

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

PFIZER INC.,
Petitioner,

v.

POGONA, LLC,
Patent Owner.

Case IPR2026-00189

Patent 11,058,757

**DECLARATION OF DR. LOUIS J. DEFILIPPI IN SUPPORT OF
PATENT OWNER'S RESPONSE**

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I, Dr. Louis J. DeFilippi, Ph.D., hereby declare as follows:

I. INTRODUCTION

1. I am over the age of eighteen (18) years and otherwise competent to make this declaration.

2. I have been retained as an expert witness on behalf of Pogona, LLC for the above-captioned *inter partes* review (“IPR”). I understand that the petition for *inter partes* review involves U.S. Patent No. 11,058,757 (the “’757 patent”), which was filed on March 31, 2017. The ’757 patent names Bruce D. Forrest and Jack D. Love as the inventors.

3. I make this declaration based on my personal knowledge, educational background and training, consideration of the materials I discuss herein, and my expert opinions.

4. I am being compensated at a rate of \$575 per hour for my time in this matter. My compensation does not depend on the outcome of this proceeding and I have no financial interest in its outcome.

5. In preparing this Declaration, I have reviewed and considered the ’757 patent and each of the documents cited herein, and I have considered them in light of general knowledge in the art in the time frame of March 31, 2016—which I understand is the earliest priority date of the ’757 patent. In formulating my opinions, I have relied upon my experience, education and knowledge as they

relate to the relevant art. I also have considered the viewpoint of a person of ordinary skill in the art in the time frame of the filing date of the '757 patent.

II. BACKGROUND AND QUALIFICATIONS

6. A copy of my curriculum vitae, which includes further details of my educational background and career, is attached as Exhibit 2021.

7. I hold a Ph.D. in biological chemistry, conferred by the Department of Biological Chemistry, The University of Michigan Medical School, and work as a consulting biochemist.

8. While at UOP, AlliedSignal and Honeywell (merged companies) and then as a consultant, I worked in such diverse areas as blood and bodily fluid preservation and storage, using enzymes to make sweeteners, to enzymatically convert natural products to commercially useful substances, applied biotechnology and novel ingredient formulations (discovered that these compounds provide a springboard into a broad spectrum of formulating applications within the personal care and over-the-counter (OTC) product categories with multi-functional properties, and as a result provide a multitude of unexpected benefits and superior characteristics to skin, hair, bath, dental and OTC products), pharmaceuticals, application of antimicrobials, biological treatment of hazardous waste, microorganisms to recycle urine and wastewater on the Space Station and Mars

Lander, as well as aiding customers in complying with OSHA, EPA, FDA and USDA regulations, mostly in the food industry.

9. I have developed the commercial scale-up for the critical enzymatic step to produce the first once-a-day AIDS treatment emtricitabine (formerly known as Coviracil).

10. I have served as an expert witness in these fields and others in a variety of legal proceedings.

11. I have been active as a Director in the Chicago Section American Chemical Society.

12. As a recipient of an NIH traineeship and as a Teaching Assistant at The University of Michigan, I performed research on the discovery of novel proteins in the blood and the purification and characterization of unique blood proteins. Much of this work involved spectrophotometry of binding and redox (reduction / oxidation) reactions, as well as related prosthetic groups, including the heme *a* from cytochrome c oxidase (aka respiration complex IV) and chemical reactivity, and immunological characterization.

13. Also, while at The University of Michigan, I taught introductory biochemistry in the undergraduate laboratory (to students which included many pre-med students), and also taught chemistry, biochemistry and applied physiology to BS Nursing students and Medical Technologists. My teaching to the Medical

Technologists included full hands-on training on performing clinical glucose tolerance tests, blood drawing, glucose analysis and relevant data work-up.

14. When I was at Cornell University, I was a Postdoctoral Scholar, performed research on blood proteins, and taught introductory biochemistry.

15. As an adjunct professor at Columbia College, I taught the general Chemistry / Biochemistry course. In each of these courses I presented lectures on enzymatic processes, including small molecule transformation processes.

16. I am a named inventor on 15 patents directed in the biotechnology, chemical, food, pharmaceutical, and biological air and wastewater treatment arts. Within that group, I am a named inventor on multiple patents involving immobilized enzymes and immobilized enzyme-catalyzed processes, including a number involving chemical crosslinking and derivatization, and enzymatic transformations, such as:

- Laszlo, Joseph A., Compton, David L., DeFilippi, Louis J. and Grall, Steven, “Methods of Making Composition Comprising a UV-Absorbing Chromophore”, U.S. Patent 7,572,610 (2009);
- Laszlo, Joseph A., Compton, David L., DeFilippi, Louis. J. and Grall, Steven, “Compositions Comprising a UV-Absorbing Chromophore”, U.S. Patent 7,727,514 (2010);

- DeFilippi, Louis J., Grall, Steven G., Kinney, James F., Laszlo, Joseph A., Compton, David L.; “Formulations with Feruloyl Glycerides and Methods of Preparation”, U.S. Patent 7,744,856 (2010)
- Laszlo, Joseph. A., Compton, David. L., DeFilippi, Louis J. and Grall, Steven, “Compositions Comprising a UV-Absorbing Chromophore”, U.S. Patent 8,357,353 (2013).

17. I have been retained as a technical expert on multiple litigation matters. Most recently (~five years) I have testified as an expert at trial and/or by deposition in the following matters:

- In the Matter of Certain Plant-Derived Recombinant Human Serum Albumins (“rHSA”) and Products Containing Same, USITC Inv. No. 337-TA-1238 (retained by respondent Wuhan Healthgen Biotechnology Corp., deposed May and July 2021, testified November 2021);
- Celanese Int’l Corp. v. Anhui Jinhe Industrial Co., Case 1:20-cv-01775-UNA and In the Matter of Certain High-Potency Sweeteners, Processes for Making Same, and Products Containing Same, USITC Inv. No. 337-TA-1264 (retained by Celanese, deposed December 2021);

- Longhorn Vaccines & Diagnostics, LLC v. Spectrum Solutions, stabilizing formulation for sputum and other biological fluids in collection tubes for later nucleic acid analysis; IPR Nos. IPR2021-00847, IPR2021-00850, IPR2021-00854, IPR2021-00857, IPR2021-00860 (retained by Longhorn Vaccines & Diagnostics, deposited April and August 2022);
- Silcotek Corp. v. Waters Corp., Silane-based vapor phase deposition coating for HPLC; C.A. No. 23-281-JPM (retained by Waters Corp., deposited January 2024);
- Bonerge Lifescience (Hunan) CO., LTD., Petitioner v. Nanjing Nutrabuilding Bio-Tech CO., LTD., (Patent Owner); U.S. Patent No. 10,278,961, involving administration of berberine metabolites for glucose tolerance (retained by Nanjing Nutrabuilding). Deposition date not set.

18. The above cases have included such subject areas as chemically or biochemically altered natural products, such as the transesterification of ferulic acid with soybean oil, transesterification of jojoba oil with hydrogenated jojoba oil (addition of hydrogen to natural molecule) as well as biologically altered natural and synthetic products.

19. If called to testify as to the contents of this report, I can and would testify truthfully and competently.

III. LEGAL PRINCIPLES

Ordinary Skill in the Art

20. My opinions in this declaration are based on the understandings of a person of ordinary skill in the art—sometimes referred to as an “ordinary artisan” or by the acronym “POSA”—as of the time of the invention, which I understand to be the March 31, 2016 filing date of the earliest application leading to the ’757 patent. I understand that the person of ordinary skill in the art is a hypothetical person who is presumed to have known the art relevant to the Challenged Claims of the ’757 patent at the time of the invention.

21. I understand that, in assessing the level of skill of a person of ordinary skill in the art, one should consider the type of problems encountered in the art, the prior solutions to those problems found in the prior art references, the rapidity with which innovations are made, the sophistication of the technology, the level of education of active workers in the field, and one's own experience working with those of skill in the art at the time of the invention.

22. I understand that Petitioner submits that a POSA at the time of the ’757 patent as “includ[ing] a research team with one or more researchers with an M.D. or Ph.D. in immunology, virology, biochemistry, chemistry, or a related

discipline, and several years of work experience in vaccinology or related fields, and one or more individuals with an advanced degree and experience in drug delivery of vaccines” (Petition at 12–13 (emphasis added)). I further understand that in a separate IPR Petition challenging the ’757 patent, a different petitioner—Merck—submitted that a POSA at the time of the ’757 patent as “an individual or team with Ph.D. degrees in the biological and chemical sciences and at least 2 years of work experience, or an M.D. degree with at least 6 years of work experience developing conjugate vaccines, including specifically growing sufficient quantities of bacteria, extracting, purifying and analyzing bacterial polysaccharides, conjugating polysaccharides to a carrier.” *Merck Sharp & Dohme LLC v. Pogona, LLC*, IPR2026-00221, Paper 2, 12–13 (PTAB Jan. 26, 2026).

23. I note that Merck’s definition does not require the underlined portion of Petitioner’s definition. In my opinion, a POSA would not need experience in drug delivery of vaccines as Petitioner’s POSA definition articulates, as an individual “with an M.D. or Ph.D. in immunology, virology, biochemistry, chemistry, or a related discipline, and several years of work experience in vaccinology or related fields” would have sufficient knowledge of drug delivery for the field of the ’757 patent. Thus, in my opinion, a POSA would include “a research team with one or more researchers with an M.D. or Ph.D. in immunology,

virology, biochemistry, chemistry, or a related discipline, and several years of work experience in vaccinology or related fields” (Petition at 12-13).

Claim Construction

24. I understand that the Challenged Claims of the ’757 patent in this IPR are generally interpreted according to their ordinary and customary meaning taking into consideration the so-called “intrinsic evidence” of the patent consisting of (1) the claim language; (2) the specification; and (3) the prosecution history.

25. I understand that claim terms may be explicitly defined in the patent specification or they may be implicitly defined through consistent usage in the specification. I also understand that the scope of claim terms may be limited by statements in the specification or prosecution history where the applicant clearly disavows or disclaims subject matter.

26. I understand that claim construction is a matter of law.

Anticipation

27. I have been informed that a claim is invalid as anticipated under 35 U.S.C. § 102 if a prior art reference discloses, either expressly or inherently, all limitations of a claim as those limitations are arranged in the claim.

28. I have been further informed that anticipation requires that a single reference describe the claimed invention with sufficient precision and detail to establish that the subject matter existed in the prior art.

29. I have also been informed that an anticipating prior art reference must disclose all elements of the claim arranged or combined in the same way as in the claim, without any need for picking, choosing, and combining various disclosures.

30. I have been informed that that where a reference contains a list of items that may be combined to form a claimed combination, the reference can only be anticipatory if the number of categories and components disclosed in the prior art reference is small enough that the claimed combination would be immediately apparent to one of ordinary skill in the art.

31. I have been informed that a limitation is disclosed inherently in a reference if it is necessarily present in the process or product described in the prior art reference. I understand that probabilities or possibilities are insufficient to show that a prior art reference inherently discloses something beyond what it discloses explicitly.

Obviousness

32. I have been instructed by counsel and understand that a combination of prior-art references may render a claim obvious if, at the time of the invention, a person of ordinary skill in the art would have selected and combined those prior-art elements in the normal course of research and development to yield the claimed invention.

33. I understand that for a reference to be considered in an obviousness analysis, it needs to be analogous to the claimed invention. I further understand that a reference is considered analogous prior art if the reference is from the same field of endeavor as the claimed invention, or if the reference is reasonably pertinent to the problem the claimed invention attempts to solve.

34. Counsel has informed me, and I understand, that an issued patent claim is invalid as obvious if it can be shown that the differences between the patented subject matter and the prior art are such that the subject matter as a whole would have been obvious, at the time the invention was made, to a person having ordinary skill in the art.

35. I understand that in making the obviousness inquiry, one should consider the *Graham* factors: the scope and content of the prior art; the differences between the claimed inventions and the prior art; the level of ordinary skill in the art; and certain secondary considerations, identified below. I further understand the obviousness analysis is to be performed on a claim-by-claim basis. I understand that a person of ordinary skill in the art is a person of ordinary creativity, not an automaton.

36. I have been instructed by counsel and understand that obviousness requires more than a mere showing that the prior art includes separate references covering each separate limitation in a claim under examination. I understand

obviousness requires the additional showing that a person of ordinary skill at the time of the invention would have been motivated to combine those references, and, in making that combination, a person of ordinary skill in the art would have had a reasonable expectation of success.

37. I also understand that an obviousness analysis must be conducted with awareness of the distortion caused by hindsight bias and with caution of arguments reliant upon *ex post* reasoning. Counsel has instructed me that when considering obviousness, I should not consider what is known today or what was learned from the asserted patents. Instead, I should put myself in the position of a person of ordinary skill in the field at the time of the invention.

38. In particular, I understand that it is improper to use the invention as a roadmap to find its prior-art components because such an approach discounts the value of combining various existing features or principles in a new way to achieve a new result.

39. I understand that an invention would not have been obvious to try when one would have had to try all possibilities in a field that is not small and easily traversed, and that is unreduced by direction of the prior art. Stated another way, when what would have been “obvious to try” would have entailed varying all parameters or trying each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which

parameters were critical or no direction as to which of many possible choices would have been likely to be successful, an invention would not have been obvious. Further, an invention is not obvious to try where prior art does not guide one toward a particular solution.

40. I am informed by counsel and I understand that the secondary considerations of nonobviousness could include factors such as commercial success, long felt but unresolved needs, the failure of others, skepticism by experts, praise by others, award and accolades, and copying.

41. Counsel has informed me, and I understand, that a reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant of the '757 patent.

Prior Art Enablement

42. For anticipation by a prior art publication or document, I understand that the reference's description must enable a POSA to practice the claimed invention without undue experimentation.

43. I understand from counsel that prior art used for obviousness must enable the claimed invention when the prior art is considered as a whole, even if a particular reference does not enable its own full disclosure.

44. I understand from counsel that prior art enablement conducts an undue experimentation inquiry that is ordinarily organized around the eight *In re Wands* factors: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

45. I understand from counsel that working examples are particularly important for functional limitations in unpredictable fields.

IV. OVERVIEW OF THE '757 PATENT AND TECHNOLOGY BACKGROUND

46. The '757 patent, entitled "Saccharide-Polypeptide Conjugate Compositions and Methods of Use Thereof," issued on July 13, 2021, claims priority to U.S. Provisional Application Nos. 62/373,807 (filed one August 11, 2016), 62/372,263 (filed on August 8, 2016), 62/330,245 (filed on May 2, 2026), and 62/316,555 (filed on March 31, 2016).

47. On July 13, 2021, the U.S. Patent and Trademark Office issued the '757 patent, which claims priority to a provisional filed on March 31, 2016, and is entitled "Saccharide-Polypeptide Conjugate Compositions and Methods of Use Thereof," to Pogona, LLC as assignee of the named inventors Bruce D. Forrest and Jack D. Love.

48. I understand that Pogona developed the novel composition of serotypes described and claimed in the '757 patent, including, for example:

Claim 1: reciting selecting at least two unique serotypes from the group of serotypes 23A, 23B, and 35B—none of which are serotypes included in PPSV23.

Claim 12: depending from claim 1 and reciting further selecting at least one additional serotype from the group of serotypes 6C, 8, 9N, 10A, 11A, 12F, 15A, 15B, 15C, 16F, 20A, 20B, 22F, and 34—of which 6C, 15A, 15C, 16F, 20A, 20B¹, and 34 are serotypes not included in PPSV23.

Claims 13/14: depending from claim 1, wherein the selected serotypes comprise/consist of 6C, 9N, 15A, 15C, 16F, 23A, 23B, and 35B.

V. CLAIM CONSTRUCTION

49. I have been informed by counsel that the Challenged Claims of the '757 patent are to be construed in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent. In forming my opinions set forth below, I have therefore applied the ordinary and customary meaning of all claim terms.

¹ PPSV includes serogroup 20, but does not specify serotypes 20A and 20B.

VI. THE CHALLENGED CLAIMS OF THE '757 PATENT ARE VALID

A. Alexander and Gu Do Not Enable a POSA to Make the Claimed Immunogenic Compositions

50. A POSA would understand that the success of any conjugation reaction depends on a combination of variables that must be evaluated together, not selected independently, for each new starting material—including reactant concentrations, the physical state and surface area of the reactants, temperature, and the use of any catalysts. (Ex. 2048 at 4; Ex. 2049 at 1.)

51. A POSA who must adjust one such variable while holding the others constant, and then test the result, is engaged in precisely the kind of iterative, trial-and-error experimentation the *Wands* factors identify as unreasonable.

52. Neither Alexander nor Gu supplies the necessary details to avoid this excessive experimentation for the claimed serotypes, as I detail below.

53. A POSA would understand that, as a matter of standard scientific practice, a researcher varies one independent variable at a time while holding the others constant, then measures the resulting dependent variable—here, the immunogenic status of the resulting composition. Where numerous variables must each be evaluated in this manner, and then evaluated again in combination with one another, the number of experiments required increases accordingly, and the immunogenic status of any particular combination cannot be predicted without testing it directly.

54. Neither Alexander nor Gu addresses whether an inert atmosphere is required, or even beneficial, as compared to a normal, oxygen-containing atmosphere, despite this being a potential stability issue: reactions conducted in the presence of oxygen risk producing unwanted side-products through oxidation. Neither reference discloses testing under different atmospheric conditions, leaving a POSA with no guidance on whether this variable would affect the immunogenic status of a conjugate of the claimed serotypes.

55. The order and rate at which reactants are combined can also be critical: adding a component too quickly can cause precipitation, or fail to dissolve materials that have undergone hydrogen bonding between polymer chains, either of which could compromise the resulting conjugate. Neither Alexander (Ex. 1008 at [1028]–[1029]) nor Gu teaches a rate of addition for any of the claimed serotypes, or what negative consequences might follow from a different rate than the one each reference happened to use in its own unrelated examples.

1. Alexander Fails Multiple Wands Factors

a. Excessive Experimentation Required (Factor 1)

56. Alexander provides no specific conjugation protocols, immunogenicity data, or technical guidance for any of the claimed serotypes.

57. While Alexander discloses general concepts for conjugating pan-DR binding peptides to capsular polysaccharides, these generic protocols are not

tailored to the claimed serotypes and provide no guidance on which conjugation approach would be appropriate for each. (Ex. 1008 at [0087]-[0093].)

58. A POSA would need to conduct substantial experimentation to determine, for each claimed serotype: appropriate activation methods for that serotype's polysaccharide structure; optimal conjugation chemistry and linker selection; solvent system and ratios (aqueous, organic, or mixed); reactant concentrations and stoichiometric ratios, including whether any reactant should be used in molar excess; temperature, pH, ionic strength, and buffer composition; whether an inert atmosphere is required; agitation method, rate, and order of addition; whether direct or linker-mediated conjugation is more suitable; purification and characterization methods; sterility and sterilization approach; and testing protocols to confirm immunogenicity.

59. Alexander's own disclosure confirms this burden: it discloses only that reactant concentrations "depend upon numerous factors including reaction conditions such as temperature and pH, and the choice and amount of acceptor saccharides to be glycosylated," without specifying values. (Ex. 1008 at [0080].)

60. Alexander further discloses that "[t]he upper limit for the concentrations of reactants that can be used in accordance with the method of the present invention is determined by the solubility of such reactants," again without providing any serotype-specific guidance. (Ex. 1008 at [0080].)

61. Alexander's only disclosed agitation step is tied to a single example, without generalizable guidance on rate or technique, and its sole reference to sterility is a citation to conventional techniques generally, with no serotype-specific protocol. (Ex. 1008 at [0117], [0128]-[0129].)

62. Alexander's only teaching on sterility is that compositions may be "sterilized by conventional, well known sterilization techniques, or may be sterile filtered." (Ex. 1008 at [0117].) Alexander does not address viscosity, which can impede sterile filtration, or otherwise provide any serotype-specific sterilization protocol.

63. Alexander provides no direction to a POSA for navigating these critical serotype-specific choices for any of the claimed serotypes. The reference's only concrete working examples involve serotypes 14, 6B, and 9V, demonstrating that even Alexander's own inventors required detailed, serotype-specific protocols to achieve successful conjugates. (Ex. 1008 at [0127]-[0139].)

64. The complete absence of such protocols for the claimed serotypes necessitates undue experimentation.

b. *Insufficient Direction or Guidance (Factor 2)*

65. Alexander offers only the conclusory statement that compositions contain "an immunogenically effective amount," without any technical direction on how to achieve immunogenicity for the claimed serotypes. (Ex. 1008 at [0105].)

While Alexander describes general pan-DR binding peptide sequences and mentions various conjugation approaches, it provides no guidance on which specific pan-DR binding peptide sequence is optimal for each claimed serotype, nor does Alexander supply guidance as to what sequences would be successful for peptides, as well as necessary protocols, other than the specific pan-DR binding peptides, which conjugation chemistry (direct vs. linker-mediated vs. spacer-mediated) is appropriate for the structural features of each claimed serotype, expected conjugation efficiency or degree of conjugation targets for each serotype, quality control parameters or acceptance criteria specific to each serotype conjugate, immunogenicity testing protocols or target immune responses for each serotype, or troubleshooting approaches when initial conjugation or immunization attempts fail. (Ex 1008 at [0058]-[0065], [0087]-[0093].)

66. Alexander's generic statements lack the specific direction necessary for enablement of conjugates including any of the claimed serotypes.

67. Alexander also merely lists some of the claimed serotypes among dozens of possible serotypes, without any technical guidance to further narrow the possible serotype combinations.

68. Nor does Alexander use the terms "two or more" or "plurality" when describing the choice among its listed serotypes for conjugation to a single

polypeptide, providing no textual signal to a POSA regarding how many serotypes to select for any particular preparation.

c. Complete Absence of Relevant Working Examples (Factor 3)

69. Alexander provides no working examples demonstrating actual immunogenic conjugates for any of the claimed serotypes.

70. The reference's sole immunogenicity data consists of antibody responses and opsonophagocytic (OPA) activity for serotype 6B conjugates, along with antibody titers for serotypes 14 and 9V. (Ex. 1008 at [0135]-[0141].) These data cannot enable the claimed serotypes. Alexander contains no immunogenicity data, ELISA results, or opsonophagocytic testing for the claimed serotypes; the structural and immunological differences between serotypes 6B, 14, 9V and the claimed serotypes are not addressed; no correlation or bridging data suggests that results for 6B, 14, or 9V would predict success for the claimed serotypes; and the detailed protocols provided for serotypes 6B, 14, and 9V are specific to those serotypes and provide no guidance for different serotypes or peptides.

d. Highly Unpredictable Art (Factor 7)

71. A POSA would have understood that pneumococcal conjugate vaccine development was highly unpredictable as of the priority date. Alexander's development approach confirms this unpredictability.

72. The reference discloses multiple different conjugation approaches, including direct conjugation and various linker-based strategies, and multiple different pan-DR binding peptide sequences, but without guidance on which to select for particular serotypes or guidance on which types of peptides other than DR binding peptides could be successfully selected. (Ex. 1008 at [0058]-[0065], [0087]-[0093].) Alexander's own data shows variability in immunogenicity across different serotypes, with serotype 14 being "the most immunogenic and serotype 9 the least." (Ex. 1008 at [0137].)

73. Based on the above factors, it is my opinion that Alexander does not enable a POSA to make the compositions recited in the '757 patent Challenged Claims without undue experimentation.

2. Gu Similarly Fails the Wands Analysis

a. Excessive Experimentation Required (Factor 1)

74. Gu also provides no specific conjugation protocols, immunogenicity data, or technical guidance for the claimed serotypes (other than claim 12's 22F).

75. While Gu discloses general activation methods using the carbonic acid derivative 1,1'-carbonyl-di-(1, 2,4-triazole) (CDT) or periodate oxidation, these generic protocols are not tailored to the claimed serotypes and provide no guidance on which activation pathway would be appropriate for each. (Ex. 1009 at 9, 22.)

76. A POSA would need to conduct substantial experimentation to determine, for each claimed serotype: whether to use CDT or periodate activation; optimal activation conditions (temperature, time, reagent concentrations); whether aqueous or organic solvent conditions—and at what ratios—are appropriate; reactant concentrations, buffer composition, and pH; ionic strength and salt content; agitation method and rate of addition; conjugation chemistry and reaction parameters; purification and characterization methods; sterility requirements; and testing protocols to confirm immunogenicity.

77. Gu’s own disclosure confirms this burden. Gu reports that “several conjugates [were] obtained...by varying different parameters (e.g. pH, temperature of the reactions and concentration of polysaccharide)” but gives no guidance on how to select those parameters for an untested serotype. (Ex. 1009 at 93:1-2.)

78. Gu also discloses various water-to-solvent ratios without explaining which ratios, or ranges of ratios, would be beneficial in other systems. (Ex. 1009 at 48.)

79. Gu’s only concrete buffer and concentration data are serotype-specific—for example, dissolving the 33F polysaccharide in 100 mM sodium phosphate buffer (pH 6.0) to a final concentration of 2 mg/ml in 25 mM buffer, and Gu’s stirring, stability-testing, and diafiltration examples likewise appear only at scattered, serotype-specific points in the disclosure, with no indication that these

parameters would translate to an untested serotype. (Ex. 1009 at 92:9-93:23; 113:5-114:2.)

80. Gu's only concrete working examples involve serotypes 22F and 33F (Ex. 1009 at 87-88, 112-119), demonstrating that even Gu's own inventors required detailed, serotype-specific protocols to achieve successful conjugates. The complete absence of such protocols for the claimed serotypes necessitates undue experimentation.

b. Insufficient Direction or Guidance (Factor 2)

81. Gu offers only the conclusory statement that glycoconjugates "can be used in the production of antibodies," without any technical direction on how to achieve immunogenicity for the claimed serotypes (other than claim 12's 22F). (Ex. 1009 at 31:32-32:2.) While the reference describes general chemical schemes for oxo-linked conjugates (Figures 1–4), it provides no guidance on which conjugation chemistry (e.g., a spacer-linked e.g., ((2-oxoethyl)thio)alkyl)carbamate glycoconjugate, (oxo-eTAC), oxo-eTAAN, or oxo-eTAAD) is appropriate for each claimed serotype, how to select activation conditions for the specific structural features of these serotypes, expected conjugation efficiency or degree of conjugation targets, quality control parameters or acceptance criteria, immunogenicity testing protocols or target immune responses, or troubleshooting approaches when initial attempts fail.

82. Gu's generic chemical schemes lack the specific direction necessary for enablement of the claimed serotypes.

83. Gu also merely lists some of the claimed serotypes among other, unclaimed serotypes, without any technical guidance to further narrow the possible serotype combinations.

84. Nor does Gu use the terms "two or more" or "plurality" when describing the choice among its listed serotypes for conjugation to a single polypeptide, providing no textual signal to a POSA regarding how many serotypes to select for any particular preparation.

c. Complete Absence of Relevant Working Examples (Factor 3)

85. Gu provides no working examples demonstrating actual immunogenic conjugates for any of the claimed serotypes.

86. Gu's sole immunogenicity data consists of OPA titers for serotype 33F conjugates in a murine model. (Ex. 1009 at 87-88.) Gu contains no immunogenicity data, ELISA results, or OPA testing for the claimed serotypes. The structural and immunological differences between serotype 33F and the claimed serotypes are not addressed. Gu provides no correlation or bridging data suggests that results for 33F would predict success for the claimed serotypes, and the detailed protocols provided for serotype 33F are specific to that serotype and provide no guidance for different serotypes.

d. Highly Unpredictable Art (Factor 7)

87. In addition to my discussion of this factor with respect to Alexander, Gu's own development approach confirms the unpredictability of this art. The reference discloses multiple different activation pathways (CDT, CDI, periodate oxidation) and conjugation chemistries (oxo-eTAC, oxo-eTAAN, oxo-eTAAD), acknowledging that different approaches may be needed for different serotypes. (Ex. 1009 at 9, 22.) Gu provides detailed protocols only for its successfully developed serotypes (22F, 33F), implicitly acknowledging that generic guidance is insufficient and that each serotype requires individual experimental development.

88. Based on the above factors, it is my opinion that Gu does not enable a POSA to make the compositions recited in the '757 patent Challenged Claims without undue experimentation.

B. The Petition Fails to Demonstrate a Reasonable Expectation of Success for Its Obviousness Grounds

89. Neither Alexander nor Gu provides any indication of how to conjugate serotypes 23A, 23B, or 35B to achieve immunogenicity, or which conjugation pathways are appropriate for these serotypes.

90. Alexander states only that "[t]he present invention is directed to vaccines which contain as an active ingredient an immunogenically effective amount of a composition comprising at least one conjugate of the present invention." (Ex. 1008 at [0105].) This conclusory statement provides no level of

immune response that constitutes “Immunogenically effective” or how to achieve it for any the claimed serotypes.

91. Gu discloses “immunogenic compositions” in its title and abstract, and states that “[g]lycoconjugates of the invention comprising a bacterial capsular polysaccharide can be used in the production of antibodies against such a bacterial capsular polysaccharide.” (Ex. 1009 at Cover, [54], [57], 31:32-32.) Like Alexander, Gu’s disclosure provides no technical direction toward achieving immunogenicity for the claimed serotypes.

92. That researchers *wanted* to include more serotypes in a pneumococcal vaccine says nothing about whether they could have a reasonable expectation that they could *successfully* select and conjugate the claimed serotypes and achieve immunogenicity.

93. For all of the above reasons, it is my opinion that a POSA would not have had a reasonable expectation of success at successfully conjugating the claimed compositions based on Alexander or Gu.

94. I currently hold the opinions expressed in this declaration, but my analysis may continue, and I may acquire additional information and/or attain supplemental insights that may result in added observations.

Under penalty of perjury, I declare that all statements made herein of my own knowledge are true and accurate and that all statements made on information and belief are believed to be true and accurate, and that these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code.

Executed this 4th day of August, 2026.



Louis J. DeFilippi, Ph.D.
President and Member,
Louis DeFilippi, LLC