A special property of pectin is its ability to produce strong gels. If a *hot water* dispersion of 0.3-0.4% pectin is cooled to room temperature [and] pH is adjusted to 2.0-3.5 and sucrose is present at a concentration of 60-65%, a gel forms on cooling.”).

271. With respect to the emulsifier (*e.g.*, gum arabic), its presence in the mixture during the heating step is beneficial because the heat increases the fluidity of the mixture which would assist the emulsifier in creating an emulsion of the proteins and fats present in the composition. Similarly, heating the composition containing these compounds (*e.g.*, starch or pectin and gum arabic) helps disperse the compounds within the composition and also promotes hydration of the gelling agents. Furthermore, it would have been common sense to add these compounds (*e.g.*, starch or pectin and gum arabic) before the heating step at the same time all of the other compounds in Giacino’s composition are combined, including taurine, thiamine, cysteine, ribose, etc. Otherwise adding one or more of these compounds

after the heating step would only necessitate an additional mixing step, which would unnecessarily complicate the process. For at least these reasons, a POSITA would add the gelling agent and emulsifier before heating the composition.

272. Hence, the combination of Giacino, Brown, and MacLeod renders obvious claim 19.

S. Claims 20, 21

273. In my opinion, Giacino discloses the limitation “[t]he food flavor additive composition of claim 10, wherein the heme flavor reaction mixture is an aqueous solution” (claim 20), and “[t]he food flavor additive composition of claim 10, wherein the heme flavor reaction mixture is an oil-based mixture” (claim 21).

274. Giacino teaches that its meaty flavoring compositions may be an aqueous solution. EX1015(Giacino), 2:23-28 (“[I]t is usually preferred to incorporate ... a vehicle which includes materials such as **water**, edible oils or fats or the like to provide a medium for the reaction ...”), 5:22-30 (“It has been found, in preparing the reaction products of this invention, that the ingredients are desirably heated in a vehicle such as **water**, a triglyceride fat, natural fat, vegetable fat or the like.... The vehicle may constitute as much as 95 percent by weight or more and as little as 10 percent by weight or less of the total weight of the pre-mix to be reacted.”), 6:36-39 (“The preferred process of this invention relative to producing beef flavor compositions involves refluxing an **aqueous pre-mix**. It is most

convenient to reflux the **aqueous mixture** for a period of from one to six hours.”), claim 12 (“[T]he heating is carried out at a temperature of from about 200° - 420° F. in an **aqueous** or fat vehicle.”).

275. Giacino also teaches that in other embodiments the meaty flavoring compositions may be an oil-based mixture. *Id.*, 2:23-28 (“[I]t is usually preferred to incorporate ... a vehicle which includes materials such as water, *edible oils or fats or* the like to provide a medium for the reaction.”), 5:22-30 (“It has been found, in preparing the reaction products of this invention, that the ingredients are desirably heated in a vehicle such as water, a *triglyceride fat, natural fat, vegetable fat* or the like.... The vehicle may constitute as much as 95 percent by weight or more and as little as 10 percent by weight or less of the total weight of the pre-mix to be reacted.”), 5:38-39 (“[The fats/oils] can be in their natural form or they can be hydrogenated.”), claim 12 (“[T]he heating is carried out at a temperature of from about 200° - 420° F. in an aqueous or **fat vehicle**.”).

276. Hence, Giacino and Brown render claims 20 and 21 obvious.

T. **Claim 23**

277. In my opinion, Giacino and Brown render obvious “[a] process for imparting a meaty flavor and/or meaty aroma to a consumable food product, comprising: adding to the consumable food product a food flavor additive

composition of claim 1; and heating the consumable food product after the adding step.”

278. As discussed above, Giacino discloses various meaty flavoring compositions (*e.g.*, food flavor additive compositions) that satisfy the limitations of claim 1. *See supra* Section XII.D. Giacino explains that these compositions impart “meaty flavor characteristics such as beef, pork and poultry flavor” to the consumable food products to which they are added. *See, e.g.*, EX1015(Giacino), 1:19-25, 1:65-68 (The compositions “can be used per se in a wide range of food stuffs, either as the dominant flavoring agent or as an aid in improving and enhancing existing flavor.”), 7:15-26 (“The flavor compositions of this invention can be used to flavor various foods, liquid or dry.... For example, they can be incorporated into gravies, sauces, soups, dressings, salads, aspics, purees and other liquid preparations [T]hey can be admixed with carrier materials or with other flavoring ingredients or foodstuffs for incorporation into finished products, illustrative of which are the dry foods such as snacks, chips, synthetic meat fibres and the like.”).

279. Giacino also discloses that the consumable food product to which the meaty flavoring compositions are added may be cooked/heated. *See id.*, 6:71-7:2 (“Where the flavor composition of this invention is added to a food which is to be subsequently heated or cooked”). Moreover, a POSITA would have understood that at least with respect to some of the consumable food products to which Giacino’s

compositions are added, such as soups, gravies, and synthetic meat fibres, the consumable food product would be heated after adding the meaty flavoring composition.

280. Hence, Giacino and Brown render obvious claim 23.

XIII. GROUNDS 3A, 3B, 3C, 3D: GIACINO, CONRAD, CRANE, PROULX, PERRET, MACLEOD

281. As I explain below, the combination of Giacino, Conrad, and Crane renders obvious claims 1-2, 4-7, 9-12, 14-15, and 20-24 (Ground 3A). The combination of Giacino, Conrad, Crane, and Proulx renders obvious claims 3 and 16 (Ground 3B). The combination of Giacino, Conrad, Crane, and Perret renders obvious claims 8 and 17 (Ground 3C). The combination of Giacino, Conrad, Crane, and MacLeod renders obvious claims 18-19 (Ground 3D).

A. Giacino, Conrad, and Crane Are Analogous Art

282. Giacino, Conrad, and Crane are analogous art to the '096 patent. For example, a POSITA would have understood that these references are in the same field of endeavor as the claimed invention. Like the '096 patent, Giacino discloses various meaty flavoring compositions that are added to other consumable food products. *See, e.g.*, EX1015(Giacino), 1:19-25, 1:65-68, 5:1-10, 7:15-26.

283. Similarly, Conrad relates to “meat replacement products, a process for the preparation of meat replacement products, as well as meat products containing such meat replacement products.” EX1013(Conrad), 1:11-14. In particular, Conrad

teaches that adding isolated hemoglobin (which is a heme-containing protein) “gives a desired taste improvement as it improves the meat flavour of the final product.” *Id.*, 4:14-16.

284. Crane teaches methods for manufacturing diverse kinds of iron-containing heme proteins, such as hemoglobin, myoglobin, and leghemoglobin, using recombinant expression systems. *See, e.g.*, EX1014(Crane), Abstract, [0021], [0060]-[0062]. Some of these heme proteins (*e.g.*, hemoglobin and myoglobin) would otherwise have to be obtained physically from previously live animals. Crane’s expression systems allow for the creation of such heme-containing proteins, which Conrad teaches enhances flavors, without having to resort to conventional animal husbandry and slaughter or costly and labor-intensive extraction methods.

285. Giacino and Conrad are also each reasonably pertinent to the problem with which the ’096 patent applicant was concerned—generally, the failure of existing food flavor additive compositions and meat substitutes containing such compositions to replicate the flavors and aromas of conventionally sourced meat. *See, e.g.*, EX1001, 1:46-62. Giacino also recognizes that prior art meaty flavoring compositions lacked the “true flavor” of meat, and thus strives to create flavoring compositions that accurately mimic the flavor and aroma of meat. *See* EX1015(Giacino), 1:47-59. Conrad too describes methods for improving the meat

flavor of its compositions, in particular, by adding hemoglobin. EX1013(Conrad), 4:14-16.

286. Crane's teachings are also pertinent to the problems faced by the '096 patent, which included creating meaty flavoring compositions that had the flavor and aroma of cooked meat without having to use conventionally sourced meat, which relies on conventional animal husbandry and slaughter practices and has substantial costs and labor associated with it. To that end, Crane teaches the use of recombinant expression systems that use recombinant yeast, bacteria, fungi, and other organisms to express heme-containing proteins, such as hemoglobin, myoglobin, and leghemoglobin. *See, e.g.*, EX1014(Crane), Abstract, [0021], [0060]-[0062].

287. For the foregoing reasons, Giacino, Conrad, and Crane are analogous art to the '096 patent.

B. A POSITA Would Have Been Motivated to Combine Giacino, Conrad, and Crane

288. A POSITA would have been motivated to combine Giacino, Conrad, and Crane to achieve the subject matter of the challenged claims.

289. Generally, a skilled artisan tasked with preparing artificial meat-flavored additive compositions would have been motivated to mimic as closely as possible the attributes of conventionally sourced meat, including flavor, aroma, and beneficial nutritional aspects, so as to encourage consumption by consumers who ordinarily enjoy consuming conventionally sourced meat. As described below, a

POSITA would have recognized that including heme-containing proteins, such as hemoglobin or leghemoglobin, in a meat-flavored composition would achieve these goals.

290. Turning to the first of these factors, flavor and aroma, a POSITA would have been motivated to mimic the natural flavor and aroma of meat in an artificial meat-flavored additive composition in order to increase the consumer's perception that the consumer is eating a familiar meat product, while minimizing the undesirable environmental and other ramifications of conventional animal husbandry practices. As a POSITA would have recognized, one characteristic of conventionally obtained meat is that, when cooked, the meat produces a meaty aroma resulting from a complex profile of volatile chemical compounds created during the process of heating precursor compounds within the meat. *See supra* Section VII.D; EX1005(McGorin), Sections V.B, V.D. Thus, a POSITA would have been motivated to prepare a meat-flavored additive composition that provides a cooked meat flavor and aroma when added to the food products so as to mimic the flavors and aromas associated with cooked meat.

291. Giacino teaches that there is a market for meat-flavored products that do not contain actual meat. *See* EX1015(Giacino), 1:26-31. Giacino asserts that prior art artificial meat flavor compositions, however, are not satisfactory because they lack the "true flavor" of meat. *Id.*, 1:51-59. Hence, a POSITA would have

understood that Giacino strives to create meaty flavoring compositions that fill this void and provide the closest approximation to the flavor and aroma of real meat as possible.

292. Moreover, a POSITA would have recognized that Giacino was ripe for modifications that would enhance the meaty flavors and aromas of its flavoring compositions. Indeed, Giacino expressly discloses that “[v]arious other materials and ingredients can be incorporated into the compositions to provide a variety of flavor characteristics” that “buil[d] upon the basic flavor” of its flavoring compositions. *Id.*, 2:38-41.

293. Conrad expressly teaches that “[t]he addition of blood/**hemoglobin** further gives a desired taste improvement as it improves the **meat flavour** of the final product.” EX1013(Conrad), 4:14-16. Conrad teaches that hemoglobin can be isolated from blood before being added to the product. *Id.*, 4:7-9 (“[P]referably the hemoglobin part [is] separated off from blood, the protein content of which is about 90% by weight”).

294. In view of Giacino’s and Conrad’s teachings, a POSITA would have been motivated to add hemoglobin, or another functionally equivalent heme-containing protein (*e.g.*, leghemoglobin), to Giacino’s meaty flavoring compositions to “improve the meat flavour of the final product” as taught by Conrad. Consistent with various well-known motivations to reduce or avoid the consumption of

conventionally sourced meat (*e.g.*, environmental, personal/religious, health, animal welfare, etc., *see supra* Section VII.A), a POSITA also would have been motivated to substitute Conrad's "hemoglobin ... of whole blood from slaughtered animals" with recombinant hemoglobins, including either native animal hemoglobins (*e.g.*, bovine hemoglobin) or non-animal hemoglobins (*e.g.*, plant/soy leghemoglobin), which a POSITA would understand could be produced via expression in well-known systems such as fungi, yeast, or bacteria and are suitable for commercial applications such as consumables. Crane teaches such recombinant expression systems used specifically to recombinantly manufacture diverse kinds of functional, fully iron-incorporated heme-containing proteins such as hemoglobin, myoglobin, and leghemoglobin, which are "completely functional" and suitable for "commercial applications." EX1014(Crane), Abstract, [0021], [0024].¹³ Using recombinant expression systems to manufacture the heme-containing protein would have also been a cost-effective option and would have produced the proteins with a high degree of purity. This would have been beneficial as it allows greater control over the amount of heme-containing protein added to the consumable, which promotes greater consistency in the end product. Using recombinantly sourced heme-containing protein in food additive compositions would also appeal to those

¹³ As my personal expertise is not in genetic engineering, I rely on Dr. Batt's opinions regarding a POSITA's understanding of Crane's disclosure in my analysis. *See generally* EX1007(Batt).

individuals who have concerns about any ethical, environmental, health, and animal welfare impacts of consuming animal products or who otherwise abstain from consuming animal products for personal/religious reasons.

295. As to mimicking meat's beneficial nutritional aspects, a POSITA would have recognized that meat is an important dietary source of iron, which in meat is supplied by heme-containing proteins. *See supra* Section VII.B.1. It was also well-known to a POSITA that heme iron has greater bioavailability than non-heme iron. *See, e.g.,* EX1019(Proulx), 1518, 1520 (citing Lynch, S.R.; Dassenko, S.A.; Morck, T.A.; Beard, J.L.; Cook, J.D. *Soy protein products and heme iron absorption in humans*. Am. J. Clin. Nutr. (1985), 41, 13-20; Layrisse, M.; Martinez-Torres, C. *Model for measuring dietary absorption of heme iron: test with a complete meal*. Am. J. Clin. Nutr. 1972, 25, 401-411.). A POSITA would have recognized that prior art artificial meat flavoring compositions, such as those described in Giacino, which contain thiamine, taurine, reducing sugars, cysteine, and other amino acids provided by hydrolyzed vegetable protein, are not significant sources of iron, and, in particular, they are not significant sources of heme iron. In light of this, a POSITA would have also been motivated to add recombinant hemoglobins, including either native animal hemoglobin (*e.g.,* bovine hemoglobin) and non-animal hemoglobins

(*e.g.*, plant leghemoglobin¹⁴), to boost the amount of heme iron in Giacino's meaty flavoring compositions. Doing so would have provided Giacino's meaty flavoring compositions additional iron that had high bioavailability and better mimicked the beneficial nutritional features of meat (*e.g.*, rich source of bioavailable heme iron).

296. In view of the foregoing, a POSITA would have been motivated to combine the teachings of Giacino, Conrad, and Crane.

1. Lipid Oxidation

297. The same opinions I made above concerning lipid oxidation apply equally here. *See supra* Section XII.B.1.

C. A POSITA Would Have Had a Reasonable Expectation of Success When Combining Giacino, Conrad, and Crane

298. A POSITA would have a reasonable expectation of success in combining the teachings of Giacino, Conrad, and Crane.

299. First, only ordinary skill would have been required to prepare and combine the compounds taught in these references into a meat flavor additive composition. Giacino already discloses various formulations, including concentration ranges of precursors, for its meaty flavoring composition. Only ordinary skill would have been required to add recombinant hemoglobin (*e.g.*,

¹⁴ It was known to a POSITA that leghemoglobin was also a source of heme iron with a high bioavailability and was, in this respect, functionally equivalent to hemoglobin sourced from animals. *See* EX1019(Proulx).

hemoglobin, leghemoglobin) to the structured protein product mixture in amounts taught by Conrad. *See, e.g.*, EX1013(Conrad), 1:56-61 (up to 10% hemoglobin, and preferably 4-6% by dry weight), 4:32-40 (adding 100g hemoglobin to a product having a total weight of 2100g, *i.e.*, 4.8% hemoglobin by dry weight). For example, only ordinary skill would have been required to mix in the recombinant hemoglobin with the meaty flavoring composition's other ingredients (*e.g.*, thiamine, taurine, cysteine, ribose, vegetable hydrolysate, and/or oil) before transferring the mixture to a heat exchanger or batchwise open vessel for heating (as taught by Giacino). *See, e.g.*, EX1015(Giacino), 6:15-6:71, 8:33-36.

300. Second, as I explain elsewhere in my declaration, the chemistry of the Maillard reaction was long known, including the identity of specific precursor compounds that, when reacted with heat, would produce a meaty flavor and aroma. *See supra* Section VII.D; EX1005(McGorin), Sections V.B, V.D.

301. Third, as Dr. Batt explains, Crane taught a POSITA how to manufacture a variety of heme-containing proteins, including proteins native to animals, plants, and other species, using recombinant technology. EX1007(Batt), ¶¶31-32. As expressly taught in Crane, such heme-containing proteins could be isolated for use in a variety of applications. *Id.*; EX1014(Crane), [0024], [0060]-[0062], [0075]. Hence, as Dr. Batt opines, a POSITA would have been able to use the teachings of Crane to successfully express recombinant heme-containing proteins from

expression systems for use in the meat/food flavor compositions of Giacino. *See* EX1007(Batt), ¶¶49-53.

D. Claim 1

302. In my opinion, Giacino, Conrad, and Crane render obvious claim 1 of the '096 patent.

1. 1[pre]: A food flavor additive composition comprising:

303. As I explained above, Giacino discloses a food flavor additive composition (*e.g.*, artificial meaty flavoring composition). *See supra* Section XII.D.1.

2. 1[a]: a) an isolated heme-containing protein

304. In my opinion, the combination of Giacino, Conrad, and Crane renders obvious a food flavor additive composition comprising an isolated heme-containing protein.

305. A skilled artisan tasked with preparing artificial meat-flavored additive compositions would have been motivated to closely replicate the attributes of conventionally sourced meat, including flavor, aroma, and beneficial nutritional aspects, so as to encourage consumption by consumers who ordinarily enjoy consuming conventionally sourced meat. As described below, a POSITA would have recognized that including heme-containing proteins, such as hemoglobin or leghemoglobin, in a meat-flavored composition would achieve these goals.

306. First, a POSITA would have been motivated to replicate the natural flavor and aroma of meat in an artificial meat-flavored composition in order to increase the consumer's perception that the consumer is eating a familiar meat product, while minimizing the undesirable environmental and other consequences of conventional animal husbandry practices. One characteristic of conventionally obtained meat known to a POSITA is that when it is cooked, the meat produces a meaty aroma resulting from a complex profile of volatile chemical compounds created during the process of heating flavor precursor compounds within the meat. *See supra* Section VII.D; EX1005(McGorin), Sections V.B, V.D. Thus, a POSITA would have been motivated to prepare a meat-flavored additive composition that provides a cooked meat flavor and aroma when added to the food products so as to mimic the flavors and aromas associated with cooked meat.

307. Giacino explains that “[t]here is considerable demand for meat-flavored products in which the actual meat such as beef, pork, chicken, turkey, duck and the like is not needed or is actually undesirable.” EX1015(Giacino), 1:26-31. Giacino provides a number of reasons and examples as to when the use of real meat would be undesirable, including: cost; convenience (*e.g.*, preparing foods such as sauces, bouillons, broths, etc. that require a meaty flavor but cannot have actual pieces of meat in them); and weight and space/storage considerations where the inclusion of meat might cause spoilage. *Id.*, 1:31-48. Giacino further explains that “[p]rior

attempts at preparing artificial meat flavor compositions Have not been entirely satisfactory, in **that true flavor is generally not achieved** in the case of spice formulations.” *Id.*, 1:51-59. Thus, a POSITA would have understood that Giacino strives to create meaty flavoring compositions that fill this void and provide the closest approximation to the flavor and aroma of real meat as possible.

308. Giacino also teaches that its disclosed compositions are not fixed in stone, and instead “[v]arious other materials and ingredients can be incorporated into the compositions to provide a variety of flavor characteristics built upon the basic flavor of the taurine-thiamine reaction product.” *Id.*, 2:38-41. Hence, Giacino explicitly considers adding additional materials and ingredients to help develop the meaty flavor of its compositions. In view of the foregoing and Giacino’s goal of providing meaty flavoring compositions that achieve “true flavor reproduction” of meat (*id.*, 1:48-51), a POSITA would have understood that modifications to Giacino’s compositions that would better mimic the true flavor of meat would be desirable and welcome by Giacino.

309. Conrad expressly teaches that “[t]he addition of blood/hemoglobin further gives a desired taste improvement as it ***improves the meat flavour*** of the final product.” EX1013(Conrad), 4:14-16. Conrad teaches that the hemoglobin can be isolated from blood before being added to the product. *Id.*, 4:7-9 (“[P]referably the

hemoglobin part [is] separated off from blood, the protein content of which is about 90% by weight”).

310. Crane teaches such recombinant expression systems used specifically to recombinantly manufacture diverse kinds of functional, fully iron-incorporated heme-containing proteins such as hemoglobin, myoglobin, and leghemoglobin, which are “completely functional” and suitable for “commercial applications.” EX1014(Crane), Abstract, [0021], [0024]; *see also* EX1007(Batt), ¶¶30-32.¹⁵ Crane also teaches that these recombinant protein expression systems produce *isolated* heme-containing proteins. EX1007(Batt), ¶32; EX1014(Crane), [0060]-[0062] (“The purified preparation of recombinant heme-binding protein of the present invention has full heme incorporation and does not contain metal-free porphyrin. The purity of the preparation is assessed by the presence or absence of un-metallated heme, which can be measured by fluorescence spectroscopy and resonance Raman spectroscopy.”); *see also id.*, [0075] (disclosing that select heme-containing proteins were purified to >95% purity). When isolated, Crane’s recombinantly produced heme proteins are useful for diverse commercial purposes. EX1014(Crane), [0062] (“Purified preparations of heme-binding proteins of the present invention have a variety of therapeutic, research, and commercial utilities.”).

¹⁵ As my personal expertise is not in genetic engineering, I rely on Dr. Batt’s opinions regarding a POSITA’s understanding of Crane’s disclosure in my analysis. *See generally* EX1007 (Batt).

311. In view of Giacino's and Conrad's teachings, a POSITA would have been motivated to add hemoglobin, or another functionally equivalent heme-containing protein (*e.g.*, leghemoglobin), to Giacino's meaty flavoring compositions to "improve the meat flavour of the final product" as taught by Conrad. Based on Crane's teachings, a POSITA would have been motivated to substitute Conrad's "hemoglobin ... of whole blood from slaughtered animals" with Crane's recombinant heme-containing proteins, including either native animal hemoglobins (*e.g.*, bovine hemoglobin) or non-animal hemoglobins (*e.g.*, plant leghemoglobin). A POSITA would understand that these recombinant heme-containing proteins would be expressed using well-known expression systems, such as fungi, yeast, or bacteria, and are suitable as cost-effective options with a high degree of purity for commercial applications such as consumables. *See* EX1007(Batt), ¶¶45-53.

312. Additionally, a POSITA would have understood that meat is an important dietary source of iron because it contains heme-containing proteins. *See supra* Section VII.B.1. It was also well-known to a POSITA that heme iron has greater bioavailability than non-heme iron. *See, e.g.*, EX1019(Proulx), 1518, 1520 (citing Lynch, S.R.; Dassenko, S. A.; Morck, T.A.; Beard, J.L.; Cook, J.D. *Soy protein products and heme iron absorption in humans*. *Am. J. Clin. Nutr.* (1985), 41, 13-20; citing Layrisse, M.; Martinez-Torres, C. *Model for measuring dietary*

absorption of heme iron: test with a complete meal. Am. J. Clin. Nutr. 1972, 25, 401-411.).

313. A POSITA would have understood that artificial meat flavoring compositions of the prior art, such as those described in Giacino, containing compounds, such as thiamine, taurine, reducing sugars, cysteine, and other amino acids provided by hydrolyzed vegetable protein, are not significant sources of iron, and, in particular, heme iron (as opposed to meat, which is a rich source of heme iron). In light of this, a POSITA would have also been motivated to add recombinant hemoglobins, including either native animal hemoglobins (*e.g.*, bovine hemoglobin) and non-animal hemoglobins (*e.g.*, plant leghemoglobin¹⁶), to boost the amount of heme iron in Giacino's meaty flavoring compositions. A POSITA would have understood that this would provide Giacino's meaty flavoring compositions additional iron that had high bioavailability and better mimicked the beneficial nutritional features of meat (*e.g.*, rich source of bioavailable heme iron).

314. Accordingly, the combination of Giacino, Conrad, and Crane renders obvious a food flavor additive composition comprising an isolated heme-containing protein.

3. 1[b]: b) a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose,

¹⁶ It was known to a POSITA that leghemoglobin was also a source of heme iron with a high bioavailability and was, in this respect, functionally equivalent to hemoglobin sourced from animals. *See* EX1019(Proulx).

maltodextrin, and galactose, and mixtures of two or more thereof; and

1[c]: c) a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof;

315. As I explained above, Giacino discloses limitations 1[b] and 1[c]. *See supra* Section XII.D.3.

4. 1[d]: wherein the flavor additive composition contains no animal products; and

316. As I explained above, Giacino’s meaty flavoring compositions satisfy this limitation. *See supra* Section XII.D.4.

317. Moreover, adding recombinant hemoglobin (*e.g.*, bovine hemoglobin or plant/soy leghemoglobin) to Giacino’s meaty flavoring composition would continue to satisfy this limitation. First, leghemoglobin is an oxygen-carrying phytoalbumin found in the nitrogen-fixing root nodules of leguminous plants, such as soy, and is thus not an animal product. *See* EX1073(Santana), 1259 (discussing how leghemoglobin present in the root nodules of leguminous plants facilitates oxygen diffusion to bacteroids responsible for expressing nitrogenase). Second, as I explained above, Patent Owner has taken the position in the parallel district court action that such proteins manufactured using recombinant techniques are not “animal products,” even if the protein is natively found in animals, such as bovine myoglobin and hemoglobin. *See supra* Section X.A.

318. Hence, Giacino's meaty flavoring compositions, as modified by Conrad and Crane, contain no animal products.

5. 1[e]: wherein cooking the food flavor additive composition results in the production of at least two volatile compounds which have a meat-associated aroma.

319. Giacino, Conrad, and Crane render this limitation obvious.

320. As I explained above, heating/cooking Giacino's meaty flavoring compositions produce at least two volatile compounds having a meat-associated aroma. *See supra* Section XII.D.5.

321. A POSITA would have understood that adding recombinant hemoglobin (*e.g.*, recombinant bovine hemoglobin or plant leghemoglobin) to Giacino's flavoring compositions would only further contribute to its meaty aroma because Conrad expressly discloses that hemoglobin "improves [] meat flavour." Notwithstanding the beneficial contributions of the heme-containing protein, however, as I explained above a POSITA would have understood that at the very least the reactions between the sulfur compounds (thiamine, cysteine) and reducing sugars (ribose) present in Giacino's compositions would have produced at least two volatile compounds having a meaty aroma.

322. Hence, Giacino, Conrad, and Crane render obvious limitation 1[e].

E. **Claims 2 and 15**

323. In my opinion, Giacino, Conrad, and Crane render obvious the limitation “[t]he food flavor additive composition of claim [1/10], wherein the heme-containing protein is selected from the group consisting of a[n] androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a **hemoglobin**, a myoglobin, a **leghemoglobin**, an erythrocrucorin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histaglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3.”

324. As discussed above, a POSITA would have added recombinant hemoglobins (*e.g.*, bovine hemoglobin or plant leghemoglobin) to Giacino’s meaty flavoring compositions. *See supra* Section XIII.D.2. Hemoglobin and leghemoglobin are compounds identified in the group of heme-containing proteins for claims 2 and 15.

325. Hence, Giacino, Conrad, and Crane render obvious claims 2 and 15.

F. **Claims 3 and 16**

326. In my opinion, Giacino, Conrad, Crane, and Proulx render obvious the limitation “[t]he food flavor additive composition of claim [1/10], wherein the heme-containing protein comprises amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID Nos: 1-26.” The ’096 patent identifies

the polypeptide of SEQ ID NO 4 as that of *Glycine max* leghemoglobin (*i.e.*, soy leghemoglobin). EX1001, 10:23-24, col. 43, Fig. 1.

327. As discussed above, a POSITA would have added recombinant hemoglobin, including either native animal (*e.g.*, bovine hemoglobin) or non-animal hemoglobins (*e.g.*, plant leghemoglobin) to Giacino's meaty flavoring compositions as taught by Conrad and Crane. *See supra* Section XIII.D.2. As to the specific type of leghemoglobin added, it would have been obvious to use soy leghemoglobin (*i.e.*, *Glycine max* leghemoglobin), which satisfies these claims.

328. Proulx discloses the use of soy leghemoglobin as an iron fortificant for foods. EX1019(Proulx), Abstract. Proulx also teaches that soy leghemoglobin "showed similar bioavailability" to that of bovine hemoglobin in a food matrix. *See, e.g., id.*

329. Thus, as Proulx teaches, using soy leghemoglobin would predictably provide the heme iron the skilled artisan desires to fortify the meaty flavoring composition. Moreover, a POSITA would have understood that using soy leghemoglobin as the recombinant hemoglobin would have been obvious to try given the finite number of hemoglobins that could be used. A POSITA would have also had a reasonable expectation of success at recombinantly expressing and using soy leghemoglobin, which would have required no more than conventional techniques (*e.g.*, use of known soy leghemoglobin sequence in a recombinant

expression system and mixing the soy leghemoglobin into the meaty flavoring composition).

330. Hence, Giacino, Conrad, Crane, and Proulx render obvious claims 3 and 16.

G. Claims 4 and 24

331. As I explained above, Giacino discloses claims 4 and 24. *See supra* Section XII.G.

H. Claim 5

332. In my opinion, Giacino, Conrad, and Crane render obvious the limitation “[t]he food flavor additive composition of claim 1, wherein the heme-containing protein is a **plant**, a yeast or filamentous fungi, or bacterial heme-containing protein.”

333. As discussed above, a POSITA would have added recombinant hemoglobin, including non-animal hemoglobins (*e.g.*, plant leghemoglobin) to Giacino’s meaty flavoring compositions as taught by Conrad and Crane. *See supra* Section XIII.D.2. A POSITA would understand that leghemoglobin is a plant heme-containing protein because it is an oxygen-carrying phytoalbumin found in the nitrogen-fixing root nodules of leguminous plants, such as soy. See EX1073(Santana), 1259 (discussing how leghemoglobin present in the root nodules

of leguminous plants facilitates oxygen diffusion to bacteroids responsible for expressing nitrogenase).

334. Hence, Giacino, Conrad, and Crane render obvious claim 5.

I. Claims 6 and 22

335. As discussed above, Giacino discloses claims 6 and 22. *See supra* Section XII.I.

J. Claim 7

336. As discussed above, Giacino discloses claim 7. *See supra* Section XII.J.

K. Claims 8 and 17

337. In my opinion, the combination of Giacino, Conrad, Crane, and Perret renders obvious the limitation “[t]he food flavor additive composition of claim [1/10], further comprising one or more of an oil selected from coconut oil, mango oil, sunflower oil, cottonseed oil, **safflower oil**, rice bran oil, cocoa butter, palm fruit oil, palm oil, soybean oil, canola oil, corn oil, sesame oil, walnut oil, flaxseed, jojoba oil, castor, grapeseed oil, peanut oil, olive oil, algal oil, and oil from bacteria or fungi.” Perret is analogous art to the ’096 patent because it too is directed to simulated meat flavoring compositions that provide a meaty aroma and flavor, but do not include meat. *See, e.g.*, EX1020(Perret), 1:10-11, 1:63-69, 2:1-38, 4:36-48.

338. Giacino discloses that its meaty flavoring compositions can include “edible oils” as a medium. *Id.*, 2:23-26, 5:22-25 (“vegetable fat”). While Giacino

does not specify the type of edible oil that can be used, a POSITA would understand based on the teachings of Perret that safflower oil can be used in meat flavoring compositions. Safflower oil is derived from the safflower plant. Like Giacino, Perret discloses various meat flavoring compositions that include “edible fat,” including “vegetable fats,” such as “safflower oil.” EX1020(Perret), 4:6-11, 4:22-29. Perret teaches incorporating such fat leads to a “roast meat flavor and odor” that is “a very pleasing product.” *See id.* In view of Giacino’s teaching that edible oils serve as a medium for its meaty flavoring compositions, and Perret’s teaching that using safflower oil leads to a “roast meat flavor and odor,” a POSITA would have been motivated to use safflower oil in Giacino’s meaty flavoring compositions. It would have also been obvious to try given the finite number of edible oils available.

339. A POSITA would have had a reasonable expectation of success given it would have required no more than routine skill in the art (*e.g.*, measuring, mixing) to add safflower oil to Giacino’s meaty flavoring compositions. Moreover, using safflower oil (as taught by Perret) would have been a simple substitution of the non-specific edible oil described in Giacino with safflower oil disclosed in Perret. This would have led to the predictable result of having meaty flavoring compositions in a medium of safflower oil.

L. Claims 9 and 22

340. As discussed above, Giacino discloses claims 9 and 22. *See supra* Section XII.L.

M. Claim 10

341. In my opinion, the combination of Giacino, Conrad, and Crane render obvious claim 10.

1. 10[pre]: A food flavor additive composition prepared by a process of:

342. As discussed above, Giacino discloses a food flavor additive composition. *See supra* Section XII.D.1.

2. 10[a]: a) combining an isolated heme-containing protein;

343. As discussed above, the combination of Giacino, Conrad, and Crane render obvious a food flavor additive composition comprising an isolated heme-containing protein. *See supra* Section XIII.D.2.

3. 10[b]: a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose and galactose, and mixtures of two or more thereof; and

4. 10[c]: a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof, to form a heme flavor reaction mixture, and

344. As discussed above, Giacino discloses a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose and galactose and a compound selected from cysteine, cystine, thiamine, and

methionine. *See supra* Section XII.D.3. The mixture of Conrad's and Crane's recombinant hemoglobin and Giacino's cysteine, taurine, thiamine, and ribose, among other ingredients in the mixture, constitute the "heme flavor reaction mixture."

5. 10[d]: b) heating the heme flavor reaction mixture to at least 150° C. for at least 1 minute to result in the food flavor additive composition;

345. As discussed above, Giacino discloses heating its compositions to at least 150°C for at least 1 minute to result in the food flavor additive composition.

See supra Section XII.M.4.

6. 10[e]: wherein the food flavoring additive composition contains no animal products; and

346. As discussed above, Giacino's meaty flavoring compositions modified to include recombinant hemoglobin (e.g., bovine hemoglobin, plant/soy leghemoglobin) do not contain any animal products. *See supra* Sections XII.D.4, XIII.D.4.

7. 10[f]: wherein the heme flavor reaction mixture has a meaty flavor and/or meaty aroma during the heating of step b) and the food flavoring additive composition has a meaty flavor and/or meaty aroma after the heating of step b).

347. Giacino, Conrad, and Crane render this limitation obvious.

348. As I explained above for limitation 1[e], a POSITA would have understood that heating Giacino's modified meaty flavoring compositions, which include, *inter alia*, sulfur compounds (e.g., thiamine and cysteine), reducing sugars

(e.g., ribose), and recombinant hemoglobin/leghemoglobin, would induce different reactions including, a Maillard reaction, that would produce many different volatiles associated with a meaty aroma and flavor. *See supra* Sections XII.D.5, XIII.D.5.

349. A POSITA would recognize that these volatiles are produced during the heating step. *See* EX1015(Giacino), 2:5-8. Moreover, a POSITA would understand that the volatiles that were produced during the heating step remain present after the heating step completes. For example, it is common knowledge that foods, such as a freshly cooked piece of meat, give off aromas after the cooking process completes.

350. Hence, Giacino, Conrad, and Crane render obvious this limitation.

N. **Claim 11**

351. In my opinion, Giacino, Conrad, and Crane render claim 11 obvious.

352. As I discussed above, a POSITA would have understood that heating Giacino's modified meaty flavoring compositions, which include, thiamine, cysteine, ribose, and recombinant hemoglobin (e.g., bovine hemoglobin, plant leghemoglobin), would produce a number of volatile compounds having a meaty flavor and aroma. *See supra* Sections XIII.D.5, XIII.M.7. In particular, a POSITA would have recognized that at the very least when the cysteine and ribose compounds are heated in Giacino's modified composition, a Maillard reaction would occur causing the production of at least, among other volatile compounds, 2,5-

dimethylpyrazine and 2-methyl-thiazole, which are both recited in claim 11. *See, e.g.,* EX1024(MacLeod), 385, Table 15 (identifying 2-methyl-thiazole and 2,5-dimethylpyrazine as volatile compounds when cysteine and ribose react). A POSITA would have understood that these two compounds are known to be associated with a meaty aroma/flavor. *See, e.g., id.*, 344, Table 1 (identifying 2,5-dimethylpyrazine as contributing to “natural beef aroma”), 351, Table 1 cont. (identifying 2-methyl-thiazole as contributing to “natural beef aroma”); EX1026(Dwivedi), 492, Table 1 (2-methylthiazole), 493, Table 1 cont. (2,5-dimethylpyrazine).

353. Hence, the combination of Giacino, Conrad, and Crane discloses claim 11.

O. Claim 12

354. In my opinion, Giacino, Conrad, and Crane render claim 12 obvious.

355. As I discussed above, a POSITA would have understood that heating Giacino’s modified meaty flavoring composition would release a variety of volatile compounds associated with a meaty flavor and/or aroma. *See supra* Sections XIII.D.5, XIII.M.7, XIII.N. A POSITA would have understood that these volatiles are released in the volume of air above the composition (*e.g.*, headspace), and therefore would be detectable during and after the heating process.

356. Hence, the combination of Giacino, Conrad, and Crane render claim 12 obvious.

P. Claim 14

357. In my opinion, Giacino, Conrad, and Crane render obvious the limitation “[t]he food flavor additive composition of claim 10, wherein the heme-containing protein is present in an amount between about 0.01% and about 5% by weight in the heme flavor reaction mixture.”

358. As I explained above, a POSITA would have modified Giacino’s meaty flavoring composition by adding recombinant hemoglobin (*e.g.*, bovine hemoglobin, plant leghemoglobin) as taught by Conrad and Crane. *See supra* Section XIII.D.2. As to the amount of such recombinant hemoglobin/leghemoglobin to add, a POSITA would have turned to the concentrations disclosed in Conrad.

359. Conrad teaches levels of heme-protein in its meat replicas that achieve these desirable meat-like properties. Specifically, to achieve these goals, Conrad discloses utilizing the “**hemoglobin part** of whole blood” in its grain-based “meat.” EX1013, 1:56-61, 4:5-10.

The wheat meat described has a brown-yellow colour deriving partly from the brown bran and partly from the yellow gluten. The colour can advantageously be transferred into meat colour by adding thereto up to 15% by weight of blood, preferably ***the hemoglobin part separated off from blood, the protein content of which is about 90% by weight and the dry substance contents are 33% by weight.***

It is to be noted that the dry substance contents of wheat meat are about 33 to 35% by weight and the addition of blood thus not changes the dry substance. The addition of blood/hemoglobin further gives a desired taste improvement as it improves the meat flavour of the final product. (EX1013, 4:3-17.)

360. Red blood cells are well-known to contain hemoglobin protein. (E.g., Weed (1963) (EX1139).) The levels of hemoglobin in red blood cells are also long known in the art. As reproduced below, Tables 1 and 2 of Weed (1963) disclose proportions of hemoglobin and other components in the “dry weight” (non-water portion) of red blood cells (versus hemoglobin-depleted “ghost” cells).

TABLE I		
<i>Hemoglobin content per cell of red blood cells and ghosts</i>		
	Red blood cells (n = 14)	Ghosts (n = 24)
Hemoglobin, g $\times 10^{-12}$	30.99 $\pm$ 0.12 (SD)	0.015 $\pm$ 0.009 (SD)
Hemoglobin, % dry weight	97	1.4

TABLE II
*Lipid content per cell of intact red blood
cells and ghosts**

Lipids	Red blood cells	Ghosts	p
Total lipid, g $\times 10^{-12}$	4.91 $\pm$ 0.33	4.95 $\pm$ 0.33	> 0.60
Total cholesterol, g $\times 10^{-12}$	1.13 $\pm$ 0.08	1.08 $\pm$ 0.06	> 0.05
Total lipid phosphorus, μ g $\times 10^{-9}$	11.89 $\pm$ 0.68	11.47 $\pm$ 0.85	> 0.40
Individual phospholipids,† μ g P $\times 10^{-9}$			
Sphingomyelin	3.12 $\pm$ 0.14	2.91 $\pm$ 0.26	> 0.05
Lecithin	3.37 $\pm$ 0.19	3.28 $\pm$ 0.22	> 0.40
Phosphatidyl serine	1.79 $\pm$ 0.22	1.84 $\pm$ 0.09	> 0.40
Phosphatidyl ethanolamine	2.39 $\pm$ 0.26	2.31 $\pm$ 0.23	> .040
Other‡	1.22 $\pm$ 0.07	1.13 $\pm$ 0.07	> 0.40

* Mean values $\pm$ SD are given for preparations from nine hematologically normal subjects. p was determined by *t* test (20).

† Plasmalogens, where present, were analyzed with the parent compounds.

‡ This includes lysolecithin, inositol phosphatide, and polyglycerol phosphatide, which together constitute about 10% of the total lipid phosphorus of the red blood cell (11).

361. A POSITA would therefore understand Conrad's reference to the "hemoglobin part" of blood used in Conrad's "grain meat" / "wheat meat" products to mean *red blood cells*.

362. Consistent with this understanding, Conrad teaches that "the *dry substance contents* [of the "hemoglobin part"] are **33% by weight.**" (EX1013, 4:5-10.) I note that Conrad refers to "protein content" values before it refers to "dry substance" values, but a POSITA would understand that the 90% "protein content" value necessarily refers to the "dry substance" because the 66% (non-dry) remainder is water, which is not protein. In particular, a POSITA would understand that this "dry weight" portion of the "hemoglobin part" refers to the components of the *red*

blood cells that are *not water*—for example, proteins or lipids that may also be present in the cells.

363. Within this “dry weight” portion of Conrad’s “hemoglobin part,” Conrad teaches that its “the *protein content*” “is *about 90% by weight*.” EX1013, 4:5-10. Although Conrad’s disclosure regarding the components of the “protein content” is not precise—for example, because Conrad does not teach particular methods for obtaining or purifying the “hemoglobin part” for use in its products—a POSITA would understand from the context of Conrad that Conrad teaches that the “*protein content*” of the “hemoglobin part” relates to *hemoglobin* itself—the protein known in the art to contribute to the desired meat-like flavor and color of Conrad’s products.

364. My interpretation of the “*protein content*” is reflected in Conrad’s choice of the term “*hemoglobin part*” to describe this fraction. My interpretation is also consistent with Conrad’s description of the components of this fraction in light of the art’s teaching of hemoglobin levels in red blood cells. Specifically, by using the term “*about*” to modify “90%,” for example, Conrad is identifying an *estimate of the levels of hemoglobin protein in the “dry weight” fraction of the “hemoglobin part.*” (Conrad does not define the scope of “about.”) In fact, the amount of hemoglobin could be different (and could potentially be higher than 90%, as taught in the art). EX1139 (Weed (1963)), 584 (“[*H*]emoglobin ... *accounts for 97% of* [a

red blood] cell's dry weight"). A POSITA would understand that Conrad is merely providing an approximation of the amount of hemoglobin in the "dry" fraction of the "hemoglobin part." Thus, when Conrad's teachings are read together, a POSITA would understand that the "*about 90%*" *term refers to the proportion of hemoglobin protein in the "dry weight" fraction.*

365. My interpretation of Conrad is consistent with its description of its Table 2 meat replica embodiment—"Wheat Meat CH" (containing "Cheese fines" and "Hemoglobin" in addition to "Wheat Meat"), reproduced below:

TABLE 2

Product	Amount in g	DS in %	Protein in DS %	Protein in g
Wheat meat	1,500	33	46	230
Cheese fines	500	33	85	140
Hemoglobin	100	33	90	30
Wheat meat <u>CH</u>	2,100	33	57	400

366. As shown in Table 2, Conrad teaches that only **30 grams** of the **100-gram** "Hemoglobin" component of the "Wheat Meat CH" embodiment are "protein." In other words, the "Hemoglobin" in "Wheat Meat CH" is only comprised of 30% protein.

367. This proportion is consistent with the teachings of Conrad explained above. If "Hemoglobin" meant only hemoglobin *protein*, for example, the "protein" value would be 100 grams (100% of the total) rather than only 30 grams. Specifically, assuming that the 100-gram "Hemoglobin" in Table 2 refers to the

“hemoglobin part” added to the “wheat meat,” 33% of that “Hemoglobin” (“hemoglobin part”) is “dry weight.” Within that “dry weight” portion of “Hemoglobin,” about 90% of the “dry weight” is hemoglobin. This translates to approximately 30% grams of hemoglobin as shown below:

“Hemoglobin” (hemoglobin part)	“Dry Weight” portion of “Hemoglobin”	Heme-Protein (hemoglobin) portion of “Hemoglobin”
<i>100 grams</i>	$(0.33 \times 100 \text{ grams}) =$ <i>33 grams</i>	$(0.9 \times 33 \text{ grams}) =$ <i>29.7 grams</i> (about 30 grams)

368. The entire Table 2 “Wheat Meat CH” embodiment is 2100 grams. The percentage of hemoglobin in this whole product is therefore 29.7 grams (hemoglobin) divided by 2100 grams (product) (which equates to 0.01415 grams), multiplied by 100. Thus, the Table 2 Wheat Meat CH” embodiment of Conrad’s meat replacement products comprises approximately **1.43%** of the heme-protein hemoglobin. This value is within the claimed 0.01%-5.0% range of (“non-animal”) heme-containing protein.

369. Conrad teaches other embodiments with slightly different heme-protein concentrations. For example, Conrad teaches adding the “hemoglobin part” “up to 10% by weight *dry weight* of the gluten-bran product *dry weight*, preferably 4-6% by weight.” EX1013(Conrad), 1:56-61. This teaching can be applied to Conrad’s Table 1 “wheat meat” embodiment, which contains 65%/35% water/non-water (dry)

components, respectively. For example, the “dry” portion of the “hemoglobin part” contributes 10% of the embodiment’s 35% dry components—i.e., 3.5%—of which 90% is heme-protein, representing **3.15%** of the total embodiment. Applying the same calculations to Conrad’s “prefer[red] 4-6% by weight” range (*id.*, 1:60-61) translates to about **1.26%** to **1.89%** by weight heme-containing protein.

370. Accordingly, based on Conrad’s disclosed concentrations of hemoglobin, a POSITA would have been motivated to add an amount of recombinant hemoglobin/legghemoglobin to Giacino’s flavoring compositions that satisfied the claim 0.01-5% range.

371. A POSITA would have had a reasonable expectation of success of adding the recombinant hemoglobin/legghemoglobin into Giacino’s flavoring compositions at the concentrations discussed above because no more than conventional methods (*e.g.*, measuring, mixing) would have been required.

372. Separately, a POSITA would have also recognized that the concentration of heme-containing protein in the flavoring composition would be adjusted as part of routine experimentation to find the precise concentration needed to obtain an optimized balance between the desired flavor profile and nutritional content (*e.g.*, iron). This experimentation would result in applications of the flavoring composition where the concentration of recombinant hemoglobin/legghemoglobin was within the claimed 0.01%-5% range.

Q. **Claim 18**

373. The combination of Giacino, Conrad, Crane, and MacLeod renders claim 18 obvious: “The food flavor additive composition of claim 10, further comprising an ingredient selected from an emulsifier and a gelling agent.”

374. As I discuss elsewhere in my declaration, Giacino satisfies this claim because it discloses that “[t]he pre-mix [composition] can also contain other ingredients normally used in the art ... such as **gum arabic**” to “stabilize the compositions.” EX1015(Giacino), 5:40-43, 9:21-27. A POSITA would have also understood that gum arabic is well-known in the art as a plant-based emulsifier. *See* EX1074(dos Santos), 233 (“Arabic gum is also known as Acacia gum and is obtained from the exudates of Acacia trees.... Arabic gum has wide industrial uses as a stabilizer, thickening agent, and **emulsifier**, mainly in the food industry.”); EX1122(Saha), 590 (“Gum arabic (Acacia gum) is widely used in the food industry mainly to impart desirable qualities because of its influence over viscosity, body and texture. Mainly it is used as an **emulsifier**”).

375. Additionally, MacLeod discloses that artificial meat flavoring compositions commonly include “agar, carageenan, cellulose, carboxymethylcellulose, gum arabic, gum tragacanth, gelatin, **pectin, and starch**.” EX1024(MacLeod), 414. Pectin and starch are well-known in the art as a gelling agents that are derived from non-animal sources (*e.g.*, apples, apricots, citrus peels,

wheat, potatoes, corn, etc.). EX1071(Flutto), 4442, 4449; EX1074(dos Santos), 231 (“Pectin Mainly finds applications as **gelling** and thickening **agent** in food industry. ...”); EX1122(Saha), 595 (“The frequently used gelling agents include **modified starch**, agar, carrageenans, [and] **pectins**”), Table 2 (listing pectin and modified starch as gelling agents).

376. A POSITA would have understood that adding pectin or starch to Giacino’s meaty flavoring composition would thicken and/or promote gelling of the mixture. Given Giacino’s teaching that its beef-flavored compositions can serve as a base for gravies and sauces (EX1015(Giacino), 7:15-22), a POSITA would have been motivated to thicken the composition. Similarly, given Giacino’s teaching that its beef-flavored compositions can be added to “synthetic meat fibres” (*id.*, 7:22-26), a POSITA would have been motivated to promote gelling to improve its texture as part of the “synthetic meat fibre” (*i.e.*, meat substitute). Moreover, Giacino invites such a modification because it teaches that many different “food additives” can be added to the meaty flavoring compositions including “carriers,” “thickeners,” and even starches (*e.g.*, cornstarch). *Id.*, 9:5-19, 11:13. A POSITA would have known to do so by adding pectin or starch (as taught by MacLeod), which are known gelling agents and thickeners.

377. Hence, Giacino, Conrad, Crane, and MacLeod render claim 18 obvious.

R. **Claim 19**

378. The combination of Giacino, Conrad, Crane, and MacLeod renders claim 19 obvious: “The food flavor additive composition of claim 10, the process further comprising adding an emulsifier and a gelling agent to the heme flavor reaction mixture prior to the heating of step b).”

379. As I discussed above for claim 18, Giacino’s compositions include gum arabic (emulsifier) and, based on the teachings of MacLeod, a POSITA would have added a gelling agent (*e.g.*, pectin or starch) to Giacino’s meaty flavoring compositions. *See supra* Section XIII.R. As I explain below, these components would have been added before the heating step b).

380. Giacino expressly discloses that “[v]arious other materials and ingredients can be incorporated into the compositions **at any time**, that is, ***before*** ... **heat treatment**.” EX1015(Giacino), 2:38-43. A POSITA would understand that with respect to gelling agents, such as starch and pectin, heat activates the desired gelling/thickening properties of these compounds. *See, e.g.*, EX1134(Lund), 249 (“Starch granules are insoluble in cold water but swell when heated in an aqueous medium. Initially, the swelling is reversible and the optical properties of the granule are retained (*e.g.*, birefringence). But when a certain temperature is reached, the swelling becomes irreversible and the structure of the granule is altered significantly. The process is called ‘gelatinization’ and the temperature at which gelatinization

occurs is called the ‘gelatinization temperature.’”); EX1136(Whistler), 114 (identifying gelatinization temperatures of various starches, which are all well above room temperature and would require heating), 124 (“A special property of pectin is its ability to produce strong gels. If a *hot water* dispersion of 0.3-0.4% pectin is cooled to room temperature [and] pH is adjusted to 2.0-3.5 and sucrose is present at a concentration of 60-65%, a gel forms on cooling.”).

381. With respect to the emulsifier (*e.g.*, gum arabic), its presence in the mixture during the heating step is beneficial because the heat increases the fluidity of the mixture which would assist the emulsifier in creating an emulsion of the proteins and fats present in the composition. Similarly, heating the composition containing these compounds (*e.g.*, starch or pectin and gum arabic) helps disperse the compounds within the composition and also promotes hydration of the gelling agents. Furthermore, it would have been common sense to add these compounds (*e.g.*, starch or pectin and gum arabic) before the heating step at the same time all of the other compounds in Giacino’s composition are combined, including taurine, thiamine, cysteine, ribose, etc. Otherwise adding one or more of these compounds after the heating step would only necessitate an additional mixing step, which would unnecessarily complicate the process. For at least these reasons, a POSITA would add the gelling agent and emulsifier before heating the composition.

382. Hence, the combination of Giacino, Conrad, Crane, and MacLeod renders obvious claim 19.

S. Claims 20, 21

383. As discussed above, Giacino discloses claims 20 and 21. *See supra* Section XII.S.

T. Claim 23

384. As discussed above, Giacino discloses claim 23. *See supra* Section XII.T.

XIV. GROUNDS 4A, 4B, 4C: GIACINO, PROULX, CONRAD, PERRET, MACLEOD

385. As I explain below, the combination of Giacino, Proulx, and Conrad (Ground 4A) renders obvious claims 1-7, 9-12, 14-16, and 20-24. The combination of Giacino, Proulx, Conrad, and Perret (Ground 4B) renders claims 8 and 17 obvious. The combination of Giacino, Proulx, Conrad, and MacLeod (Ground 4C) renders obvious claims 18-19.

A. Giacino, Proulx, and Conrad Are All Analogous Art

386. Giacino, Proulx, and Conrad are analogous art to the '096 patent. For example, a POSITA would have understood that these references are in the same field of endeavor as the claimed invention. As I discussed above in connection to Grounds 2 and 3, like the '096 patent, **Giacino** discloses various meaty flavoring compositions that are added to other consumable food products. *See, e.g.,*

EX1015(Giacino), 1:19-25, 1:65-68, 5:1-10, 7:15-26. Similarly, Conrad relates to “meat replacement products, a process for the preparation of meat replacement products, as well as meat products containing such meat replacement products.” EX1013(Conrad), 1:11-14. In particular, Conrad teaches that adding isolated hemoglobin (which is a heme-containing protein) “gives a desired taste improvement as it improves the meat flavour of the final product.” *Id.*, 4:14-16. **Proulx** teaches methods for preparing isolated soy leghemoglobin and use of such soy leghemoglobin as a food additive to fortify foods with iron. *See, e.g.*, EX1019(Proulx), 1518.

387. Giacino, Proulx, and Conrad are also each reasonably pertinent to the problem with which the '096 patent applicant was concerned—generally, the failure of existing food flavor additive compositions and meat substitutes containing such compositions to replicate the flavors and aromas of conventionally sourced meat. *See, e.g.*, EX1001, 1:46-62. Giacino recognizes that prior art meaty flavoring compositions lacked the “true flavor” of meat, and thus strives to create flavoring compositions that accurately mimic the flavor and aroma of meat. *See* EX1015(Giacino), 1:47-59. To address this deficiency, Giacino discloses meaty flavoring compositions containing taurine, thiamine, cysteine, vegetable protein hydrolysate, and reducing sugars that provide “a meaty flavor.” *See, e.g., id.*, 2:5-8,

3:3-25, 5:1-10, 6:1-7. Similarly, Conrad strives to enhance “meaty flavour” by adding hemoglobin to its food products. EX1013(Conrad), 4:14-16.

388. Proulx’s teachings are also pertinent to one of the problems faced by the ’096 patent applicant, which included minimizing or eliminating the use of conventionally sourced meat to avoid wasteful and harmful animal husbandry and slaughter practices and associated costs. Proulx teaches methods for preparing isolated soy leghemoglobin and using the soy leghemoglobin as a food additive to fortify foods with iron. *See, e.g.*, EX1019(Proulx), 1518. A POSITA would have recognized that Proulx’s methods for preparing soy leghemoglobin, which contains heme iron, provide an animal free alternative to obtaining heme iron. A POSITA would have also recognized that Proulx’s teachings are relevant because they provide an animal free source of heme iron to use as a fortificant and replicate the nutritional content of meat in a non-meat-based food flavor additive.

389. For at least the above reasons, Giacino, Proulx, and Conrad are analogous art to the ’096 patent.

B. A POSITA Would Have Been Motivated to Combine Giacino, Proulx, and Conrad to Achieve the Claimed Subject Matter

390. A POSITA would have been motivated to combine Giacino, Proulx, and Conrad to achieve the subject matter of the challenged claims for a variety of reasons. Generally, a POSITA would have been motivated to create a meat-flavored additive composition, such as those described in Giacino, that closely mimics the

attributes of conventionally sourced meat, including flavor, aroma, and beneficial nutritional aspects, so as to encourage consumption by consumers who ordinarily enjoy consuming conventionally sourced meat, but for health, environmental, and/or personal preferences (*e.g.*, religious) choose not to consume animal products. As described below, a POSITA would have recognized that including a heme-containing protein, such as leghemoglobin, in Giacino's meaty flavoring compositions would achieve these goals.

391. First, a POSITA would have been motivated to mimic beneficial aspects of meat's nutritional content. Specifically, a POSITA would have recognized that meat (*e.g.*, beef) is an important dietary source of iron, which is supplied by heme-containing proteins. *See supra* Section VII.B.1. It was also well-known to a POSITA that heme iron has greater bioavailability than non-heme iron. *See, e.g.*, EX1019(Proulx), 1518, 1520 (citing Lynch, S. R.; Dassenko, S. A.; Morck, T. A.; Beard, J. L.; Cook, J. D. *Soy protein products and heme iron absorption in humans*. Am. J. Clin. Nutr. (1985), 41, 13-20; citing Layrisse, M.; Martinez-Torres, C. *Model for measuring dietary absorption of heme iron: test with a complete meal*. Am. J. Clin. Nutr. 1972, 25, 401-411.). A POSITA would have recognized that prior art artificial meat flavoring compositions, such as those described in Giacino, which contain taurine, thiamine, reducing sugars, cysteine, and other amino acids provided by vegetable protein hydrolysate, are not significant sources of iron, and, in

particular, they are not significant sources of heme iron. In light of this, a POSITA would have recognized a need to fortify Giacino's meaty flavoring compositions to better approximate the iron content of meat.

392. Proulx describes methods for supplementing foods with heme iron. As Proulx acknowledges, it was well-known in the art that iron bioavailability of heme iron is higher than non-heme iron. EX1019(Proulx), 1518, 1520 (citing Lynch, S. R.; Dassenko, S. A.; Morck, T. A.; Beard, J. L.; Cook, J. D. *Soy protein products and heme iron absorption in humans*. Am. J. Clin. Nutr. (1985), 41, 13-20; citing Layrisse, M.; Martinez-Torres, C. *Model for measuring dietary absorption of heme iron: test with a complete meal*. Am. J. Clin. Nutr. 1972, 25, 401-411.). Proulx teaches that heme iron may be sourced from leghemoglobin found in soy root nodules. Notably, Proulx discloses that soy leghemoglobin “showed similar bioavailability” to that of bovine hemoglobin in a food matrix. *See, e.g.*, EX1019(Proulx), Abstract.

393. In view of the foregoing, a POSITA would have been motivated to add isolated soy leghemoglobin as taught by Proulx into Giacino's meaty flavoring compositions to fortify the compositions with heme iron, which has a significantly higher bioavailability than non-heme iron. Doing so would allow the meaty flavoring compositions to better mimic the nutritional profile (*e.g.*, iron content) of conventionally sourced meat and encourage consumers to consume meat substitutes

made with the fortified meat-flavored compositions. A POSITA would have been further motivated to use Proulx's leghemoglobin as a fortificant because of the "high heat stability of ... [heme] iron." EX1019(Proulx), 1520, 1522. Additionally, Proulx teaches that "[s]oy root nodules have no current use in agriculture production and as such may provide a novel value-added product for soy producers," which for efficiency and cost reasons would serve as an additional motivation to use soy leghemoglobin. *Id.*, 1522. For all of these reasons, a POSITA would have recognized that "plant hemoglobins may have great potential to be used as a fortificant for improving nutrition." *Id.*

394. I understand that Patent Owner also agrees that soy leghemoglobin serves as an iron fortificant in light of Proulx's teachings. I understand that Patent Owner stated in its "generally recognized as safe" (GRAS) submission to the FDA for the use of soy leghemoglobin that:

2.3.2 Purposes

The primary purpose of the characterizing component, soy leghemoglobin protein, in LegH Prep is to create a flavor impact in ground beef analogue products. In addition, soy leghemoglobin has a nutritive value as a source of iron, analogous to the role of myoglobin as an iron source in meat. Once cooked and digested, both soy leghemoglobin and animal-based myoglobin release identical heme B molecules into the digestive system (Annex 1). Studies using cell models of iron bioavailability have shown that the bioavailability of iron in soy leghemoglobin is equivalent to that of bovine myoglobin when in a food-like substrate (Proulx & Reddy, 2006). Thus, the use of LegH Prep in ground beef analogue products will enhance both the flavor and the dietary profile of those products (Carpenter & Mahoney, 1992).

EX1052, 7. In particular, Patent Owner expressly relied on Proulx to show that it was known in the art that the bioavailability of iron in soy leghemoglobin was

equivalent to that of animal heme sources (*e.g.*, bovine myoglobin) in food. Hence, Patent Owner agrees that soy leghemoglobin has a nutritive value as a source of iron and that adding it to meat-flavored compositions would enhance their dietary profile.

395. Additionally, a POSITA would have been motivated to mimic the natural flavor and aroma of cooked meat in Giacino's meaty flavoring compositions in order to increase the consumer's perception that the consumer is eating a familiar meat product while minimizing the undesirable environmental and other ramifications of conventional animal husbandry practices. As a POSITA would have recognized, one characteristic of conventionally obtained meat is that, when cooked, the meat produces a meaty aroma resulting from a complex profile of volatile chemical compounds created during the process of heating precursor compounds within the meat. *See supra* Section VII.D; EX1005(McGorin), Sections V.B, V.D. Thus, a POSITA would have been motivated to prepare a food flavor additive composition that provides a meaty flavor and aroma when added to the meat substitute product so as to mimic the flavors and aromas associated with cooked meat.

396. To achieve this goal, Giacino teaches that heating reducing sugars, such as ribose, with taurine, thiamine, cysteine, and potentially other flavor precursors produces a meaty flavoring composition having "meaty flavor." *See, e.g.*, EX1015(Giacino), 1:19-25, 2:5-8, 3:3-25, 5:1-10. Similarly, Conrad expressly

teaches that “[t]he addition of blood/hemoglobin further gives a desired taste improvement as it improves the meat flavour of the final product.” EX1013(Conrad), 4:14-16. Conrad teaches that hemoglobin can be isolated from blood before being added to the product. *Id.*, 4:7-9 (“[P]referably the hemoglobin part separated off from blood, the protein content of which is about 90% by weight”). A POSITA would have understood that, like bovine hemoglobin, soy leghemoglobin is also a heme-containing protein and would thus improve “meat flavour” as taught by Conrad. Hence, a POSITA would have been motivated to include soy leghemoglobin in Giacino’s compositions for the additional reason of improving their flavor profile.

397. Accordingly, whether to fortify the composition with heme iron *and/or* to enhance meat flavor, a POSITA would have been motivated to add soy leghemoglobin to Giacino’s compositions.

398. Moreover, given soy leghemoglobin is a plant protein (*e.g.*, soy), a POSITA would have understood that soy leghemoglobin provides a non-animal source of heme iron, which obviates the need to rely on heme-containing proteins obtained physically from animals (*e.g.*, bovine myoglobin or hemoglobin) that are associated with conventional animal husbandry. This would have been appealing to consumers who desired a vegetarian product for health or religious reasons and/or those concerned about the environmental impacts of conventional animal husbandry.

399. In view of the foregoing, a POSITA would have been motivated to combine the teachings of Giacino, Proulx, and Conrad to modify Giacino's meaty flavoring compositions to include soy leghemoglobin.

1. Lipid Oxidation

400. The same opinions I made above concerning lipid oxidation apply equally here. *See supra* Section XII.B.1.

C. A POSITA Would Have Had a Reasonable Expectation of Success When Combining Giacino, Proulx, and Conrad

401. A POSITA would have had a reasonable expectation of success in combining the teachings of Giacino, Proulx, and Conrad to achieve the claimed invention.

402. First, only ordinary skill would have been required to prepare and assemble the ingredients taught in these references into a meaty flavoring composition. Giacino discloses detailed ingredient lists, including amounts and process steps, for its meaty flavoring compositions. Proulx teaches conventional extraction methods for obtaining soybean leghemoglobin from plants for use in foodstuffs, which would require only ordinary skill to practice. For example, Proulx teaches that root nodules "were mechanically harvested [and] ground... [T]he aqueous extract was also used to prepare partially purified LHb ... by using ... precipitation Ion exchange chromatography ... was used to further purify the LHb obtained from ... precipitation." EX1019(Proulx), 1519 (describing "LHb

Preparation” and bioavailability study design). Only ordinary skill would have been required to follow these steps. *See id.*, 1519. Similarly, only ordinary skill (*e.g.*, mixing) would have been needed to add the isolated soy leghemoglobin to Giacino’s meaty flavoring compositions, *e.g.*, by adding it to the mixture of taurine, thiamine, cysteine, vegetable protein hydrolysate, and reducing sugars used to prepare the meaty flavoring compositions. EX1015(Giacino), 2:5-8, 3:3-25, 5:1-10.

403. Second, as explained further above, the chemistry of the Maillard reaction was long known, including the identity of specific precursor compounds that, when reacted with heat, would produce a meaty flavor and aroma. *See supra* Section VII.D; EX1005(McGorin), Sections V.B, V.D. As taught in Giacino, a POSITA would have been motivated to use reducing sugars, such as ribose, and sulfur compounds, such as thiamine and cysteine, to serve as precursors for the Maillard reaction (and other chemical reactions that occur during cooking), as the Maillard reaction was long known to produce volatile compounds associated with a desirable meaty flavor and aroma.

D. Claim 1

404. In my opinion, Giacino, Proulx and Conrad render obvious claim 1 of the ’096 patent.

1. 1[pre]: A food flavor additive composition comprising:

405. As I explained above, Giacino discloses a food flavor additive composition (*e.g.*, artificial meaty flavoring composition). *See supra* Section XII.D.1.

2. 1[a]: a) an isolated heme-containing protein

406. In my opinion, the combination of Giacino, Proulx, and Conrad render obvious a food flavor additive composition comprising an isolated heme-containing protein.

407. When preparing a meaty flavoring composition as taught by Giacino, a POSITA would have been motivated to replicate various attributes associated with conventionally sourced meat, such as conventionally sourced beef, including beef flavor, beef aroma, and beef's nutritional profile. This would encourage consumption by consumers who ordinarily enjoy consuming conventionally sourced meat. A POSITA would have recognized that beef serves as a robust source of dietary iron due to the heme-containing proteins (*e.g.*, hemoglobin and myoglobin) it contains. A POSITA would have further recognized that prior art artificial meat flavoring compositions, such as those described in Giacino, which contain taurine, thiamine, reducing sugars, cysteine, and other amino acids provided by vegetable protein hydrolysate, are not significant sources of iron, and, in particular, they are not significant sources of heme iron. In light of this, a POSITA would have

recognized a need to fortify Giacino's meaty flavoring compositions to better approximate the iron content of beef.

408. Proulx describes methods for supplementing foods with heme iron. As Proulx acknowledges, it was well-known in the art that iron bioavailability is higher in heme iron than non-heme iron. EX1019(Proulx), 1518, 1520 (citing Lynch, S.R.; Dassenko, S.A.; Morck, T.A.; Beard, J. L.; Cook, J.D. *Soy protein products and heme iron absorption in humans*. Am. J. Clin. Nutr. (1985), 41, 13-20; citing Layrisse, M.; Martinez-Torres, C. *Model for measuring dietary absorption of heme iron: test with a complete meal*. Am. J. Clin. Nutr. 1972, 25, 401-411.). In particular, Proulx teaches that heme iron may be sourced from leghemoglobin found in soy root nodules. Proulx also teaches methods for isolating the soy leghemoglobin to various levels of purity. *Id.*, 1519-20 (disclosing 21% purity of leghemoglobin in soy root nodule (SRN) extract, 54% purity for “partially purified” leghemoglobin (“LHb_A”), and 73% purity for “LHb_D”). Notably, Proulx's disclosures teach a POSITA that soy leghemoglobin provided substantially similar bioavailability to that of bovine hemoglobin in the presence of food. *See generally id.*, 1519-22 (27% ± 6% higher bioavailability than ferrous sulfate for LHb_A and 33% ± 10% higher bioavailability for bovine hemoglobin). Accordingly, a POSITA would have understood based on Proulx's teachings that isolated soy leghemoglobin could be used to fortify foods with heme iron.

409. I understand that Patent Owner came to the same conclusion regarding the use of soy leghemoglobin as an iron fortificant in light of Proulx's teachings. For example, Patent Owner admitted in its "generally recognized as safe" (GRAS) submission to the FDA for the use of soy leghemoglobin that:

2.3.2 Purposes

The primary purpose of the characterizing component, soy leghemoglobin protein, in LegH Prep is to create a flavor impact in ground beef analogue products. In addition, soy leghemoglobin has a nutritive value as a source of iron, analogous to the role of myoglobin as an iron source in meat. Once cooked and digested, both soy leghemoglobin and animal-based myoglobin release identical heme B molecules into the digestive system (Annex 1). Studies using cell models of iron bioavailability have shown that the bioavailability of iron in soy leghemoglobin is equivalent to that of bovine myoglobin when in a food-like substrate (Proulx & Reddy, 2006). Thus, the use of LegH Prep in ground beef analogue products will enhance both the flavor and the dietary profile of those products (Carpenter & Mahoney, 1992).

EX1052, 7. Hence, Patent Owner concedes that soy leghemoglobin has a nutritive value as a source of iron and that adding it to meat analogue products would enhance their dietary profile. In particular, Patent Owner expressly relied on Proulx as authoritative to show that it was known in the art that the bioavailability of iron in soy leghemoglobin was equivalent to that of animal heme sources (*e.g.*, bovine myoglobin) in food.

410. In view of the foregoing, a POSITA would have been motivated to add isolated soy leghemoglobin (*e.g.*, LHb_A or LHb_D) as taught by Proulx into Giacino's meaty flavoring compositions to fortify the compositions with heme iron, which has a relatively high degree of bioavailability compared to non-heme iron. Doing so would allow the meaty flavoring compositions to better mimic the nutritional profile

(*e.g.*, iron content) of conventionally sourced beef and encourage consumers to consume meat substitutes made with the fortified meaty flavoring compositions. Additionally, Proulx’s teachings that heme iron exhibits higher heat stability and that “soy root nodules have no current use in agriculture production and as such may provide a novel value-added product for soy producers” would further motivate a POSITA to add soy leghemoglobin into Giacino’s meaty flavoring compositions. *See* EX1019(Proulx), 1521-22.

411. Additionally, as taught by Proulx, a POSITA would have understood that the different soy leghemoglobin preparations described in Proulx (*e.g.*, LHb_A or LHb_D) could be used. For instance, LHb_A would have been used for applications where cost was a concern (EX1019 (Proulx), 1521 (LHb_D “adds higher cost”)), while LHb_D would have been used where greater control over the amount of heme iron being added was required.¹⁷

412. A POSITA would have had a reasonable expectation of success because Proulx provides detailed teachings on the process used for isolating the soy leghemoglobin from the soy nodules (*see id.*, 1519). Moreover, adding the isolated soy leghemoglobin to a meaty flavoring composition would have involved nothing more than conventional techniques (*e.g.*, mixing as described above).

¹⁷ A POSITA would have understood that isolated preparations provide greater certainty as to the contents of the preparation and amount of the ingredient-at-issue being added.

413. In addition to providing an improved nutritional profile, a POSITA would have also been motivated to add Proulx's soy leghemoglobin to Giacino's meaty flavoring compositions to provide enhanced meat flavor and aroma as taught by Conrad. Conrad discloses that "[t]he addition of blood/hemoglobin further gives a desired taste improvement as it *improves the meat flavour* of the final product." EX1013(Conrad), 4:14-16. Conrad further teaches that hemoglobin can be isolated from blood before being added to the product. *Id.*, 4:7-9 ("[P]referably the hemoglobin part separated off from blood, the protein content of which is about 90% by weight"). In view of Conrad's teachings, a POSITA would have been motivated to add Proulx's leghemoglobin (which contains heme iron) to Giacino's meaty flavoring compositions to enhance their "meat flavour." A POSITA would have also had a reasonable expectation of success of combining Conrad's teachings with Giacino and Proulx. *See supra* Section XIV.C.

414. Accordingly, the combination of Giacino, Proulx, and Conrad renders obvious a food flavor additive composition comprising an isolated heme-containing protein.

3. **1[b]: b) a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose,**

maltodextrin, and galactose, and mixtures of two or more thereof; and

1[c]: c) a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof;

415. As I explained above, Giacino discloses limitations 1[b] and 1[c]. *See supra* Section XII.D.3.

4. 1[d]: wherein the flavor additive composition contains no animal products; and

416. As I explained above, Giacino's meaty flavoring compositions satisfy this limitation. *See supra* Section XII.D.4.

417. Moreover, soy leghemoglobin is derived from soy root nodules and does not contain animal products. Hence, the addition of soy leghemoglobin maintains the no-animal product status of Giacino's compositions.

418. Accordingly, the Giacino, Proulx, and Conrad also satisfy this limitation.

5. 1[e]: wherein cooking the food flavor additive composition results in the production of at least two volatile compounds which have a meat-associated aroma.

419. Giacino, Proulx, and Conrad render this limitation obvious.

420. As I explained above, heating/cooking Giacino's meaty flavoring compositions produce at least two volatile compounds having a meat-associated aroma. *See supra* Section XII.D.5.

421. A POSITA would have understood that adding heme-containing protein (*e.g.*, soy leghemoglobin) to Giacino's flavoring compositions would only further contribute to the desirable aroma produced since Conrad teaches that heme-containing protein, such as hemoglobin, enhances the "meat flavour" of the composition. Notwithstanding the beneficial contributions of the heme-containing protein, however, as I explained above a POSITA would have understood that at the very least the reactions between the sulfur compounds (thiamine, cysteine) and reducing sugars (ribose) present in Giacino's compositions would have produced at least two volatile compounds having a meaty aroma.

422. Hence, Giacino, Proulx, and Conrad render obvious limitation 1[e].

E. **Claims 2 and 15**

423. In my opinion, Giacino, Proulx, and Conrad render obvious the limitation "[t]he food flavor additive composition of claim [1/10], wherein the heme-containing protein is selected from the group consisting of a[n] androglobin, a cytoglobin, a globin E, a globin X, a globin Y, a hemoglobin, a myoglobin, a **leghemoglobin**, an erythrocrucorin, a beta hemoglobin, an alpha hemoglobin, a protoglobin, a cyanoglobin, a cytoglobin, a histaglobin, a neuroglobins, a chlorocruorin, a truncated hemoglobin, a truncated 2/2 globin, and a hemoglobin 3."

424. As discussed above, a POSITA would have added soy leghemoglobin to Giacino's meaty flavoring compositions. *See supra* Section XIV.D.2.

Leghemoglobin is one of the elements identified in the group of heme-containing proteins for claims 2 and 15.

F. Claims 3 and 16

425. In my opinion, Giacino, Proulx, and Conrad render obvious the limitation “[t]he food flavor additive composition of claim [1/10], wherein the heme-containing protein comprises amino acid sequence having at least 80% sequence identity to a polypeptide set forth in SEQ ID NOs: 1-26.” The ’096 patent identifies the polypeptide of SEQ ID NO 4 as that of *Glycine max* leghemoglobin (*i.e.*, soy leghemoglobin). EX1001, 10:23-24, col. 43, FIG. 1.

426. As discussed above, a POSITA would have added soy leghemoglobin (same polypeptide as SEQ ID NO 4) to Giacino’s meaty flavoring compositions. *See supra* Section XIV.D.2. Hence, the Giacino, Proulx, and Conrad render claims 3 and 16 obvious.

G. Claims 4 and 24

427. As I explained above, Giacino discloses claims 4 and 24. *See supra* Section XII.G.

H. Claim 5

428. In my opinion, Giacino, Proulx, and Conrad render obvious the limitation “[t]he food flavor additive composition of claim 1, wherein the heme-containing protein is a plant, a yeast or filamentous fungi, or bacterial heme-containing protein.”

429. As discussed above, a POSITA would have been motivated to add soy leghemoglobin to Giacino's meaty flavoring compositions. *See supra* Section XIV.D.2. Soy leghemoglobin is a plant heme-containing protein.

I. Claims 6 and 22

430. As discussed above, Giacino discloses claims 6 and 22. *See supra* Section XII.I.

J. Claim 7

431. As discussed above, Giacino discloses claim 7. *See supra* Section XII.J.

K. Claims 8 and 17

432. In my opinion, the combination of Giacino, Proulx, Conrad, and Perret render obvious claims 8 and 17 for the same reasons that Giacino, Conrad, Crane, and Perret render these claims obvious. Namely, a POSITA would have been motivated to add Perret's safflower oil as the edible oil vehicle/medium for Giacino's compositions. *See supra* Section XIII.K.

L. Claims 9 and 22

433. As discussed above, Giacino discloses claims 9 and 22. *See supra* Section XII.L.

M. Claim 10

434. In my opinion, Giacino, Proulx, and Conrad render obvious claim 10.

1. 10[pre]: A food flavor additive composition prepared by a process of:

435. Giacino discloses a food flavor additive composition. *See supra* Section XII.D.1.

2. 10[a]: a) combining an isolated heme-containing protein;

436. As discussed above, the combination of Giacino, Proulx, and Conrad renders obvious a food flavor additive composition comprising an isolated heme-containing protein (*e.g.*, soy leghemoglobin). *See supra* Section XIV.D.2.

3. 10[b]: a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose and galactose, and mixtures of two or more thereof; and

10[c]: a compound selected from cysteine, cystine, thiamine, methionine, and mixtures of two or more thereof, to form a heme flavor reaction mixture, and

437. As discussed above, Giacino discloses a compound selected from glucose, ribose, fructose, lactose, xylose, arabinose, glucose-6-phosphate, maltose and galactose and a compound selected from cysteine, cystine, thiamine, and methionine. *See supra* Section XII.D.3. The mixture of Proulx's soy leghemoglobin and Giacino's taurine, thiamine, cysteine, and ribose, and other ingredients in the flavoring composition, constitute the "heme flavor reaction mixture."

4. **10[d]: b) heating the heme flavor reaction mixture to at least 150° C. for at least 1 minute to result in the food flavor additive composition;**

438. The same reasons for why Giacino discloses this limitation for the combination of Giacino and Brown is equally applicable here for the combination of Giacino, Proulx, and Conrad. *See supra* Section XII.M.4.

5. **10[e]: wherein the food flavoring additive composition contains no animal products; and**

439. As discussed above, Giacino's meaty flavoring compositions modified to include soy leghemoglobin do not contain any animal products. *See supra* Sections XII.D.4, XIV.D.4.

6. **10[f]: wherein the heme flavor reaction mixture has a meaty flavor and/or meaty aroma during the heating of step b) and the food flavoring additive composition has a meaty flavor and/or meaty aroma after the heating of step b).**

440. As explained above, a POSITA would have understood that heating Giacino's modified meaty flavoring compositions, which include, *inter alia*, sulfur compounds (*e.g.*, thiamine and cysteine), reducing sugars (*e.g.*, ribose), and soy leghemoglobin, would induce different reactions including, a Maillard reaction, that would produce many different volatiles associated with a meaty aroma and flavor. *See supra* Sections XII.D.5, XIV.D.5.

441. A POSITA would recognize that these volatiles are produced during the heating step. *See* EX1015(Giacino), 2:5-8. Moreover, a POSITA would understand that the volatiles that were produced during the heating step remain

present after the heating step completes. For example, it is common knowledge that foods, such as a freshly cooked piece of meat, give off aromas after the cooking process completes.

442. Hence, Giacino, Proulx, and Conrad render obvious limitation 10[f].

N. **Claim 11**

443. In my opinion, Giacino, Proulx, and Conrad render obvious the limitation “[t]he food flavor additive composition of claim 10, wherein the food flavoring additive composition further comprises a compound selected from the group consisting of 2-methyl-furan, bis(2-methyl-3-furyl)disulfide, 2-pentyl-furan, 3,3'-dithiobis-2-methyl-furan, **2,5-dimethyl-pyrazine**, 2-methyl-3-furanthiol, bis(2-methyl-4,5-dihydro-3-furyl) disulfide, dihydro-3-(2H)-thiophenone, 5-methyl-2-thiophenecarboxaldehyde, 3-methyl-2-thiophenecarboxaldehyde, **2-methyl-thiazole**, dimethyl sulfide, decanal, 5-ethyl-dihydro-2(3H)-furanone, dihydro-5-pentyl-2(3H)-furanone, 2-octanone, 3,5-octadien-2-one, p-Cresol, and hexanoic acid.”

444. As I discussed above, a POSITA would have understood that heating Giacino’s modified meaty flavoring compositions, which include, thiamine, cysteine, ribose, and soy leghemoglobin, would produce a number of volatile compounds having a meaty flavor and aroma. *See supra* Sections XIV.D.5, XIV.M.6. In particular, a POSITA would have recognized that heating cysteine with ribose would result in the production of at least, among other volatile compounds,

2,5-dimethylpyrazine and **2-methyl-thiazole** (both recited in claim 11, see above).

See, e.g., EX1024(MacLeod), 384 Table 14 (identifying 2,5-dimethylpyrazine as volatile compound when cysteine and glucose react), 385, Table 15 (identifying 2-methyl-thiazole and 2,5-dimethylpyrazine as volatile compounds when cysteine and ribose react). A POSITA would have understood that these two compounds are well known to be associated with a meaty aroma/flavor. *See, e.g.*, EX1024(MacLeod), 344, Table 1 (identifying 2,5-dimethylpyrazine as contributing to “natural beef aroma”), 351, Table 1 cont. (identifying 2-methyl-thiazole as contributing to “natural beef aroma”); EX1026(Dwivedi), 492, Table 1 (2-methylthiazole), 493, Table 1 cont. (2,5-dimethylpyrazine).

445. Accordingly, Giacino, Proulx, and Conrad render obvious claim 11.

O. Claim 12

446. In my opinion, Giacino, Proulx, and Conrad render obvious the limitation “[t]he food flavor additive composition of claim 11, wherein the compound is detectable in the headspace above the heme flavor reaction mixture during the heating of step b) or in the headspace above the food flavoring additive composition after the heating of step b).”

447. As discussed above, a POSITA would understand that heating Giacino’s meaty flavoring composition would release a variety of volatile compounds associated with a meaty flavor and/or aroma. *See supra* Sections

XIV.D.5, XIV.M.6, XIV.N. A POSITA would understand that these volatiles are released (and therefore would be detectable) during and after the heating process in the volume of air above (*e.g.*, headspace) the meaty flavoring composition.

448. Accordingly, Giacino, Proulx, and Conrad render obvious claim 12.

P. Claim 14

449. In my opinion, Giacino, Proulx, and Conrad render obvious the limitation “[t]he food flavor additive composition of claim 10, wherein the heme-containing protein is present in an amount between about 0.01% and about 5% by weight in the heme flavor reaction mixture.”

450. As I explained above, in view of Proulx’s and Conrad’s teachings, a POSITA would have modified Giacino’s meaty flavoring composition by adding soy leghemoglobin. *See supra* Section XIV.D.2. As to the amount of soy leghemoglobin added, as I discussed elsewhere in my declaration, a POSITA would have turned to Conrad’s teachings concerning the concentration of heme-containing protein to include in Giacino’s meaty flavoring composition, which are within or at least overlap with the claimed 0.01%-5% by weight range. *See supra* Section XIII.P. The same arguments equally apply here as to the amount of soy leghemoglobin a POSITA would have been motivated to add to Giacino’s flavoring compositions.

Q. Claims 18 and 19

451. In my opinion, the combination of Giacino, Proulx, Conrad, and MacLeod render obvious claims 18 and 19 for the same reasons that Giacino, Conrad, Crane, and MacLeod render these claims obvious. *See supra* Sections XIII.Q, XIII.R.

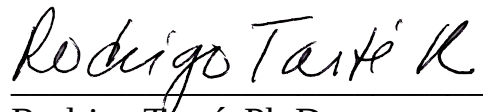
R. Claims 20, 21, 23

452. As discussed above, Giacino discloses claims 20, 21, and 23. *See supra* Sections XII.S, XII.T.

XV. CONCLUSION

453. In signing this Declaration, I recognize that the Declaration will be filed as evidence in a contested case before the Patent Trial and Appeal Board of the United States Patent and Trademark Office. I also recognize that I may be subject to cross-examination in the case and that cross-examination will take place within the United States. If cross-examination is required of me, I will appear for cross-examination within the United States during the time allotted for cross-examination.

454. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on the 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 of Title 18 of the United States Code.


Rodrigo Tarté, Ph.D.

Dec. 7, 2022

Date