

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NATIONAL BEEF PACKING COMPANY, LLC
Petitioner

v.

INSTITUTE FOR ENVIRONMENTAL HEALTH, INC.
Patent Owner

IPR2024-01156
Patent 9,845,486

PETITION FOR *INTER PARTES* REVIEW

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Other Authorities

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PETITIONER’S EXHIBIT LIST

Ex.	Description
1001	U.S. Patent No. 9,845,486 B2 (“the ’486 Patent”) to Samadpour, titled “Enrichment Methods for the Detection of Pathogens and Other Microbes”
1002	Complaint for Patent Infringement, <i>Inst. for Env’tl. Health, Inc. v. Nat’l Beef Packing Co., LLC</i> , No. 1:23-cv-00826 (D. Del. Aug. 1, 2023)
1003	Prosecution History for U.S. Provisional Patent Appl. No. 60/470,975
1004	U.S. Patent No. 7,531,163 B2 (“the ’163 Patent”) to Samadpour, titled “Enrichment Methods for the Detection of Pathogens and Other Microbes”
1005	Prosecution History for U.S. Patent Appl. No. 10/848,253, which issued as the ’163 Patent
1006	Prosecution History for U.S. Patent Appl. No. 12/360,646, which issued as the ’486 Patent
1007	U.S. Patent No. 10,724,068 B2 (“the ’068 Patent”) to Samadpour, titled “Enrichment Methods for the Detection of Pathogens and Other Microbes”
1008	Prosecution History for U.S. Patent Appl. No. 15/844,407, which issued as the ’068 Patent
1009	Judith M. Anderson & A.C. Baird-Parker, “A Rapid and Direct Plate Method for Enumerating <i>Escherichia Coli</i> biotype I in Food,” J. Appl. Bact., vol. 39, no. 2, pages 111-117 (October 1975) (“Anderson”)
1010	M. K. Rayman et al., “ICMSF methods studies. XIII. An international comparative study of the MPN procedure and the Anderson–Baird-Parker direct plating method for the enumeration of <i>Escherichia coli</i> biotype I in raw meats,” Can. J. Microbiol., vol. 25, no. 11, pages 1321-1327 (November 1979) (“Rayman”)

1011	“An Evaluation of the Role of Microbiological Criteria for Foods and Food Ingredients,” U.S. National Research Council, Food Protection Committee, Subcommittee on Microbiological Criteria, National Academy Press, Appendix (1985) (“NRC”)
1012	European Patent Application Publication No. EP 1,253,203 A1 to Nagar et al., which was published on October 30, 2002 (“Nagar”)
1013	“Microorganisms in Foods 2: Sampling for Microbiological Analysis: Principles and Specific Applications,” Int’l Comm’n on Microbiological Spec’s for Foods (ICMSF), Univ. Toronto Press, Chapters 2-4, 6, 9, 11-13, 15, 16, 24, Glossary (2nd ed. 1986) (“ICMSF 1986”) or (“ICMSF 2”)
1014	“Microorganisms in Foods 7: Microbiological Testing in Food Safety Management,” Int’l Comm’n on Microbiological Spec’s for Foods, Kluwer Academic/Plenum Publishers, Chapters 6, 10, 12, 15–17 (2002) (“ICMSF 2002”), (“ICMSF 7”), or (“ICMSF”)
1015	International Publication No. WO 94/21816 to Hird et al., which was published on September 29, 1994 (“Hird”)
1016	International Publication No. WO 01/12853 A1 to Karlsen, which was published on February 22, 2001 (“Karlsen”)
1017	Pathogen Reduction; Hazard Analysis and Critical Control Point (HACCP) Systems; Final Rule, 61 Fed. Reg. 38805 (July 25, 1996) (codified at 9 CFR Part 304, et al.) (“PR/HACCP”) or (“MegaReg”)
1018	U.S. Food & Drug Admin., “Bacteriological Analytical Manual,” Table of Contents, Introduction, About the Bacteriological Analytical Manual, Chapters 1, 4, 4A, 5, 10, Appendix 1 (April 2003) (“BAM 2003”)
1019	U.S. Dept. of Agric. Food Safety and Inspection Service (FSIS), “Microbiology Laboratory Guidebook,” Table of Contents, Cover, Foreword, General Considerations, Chapters 4, 5.03, 8.03 (April 2003) (“MLG 2003”) or (“MLG”)
1020	Expert Declaration of James S. Dickson, Ph.D.
1021	Curriculum Vitae of James S. Dickson, Ph.D.

1022	Expert Declaration of James L. Mullins, Ph.D. (“Mullins Decl.”)
1023	Mullins Decl. Appendix A - Curriculum Vitae of James L. Mullins, Ph.D.
1024	Mullins Decl. Appendices A-1, A-2, A-3, and A-4
1025	Mullins Decl. Appendices B-1, B-2, B-3, and B-4
1026	Mullins Decl. Appendices C-1, C-2, C-3, and C-4
1027	Mullins Decl. Appendices D-1, D-2, and D-3
1028	Mullins Decl. Appendices E-1, E-2, E-3, and E-4
1029	Mullins Decl. Appendices F-1, F-2, F-3, F-4, and F-5
1030	Mullins Decl. Appendices G-1, G-2, G-3, G-4, and G-5
1031	Federal Court Management Statistics, District of Delaware (Reporting Period End Date: Dec. 31, 2023), available at https://www.uscourts.gov/statistics/table/na/federal-court-management-statistics/2023/12/31-1 , (last visited June 19, 2024)
1032	Declaration of Kevin B. Laurence
1033	Proposed Scheduling Order, <i>Inst. for Env'tl. Health, Inc. v. Nat'l Beef Packing Co., LLC</i> , No. 1:23-cv-00826 (D. Del. May 16, 2024)
1034	Robert O. Elder et al., “Correlation of enterohemorrhagic <i>Escherichia coli</i> O157 prevalence in feces, hides, and carcasses of beef cattle during processing,” <i>Proc. Natl. Acad. Sci.</i> , vol. 97, no. 7, pages 2999-3003 (March 2000) (“Elder”)

CLAIMS LISTING

Claim 1 of the '486 Patent	
Preamble	A method for detection of a particular bacterial pathogen or bacterial microbe, comprising:
First Step	obtaining a test sample, the sample being solid or semi-solid;
Second Step	diluting the sample with liquid enrichment medium at a ratio of sample to diluent between about 1:0.1 to about 1:5 (wt./vol.) or lesser dilution;
Third Step	incubating, in an incubator, the diluted sample at an optimal temperature for the particular bacterial pathogen or bacterial microbe to be detected for a time period sufficient to allow levels of the particular bacterial pathogen or microbe to reach levels detectable by use of an assay suitable to detect the particular bacterial pathogen or bacterial microbe; and
Fourth Step	determining, by assaying the diluted incubated test sample, or a portion thereof, with the assay suitable to detect the particular bacterial pathogen or bacterial microbe, whether the sample is contaminated with the particular bacterial pathogen or bacterial microbe.

Claims Depending from Claim 1 of the '486 Patent	
2	The method of claim 1, wherein diluting is at a ratio of sample to diluent between about 1:0.1 to about 1:0.5 (wt./vol.) or lesser dilution.
3	The method of claim 1, wherein diluting is at a ratio of sample to diluent between about 1:0.1 to about 1:0.3 (wt./vol.) or lesser dilution.
4	The method of claim 1, wherein the optimal temperature is within the optimal growth temperature range of the particular bacterial pathogen or bacterial microbe in the liquid enrichment medium.

Claims Depending from Claim 1 of the '486 Patent — cont'd	
5	The method of claim 4, wherein the optimal temperature range is from about 25° C. to about 45° C.
6	The method of claim 1, wherein the assay suitable for detection of the particular bacterial pathogen or bacterial microbe contamination is selected from the assay group consisting of immunoassays, nucleic acid amplification-based assays, PCR-based assays, nucleic acid hybridization-based assays, bio-sensor assays, immunostaining-microscopy-based assays, nucleic acid-array-based assays, DNA chip-based assays, classical microbiology-based assays, and chemical or biochemical assays based on the detection of compounds associated with the particular bacterial pathogen or bacterial microbe, and combinations thereof.
7	The method of claim 1, wherein the particular bacterial pathogen or bacterial microbe is selected from the group consisting of <i>Escherichia coli</i> O157:H7 (<i>E. coli</i> O157:H7), enterohemorrhagic <i>Escherichia coli</i> (EHEC), enterotoxigenic <i>Escherichia coli</i> (ETEC), enteroinvasive <i>Escherichia coli</i> (EIEC), enteropathogenic <i>Escherichia coli</i> (EPEC), <i>Salmonella</i> , <i>Listeria</i> , <i>Yersinis</i> , <i>Campylobacter</i> , <i>Clostridial</i> species, <i>Staphylococcus</i> spp.; frank and opportunistic bacteria, indicator organisms including heterotrophes, generic <i>E. Coli</i> , total and fecal coliforms and enterococcus; spoilage organisms including <i>Pseudomonas</i> , and combinations thereof.
8	The method of claim 7, wherein the particular bacterial pathogen or bacterial microbe is <i>Escherichia coli</i> O157:H7 (<i>E. coli</i> O157:H7, or H negative), <i>Salmonella</i> , <i>Listeria</i> , EHEC, and <i>Campylobacter</i> .
9	The method of claim 1, wherein obtaining a sample is obtaining a standard Lot-unit sample.
10	The method of claim 1, wherein the sample is a composite-Lot sample, corresponding to a combination of samples selected from the group consisting of samples or subsamples taken from sublots/lots of raw or processed samples, environmental samples, industrial samples, pharmaceutical samples, bio-solid samples, samples taken by spore traps, settled dust, impingers, or filtration, and combinations thereof.

Claims Depending from Claim 1 of the '486 Patent — cont'd	
17	The method of claim 1, where in the sample is selected from the group consisting of beef, pork, sheep, bison, deer, elk, poultry, fish, produce, dairy products, dry goods, raw and processed foods, environmental samples, soil, sludge, surface samples, samples taken by impingers and filtration, pharmaceuticals, and samples analyzed using enrichment-detection protocols.
19	The method of claim 1, wherein the diluting comprises addition to the sample of a supplement selected from the group consisting of water, sugars, proteins, minerals, organics, vitamins and cofactors, antibiotics, dyes, indicators, buffers, agents to adjust the pH, water activity, nutritional contents, selective pressure to optimize the growth conditions for the particular bacterial pathogen or bacterial microbe, and combinations thereof.
21	The method of claim 1, wherein the obtaining and diluting of the solid or semi-solid sample with liquid enrichment medium is at a first location, wherein incubating the diluted sample at an optimal temperature in the incubator is during transit of the diluted sample to a second location that is not the site of sample collection and dilution, and wherein determining by assaying the diluted incubated test sample, or a portion thereof, with the assay suitable to detect the particular bacterial pathogen or bacterial microbe, whether the sample is contaminated with the particular bacterial pathogen or bacterial microbe, is at the second location.
22	The method of claim 21, further comprising addition to the sample, prior to or during incubation, of a supplement selected from the group consisting of water, sugars, proteins, minerals, organics, vitamins and cofactors, antibiotics, dyes, indicators, buffers, agents to adjust the pH, water activity, nutritional contents, selective pressure to optimize the growth conditions for the particular bacterial pathogen or bacterial microbe, and combinations thereof.
23	The method of claim 21, wherein the second location is an in-house or local lab, or a remote location.

Claims Depending from Claim 1 of the '486 Patent — cont'd	
27	The method of claim 1, wherein diluting is at a ratio of sample to diluent between about 1:0.1 to about 1:2 (wt./vol.) or lesser dilution.

Claim 11 of the '486 Patent	
Preamble	A method for detection of a particular bacterial pathogen or bacterial microbe, comprising:
First Step	obtaining a liquid sample;
Second Step	diluting the sample with liquid enrichment medium at a ratio of sample to diluent between about 1:0.1 to about 1:5 (vol./vol.) or lesser dilution, or not diluting the sample;
Third Step	incubating, in an incubator, the diluted or the not diluted sample at an optimal temperature for the particular bacterial pathogen or bacterial microbe to be detected for a time period sufficient to allow levels of the particular bacterial pathogen or bacterial microbe to reach levels detectable by use of an assay suitable to detect the particular bacterial pathogen or bacterial microbe; and
Fourth Step	determining, by assaying the diluted or the not diluted incubated test sample, or a portion thereof, with the assay suitable to detect the particular bacterial pathogen or bacterial microbe, whether the sample is contaminated with the particular bacterial pathogen or bacterial microbe.

Claims Depending from Claim 11 of the '486 Patent	
12	The method of claim 11, wherein the optimal temperature is within the optimal growth temperature range of the particular bacterial pathogen or bacterial microbe in the liquid enrichment medium.

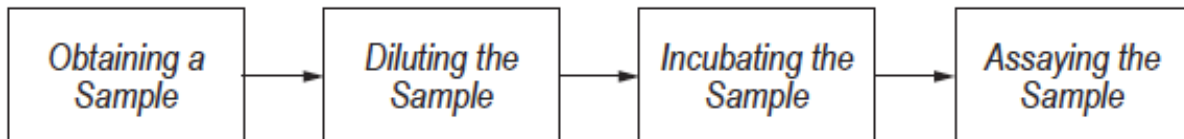
Claims Depending from Claim 11 of the '486 Patent — cont'd	
13	The method of claim 12, wherein the optimal temperature range is from about 25° C. to about 45° C.
14	The method of claim 11, wherein the assay suitable for detection of the particular bacterial pathogen or bacterial microbe contamination is selected from the assay group consisting of immunoassays, nucleic acid amplification-based assays, PCR-based assays, nucleic acid hybridization-based assays, bio-sensor assays, immunostaining-microscopy-based assays, nucleic acid-array-based assays, DNA chip-based assays, classical microbiology-based assays, and chemical or biochemical assays based on the detection of compounds associated with the particular bacterial pathogen or bacterial microbe, and combinations thereof.
15	The method of claim 11, wherein the particular bacterial pathogen or bacterial microbe is selected from the group consisting of <i>Escherichia coli</i> O157:H7 (<i>E. coli</i> O157:H7), enterohemorrhagic <i>Escherichia coli</i> (EHEC), enterotoxigenic <i>Escherichia coli</i> (ETEC), enteroinvasive <i>Escherichia coli</i> (EIEC), enteropathogenic <i>Escherichia coli</i> (EPEC), <i>Salmonella</i> , <i>Listeria</i> , <i>Yersinia</i> , <i>Campylobacter</i> , <i>Clostridial</i> species, <i>Staphylococcus</i> spp.; frank and opportunistic bacteria, indicator organisms including heterotrophes, generic <i>E. Coli</i> , total and fecal coliforms and enterococcus; spoilage organisms including <i>Pseudomonas</i> , and combinations thereof.
16	The method of claim 15, wherein the particular bacterial pathogen or bacterial microbe is <i>Escherichia coli</i> O157:H7 (<i>E. coli</i> O157:H7, or H negative), <i>Salmonella</i> , <i>Listeria</i> , EHEC, and <i>Campylobacter</i> .
18	The method of claim 11, where in the sample is selected from the group consisting of beef, pork, sheep, bison, deer, elk, poultry, fish, produce, dairy products, dry goods, raw and processed foods, environmental samples, soil, sludge, surface samples, samples taken by impingers and filtration, pharmaceuticals, and samples analyzed using enrichment-detection protocols.

Claims Depending from Claim 11 of the '486 Patent — cont'd	
20	The method of claim 11, wherein the diluting comprises addition to the sample of a supplement selected from the group consisting of water, sugars, proteins, minerals, organics, vitamins and cofactors, antibiotics, dyes, indicators, buffers, agents to adjust the pH, water activity, nutritional contents, selective pressure to optimize the growth conditions for the particular bacterial pathogen or bacterial microbe, and combinations thereof.
24	The method of claim 11, wherein the obtaining and diluting of the liquid sample with liquid enrichment medium is at a first location, wherein incubating the diluted sample at an optimal temperature in the incubator is during transit of the diluted sample to a second location that is not the site of sample collection and dilution, and wherein determining by assaying the diluted incubated test sample, or a portion thereof, with the assay suitable to detect the particular bacterial pathogen or bacterial microbe, whether the sample is contaminated with the particular bacterial pathogen or bacterial microbe, is at the second location.
25	The method of claim 24, further comprising addition to the sample, prior to or during incubation, of a supplement selected from the group consisting of water, sugars, proteins, minerals, organics, vitamins and cofactors, antibiotics, dyes, indicators, buffers, agents to adjust the pH, water activity, nutritional contents, selective pressure to optimize the growth conditions for the particular bacterial pathogen or bacterial microbe, and combinations thereof.
26	The method of claim 24, wherein the second location is an in-house or local lab, or a remote location.
28	The method of claim 11, wherein diluting is at a ratio of sample to diluent between about 1:0.1 to about 1:2 (vol./vol.) or lesser dilution.
29	The method of claim 11, wherein diluting is at a ratio of sample to diluent between about 1:0.1 to about 1:0.5 (vol./vol.) or lesser dilution.
30	The method of claim 11, wherein diluting is at a ratio of sample to diluent between about 1:0.1 to about 1:0.3 (vol./vol.) or lesser dilution.

I. INTRODUCTION

National Beef Packing Company, LLC (“National Beef” or “Petitioner”) requests *inter partes* review (IPR) of claims 1–30 (the “Challenged Claims”) of Patent No. 9,845,486 (“the ’486 Patent”) owned by the Institute for Environmental Health, Inc. (“IEH”).

The ’486 Patent relates to methods for detecting microorganisms in samples, such as meat, at particular dilution ratios. Ex. 1001, Abstract. The ’486 Patent has two independent claims, which each recite four steps, as depicted below.



As summarized in the Background section of the ’486 Patent, it was well known to obtain a sample, dilute the sample with liquid enrichment medium, incubate the sample to enable a particular pathogen or microbe to grow to detectable levels, and then assay the sample to determine whether the sample is contaminated with the particular pathogen or microbe. *See id.*, 2:14–48 (describes sampling, diluting, incubating, and assaying beef and citrus juices for *E. coli*). *See* § IV-B *infra*.

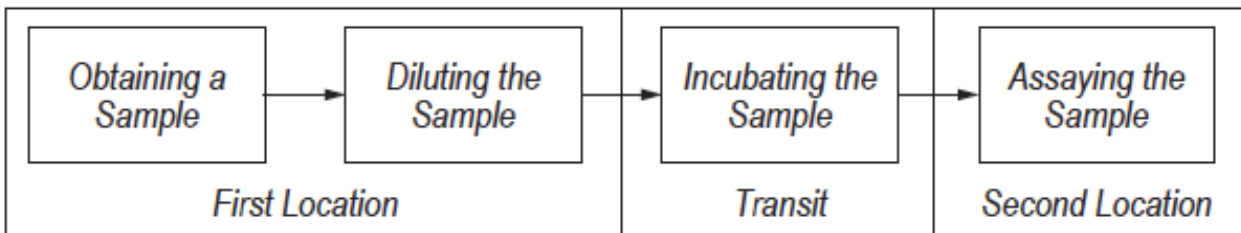
The Background section focuses on examples related to the second step, the diluting step. These examples describe enriching samples using a 1:10 dilution, which is a ratio of sample to diluent of 1:9 (weight/volume) or (volume/volume)

commonly referred to as decimal dilution. Ex. 1001, 1:58-5:34. The diluting step in the independent claims recites dilutions less than decimal dilution. The Examiner considered this recitation sufficiently different from the prior art for allowance of the claims. *See* § VII-B *infra*.

The two independent claims of the '486 Patent differ primarily in that the sample of the first independent claim is a solid or semi-solid sample, while the sample of the second independent claim is a liquid sample. The independent claims also differ because the second independent claim recites “diluting the sample . . . or not diluting the sample,” whereas the first independent claim requires at least some dilution.

It was known to dilute samples with a 1:5 dilution (i.e., a ratio of sample to diluent of 1:4) at least as early as 1975 as disclosed by Anderson. Ex. 1009, 113. Anderson’s method was later analyzed and compared by Rayman in 1979. Ex. 1010, 1322. Subsequently, the methods of Anderson and Rayman were summarized by the National Research Council (“NRC”) in 1985. Ex. 1011, 353. Rayman and other references that disclose even lower diluent volumes are relied on in this Petition. During prosecution of the application that yielded the '486 Patent, a single reference, the FDA’s Bacteriological Analytical Manual (“BAM”) was considered for its teaching of dilution even though it only discloses decimal dilution like the examples in the Background section.

The four steps recited in the independent claims are not limited to being done at specific locations. However, dependent claims 21–26 (“the Transportation Claims”) require that the obtaining and diluting steps occur at a first location, the incubating step occurs during transit to a second location, and that the assaying step occurs at the second location. These requirements are depicted in the diagram below.



Nagar discloses this same scheme for incubating a sample during transit from a first location to a second location. See §§ VIII-A-3, IX-C-1-g *infra*.

Because Rayman, Nagar, and other references have not been considered by the Office relative to the Challenged Claims, each ground presents new art and new arguments. See § X-B-1 *infra*.

A family tree is provided at § VI *infra*. A declaration from Professor James S. Dickson, Ph.D. (Ex. 1020, “Dickson”) supports this Petition.

II. IPR REQUIREMENTS

A. Standing

Petitioner is not barred or estopped from requesting IPR of the Challenged Claims on the grounds identified herein and certifies the '486 Patent is available for IPR.

B. Identification of Challenges Under 37 C.F.R. § 42.104(b)

Petitioner requests IPR of the Challenged Claims and cancellation of the same as unpatentable.

C. Art Relied on for Challenges

The publications relied upon for unpatentability grounds include:

Reference	Exhibit	Published
Rayman	1010	1979
PR/HACCP	1017	1996
Nagar	1012	2002
Karlsen	1016	2001
ICMSF	1014	2002

As explained at §§ VII-A and VII-B *infra*, the priority date for claims 11, 12, 20, 24-26 is the filing date of the Provisional Application No. 60/470,975 on May 16, 2003, while the priority date for the other claims is the filing date of Application No. 10/848,253 on May 17, 2004. However, each publication was prior art as of the

earliest priority date of May 16, 2003 under 35 U.S.C. § 102(b) (pre-AIA). Public availability of these references is established by the declaration of James L. Mullins, Ph.D. (Ex. 1022).

D. Statutory Grounds for Challenges

This Petition requests cancellation of the Challenged Claims as unpatentable based on the following grounds under 35 U.S.C. §§ 102 and 103.

Grounds 1–5				
Ground	References	§	Ind. Claims	Dependent Claims
1	Rayman	102	1	4–8, 17, and 19
2	Rayman and PR/HACCP	103		1, 11
3	Nagar and Rayman		4–8 and 12–26	
4	Nagar and Karlsen		4–8 and 12–28	
5	Nagar and PR/HACCP		2–8 and 12–30	

Grounds 6–7 for Dependent Claims Only			
Ground	References	§	Dep. Claims
6	Rayman and ICMSF	103	9 and 10
7	Rayman and AAPA		

III. TECHNOLOGY BACKGROUND

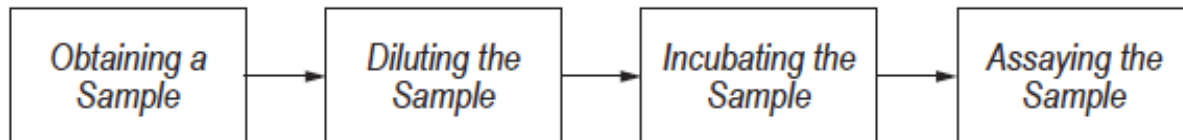
Professor Dickson summarizes developments leading to efficient and effective sampling, diluting, incubating, and assaying. Dickson ¶¶ 39–49.

IV. THE '486 PATENT

A. Independent Claims

The independent claims recite four steps as depicted in the diagram below.

Dickson ¶¶ 53–59.



In the first step, the **sampling** step, a sample is obtained that is recited as “solid or semi-solid” in claim 1 and as “liquid” in claim 11.

The second step, the **diluting** step, is recited in claim 1 as “diluting the sample with liquid enrichment medium at a ratio of sample to diluent between about 1:0.1 to about 1:5 (wt./vol.) or lesser dilution.” The term “lesser dilution” modifies the lower endpoint of the 1:0.1 ratio, as discussed in the analysis of the prosecution history. *See* § VII-B *infra*.

The second step is recited in claim 11 with two differences relative to claim 1. First, the ratio is recited with (vol./vol) since the sample and medium are both liquids. Second, claim 11 includes an alternative to diluting because claim 11 recites “or not diluting the sample.” Thus, the dilution recited in claim 11 is merely optional.

The third step, the **incubating** step, requires incubating in an incubator. Both independent claims further recite an “optimal temperature for the particular bacterial pathogen or bacterial microbe to be detected for a time period sufficient to allow levels of the particular bacterial pathogen or bacterial microbe to reach levels detectable by use of an assay suitable to detect the particular bacterial pathogen or bacterial microbe.” This functional recitation of time and temperature merely recites standard incubating conditions.

The fourth step, the **assaying** step, generically covers, in both independent claims, use of an “assay suitable to detect the particular bacterial pathogen or bacterial microbe, whether the sample is contaminated with the particular bacterial pathogen or bacterial microbe.”

B. AAPA

The '486 Patent includes applicant-admitted prior art (AAPA). More specifically, the '486 Patent states “[p]rior art methods, as summarized herein, under the ‘Background’ section, are based on 1:10 (wt./vol.) dilutions of the sample.” Ex. 1001, 8:24-25. Accordingly, the range of dilution ratios recited in the diluting step of the independent claims is the only aspect of the independent claims that IEH has not admitted is in the prior art. Dickson ¶ 50.

1. AAPA Re Steps of Independent Claim 1

The '486 Patent includes AAPA admitting that, with the exception of the claimed dilution ratio range, all the steps of independent claim 1 are in the prior art. For example, the '486 Patent discloses these steps in stating “[f]or the detection of *Escherichia coli* O157:H7 in food, **25 g of ground beef is incubated in 225 ml of selective enrichment medium** for 16 to 18 h at 37° C. with agitation **Enzyme-linked immunosorbent assay (ELISA) is used to detect the pathogen from the enriched culture.**” Ex. 1001, 2:10-42; *see also id.*, 1:58-2:9, 2:49-5:34, 13:54-14:32; Dickson ¶ 51.

2. AAPA Re Steps of Independent Claim 11

The '486 Patent includes AAPA admitting that, with the exception of the claimed dilution ratio range, all the steps of independent claim 11 are in the prior art. For example, the '486 Patent discloses these steps in stating:

Escherichia coli. The assay for the detection of *E. coli* in **citrus juices**, as described in the Bacteriological Analytical manual (BAM) (United States Food & Drug Administration, and Center for Food Safety & Applied Nutrition, Bacteriological Analytical Manual, Chapter 4, Enumeration of *Escherichia coli* and the Coliform Bacteria, September 2002), is carried out in duplicate. Basically, a **10-mL portion of juice** is aseptically

inoculated into **90 mL of Universal Pre-enrichment Broth** (UPEB) and **incubated** at 35° C. for 24 h. After enrichment, **the sample is mixed and 1 mL** is transferred from each UPEB enrichment broth into **9 mL of EC broth** containing a CC disc, and EC/CC broth tubes are **incubated** at 44.5° C. in a circulating water bath for 24 h. Preferably, positive (tube inoculated with a MUG (+) *E. coli* strain) and negative (tube inoculated with *K. pneumoniae*) controls are included. The tubes are checked in the dark and under long wave UV light. **The presence of blue fluorescence in either tube is indicative that *E. coli* is present in the sample.**

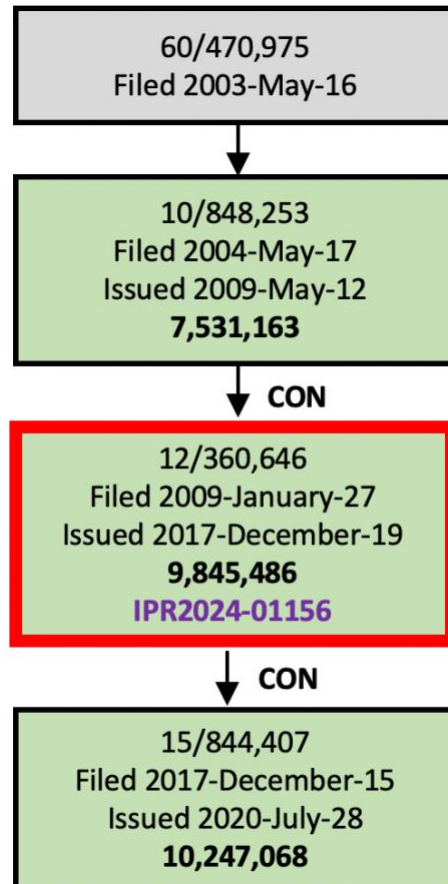
Ex. 1001, 2:10-32; *see also id.*, 1:58-2:9, 4:35-44; Dickson ¶ 52.

V. PERSON OF ORDINARY SKILL IN THE ART

A person of ordinary skill in the art (“POSA”) at the time of invention would have a working knowledge of microbiology and would have been involved in developing testing methodologies for analysis of samples such as food products (“validation methodologies”). The POSA would most likely have an advanced degree in microbiology, food science, or animal science and at least two years of work experience but may alternatively have a bachelor’s degree in those areas and at least four years of experience with validation methodologies. The POSA would have been familiar with relevant scientific literature and industry regulations, directives, and guidelines relating to validation methodologies. Dickson ¶¶ 22–24.

VI. FAMILY TREE

A family tree diagram below depicts the '486 Patent; its parent, No. 7,531,163 (“the ’163 Patent”); and its child, No. 10,247,068 (“the ’068 Patent”).



Dickson ¶¶ 80–81.

VII. PROSECUTION HISTORY OF THE '486 PATENT

A. Provisional Application No. 60/470,975

The '486 Patent claims priority to Provisional Application No. 60/470,975, which was filed on May 16, 2003. Ex. 1003, 1. No. 60/470,975 includes only two

paragraphs on a single page. *Id.*, 2. IEH’s method was disclosed as relying on a dry or semi-dry enrichment process, which “would allow for incubation of the food samples without the addition of enrichment media.” *Id.* Additionally, IEH states that liquid “samples can be enriched directly with or without a concentration step.” *Id.* That statement supports the limitation in independent claim 11 of the ’486 Patent that recites “or not diluting the sample.” However, the other claims of the ’486 Patent are not supported and thus priority for these claims cannot be claimed based on the provisional application.

The provisional application lacks any disclosure that supports the recitation in claim 1 of the ’486 Patent of “diluting the sample with liquid enrichment medium at a ratio of sample to diluent between about 1:0.1 to about 1:5 (wt./vol.) or lesser dilution.” Thus, priority cannot be claimed for claim 1 or its dependent claims, claims 2–10, 17, 19, 21–23, 27, 29, and 30. The same applies to the claims that depend from claim 11.

B. Application No. 10/848,253 Issued as Patent No. 7,531,163

Application No. 10/848,253 (“the ’253 Application”) was filed on May 17, 2004 and issued as the ’163 Patent on May 12, 2009. The ’163 Patent has three independent claims, claims 1, 12, and 22.

Claims 1 and 22 of the ’163 Patent, like claim 1 of ’486 Patent, are directed to samples that are solid or semi-solid. Ex. 1004, 20:32–48, 21:42–56. These

solid/semi-solid claims differ primarily in two respects. First, claims 1 and 22 of the '163 Patent more narrowly recite a dilution ratio of sample to diluent between “about 1:0.1 to about 1:2 (wt./vol.), or lesser dilution.” *Id.* Second, claims 1 and 22 of the '163 Patent, like dependent claim 21 of the '486 Patent, recite obtaining a test sample at a first location, incubating the sample in transit to a second location, and assaying the sample at the second location. *Id.*

Claim 12 of the '163 Patent is similar to claim 11 of the '486 Patent. Both claims are directed to liquid samples. *Id.*, 21:31–46. However, these independent claims differ from each other in the same way that the solid/semi-solid claims differ.

1. Summary of Prosecution History

The '253 Application was allowed over art disclosing decimal dilution. The '253 Application was pending for five years while the Examiner and IEH's patent attorney wrangled over claim terms. The most important change was replacing the term “greater ratio” with “lesser dilution” in the diluting step of each independent claim.

2. Details of Prosecution History

An Office Action issued on October 3, 2005. Ex. 1005, 169–176. The claims were rejected under 35 U.S.C. § 112 as indefinite including the independent claims based on the recitation of “a second location that is a remote test location.” *Id.*, 173.

The claims were also rejected under 35 U.S.C. § 103 as obvious based on U.S. Patent No. 6,060,266 to Naqui in view of the FDA's BAM, Chapters 4, 4a, 5-7, 9, and 10. *Id.*, 174-75. It is unclear from the prosecution history, which version of BAM, was used because it is not dated in the information disclosure statement. *Id.*, 246. The Examiner relied on Naqui for its teachings of a self-contained incubator for growth of microorganisms, which can be used "for concurrent shipment and incubation of a sample that may contain a microorganism" and "if it is used as a shipping container, upon arrival at a testing facility, the growth of the organism(s) is complete or nearly complete and the result can be rapidly detected by facility personnel." *Id.*, 175 (citing Naqui at 1:66–2:10). BAM was relied on for its teachings of the other limitations including its teachings for the ratio. *Id.*

A response was filed on April 3, 2005. *Id.*, 143–65. The first and second independent claims were amended to recite that the second remote location is "not the site of sample collection." *Id.*, 153, 155. Additionally, the independent claims were amended to recite a ratio of sample to diluent of between about 1:0.1 to about 1:2 (wt./vol.), or greater ratio. *Id.*, 153, 155, 157. IEH asserted patentability of the claims because BAM teaches decimal dilution. *Id.*, 163.

A final Office Action issued on June 9, 2006. *Id.*, 137–42. The rejection of the claims under 35 U.S.C. § 112 as indefinite was withdrawn. However, the rejection of the claims under 35 U.S.C. § 103 as obvious based on Naqui in view of

BAM was maintained because the recitation of “or greater ratio” after the listed ratio “also encompasses any ratio greater than the listed ratio.” *Id.*, 140.

A response was filed on June 16, 2006. *Id.*, 124–36. The claims were not substantively amended. *Id.*, 127–31. IEH argued “a ratio in the range of 1/0.1 (**10**) to 1/2 (**0.5**) is, in fact, a greater ratio, than, for example, 1/100 (0.01) or 1/1000 (**0.001**), because the quotients (i.e., “the number resulting from the division of one number by another’) is greater; namely a number in the range of **10** to **0.5** is greater than the number **0.01** or **0.001**.” *Id.*, 133–34 (emphasis in original). Based on this position, IEH asserted that the “recitation of ‘wherein diluting is at a ratio of 1:0.1 to about 1:2 (wt/vol.) or greater ratio’, **does not** encompass ratios taught by the art (e.g., 1/10, 1/100 or 1/1000).” *Id.*, 134 (emphasis in original). IEH further argued that BAM teaches away from the recited range based on its teaching that dilutions are 1:10. *Id.*

An Advisory Action was issued on August 1, 2006. *Id.*, 120–23. The Examiner indicated that “[r]elatively large dilutions (i.e., 1:10, as pervasively used in the art, and as explicitly taught in the BAM manual) are standard in the relevant art to provide for at least some expansion of the target microorganism.” *Id.*, 122. Thus, the Examiner concluded the recitation of “greater ratio” therefore “includes the ratios taught by the cited reference.” *Id.*

IEH filed a Request for Continued Examination with a response on December 11, 2006. *Id.*, 103–19. IEH repeated arguments about the recitation of “a greater ratio” and concluded that “a lesser dilution corresponds to a greater ratio.” *Id.*, 115. However, the claims were not substantively amended to reflect this position. *Id.*, 105–09. IEH also attacked Naqui and asserted it only teaches adding a liquid sample to a vessel, and then adding a solid growth medium to the aqueous samples. *Id.*, 112–13.

An Advisory Action issued on January 18, 2007. *Id.*, 98–102. The rejection under 35 U.S.C. § 103 was maintained. *Id.*, 100–01.

On July 18, 2007, IEH filed a Response and Amendment. *Id.*, 86–97. The independent claims were amended to replace “greater ratio” with “lesser dilution.” *Id.*, 87, 89, 91.

An Office Action issued on October 3, 2007. *Id.*, 81–85. The Examiner withdrew the rejection of the claims based on Naqui. *Id.*, 83. The claims were rejected under 35 U.S.C. § 112 as being indefinite. *Id.*, 83–85.

On October 29, 2007, a telephonic interview was held by IEH’s patent attorney and the Examiner. *Id.*, 79–80. They discussed the rejection of the claims as being indefinite. *Id.*, 80.

IEH filed an amendment on December 18, 2007. *Id.*, 65–76. IEH made minor amendments to the independent claims. *Id.*, 66–72. For example, the incubating step was modified to recite that the incubation occurred “for a particular pathogen or other microbe to be detected.” *Id.*, 67, 69, 71. IEH discussed the Examiner’s suggestions for revisions to the claims and the related amendments. *Id.*, 74–75.

An Office Action issued on March 21, 2008. *Id.*, 59–64. The rejection under 35 U.S.C. § 112 as being indefinite for a “particular” enrichment medium, was withdrawn. However, the rejection for indefiniteness for “optimal temperature” was maintained and a related rejection was made for additional claims that had an antecedent basis problem. *Id.*, 62–63.

IEH filed a Response and Amendment on May 21, 2008. *Id.*, 45–56. The dependent claims were amended to eliminate the antecedent basis problem. *Id.*, 46–51. However, the rejection of the dependent claims was maintained in an Office Action dated December 9, 2008. *Id.*, 22–25. The problematic dependent claims were cancelled in a Response and Amendment dated January 20, 2009. *Id.*, 11–19. A Notice of Allowance issued on March 6, 2009. *Id.*, 5–10.

C. Application No. 12/360,646 Issued as Patent No. 9,845,486

Application No. 12/360,646 (“the ’646 Application”) was filed on January 27, 2009 and issued as the ’486 Patent on December 19, 2017.

1. Summary of Prosecution History

Over the course of 15 years, IEH's patent attorney, Barry Davison, prosecuted three applications, including the '646 Application, its parent, and its child, which were examined by the same examiner, Examiner Swartz. During the entire prosecution of this patent family, only a single obviousness rejection was made based on Naqui and BAM, as summarized above regarding the '253 Application.

The '646 Application was pending for nearly nine years. At the end of the process, the independent claims differed little from their content as presented in a Preliminary Amendment. For the eight years after the filing of the Preliminary Amendment, the Examiner and IEH's patent attorney exchanged Office Actions and Responses that advanced prosecution in small steps without any changes to the claims that were especially substantive. During this slow-paced, incremental prosecution, no rejections were made based on prior art and the claims were only rejected under 35 U.S.C. § 112 as being indefinite, as provided below.

2. Details of Prosecution History

A Preliminary Amendment was filed on July 14, 2009. Ex. 1006, 255–66. The claims were revised to present two independent claims reciting that the “ratio of sample to diluent” was “substantially less than 1:10.”

An Office Action issued on December 17, 2010. *Id.*, 194–98. The independent claims were rejected under 35 U.S.C. § 112 as indefinite based on their recitation of a dilution ratio that is “substantially less” than 1:10.

A Response and Amendment was filed on June 17, 2011. *Id.*, 172–84. The first and second independent claims were amended to recite a ratio of sample to diluent of “between about 1:0.1 to about 1:5 (wt./vol.) or lesser dilution.” IEH asserted that the amendment overcame the rejection based on indefiniteness. *Id.*, 182, 183.

An Office Action issued on August 31, 2011. *Id.*, 162–66. The claims were allowed with the exception of a claim that depends from claim 1 and recited liquids, conflicting with the recitation in claim 1 of a “semi solid” sample. *Id.*, 164, 165.

A Response and Amendment was filed on February 6, 2012. *Id.*, 146–55. The dependent claim that was rejected was amended to remove liquid samples. *Id.*, 157. IEH asserted that the amendment overcame the rejection based on indefiniteness. *Id.*, 154, 155. An interview was held on February 6, 2012 between IEH’s patent attorney and the Examiner. *Id.*, 145. IEH filed a Terminal Disclaimer regarding the ’163 Patent. *Id.*, 155–59. A Request for Continued Examination was filed on February 29, 2012. *Id.*, 141–42.

An Office Action issued on November 14, 2012. *Id.*, 123–28. The claims were rejected under 35 U.S.C. § 112 as indefinite for omitting essential steps. *Id.*

A Response and Amendment was filed on April 15, 2013. *Id.*, 110–20. The independent claims were amended to add a recitation of incubating for “a time period sufficient to allow levels of the particular pathogen or other microbe to reach detectable levels.” *Id.*, 111, 113, 118, and 119.

An Office Action issued on August 15, 2013. *Id.*, 105–09. The claims were rejected under 35 U.S.C. § 112 as indefinite because the claims did not specify the length of the time period. *Id.*, 107. Also, the second independent claim was rejected under 35 U.S.C. § 112 as indefinite for reciting “not diluting the sample.” *Id.*, 108.

A Response and Amendment was filed on January 24, 2014. *Id.*, 92–102. The claims were amended to address numerous rejections based on indefiniteness raised in the Office Action. *Id.*

An Office Action issued on July 17, 2014. *Id.*, 83–88. The claims were rejected under 35 U.S.C. § 112 as indefinite based on the recited incubation temperature. *Id.*

A Response and Amendment was filed on January 20, 2015. *Id.*, 71–80. Minor amendments were made to the claims. *Id.*

An Office Action issued on May 13, 2015. *Id.*, 65–70. The claims were rejected under 35 U.S.C. § 112 as indefinite and for typographical errors. *Id.*

A Response and Amendment was filed on November 13, 2015. *Id.*, 52–62. Additional minor amendments were made to the claims to address indefiniteness rejections. *Id.*

An Office Action issued on March 3, 2016. *Id.*, 47–51. The claims were rejected under 35 U.S.C. § 112 as indefinite and for typographical errors. *Id.*, 49, 50.

A Response and Amendment was filed on September 2, 2016. *Id.*, 33–43. The second independent claim was amended so the numerator in the dilution ratio recited volume instead of weight. *Id.*, 36.

An Office Action issued on December 16, 2016. *Id.*, 28–32. The claims were allowed with the exception of claims with typographical errors. *Id.*, 30, 31.

IEH filed a Response and Amendment on June 15, 2017. *Id.*, 12–22. Dependent claims were amended to correct typographical errors. *Id.*, 21. A Notice of Allowance issued on September 5, 2017. *Id.*, 5–11.

D. Application No. 15/844,407 Issued as Patent No. 10,724,068

Appl. No. 15/844,407 (“the ’407 Application”) was filed on December 15, 2017 and issued as Patent No. 10,724,068 (“the ’068 Patent”) on July 28, 2020.

When the '407 Application was filed, it was accompanied by a Preliminary Amendment. Ex. 1008, 165–76. The claims were revised to present two independent claims, which recited that the “ratio of sample to diluent” was “between about 1:0.1 to about 1:9 (wt./vol.), or lesser dilution.” *Id.*, 167, 169. On April 30, 2019, a Notice of Non-Complaint Amendment was mailed. *Id.*, 139–43. A Response to the Notice was filed on September 19, 2019 to enter the necessary corrections. *Id.*, 106–37.

An Office Action issued on December 19, 2019. *Id.*, 48–59. The claims were objected to for informalities and were rejected under 35 U.S.C. § 112 as being indefinite. *Id.*, 51–54. Additionally, terminal disclaimers were required to overcome a nonstatutory double patenting rejection based on the '163 and '486 Patents. *Id.*, 54–55.

IEH filed a Response and Amendment on March 19, 2019. *Id.*, 23–40. Terminal Disclaimers were filed. *Id.*, 39, 43–47. Minor changes to the claims were made to correct typographical errors and to address indefiniteness rejections. *Id.*, 21. A Notice of Allowance issued on April 1, 2020. *Id.*, 6–15.

VIII. PRIOR ART

A. Ground References

1. Rayman

Rayman states “the present concern about the enumeration of fecal coliforms, or more specifically *Escherichia coli* in foods, is the length of time and the amount of media and analysts’ time required to complete the analyses.” Ex. 1010, 1322. One solution identified and tested by Rayman is “direct plating onto membranes overlying tryptone bile agar (Anderson and Baird-Parker 1975).” *Id.*

The technique disclosed by Anderson and Baird-Parker involved diluting samples of food “1 in 5 or 1 in 10 with 0.1% (w/v) peptone water” and then homogenizing. Ex. 1009, 113. Thus, Rayman tested “1.0-mL volumes of the 1:5 and 1:10 dilutions of solid samples.” Ex. 1010, 1322–23.

Rayman describes obtaining samples of meat including “raw red meats . . . and surface swabs of carcasses.” *Id.*, 1322. The solid samples were “weighed and homogenized in 4 parts (v/w) of 0.1% peptone water” yielding a “homogenate (1:5).” *Id.*

Rayman concluded that the direct plating method of Anderson and Baird-Parker was superior to other methods. Dickson ¶¶ 89–92.

NRC reported that:

By placing 1 ml of a 1:5 dilution of meat on duplicate filters a lower limit of detection of 2.5 cells per gram of meat could be reached (Rayman et al., 1979). With 1 ml of a 1:10 dilution, the lower limit of detection would be <10 per gram of food.

Ex. 1011, 353.

2. PR/HACCP

The USDA FSIS issued its landmark final rule, PR/HACCP, in 1996. Ex. 1017, 38805; *see also* Ex. 1034, 300 (citing to PR/HACCP as “standard protocols” for carcass sampling); Dickson ¶¶ 93–95. PR/HACCP requires routine microbiological testing of carcasses. *Id.*, 38806. PR/HACCP describe the sampling and testing procedures for beef, pork and poultry carcasses. *Id.*, 38835.

Prior to PR/HACCP, FSIS required excision samples for beef and pork carcasses, however this was changed to non-destructive swab (sponge) sampling. A 300 cm² sample (3, 10x10 cm samples with a single sponge) for beef or pork carcasses are considered representative of the carcass. *Id.*, 38931. Although excision samples could be reported as populations per gram of sample, the assay described in PR/HACCP is reported as population per cm². *Id.*, 38840. The beef or pork carcass sampling combines 300 cm² of sampled area with 25 mls of buffer, so that 1 ml of the buffer is equivalent to 12 cm² of the carcass surface. *Id.*, 38933. The assay method includes an option for further diluting the samples, but the

industry has often found that further dilution was unnecessary. *Id.*, 38933. Both excision and sponge sampling methods rely on the concept of transferring bacteria from a solid surface into a liquid medium for further analysis. *Id.*, 38943.

3. Nagar

Nagar is a published European patent application filed by Becton, Dickinson and Company. Dickson ¶¶ 96–100. Nagar discloses a method including the steps of:

placing a sample in a container containing a resuscitation/growth medium; optionally homogenizing the sample; placing a capture matrix in the sampling bag with the sample; incubating the sample in the resuscitation/growth medium for a pre-determined amount of time at an elevated temperature while optionally shaking; optionally removing the capture matrix from the container; performing detection assays to detect the presence of the target pathogens in the sample.

Ex. 1012, ¶ [0023].

Nagar’s method is used with a variety of samples including “ground beef, milk, cheese, vegetables, apple cider, etc.” *Id.*, ¶ [0036]. Moreover, Nagar’s method:

can also be used during transportation of a test sample (e.g., soil, etc.) from the collection site to the testing

laboratory. This may be achieved by placing the capture matrix inside a sampling/transportation device containing suitable resuscitation/growth medium, thus facilitating the capture, resuscitation and growth of the target pathogen for rapid detection.

Id., ¶ [0031].

4. Karlsen

Karlsen is an international patent application, WO 01/12853, filed by Nye Colifast AS. Dickson ¶¶ 101-03.

Karlsen discloses a method comprising:

(1) providing a liquid or liquified sample (which may include treating the sample with a culture media to enrich microorganisms present in the sample); (2) recovering microorganisms from the treated sample; . . . (7) detecting the presence of the amplicon . . . ; and (8) making a determination about the presence or absence of the microorganism in the original liquid or liquified sample based on presence or absence of the amplicon.

Ex. 1015, 10.

Karlsen describes a spectrum of solid, semi-solid, and liquid samples:

The term “liquid or liquified sample” may be used herein interchangeably with the term “test sample”. . . . Examples of the liquid or liquified sample include but are

not limited to drinking water, . . . juices, soft drinks, wine or other alcoholic beverages, milk, milk products, cheeses, and yogurt.

Id., 14.

Karlsen discloses a ratio of sample to diluent of 1:1 (vol./vol.):

an approximately 10 ml portion of the liquid or liquified sample (as defined elsewhere) herein which is desired to be tested for bacteria is mixed with approximately 10 ml of an enrichment media for enhancing growth of bacteria which may be present in the sample and is incubated.

Id., 23; *see also* Ex. 1015, 14:26–28 (Hird discloses a liquid sample, tomato soup, diluted using a ratio of sample to diluent of 1:5 (vol./vol.)).

5. ICMSF

International Commission on Microbiological Specifications for Foods publishes a series of books titled “Microorganisms in Foods,” referred to in the industry as the ICMSF guidelines or more specifically by their series number such as ICMSF 7. Dickson ¶¶ 104–09. Exhibit 1014, which includes Chapters 6, 10, 12, and 15–17 of ICMSF 7, is referred to herein as ICMSF.

Chapter 6 discusses lots in a consignment. Ex. 1014, 119. ICMSF 2 defines a consignment as “a quantity, large or small, of food destined, in commerce, to a particular recipient, usually consisting of multiple containers of food from one or

more lots.” Ex. 1013, 275. Chapters 6, 10, 12, and 17 of ICMSF 7 describe: (a) collecting, according to a sampling plan, sub-samples representative of meat lots in a consignment; (b) combining the sub-samples to yield composited lot samples while maintaining traceability; (c) enriching the composited lot samples to provide a set of enriched, composited lot samples; and (d) testing to obtain a negative result. Ex. 1014, 113–21, 183–97, 225–36, 326–27. Chapters 15–17 respectively focus on *Salmonella*, *Listeria*, and *E. coli*. *Id.*, 273–332.

C. State-of-the-Art References

1. BAM

The Bacteriological Analytical Manual (BAM) is the FDA’s official methods of microbiological analysis for foods. Dickson ¶¶ 110–14. Exhibit 1018 includes Chapters 1, 4, 4A, 5, 10, and Appendix 1 of BAM 2003. Chapter 1 provides guidance on collecting sub-samples according to a statistical sampling procedure. Chapters 4, 4A, 5, and 10 describe testing procedures for *E. coli*, *Salmonella* and *Listeria*. Appendix 1 discusses rapid methods for detecting foodborne pathogens.

2. MLG

The USDA FSIS publishes guidelines for analytical methods for meat and poultry, known as the Microbiology Laboratory Guidebook (MLG). Exhibit 1019

includes chapters 4, 5.03, and 8.03, which respectively relate to *Salmonella*, *E. coli*, and *Listeria*, of MLG 2003. Dickson ¶¶ 115–121.

IX. DETAILED ANALYSIS OF CHALLENGE GROUNDS

A. Grounds 1 and 2: Claim 1 Was Anticipated by Rayman And Was Obvious Based on Rayman in View of PR/HACCP

As provided below, Rayman anticipates claim 1 in Ground 1 and claim 1 also would have been obvious based on Rayman in view of the PR/HACCP in Ground 2.

Ground	References	§	Indep. Claim
1	Rayman	102	1
2	Rayman and PR/HACCP	103	

1. Claims 1 and 11

a. Preamble

Claim 1 — Preamble
A method for detection of a particular bacterial pathogen or bacterial microbe, comprising:

Preamble	Rayman in Grounds 1–3
Rayman is titled “ICMSF methods studies. XIII. An international comparative study of the MPN procedure and the Anderson–Baird-Parker direct plating method for the enumeration of <i>Escherichia coli</i> biotype I in raw meats.” Ex. 1010, 1321.	

Preamble	PR/HACCP in Grounds 2 and 5
PR/HACCP includes regulations for “all slaughter establishments . . . to test carcasses for generic <i>E. coli</i> as a tool to verify process control. This document outlines the sampling and microbial testing that should be followed to meet this requirement.” Ex. 1017, 38929.	

Rayman and PR/HACCP each respectively teach methods for detecting *E. coli*.

Dickson ¶¶ 124–26.

b. First Step — Sampling

Claim 1 — Sampling Step
obtaining a test sample, the sample being solid or semi-solid;

Sampling Step	Rayman in Grounds 1–3
Rayman lists samples under the heading, <i>Samples</i> , as provided below: Raw red meats , poultry and pork, and washings and surface-swabs of carcasses thereof were examined. All samples, frozen and non-frozen, were obtained in the country of the participating laboratory and were naturally contaminated. Ex. 1010, 1322 (emphases added); Dickson ¶¶ 131, 132.	

Sampling Step	PR/HACCP in Grounds 2 and 5
PR/HACCP includes “Appendix F—Guidelines for Escherichia coli Testing for Process Control Verification in Cattle and Swine Slaughter Establishments.” Ex. 1017, 38929. PR/HACCP describes “Specific Sample Collection Procedures” for cattle carcasses using “[a] sampling sponge (which usually comes dehydrated and prepackaged in a sterile bag) . . . [to] swab the areas in the sequence indicated in this sampling protocol.” <i>Id.</i> , 38931.	

Rayman’s meat samples meet the sampling step of claim 1. PR/HACCP’s beef and pork samples meet the sampling step of claim 1. Dickson ¶ 133.

c. Second Step — Diluting

Claim 1 — Diluting Step
diluting the sample with liquid enrichment medium at a ratio of sample to diluent between about 1:0.1 to about 1:5 (wt./vol.) or lesser dilution;

Diluting Step	Rayman in Grounds 1–3
Rayman tested the technique of Anderson and Baird-Parker, which involved diluting samples of food “1 in 5 or 1 in 10 with 0.1% (w/v) peptone water” and then homogenizing. Ex. 1009, 113 (emphasis added). Rayman reported “solids were weighed and homogenized in 4 parts (v/w) of 0.1 % peptone water” yielding “a homogenate (1:5).” Ex. 1010, 1322 (emphasis added). Rayman’s results were confirmed by NRC, which reported: By placing 1 ml of a 1:5 dilution of meat on duplicate filters a lower limit of detection of 2.5 cells per gram of meat could be reached (Rayman et al., 1979). Ex. 1011, 353 (emphasis added); Dickson ¶¶ 139, 140.	

Diluting Step	PR/HACCP in Grounds 2 and 5
	PR/HACCP includes “Appendix F—Guidelines for Escherichia coli Testing for Process Control Verification in Cattle and Swine Slaughter Establishments” which includes the following steps under the “Collection” heading: 1. “Carefully pour about half the contents of the sterile BPD [Butterfield's phosphate diluent] bottle (approximately 10 ml) into the sponge bag to moisten the sponge.” Ex. 1017, 38931 (Appendix F, Collection, Step 7); 2. Swab three 100 cm² areas of the carcass with the same hydrated sponge for a total area of 300 cm². <i>Id.</i> (Appendix F, Collection, Steps 14–17); and 3. “Add the additional BPD (about 15 ml) to the sample bag to bring the total volume to approximately 25 ml.” <i>Id.</i> (Appendix F, Collection, Step 23). Based on the foregoing, the total buffer is 25 ml and the total area equals 300 cm². Dividing 300 cm² by 25 ml equals 12 cm² per 1 ml or 1 cm² = 0.083 ml, which equates to a sample to diluent ratio of 1:0.083. Dickson ¶ 141. Some POSA only count the 15 ml added to the bag so on that basis, dividing 300 cm² by 15 ml equals 20 cm² per 1 ml or 1 cm² = 0.05 ml, which equates to a sample to diluent ratio of 1:0.05. Dickson ¶ 141. In either case, the dilution is less than 1:0.1.

Rayman meets the limitation of the second step of claim 1, the diluting step, because the sample is diluted with liquid enrichment medium for a 1:5 dilution, which is a ratio of sample to diluent of 1:4 (wt./vol.). Dickson ¶¶ 139, 140.

PR/HACCP meets the diluting step of claim 1 because the sample is diluted with liquid enrichment medium using a ratio of sample to diluent that is less than 1:0.1. Dickson ¶ 141.

d. Third Step — Incubating

Claim 1 — Incubating Step
incubating, in an incubator, the diluted sample at an optimal temperature for the particular bacterial pathogen or bacterial microbe to be detected for a time period sufficient to allow levels of the particular bacterial pathogen or microbe to reach levels detectable by use of an assay suitable to detect the particular bacterial pathogen or bacterial microbe; and

Incubating Step	Rayman in Grounds 1–3
Rayman characterized the technique of Anderson and Baird-Parker, which Rayman tested, as involving “direct incubation at an elevated temperature of 44.0–44.5°C.” Ex. 1010, 1322. Rayman further characterized the technique as incubating plates “in the upright position in stacks of not more than three in a 44.5±0.5°C water-jacketed or similarly accurate incubator for 24 h. It is important that this temperature range be maintained throughout the incubation period. ” <i>Id.</i> , 1323 (emphasis added); Dickson ¶¶ 148, 149.	

Incubating Step	PR/HACCP in Grounds 2 and 5
PR/HACCP states “[s]amples must be analyzed using one of the <i>E. coli</i> (Biotype I) quantitation methods found in the Official Methods of Analysis of the Association of Official Analytical Chemists (AOAC), International, 16 th edition.” Ex. 1017, 38933 (Appendix F, Analytical Methods). AOAC Official Methods of Analysis for <i>E. coli</i> include incubation. Dickson ¶ 150.	

The '486 Patent indicates that the incubator recited in the third step of claim 1, the incubating step, is not unique because it states that “[s]uitable incubators are known in the art.” Ex. 1001, 13:30. Rayman refers to conventional incubators, such as “incubating plates.” *Id.*, 1323. Thus, Rayman meets the limitation of the

incubating step of claim 1 because the sample is incubated in an incubator at an elevated temperature throughout the incubation period. Dickson ¶¶ 148, 149.

PR/HACCP meets the incubating step of claim 1 because the sample is incubated according to AOAC methods. Dickson ¶ 150.

e. Fourth Step — Assaying

Claim 1 — Assaying Step
determining, by assaying the diluted incubated test sample, or a portion thereof, with the assay suitable to detect the particular bacterial pathogen or bacterial microbe, whether the sample is contaminated with the particular bacterial pathogen or bacterial microbe.

Assaying Step	Rayman in Grounds 1–3
Rayman describes various options to assay for <i>E. coli</i> in food and notes: the ICMSF selected as most promising the direct plating method of Anderson and Baird-Parker (1975). Ex. 1010, 1322; <i>see also id.</i> , 1322, 1323 (description of direct plating (DP) method); Dickson ¶¶ 156, 157.	

Assaying Step	PR/HACCP in Grounds 2 and 5
PR/HACCP indicates “Samples must be analyzed using one of the <i>E. coli</i> (Biotype I) quantitation methods found in the Official Methods of Analysis of the Association of Official Analytical Chemists (AOAC), International, 16th edition.” Ex. 1017, 38933 (Appendix F, Analytical Methods). AOAC Official Methods of Analysis for <i>E. coli</i> include assaying. Dickson ¶¶ 150, 158.	

Rayman meets the limitation of the fourth step of claim 1, the assaying step, because Rayman describes determining, by assaying with an assay suitable to detect *E. coli* in meat samples. Dickson ¶¶ 156, 157. In Ground 2, the teachings of PR/HACCP complement those of Rayman. Additionally, PR/HACCP meets the assaying step of claim 1 because the sample is assayed according to AOAC methods. Dickson ¶¶ 150, 158.

2. Ground 1: Anticipation Summary

As summarized at VII-C-1 *supra*, the Examiner considered the independent claims to be allowable because the Examiner thought decimal dilution was the only known dilution ratio. The other three steps are well-known steps for techniques for detecting a particular bacterial pathogen or bacterial microbe, such as *E. coli*. See § IV-B-1. Because Rayman discloses a ratio of sample to diluent of 1:4 (wt./vol.) (i.e., a 1:5 dilution), as well as the other well-known steps, Rayman anticipates claim 1. Dickson ¶ 163.

3. Ground 2: Obviousness Rationales

Rayman states “the present concern about the enumeration of fecal coliforms, or more specifically *Escherichia coli* in foods, is the length of time and the amount of media and analysts’ time required to complete the analyses.” Ex. 1010, 1322. Rayman concludes that the method of Anderson and Baird-Parker “reduces the requirement of analyst’ time.” *Id.* Rayman also describes obtaining samples of meat including “washings and surface swabs of carcasses.” Ex. 1010, 1322.

A POSA would have been aware of the PR/HACCP. Given Rayman’s emphasis on reducing analysis time and reference to swabbing, a POSA utilizing the method of Rayman would have looked to the PR/HACCP requirements for swabbing, to utilize even less liquid enrichment medium than Rayman’s 1:5 dilution. In addition to obtaining a solid sample and performing a 1:5 dilution, Rayman discloses the other well-known steps of incubating and assaying. See §§ IX-A-1-a to X-A-1-e *supra*. A POSA would have been motivated to replace Rayman’s 1:5 dilution for a solid sample with the PR/HACCP’s lesser dilutions (i.e., ratios of sample to diluent of 1:0.083 and 1:0.05) with the objectives of rapid analysis and reduction in the amount of enrichment media that is required. Dickson ¶ 164.

A POSA would have been motivated to modify Rayman based on the PR/HACCP under the teaching-suggestion-motivation test so Rayman’s samples are less dilute, with a reasonable expectation of success for efficient analysis. Dickson

¶ 164. Moreover, a POSA would have improved Rayman with the similar methods of PR/HACCP to yield rapid and efficient analysis, which is a predictable result. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). In this combination, a POSA would have simply substituted the dilution step of Rayman, as described above, with the dilution step of the PR/HACCP for predictably efficient analysis. MPEP § 2143(I)(B); Dickson ¶ 164.

Thus, a POSA would have found claim 1 to be obvious based on Rayman in view of PR/HACCP

B. Grounds 3–5: Independent Claims Would Have Been Obvious Based on *Nagar* in View of *Rayman*, *Karlsen*, or *PR/HACCP*

As provided below, the independent claims would have been obvious based on Nagar in view of Rayman in Ground 3, Nagar in view of Karlsen in Ground 4, and Nagar in view of PR/HACCP in Ground 5.

Ground	References	§	Indep. Claims
3	Nagar and Rayman	103	1 and 11
4	Nagar and Karlsen		
5	Nagar and PR/HACCP		

1. Claims 1 and 11

a. Preamble

Claim 1	Claim 11
A method for detection of a particular bacterial pathogen or bacterial microbe, comprising:	

Preamble	Nagar in Grounds 3–5
Nagar states: Target pathogens that can be detected and identified using the method and system of the present invention include Gram (-) organisms such as the <i>Enterobacteriaceae</i>, including <i>E. coli</i>. Ex. 1012, ¶ [0035].	

Preamble	Karlsen in Ground 4
Karlsen describes “[a] method for the identification of the presence of <i>E. coli</i>. . . in a liquid or liquified sample. Ex. 1016, Abstract.	

Nagar, Rayman (*see* § IX-A-1-a *supra*), Karlsen, and PR/HACCP (*see* § IX-A-1-a *supra*) each respectively teach methods for detecting *E. coli*. Dickson ¶¶ 124–29.

b. First Step — Sampling

Claim 1	Claim 11
obtaining	

a test	a liquid
sample,	
the sample being solid or semi-solid;	

Sampling Step	Nagar in Grounds 3–5
Nagar states: For example, in testing a food sample, the rapidly growing target pathogens that could be tested for could include, but are not limited to, <i>Salmonella</i> and/or <i>E. coli</i>. Since these pathogens which are often found in a variety of foods (e.g., ground beef, milk, cheese, vegetables, apple cider, etc.), they are often “targeted” for testing in order to determine if they are present in a food sample. Ex. 1012, ¶ [0036] (emphases added); Dickson ¶¶ 134, 135.	

Sampling Step	Karlsen in Ground 4
Karlsen states: The term “liquid or liquified sample” may be used herein interchangeably with the term “test sample”. The liquid or liquified sample may comprise . . . food, feed, and water. It is therefore contemplated that the liquid or liquified sample comprise any number of sample types, both environmental and clinical. Examples of the liquid or liquified sample include but are not limited to drinking water, bathing water, cerebrospinal fluid, blood, juices, soft drinks, wine or other alcoholic beverages, milk, milk products, cheeses, and yogurt. Ex. 1016, 14 (emphasis added); Dickson ¶ 136.	

Nagar food samples of meat, cheese, and apple cider meet the sampling step of claims 1 and 11. Rayman and PR/HACCP sample meat. See § IX-A-1-b *supra*.

Karlsen's cheese and liquids meet the sampling step of claims 1 and 11. Dickson ¶ 137.

c. Second Step — Diluting

Claim 1	Claim 11
diluting the sample with liquid enrichment medium at a ratio of sample to diluent between about 1:0.1 to about 1:5	
(wt./vol.) or lesser dilution;	(vol./vol.) or lesser dilution, or not diluting the sample;

Diluting Step	Nagar in Grounds 3–5
Nagar discloses use of decimal dilution in a feasibility study in which ground beef was artificially inoculated with <i>E. coli</i> O157:H7 pathogen. Samples of ground beef weighing 25 g were placed in stomacher bags and then 225 ml resuscitation/growth medium was added to each bag. Ex. 1012, ¶ [0050] (emphases added); Dickson ¶ 142.	

Diluting Step	Karlsen in Ground 4
Karlsen indicates: an approximately 10 ml portion of the liquid or liquified sample (as defined elsewhere) herein which is desired to be tested for bacteria is mixed with approximately 10 ml of an enrichment media for enhancing growth of bacteria which may be present in the sample. Ex. 1016, 23 (emphasis added); Dickson ¶ 143. Thus, Karlsen discloses a 1:1 ratio of sample to diluent (i.e., a 1:2 dilution).	

Nagar discloses decimal dilution. A POSA would have modified the teachings of Nagar for obtaining and decimal diluting samples based on the

teachings of Rayman, Karlsen, or PR/HACCP to only dilute the sample with liquid enrichment medium at a ratio of sample to diluent respectively to 1:4, 1:1, or less than 1:0.1. *See* § IX-A-1-c *supra*. Dickson ¶ 145.

d. Third Step — Incubating

Claim 1	Claim 11
incubating, in an incubator,	
the diluted sample	the diluted or the not diluted sample
at an optimal temperature for the particular bacterial pathogen or bacterial microbe to be detected for a time period sufficient to allow levels of the particular bacterial pathogen or microbe to reach levels detectable by use of an assay suitable to detect the particular bacterial pathogen or bacterial microbe; and	

Incubating Step	Nagar in Grounds 3–5
Nagar states the method and system include the steps of: placing a sample in a container containing a resuscitation/growth medium; optionally homogenizing the sample; placing a capture matrix in the sampling bag with the sample; incubating the sample in the resuscitation/growth medium for a pre-determined amount of time at an elevated temperature while optionally shaking; optionally removing the capture matrix from the container; performing detection assays to detect the presence of the target pathogens in the sample. Ex. 1012, ¶ [0023] (emphases added); <i>see also id.</i>, [0044], [0045] (discussion of incubating in a container then performing detection assays after “the end of the incubation period”); Dickson ¶¶ 151, 152.	

Incubating Step	Karlsen in Ground 4
Karlsen indicates: an approximately 10 ml portion of the liquid or liquified sample . . . mixed with approximately 10 ml of an enrichment media for enhancing growth of bacteria which may be present in the sample and is incubated , preferably at about 41° to about 44°C for about three to about five hours. Ex. 1016, 23 (emphases added); Dickson ¶¶ 153, 154.	

The '486 Patent indicates that the incubator recited in the third step of claim 1, the incubating step, is not unique because it states that “[s]uitable incubators are known in the art.” Ex. 1001, 13:30. Nagar meets the same step for claims 1 and 11 because the sample is incubated “in a container” at an elevated temperature for an incubation period sufficient for the “assays to **detect the presence of the target pathogens in the sample.**” Ex. 1012, ¶ [0023]. In Ground 3, the teachings of Rayman complement those of Nagar. *See* § IX-A-1-d *supra*. In Grounds 4 and 5, the teachings of Karlsen and PR/HACCP respectively complement those of Nagar. Dickson ¶¶ 150–154.

e. Fourth Step — Assaying

Claim 1	Claim 11
determining, by assaying	
the diluted incubated test sample, or a portion thereof,	the diluted or the not diluted incubated test sample, or a portion thereof,

with the assay suitable to detect the particular bacterial pathogen or bacterial microbe, whether the sample is contaminated with the particular bacterial pathogen or bacterial microbe.

Assaying Step	Nagar in Grounds 3–5
Nagar states: performing detection assays to detect the presence of the target pathogens in the sample. Ex. 1012, ¶ [0023] (emphases added); Dickson ¶¶ 160, 161. Nagar describes various assaying options: The presence/absence test may be run on one part of the two-part device and, if present, the other part of the two-part device can be used for culturing and confirming target pathogen(s) using, but not limited to, detection methodologies, such as enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR), or manual strand displacement amplification (SDA). Ex. 1012, ¶ [0026] (emphases added). Nagar describes various assaying options: At the end of the incubation period, specific detection assays can be performed on the capture matrix to detect the presence of the target microorganism. One method of detection is through the use of biochemical tests or assays. Ex. 1012, ¶ [0045], [0046] (emphases added); <i>see also id.</i> ¶ [0046], [0047] (long list of biochemical assays followed by alternative assays).	

Assaying Step	Karlsen in Ground 4
Karlsen indicates: The method of detection and identification preferably involves enrichment of the bacteria using selective culture media, recovery of bacteria from media, lysing of the bacteria to release DNA, polymerase chain reaction (PCR) amplification of the target sequences using the novel oligonucleotides, and specific detection of PCR products. Ex. 1016, 8 (emphases added); Dickson ¶ 162.	

Nagar meets the assaying step for claims 1 and 11 because Nagar describes performing detection assays to detect the presence, in the sample, of the target pathogens such as *E. coli*. In Ground 3, the teachings of Rayman complement those of Nagar. Dickson ¶¶ 156, 157, 159–61. In Grounds 4 and 5, the teachings of Karlsen and PR/HACCP respectively complement those of Nagar. Dickson ¶¶ 158, 160–62.

2. Ground 3: Obviousness Rationales

Nagar is focused on methods for rapidly detecting microorganisms. Ex. 1012, Title. Rayman has the same focus. Rayman states “the present concern about the enumeration of fecal coliforms, or more specifically *Escherichia coli* in foods, is the length of time and the amount of media and analysts’ time required to complete the analyses.” Ex. 1010, 1322. Rayman concludes that the method of Anderson and Baird-Parker “reduces the requirement for analysts’ time.” *Id.*

Given that Nagar and Rayman were trying to solve the same problem, a POSA utilizing the method of Nagar would have looked to the teachings of Rayman, which included 1:5 dilutions in the Anderson and Baird-Parker method. Dickson ¶ 165. Nagar discloses obtaining a solid or liquid sample, decimal dilution, and the other well-known steps of incubating and assaying. See §§ IX-A-1-a to X-A-1-e *supra*. A POSA would have been motivated to replace Nagar's decimal dilution (1:10) for any solid or liquid sample with Rayman's more concentrated dilution (1:5) with the objective of rapid analysis. Dickson ¶ 165. The modification also reduces the amount of enrichment media that is required. *Id.*

A POSA would have been motivated to modify Nagar based on Rayman under the teaching-suggestion-motivation test so Nagar's samples are less dilute, with a reasonable expectation of success for efficient analysis. *Id.* Moreover, a POSA would have improved Nagar with the similar methods of Rayman to yield rapid and efficient analysis, which is a predictable result. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). In this combination, a POSA would have simply substituted the dilution step of Nagar, as described above, with the dilution step of Rayman for predictably efficient analysis. MPEP § 2143(I)(B); Dickson ¶ 165.

Thus, a POSA would have found claims 1 and 11 to be obvious based on Nagar in view of Rayman.

3. Ground 4: Obviousness Rationales

Like Nagar and Rayman, Karlsen is also focused on methods for rapidly detecting microorganisms. Ex. 1016, 3, 5, 24. Given that Nagar and Karlsen were trying to solve the same problem, a POSA utilizing the method of Nagar would have looked to the teachings of Karlsen, which included a 1:2 dilution. Dickson ¶ 165. Nagar discloses obtaining a solid or liquid sample, decimal dilution, and the other well-known steps of incubating and assaying. See §§ IX-A-1-a to IX-A-1-e *supra*. A POSA would have been motivated to replace Nagar's decimal dilution (1:10) for any solid or liquid sample with Karlsen's more concentrated dilution (1:2) with the objective of reducing the time for analysis. Dickson ¶ 165. The modification also reduces the amount of enrichment media that is required. *Id.*

A POSA would have been motivated to modify Nagar based on Karlsen under the teaching-suggestion-motivation test so Nagar's samples are less dilute, with a reasonable expectation of success for efficient analysis. *Id.* Moreover, a POSA would have improved Nagar with the similar methods of Karlsen to yield rapid and efficient analysis, which is a predictable result. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). In this combination, a POSA would have simply substituted the dilution step of Nagar, as described above, with the dilution step of Karlsen for predictably efficient analysis. MPEP § 2143(I)(B); Dickson ¶ 165.

Thus, a POSA would have found claims 1 and 11 to be obvious based on Nagar in view of Karlsen.

4. Ground 5: Obviousness Rationales

Nagar is focused on methods for rapidly detecting microorganisms. Ex. 1012, Title. A POSA would have been aware of the PR/HACCP. Dickson ¶ 165. A POSA utilizing the method of Nagar would have looked to the PR/HACCP requirements for swabbing, to utilize even less liquid enrichment medium than Nagar's decimal dilution. *Id.* In addition to obtaining a sample (solid or liquid) and using decimal dilution, Nagar discloses the other well-known steps of incubating and assaying. See §§ IX-B-1-a to IX-B-1-e *supra*. A POSA would have been motivated to replace Nagar's decimal dilution for a solid or liquid sample with the PR/HACCP's more concentrated dilution of a ratio of sample to diluent of less than 1:0.1 with the objectives of rapid analysis and reduction in the amount of enrichment media that is required. Dickson ¶ 165.

A POSA would have been motivated to modify Nagar based on the PR/HACCP under the teaching-suggestion-motivation test so Nagar's samples are less dilute, with a reasonable expectation of success for efficient analysis. *Id.* Moreover, a POSA would have improved Nagar with the similar methods of PR/HACCP to yield rapid and efficient analysis, which is a predictable result. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). In this combination, a POSA

would have simply substituted the dilution step of Nagar, as described above, with the dilution step of the PR/HACCP for predictably efficient analysis. MPEP § 2143(I)(B); Dickson ¶ 165.

Thus, a POSA would have found claims 1 and 11 to be obvious based on Nagar in view of PR/HACCP.

C. Grounds 1–7: Dependent Claims 2–10 and 12–30 Would Have Been Obvious

As provided below, the dependent claims 2–10 and 12–30 would have been obvious based on Grounds 1–7.

Grounds 1–7 and Dependent Claims		
Ground	References	Dependent Claims
1	Rayman	4–8, 17, 19
2	Rayman and PR/HACCP	2–8, 17, 19, 27
3	Nagar and Rayman	4–8, 12–26
4	Nagar and Karlsen	4–8, 12–28
5	Nagar and PR/HACCP	2–8 and 12–30
6	Rayman and ICMSF	9 and 10
7	Rayman and AAPA	

The dependent claims are listed below grouped by their dependency from claim 1 or 11 and correlated to their recited subject matter.

Claim 1	Claim 11	Subject Matter
2, 3, 27	28–30	Dilution Ratios

4, 5	12, 13	Temperature
6	14	Assay Type
7, 8	15, 16	Pathogen Type
9, 10		Lot Sample
17	18	Sample Types
19	20	Supplement
21–23	24–26	Locations

1. Grounds 1–5 and Dependent Claims 2–8 and 12–30

a. Claims 2, 3, and 27–30 — Dilution Ratios

27	The method of claim	1	wherein diluting is at a ratio of sample to diluent between about 1:0.1 to about	1:2 (wt./vol.)	or lesser dilution.
28		11		1:2 (vol./vol.)	
2		1		1:0.5 (wt./vol.)	
29		11		1:0.5 (vol./vol.)	
3		1		1:0.3 (wt./vol.)	
30		11		1:0.3 (vol./vol.)	

Karlsen discloses diluting at a ratio of sample to diluent of 1:1 as required by claims 27 and 28. X-B-1-c. Thus, claims 27 and 28 would have been obvious based on Ground 4. Dickson ¶ 168.

PR/HACCP discloses diluting at a ratio of sample to diluent of less than 1:0.1, which is a lesser dilution than that required by the range in claims 2, 3, 29, and 30. See §§ IX-A-1-c and IX-B-1-c *supra*. Thus, claims 2 and 3 would have been obvious

based on Grounds 2 and 5 and claims 29 and 30 would have been obvious based on Ground 5. Dickson ¶¶ 169, 170.

b. Claims 4, 5, 12, and 13 — Temperature

Claim 4	Claim 12
The method of claim 1,	The method of claim 11,
wherein the optimal temperature is within the optimal growth temperature range of the particular bacterial pathogen or bacterial microbe in the liquid enrichment medium.	

Claim 5	Claim 13
The method of claim 4,	The method of claim 12,
wherein the optimal temperature range is from about 25° C. to about 45° C.	

Rayman characterized the technique of Anderson and Baird-Parker, which Rayman tested, as involving “direct **incubation** at an **elevated temperature** of 44.0–44.5°C.” Ex. 1010, 1322. Rayman further characterized the technique as **incubating** plates “in the upright position in stacks of not more than three in a 44.5±0.5°C water-jacketed or similarly accurate **incubator** for 24 h. It is important that this temperature range be maintained throughout the **incubation period.**” *Id.*, 1323 (emphasis added); Dickson ¶ 171.

Nagar describes a feasibility study, which showed the capture of target pathogen, *E. coli* O157:H7, in beef and incubation at 37°C. Ex. 1012, ¶ [0050].

Nagar describes, in its section titled Background of the Technology, the well-known conventional process for culturing a food sample for the presence of *Salmonella* with reference to the well-known optimal temperature range for optimal growth, approximately 35°C +/- 2°C. *Id.*, ¶ [0009]; Dickson ¶ 172.

Thus, claims 4 and 5 were anticipated by Rayman; claims 4 and 5 would have been obvious based on Ground 2; and claims 4, 5, 12 and 13 would have been obvious based on Grounds 3–5. Dickson ¶¶ 171, 172.

c. Claims 6 and 14 — Assay Types

Claim 6	Claim 14
The method of claim 1,	The method of claim 11,
wherein the assay suitable for detection of the particular bacterial pathogen or bacterial microbe contamination is selected from the assay group consisting of immunoassays, nucleic acid amplification-based assays, PCR-based assays, nucleic acid hybridization-based assays, bio-sensor assays, immunostaining-microscopy-based assays, nucleic acid-array-based assays, DNA chip-based assays, classical microbiology-based assays, and chemical or biochemical assays based on the detection of compounds associated with the particular bacterial pathogen or bacterial microbe, and combinations thereof.	

Rayman describes various options to assay for *E. coli* in food and notes “the ICMSF selected as most promising the direct plating method of Anderson and Baird-Parker (1975).” Ex. 1010, 1322; *see also id.*, 1322–23 (description of direct plating

(DP) method). Dickson ¶ 173. Direct plating is an example of a “classical microbiology-based assay.” *Id.*

Nagar states:

One method of detection is through the use of biochemical tests or assays. Examples of **biochemical assays** include enzyme detection, products of bacterial metabolism, immunochemical markers, specific stains, chemiluminescence, and bioluminescence.

Ex. 1012, ¶ [0046] (emphasis added); *see also id.*, claims 3 and 4; Dickson ¶ 174.

Nagar also describes use of an assay suitable for detection of a particular bacterial pathogen, *Salmonella*.

a **detection step** . . . can include plating the secondary enrichment broth onto solid media or by utilizing other methods, such as the use of specific enzyme markers, **biochemical testing, immunological assays or DNA probes.**

Ex. 1012, ¶ [0009] (emphases added).

Thus, claim 6 was anticipated by Rayman; claim 6 would have been obvious based on Ground 2; and claims 6 and 14 would have been obvious based on Grounds 3–5. Dickson ¶¶ 173, 174.

d. Claims 7, 8, 15, and 16 — Bacterial Pathogen or Microbes

Claim 7	Claim 15
The method of claim 1,	The method of claim 11,
wherein the particular bacterial pathogen or bacterial microbe is selected from the group consisting of <i>Escherichia coli</i> O157:H7 (<i>E. coli</i> O157:H7), enterohemorrhagic <i>Escherichia coli</i> (EHEC), enterotoxigenic <i>Escherichia coli</i> (ETEC), enteroinvasive <i>Escherichia coli</i> (EIEC), enteropathogenic <i>Escherichia coli</i> (EPEC), <i>Salmonella</i> , <i>Listeria</i> , <i>Yersinia</i> , <i>Campylobacter</i> , <i>Clostridial</i> species, <i>Staphylococcus</i> spp.; frank and opportunistic bacteria, indicator organisms including heterotrophes, generic <i>E. Coli</i> , total and fecal coliforms and enterococcus; spoilage organisms including <i>Pseudomonas</i> , and combinations thereof.	

Claim 8	Claim 16
The method of claim 7,	The method of claim 15,
wherein the particular bacterial pathogen or bacterial microbe is <i>Escherichia coli</i> O157:H7 (<i>E. coli</i> O157:H7, or H negative), <i>Salmonella</i> , <i>Listeria</i> , EHEC, and <i>Campylobacter</i> .	

Rayman is titled “An international comparative study of the MPN procedure and the Anderson–Baird-Parker direct plating method for the enumeration of *Escherichia coli* biotype I in raw meats.” Ex. 1010, 1321; Dickson ¶ 175.

Nagar further discloses a process for detecting target pathogens including: “Gram (-) organisms such as the *Enterobacteriaceae*, including *E. coli*, and Gram (+) organisms, including *Staphylococcus aureus* and *Enterococcus faecalis*.” Ex.

1012, ¶ [0035]; *see also id.*, ¶ [0036] (describing testing food samples for “*Salmonella* and/or *E. coli*.”); Dickson ¶ 176.

Thus, claims 7 and 8 were anticipated by Rayman; claims 7 and 8 would have been obvious based on Ground 2; and claims 7, 8, 15 and 16 would have been obvious based on Grounds 3–5. Dickson ¶¶ 175, 176.

e. Claims 17 and 18 — Sample Types

17	The method of claim 1,	where in the sample is selected from the group consisting of beef, pork, sheep, bison, deer, elk, poultry, fish, produce, dairy products, dry goods, raw and processed foods, environmental samples, soil, sludge, surface samples, samples taken by impingers and filtration, pharmaceuticals, and samples analyzed using enrichment-detection protocols.
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18	The method of claim 11,	wherein the liquid sample is selected from the group consisting of fruit juice, vegetable juice, milk and dairy products, raw and processed liquid foods, environmental samples, water, wastewater, samples taken by impingers and filtration, botanical liquid, industrial liquids, pharmaceutical liquids, and other liquid samples analyzed using enrichment-detection protocols.
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Rayman describes types of samples that are tested:

Raw red **meats**, **poultry** and **pork**, and washings and surface-swabs of carcasses thereof were examined. All samples, frozen and non-frozen, were obtained in the country of the participating laboratory and were naturally contaminated.

Ex. 1010, 1322 (emphases added); Dickson ¶ 177.

Nagar also describes types of foods that are tested:

For example, in **testing a food sample**, the rapidly growing target pathogens that could be tested for could include, but are not limited to, *Salmonella* and/or *E. coli*. Since these pathogens which are often found in a variety of foods (e.g., **ground beef**, **milk**, cheese, vegetables, **apple cider**, etc.), they are often “targeted” for testing in order to determine if they are present in a food sample.

Ex. 1012, ¶ [0036] (emphases added); Dickson ¶ 178.

Thus, claim 17 was anticipated by Rayman; claim 17 would have been obvious based on Ground 2; and claims 17 and 18 would have been obvious based on Grounds 3–5. Dickson ¶¶ 177, 178.

f. Claims 19 and 20 — Supplement

Claim 19	Claim 20
The method of claim 1,	The method of claim 11,
wherein the diluting comprises addition to the sample of a supplement selected from the group consisting of water, sugars, proteins, minerals, organics, vitamins and cofactors, antibiotics, dyes, indicators, buffers, agents to adjust the pH, water activity, nutritional contents, selective pressure to optimize the growth conditions for the particular bacterial pathogen or bacterial microbe, and combinations thereof.	

Rayman describes diluting samples with 0.1% peptone water. Ex. 1010, 1322; Dickson ¶ 179.

Nagar discloses the standard use of pre-enrichment or non-selective medium and selective medium. These mediums or broths may contain sugars. For example, Nagar cites to use of “a pre-enrichment broth that comprises . . . glucose.” Ex. 1012, ¶ [0016]; Dickson ¶ 180. Nagar further discloses that:

The medium located inside the container is not particularly limited, and includes items such as a growth medium, a **buffer**, **water**, solvent, semi-solid growth medium, resuscitation medium, a process solution, or a simple growth medium. A resuscitation/growth medium is most preferred.

Ex. 1012, ¶ [0039] (emphases added); *see also id.*, claim 2.

Thus, claim 19 was anticipated by Rayman; claim 19 would have been obvious based on Ground 2; and claims 19 and 20 would have been obvious based on Grounds 3–5. Dickson ¶¶ 179, 180.

g. Claims 21–26 — Location

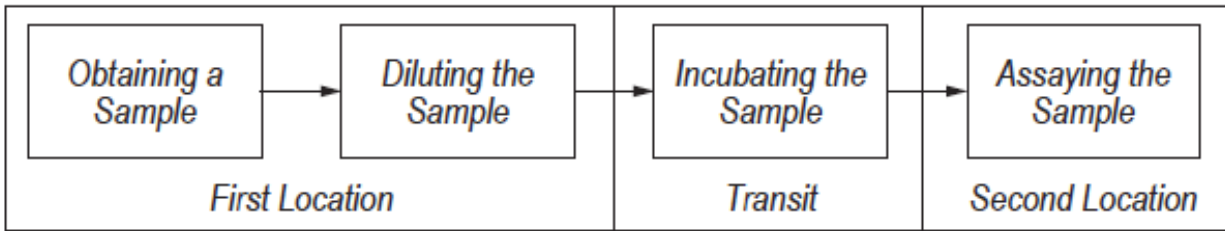
Claim 21	Claim 24
The method of claim 1,	The method of claim 11,
wherein the obtaining and diluting of the solid or semi-solid sample with liquid enrichment medium is at a first location, wherein incubating the diluted sample at an optimal temperature in the incubator is during transit	

of the diluted sample to a second location that is not the site of sample collection and dilution, and wherein determining by assaying the diluted incubated test sample, or a portion thereof, with the assay suitable to detect the particular bacterial pathogen or bacterial microbe, whether the sample is contaminated with the particular bacterial pathogen or bacterial microbe, is at the second location.

Claim 22	Claim 25
The method of claim 21,	The method of claim 24,
further comprising addition to the sample, prior to or during incubation, of a supplement selected from the group consisting of water, sugars, proteins, minerals, organics, vitamins and cofactors, antibiotics, dyes, indicators, buffers, agents to adjust the pH, water activity, nutritional contents, selective pressure to optimize the growth conditions for the particular bacterial pathogen or bacterial microbe, and combinations thereof.	

Claim 23	Claim 26
The method of claim 21,	The method of claim 24,
wherein the second location is an in-house or local lab, or a remote location.	

Dependent claims 21–23 and 24–26, respectively depend directly or indirectly from independent claims 1 and 11. Claims 21–26 (“the Transportation Claims”) require that the obtaining and diluting steps occur at a first location, the incubating step occurs during transit to a second location, and that the assaying step occurs at the second location. These requirements are depicted in the diagram below.



Dickson ¶ 181.

Nagar states that “pathogens are often subjected to unfavorable growth conditions during transportation” and that “[i]ntrinsic factors that affect the growth of pathogens include nutrients, growth factors/inhibitors, water activity. . .” Ex. 1012, ¶ [0028]. Nagar further states:

The method and system of the invention can also be used **during transportation of a test sample (e.g., soil, etc.) from the collection site to the testing laboratory.** This may be achieved **by placing the capture matrix inside a sampling/transportation device containing suitable resuscitation/growth medium,** thus facilitating the capture, resuscitation and growth of the target pathogen for rapid detection.

Id., ¶ [0031] (emphases added). Based on the above quoted paragraph, Nagar discloses obtaining a sample at a first location, which is a collection site, then diluting the sample in “a sampling/transportation device containing suitable resuscitation/growth medium.” *Id.* The incubating step occurs during transit to a second location, which is “the testing laboratory.” Dickson ¶ 182.

Thus, claims 21–26 would have been obvious based on teachings of Nagar in Grounds 3–5. Dickson ¶¶ 181, 182.

2. Grounds 6 and 7: Obviousness of Claims 9 and 10 Based On *Rayman* in View of *ICMSF* and *Rayman* in View of *AAPA*

a. Claims 9 and 10 — Lot Samples

9		wherein obtaining a sample is obtaining a standard Lot-unit sample.
10	The method of claim 1,	wherein the sample is a composite-Lot sample, corresponding to a combination of samples selected from the group consisting of samples or subsamples taken from sublots/lots of raw or processed samples, environmental samples, industrial samples, pharmaceutical samples, bio-solid samples, samples taken by spore traps, settled dust, impingers, or filtration, and combinations thereof.

In contrast to *Rayman*, *ICMSF* and *AAPA* describe a production environment in which samples are collected from lots and combined.

Regarding claim 9, the '486 Patent states “[a] **prior art ‘Lot-unit sample’** refers to a **375 g composite sample . . .**” Ex. 1001, 9:66–67 (emphasis added). “In **prior art sampling plans**, the **Lot-unit** represents raw [sic] the material (**composite trim**) upon which sampling, testing and acceptance or rejection is based.” *Id.*, 9:57–60 (emphasis added). Trim is “small pieces of meat and fat . . . excised during the fabrication process.” *Id.*, 9:46–48. Thus, the “Lot-unit sample” of claim 9 is a 375 g composite sample of trim.

Regarding claim 10, the '486 Patent states “[a] **typical trim-testing plan . . .** comprises analysis of a single **composite-Lot sample** of about **375 g, ...** [T]est results under **these prior art systems** reflect random . . . sampling . . . [as] only a sub-fraction of the **composite-Lot sample** is used for the pathogen-testing assay (e.g., when large pieces of **trim** are collected).” Ex. 1001, 13:61-14:7 (emphasis added). Therefore, the “composite-Lot sample” of claim 10 is also a 375 g composite sample of trim.

ICMSF discloses obtaining a 375 g composite sample of trim for testing:

The method can be adjusted for analysis of 15 analytical units into **a single 375 g composite sample. Research has validated that . . . trimmings can be composited without significant loss in . . . detection sensitivity** (Silliker & Nickelson, 1995). This permits testing at a more reasonable cost and makes it more practical to screen lots to detect those of higher prevalence.

Ex. 1014, 327 (emphasis added).

Additionally, ICMSF describes collecting samples from lots or consignments (e.g., multiple lots) and combining (i.e., compositing) those samples to “reduce laboratory effort” and gain a “very great technical advantage”. *Id.*, 187-88, 224; Dickson ¶¶ 187, 188.

Thus, ICMSF discloses obtaining a standard Lot-unit sample as recited by claim 9 and ICMSF also discloses a composite-Lot sample corresponding to a combination of samples as recited by claim 10.

Furthermore, as described above, the '486 Patent refers to both the “Lot-unit sample” of claim 9 and the “composite-Lot sample” of claim 10 as “prior art.” Thus, this AAPA indicates that a POSA would have been familiar with obtaining samples as recited by claims 9 and 10.

Accordingly, claims 9 and 10 would have been obvious based on the teachings of Rayman in view of ICMSF in Ground 6 and Rayman in view of AAPA in Ground 7.

b. Grounds 6 and 7: Obviousness Rationales

Rayman describes obtaining a variety of samples including meat. Ex. 1010, 1322; *see* § IX-A-1-b *supra*. However, Rayman is written for a POSA who already understands the details of collecting samples from lots and combining those samples. ICMSF provides those details and a POSA would be quite familiar with ICMSF and the procedures it describes for collecting and combining samples, such as obtaining a 375 g composite sample of trim. Dickson ¶¶ 191, 192. Likewise, the AAPA provides these details as well to indicate that a POSA would know how to collect and combine samples as recited in claims 9 and 10. *Id.*

A POSA would have been motivated to combine the teachings of Rayman with ICMSF or AAPA under the teaching-suggestion-motivation test because ICMSF indicates that combining analytical units (samples or subsamples) reduces “laboratory effort” and the AAPA indicates that collecting and testing composites was known in the art. Dickson ¶ 192. Moreover, a POSA would have improved Rayman with the similar methods of ICMSF or AAPA to yield more efficient analysis, which is a predictable result. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). In this combination, a POSA would have simply substituted the sampling step of Rayman, as described above, with the sampling and combining steps of ICMSF or AAPA for predictably efficient analysis. MPEP § 2143(I)(B); Dickson ¶ 192.

Thus, a POSA would have found claims 9 and 10 to be obvious based on Rayman in view of ICMSF and Rayman in view of AAPA. Dickson ¶¶ 191, 192.

X. THE BOARD SHOULD REACH THE MERITS OF THIS PETITION

A. Section 314(a): *Fintiv* Factors Favor Institution

The district court litigation is listed at XII-B *infra*. See Ex. 1002. The *Fintiv* factors weigh against discretionary denial in view of the parallel district court litigation in this case. See *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 (Mar. 20, 2020) (precedential).

1. Institution Will Increase the Likelihood of a Stay

If this IPR is instituted and the litigation is still pending, National Beef will seek a stay. Institution would enable the Board to resolve patentability issues, advancing judicial efficiency by freeing the district court from having to assess validity. The early stage of the litigation and the potential for issue simplification increases the likelihood that a stay will be granted based on institution. Thus, this factor favors institution.

1. Timing

A final written decision (FWD) in this IPR would likely issue in February 2026. Based on the filing of IEH's complaint in the District of Delaware on August 1, 2023 and the 38-month period reported in the most recent statistics on median time-to-trial for civil actions in the District of Delaware, any potentially foreseeable court trial date is on October 1, 2026. Exs. 1031, 1032. Thus, factor two favors institution.

2. Litigation Stage

On May 16, 2024, IEH and National Beef jointly submitted to the district court a Proposed Scheduling Order. Ex. 1033. The Proposed Scheduling Order indicates claim construction briefing will be completed by February 19, 2025. *Id.*, 8. Based on this proposed schedule, it would be very unlikely for trial in the litigation to be

reached before issuance of the FWD in February 2026. Thus, the early stage of the litigation favors institution.

3. No Overlap

Based on the likely timing for a FWD and the lack of a trial date, a FWD will issue before the district court's trial date. Thus, the estoppel that would attach from the FWD pursuant to 35 U.S.C. § 315(e) would prevent grounds that were raised or reasonably could have been raised in this IPR from being raised at trial in the litigation. Because there is no possibility for overlap between the IPR and the related litigation, this factor favors institution.

4. Same Party

National Beef is the Petitioner and the defendant. However, that is typically the scenario for a patent asserted in district court and challenged at the Board. *Fintiv* “says nothing about situations in which the Petitioner is the same as, or is related to, the district court defendant.” *Cisco Sys., Inc. v. Ramot at Tel Aviv Univ. Ltd.*, IPR2020-00122, Paper 15 at 10 (May 15, 2020) (“the factor is neutral.”).

5. Other Circumstances

As evidenced by the analysis at §§ IX-A to IX-C *supra*, National Beef's patentability challenge presents a compelling merits case that all Challenged Claims are not patentable. This factor therefore favors institution regardless of other factors.

Thus, in view of the facts presented in this Petition, the *Fintiv* factors do not support discretionary denial.

B. Section 325(d): *Advanced Bionics* Favors Institution

1. Substantially Same Art/Arguments Not Considered

Discretionary denial under § 325(d) is not appropriate given this Petition does not present the same or substantially the same grounds/arguments previously presented to and considered by the Office. *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 at 8–9 (Feb. 13, 2020) (precedential). Moreover, there are material differences between the art/arguments in this Petition and those during prosecution and reexamination.

Each ground includes a reference that teaches use of a dilution ratio of sample to diluent that is within the dilution range recited by the claims. Neither Rayman, the PR/HACCP, Nagar, Karlsen, or ICMSF were considered previously by the Office. Thus, each ground presents new art and new arguments that are different and stronger relative to the rejection based on BAM.

2. Office Erred

If the Board concludes the same or substantially the same art or arguments were previously presented to the Office, then institution should not be denied

because the Office erred in a manner material to the patentability of challenged claims. *Advanced Bionics* at 8–9.

The '486 Patent was improvidently granted because it was based on the Examiner's misunderstanding of the state of the art, which includes numerous examples of dilutions that are less dilute than decimal dilution. During the five-year pendency of the '253 Application (the parent application to the application that yielded the '486 Patent), **a single prior art rejection was made** based on the teachings of decimal dilution in BAM. *See* § VII-B *supra*. During the nine-year pendency of the '646 Application, which yielded the '486 Patent, **no prior art rejection was made**. *See* § VII-B *supra*. While BAM is an important reference in the industry, more relevant teachings regarding dilution should have been considered over the course of 14.5 years from the filing of parent application to issuance of the '486 Patent. The prosecution histories of the three applications in this family indicate that the Examiner's misunderstanding of the state of the art was not corrected. *See* § VII-C *supra*.

XI. MANDATORY NOTICES

A. Real Party-in-Interest (37 C.F.R. § 42.8(b)(1))

National Beef Packing Company, LLC certifies it is the real party-in-interest and no other party exercised control over preparation or filing of this Petition.

B. Related Matters (37 C.F.R. § 42.8(b)(2))

The '486 Patent is the subject of a district court proceeding: *Inst. for Env'tl. Health, Inc. v. Nat'l Beef Packing Co.*, No. 1:23-cv-00826 (D. Del. Aug. 1, 2023).
See Ex. 1002.

C. Lead and Backup Counsel (37 C.F.R. § 42.8(b)(3)) and Service Information (37 C.F.R. § 42.8(b)(4))

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XII. CONCLUSION

Petitioner respectfully requests that a trial be instituted.

Respectfully Submitted,

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WORD-COUNT CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned hereby certifies that this Petition complies with the type-volume limitation of 37 C.F.R. § 42.24(a)(1)(i). The Petition contains 13,204 words, excluding parts of this Petition exempted under 37 C.F.R. § 42.24(a), as measured by the word-processing system used to prepare this Petition, and by adding words appearing as annotations to Patent Owner's diagrams and those included on Petitioner's diagrams.

Respectfully submitted,

Dated: July 31, 2024

By: /Kevin Laurence/
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CERTIFICATE OF SERVICE

The undersigned certifies service pursuant to 37 C.F.R. §§ 42.6(e) and 42.105(b) of the following materials:

- Petition for *Inter Partes* Review of U.S. Patent No. 9,845,486 under 35 U.S.C. § 312 and 37 C.F.R. § 42.104
- Exhibit List
- Exhibits for Petition for *Inter Partes* Review of U.S. Patent No. 9,845,486 (Exs. 1001–1034)
- Power of Attorney
- Word Count Certification Under 37 CFR § 42.24(d)

on IEH for next day delivery at the correspondence address of record for the subject patent as listed in the records of the United States Patent and Trademark Office:

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