

Filed: April 6, 2026

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

**PATENT OWNER'S PRELIMINARY RESPONSE
UNDER 35 U.S.C. § 313 AND 37 C.F.R. § 42.107**

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I. INTRODUCTION

On December 23, 2025, Petitioner Pfizer Inc. filed a Petition seeking inter partes review of all claims of U.S. Patent No. 11,058,757 (the “’757 patent”), which is assigned to Patent Owner Pogona, LLC. The ’757 patent claims a novel composition of pneumococcal serotypes for use in pneumococcal conjugate vaccines (“PCV”)—serotypes that had never before been included in any pneumococcal vaccine and that represent a fundamental departure from decades of industry practice.

For over forty years, the pharmaceutical industry developed pneumococcal vaccines by selecting serotypes exclusively from the original 23 serotypes included in Merck’s 1983 PPSV23 polysaccharide vaccine. The ’757 patent’s inventors took a different approach. Based on epidemiological data and the hypothesis that widespread use of Pfizer’s own Prevnar 13 vaccine would shift disease burden toward non-PPSV23 serotypes, they identified a novel composition targeting emerging invasive disease serotypes—including serotypes 23A, 23B, and 35B, none of which had previously been included in PPSV23 or any other pneumococcal vaccine. This hypothesis proved correct: by 2016, disease caused by Prevnar 13 serotypes had dropped to 25%, while non-pneumococcal conjugate vaccines (“PCV”) and non-PPSV23 serotypes like those claimed in the ’757 patent became the predominant causes of invasive pneumococcal disease.

Petitioner’s anticipation and obviousness challenges against this ’757 patent fail for multiple independent reasons. **First**, the prior art references on which Petitioner relies—Alexander (Ex. 1008) and Gu (Ex. 1009)—disclose vast universes of possible vaccine formulations without identifying the claimed invention. Alexander’s laundry list of serotypes creates between 2.25 and 31.5 quadrillion possible combinations. Gu lists 8 serotypes creating 192 distinct combinations. Neither reference provides any guidance directing a person of ordinary skill in the art (“POSA”) to select the specific serotype combinations claimed in the ’757 patent. Petitioner’s challenges thus require the impermissible “picking and choosing” that Federal Circuit and Board precedent explicitly prohibits in an anticipation analysis.

Second, neither Alexander nor Gu discloses the critical “immunogenic” limitation recited in every claim. As the Board held in *Merck v. Wyeth*, invalidating prior art must provide actual evidence of immunogenicity for the specific claimed serotypes, not merely aspirational statements of intent. Neither reference provides such evidence; instead, they make only generic, conclusory statements about immunogenicity as an overall goal.

Third, Petitioner’s obviousness grounds fail to establish a reasonable expectation of success. Petitioner’s entire showing consists of conclusory assertions unsupported by technical analysis or evidence. This deficiency is particularly

glaring given that Petitioner itself—in prior proceedings before the Board defending its own pneumococcal vaccine patents—has repeatedly told the Board that pneumococcal conjugate vaccine development is “an unpredictable field characterized more by failures than successes,” and plagued by immune interference, carrier-induced epitope suppression, and formulation instability challenges. *Merck Sharp & Dohme Corp. v. Wyeth LLC*, IPR2017-00390, Paper 15, 5 (PTAB Sept. 13, 2017). The fact that only 13 of the roughly 100 known pneumococcal serotypes had been successfully incorporated into conjugate vaccines by 2016—despite decades of research and commercial incentive—demonstrates that technical feasibility, not mere knowledge or desire, limits vaccine development.

For these reasons, detailed below, the Board should deny institution of inter partes review.

II. LEVEL OF ORDINARY SKILL

Petitioner defines the POSA 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).) Pogona does not agree with the underlined portion of the Petitioner’s definition, ,

as the invention is directed toward “saccharide-polypeptide conjugates, and not drug delivery of vaccines. (Ex. 1001 at abstract.) Pogona notes that Merck has also filed a Petition against the ’757 patent, and defines a POSA 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). Merck’s definition notably does not require the underlined portion of Petitioner’s definition.

III. BACKGROUND TECHNOLOGY AND OVERVIEW OF THE ’757 INVENTION

Patent Owner Pogona is a biotechnology company advancing innovative discoveries and biotechnology that improves PCVs. Pogona and its predecessor entities were established to create and bring to market an improved, next-generation PCV utilizing a novel composition of serotypes, as claimed in the ’757 patent.

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—Pogona’s CSO and Manager—and Jack D. Love—Pogona’s Head of Regulatory. Dr. Forrest was formerly the global clinical team leader for Prevnar® and as SVP, Late Phase Programs, Vaccines Research & Development at Wyeth/Pfizer, led the organization responsible for the development of Prevnar 13®. Dr. Love was formerly the head of global regulatory affairs for Wyeth/Pfizer Vaccines Research & Development, and oversaw Prevnar and Prevnar 13 regulatory submissions.

“*Streptococcus pneumoniae* (pneumococcus) can cause serious illness, including sepsis, meningitis, and pneumonia with bacteremia (invasive) or pneumonia without bacteremia (noninvasive).” (Ex. 2007 at 1.) As of the priority date of the ’757 patent, there were two pneumococcal vaccines licensed for use in the United States. (*Id.*) The first is Merck’s Pneumovax 23 pneumococcal polysaccharide vaccine (“PPSV23”), for which the serotype composition was determined from epidemiology developed in the 1970s. PPSV23 is directed to serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F. Since the early 1980s, PPSV23 has been recommended for individuals aged two and older who have certain medical conditions, as well as for all adults aged sixty-five and older. Pneumococcal polysaccharide vaccines—unlike PCVs—are not immunogenic in children under the age of two.

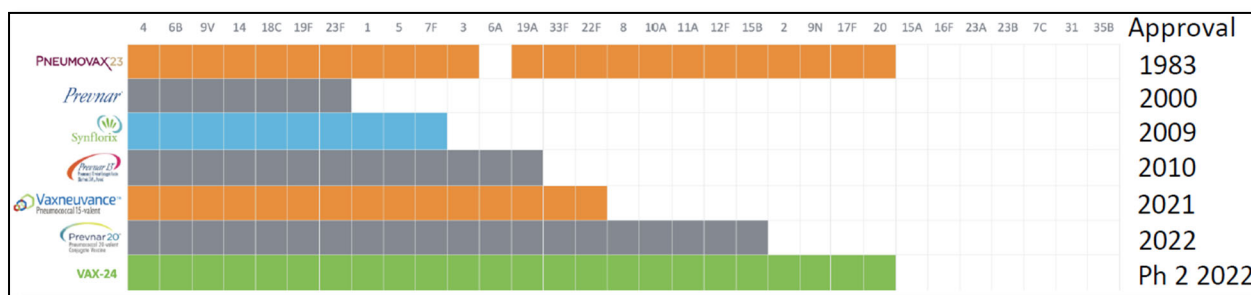
The second is Wyeth/Pfizer's Prevnar 13 PCV ("PCV13"), which replaced the 7-valent PCV, Prevnar. Prevnar was approved in 2000 and developed by conjugating CRM197 to a polysaccharide containing the seven most important serotypes from PPSV23. Prevnar is directed to serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F—all of which are a subset of the serotypes in PPSV23. When Prevnar was launched, pneumococcus remained the most common cause of severe pneumonia and bacterial meningitis, leading to a global estimate at that time of 735,000 deaths per year among children under 5 years old.

PCVs overcame the challenge of poor immunogenicity in infants and young children by using conjugation technology. In PCVs, polysaccharides (or their derivatives) are covalently linked to carrier proteins. However, due to the complexity of the conjugation process, PCVs have contained fewer serotypes than the 23 included in PPSV23.

Prevnar 13 ("PCV13"), which was approved in 2010, was developed by conjugating CRM197 to polysaccharide for what were—at one time—the thirteen most important serotypes from PPSV23. PCV13 is directed to serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F—all of which are a subset of the serotypes in PPSV23, minus serotype 6A. Serotype 6A is the only serotype to be added to PCVs beyond the serotypes included in the original PPSV23 before the '757 patent's priority date. PCV13 has been included in the routine pediatric

immunization schedule since 2010 (until well after the priority date) and since 2014 (until well after the priority date) has been recommended for all adults aged 65 and over in combination with PPSV23.

Since PPSV23 was approved in 1983, pharmaceutical companies have ignored most of the over 100 immunologically distinct serotypes of pneumococcus that have been identified, and have almost exclusively developed new pneumococcal vaccines by conjugating additional serotypes from the original PPSV23 composition backbone, as shown in the graphic below:



Pogona took a different approach, focusing not on the PPSV23 composition serotypes, but on aligning vaccine coverage with emerging invasive disease serotypes. Pogona took this approach based on the hypothesis of the '757 patent inventors that the effectiveness of PCV13 and its inclusion in routine immunization schedules would increase the importance of non-PPSV23 serotypes.

In the course of Pogona's study of PCVs, Pogona's inventors identified that the marketed and investigational PCVs at the time were likely to provide inadequate coverage against invasive pneumococcal disease ("IPD"), and

identified a novel composition of pneumococcal serotypes currently causing IPD that had not previously been included in any pneumococcal vaccine—whether polysaccharide or conjugate. The '757 patent embodies these discoveries and covers the novel composition of pneumococcal serotypes that the '757 patent's inventors discovered.

Pogona's team worked for years on an improved PCV for the prevention of pneumococcal disease not currently covered by Prevnar 13. Specifically, Pogona's team was working toward FDA approval of a vaccine containing a combination of serotypes claimed in the '757 patent, which, based on current epidemiological surveillance, are the serotypes causing most invasive pneumococcal disease in adults, and which is a combination of serotypes different than those in Prevnar 13. Through this approach, 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.

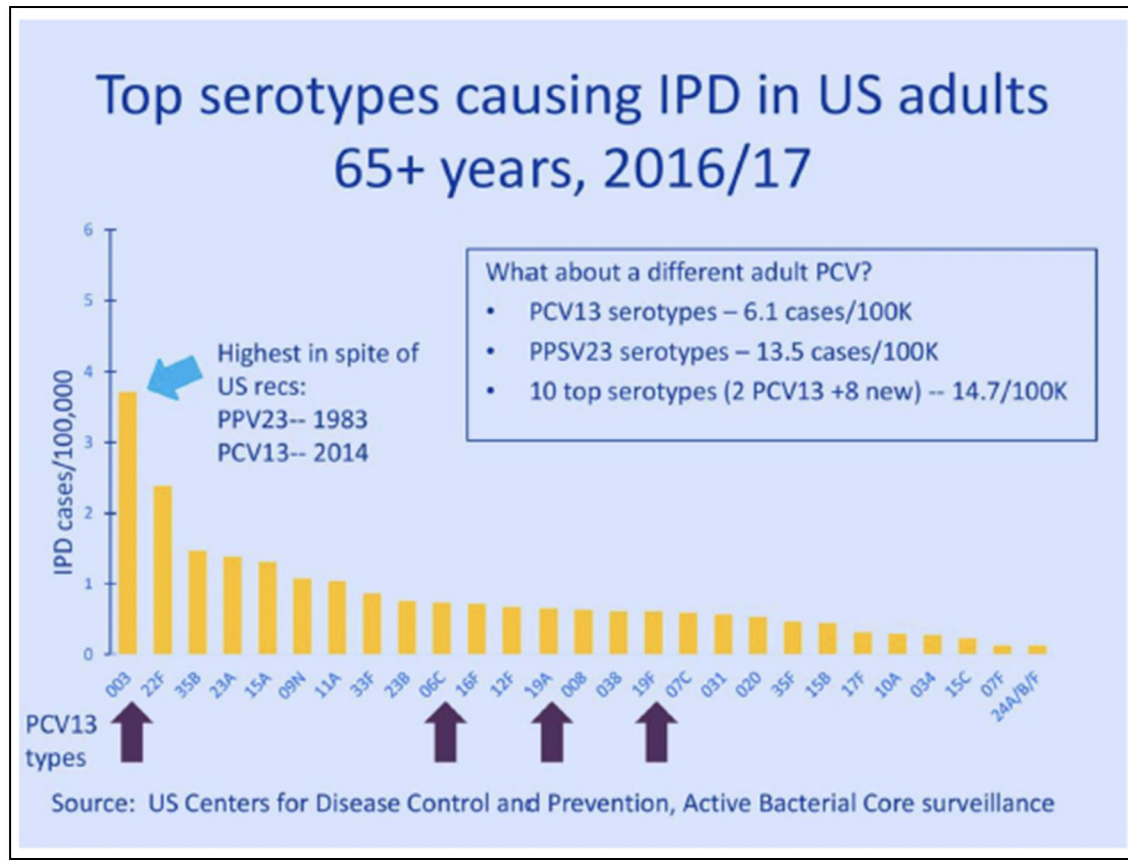
Claim 12: depending from claim 1 and reciting further selecting at least one additional serotype from the group of serotypes 6C, 8, 9N, 10A, 11A, 12F, 15A, 15B, 15C, 16F, 20A, 20B, 22F, and 34—of

which 6C, 15A, 15C, 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.

Pogona's approach proved to be correct. Initially, the serotypes included in PCV13 accounted for approximately 85% of the PPSV23 serotypes that cause disease. As Pogona's inventors predicted, the effectiveness of PCV13 resulted in a decrease in disease caused by the 13 PCV13 serotypes, from 75% in the late 1990s to 25% by 2016. Consequently, this decrease in the percentage of disease caused by PCV13 serotypes resulted in an increased rate of disease being caused by non-PCV and non-PPSV23 serotypes, as shown in the graphic below:

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



(Ex. 2008 at 28.)

Over a year after the '757 patent's priority date—on October 26, 2017—the Center for Disease Control and Prevention's ("CDC") National Center for Immunization & Respiratory Diseases ranked the non-PCV13 serotypes causing invasive pneumococcal disease, as shown in the graphic below:

Rank order of non-PCV13 serotypes causing IPD, 2015-2016

Children < 5 years

TYPE	Cases/100,000
23B	0.62
22F	0.62
33F	0.57
15C	0.52
15A	0.48
35B	0.43
10A	0.33
12F	0.29
15B	0.29
38	0.19
other	1.67

Adults ≥ 65 years

TYPE	Cases/100,000
22F	2.57
23A	1.33
35B	1.31
15A	1.16
33F	0.97
16F	0.88
11A	0.82
9N	0.72
23B	0.67
12F	0.61
other	4.66

Green denotes serotypes common to both age groups

(Ex. 2009 at 9.)

This is what the '757 patent's inventors understood—over a year earlier—when they described and recited in claim 1 a vaccine reciting selecting at least two unique serotypes from the group of serotypes 23A, 35B (top two non-PPSV23 serotypes causing IPD in adults sixty-five and older), and 23B (top non-PPSV23 serotype causing IPD in children under five years). Additionally, claim 12, which depends from claim 1, recites further selecting at least one additional serotype from a group that includes the following additional serotypes from the CDC's list: serotypes 9N, 10A, 11A, 12F, 15A, 15B, 15C, 16F, and 22F.

Based on the CDC's data, in a marked departure from decades of pharmaceutical companies developing new pneumococcal vaccines by conjugating

additional serotypes from the original PPSV23 composition backbone, CDC advised the pharmaceutical industry in 2018 to update pneumococcal vaccine coverage in adults to include circulating serotypes.

IV. CHALLENGED CLAIMS

Petitioner challenges all claims of the '757 patent.

V. CLAIM CONSTRUCTION

The Challenged Claims of the '757 patent are construed “using the same claim construction standard that would be used to construe the claim in a civil action under 35 U.S.C. 282(b).” 37 C.F.R. § 42.100(b) (Nov. 13, 2018). The '757 patent claim terms are therefore 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.” *Id.*

Patent Owner agrees with Petitioner that, for purposes of this Preliminary Response only, all terms of the '757 patent have their plain and ordinary meaning.

VI. STANDARD FOR GRANTING *INTER PARTES* REVIEW

A petition for IPR may only be granted when “the information presented in the petition ... shows that there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.” 35 U.S.C. § 314(a); *see also* 37 C.F.R. § 42.108(c). Petitioner has the burden of proof to show that the statutory threshold is satisfied. (*See* Office Patent Trial Practice Guide, 77 Fed. Reg. 48756 (Aug. 14, 2012).)

IPR institution is discretionary. *See SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1356 (2018) (“[Section] 314(a) invests the Director with discretion on the question whether to institute review ...”) (emphasis omitted). “In exercising that discretion, [the Board is] guided by the statutory requirement, in promulgating regulations for *inter partes* review, to consider the effect of any regulations on ‘the efficient administration of the Office [and] the ability of the Office to timely complete proceedings,’ 35 U.S.C. § 316(b), as well as the requirement to construe the PTAB’s rules to ‘secure the just, speedy, and inexpensive resolution of every proceeding,’ 37 C.F.R. § 42.1(b).”

For example, “the Board may consider the number of claims and grounds that meet the reasonable likelihood standard when deciding whether to institute *inter partes* review under 35 U.S.C. § 314(a).” *Deeper, UAB v. Vexilar, Inc.*, IPR2018-01310, Paper 7, 42 (PTAB Jan. 24, 2019)) (Informative).

VII. IPR SHOULD NOT BE INSTITUTED

A. Alexander and Gu’s Disclosures of Hundreds to Quadrillions of Options for Serotype Selection Do Not Anticipate the ’757 Patent

Two fundamental requirements define the anticipation standard. First, 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.” *Wasica Fin. GmbH v. Cont’l Auto. Sys., Inc.*, 853 F.3d 1272, 1284 (Fed. Cir. 2017) (emphasis added). Second, the prior art reference must disclose all

elements of the claim “arranged or combined in the same way as in the claim.” *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369–70 (Fed. Cir. 2008).

Neither Alexander nor Gu satisfies these fundamental requirements. Neither reference describes the claimed invention with the precision and detail required to show the invention previously “existed in the prior art”—instead, both provide generic lists of serotypes disclosing vast numbers of possible combinations without specifically identifying the claimed invention. (*See* Petition at 24–25, 42.)

Moreover, neither reference discloses serotypes “arranged or combined in the same way” as the claims require. The claims, among other requirements, demand a specific combination pattern: glycoconjugates that include at least two serotypes selected from the group consisting of 23A, 23B, and 35B. (Ex. 1001 at claims.)

Alexander and Gu merely list serotypes without teaching how to arrange or combine them to satisfy this specific pattern. (*See, id.*) A POSA reviewing these references would find bare lists without any teaching about which serotypes to select, how many to select, or which combination patterns correspond to the claimed invention.

1. The Mathematical Scope of Alexander and Gu’s Disclosures Renders Anticipation Impossible

A straightforward mathematical analysis reveals the fundamental problem with Petitioner’s anticipation theories: both Alexander and Gu disclose such vast universes of possible vaccine formulations that a POSA could not identify the

claimed invention without impermissible “picking and choosing” from extensive possibilities.

a. Alexander Reference

Alexander discloses a list of pneumococcal serotypes that creates an astronomical number of possible vaccine combinations. Specifically, Alexander “states that ‘the compositions of the invention comprise a mixture of conjugates of a separate [polypeptide] of the invention with capsular polysaccharides from 2’ up to **‘30 or more** of the following serotypes,’ followed by a list of **53 serotypes...**” (Petition at 24–25 (emphasis added).) Accepting Petitioner’s (unavailing) argument that “the POSA would thus understand ‘35’ to encompass 35B” as well as 35A and 35F, then Alexander’s list of 53 serotypes—which includes serotype 35—would expand the list to 55 serotypes (converting 35 to 35A, 35B, and 35F). (Petition at 25 n.2). Additionally, because Alexander limits the number of chosen serotypes only by the size of its list—disclosing combinations of up to “30 or more” of its listed serotypes—the number of serotypes that a POSA could choose from Alexander would also be 33 (scenario 1) or 35—under Petitioner’s incorrect serotype 35 argument (scenario 2).

Under Scenario 1 (treating Alexander’s disclosure of 53 serotypes as including only 23A and 23B from the required group, not 35B), a POSA could

select **2,251,799,813,685,248** possible combinations from Alexander’s list—approximately **2.25 quadrillion combinations**.²

Under Scenario 2 (expanding Alexander’s generic reference to serogroup “35” to include serotypes 35F, 35A, and 35B, resulting in 55 total serotypes), then a POSA could select **31,525,197,391,593,472** possible combinations from Alexander’s list—approximately **31.5 quadrillion combinations**.³

² The calculations for Alexander scenario 1 are as follows:

- Available serotypes from required group: 23A and 23B
- Ways to select 2 from available {23A, 23B}: $C(2,2) = 1$
 - Must select both 23A and 23B
- Remaining serotypes available: $53 - 2 = 51$
- Additional serotype combinations: $2^{51} = 2,251,799,813,685,248$

Total combinations: $1 \times 2,251,799,813,685,248 = 2,251,799,813,685,248$

Result: 2.25 quadrillion combinations

³ The calculations for Alexander scenario 2 are as follows:

Case 1: Exactly 2 from {23A, 23B, 35B}

- Ways to select 2 from {23A, 23B, 35B}: $C(3,2) = 3$
- Remaining serotypes: $55 - 2 = 53$
- Additional combinations: $2^{53} = 9,007,199,254,740,992$
- Subtotal: $3 \times 9,007,199,254,740,992 = 27,021,597,764,222,976$

Case 2: All 3 from {23A, 23B, 35B}

- Ways to select all 3: $C(3,3) = 1$

These numbers exceed human comprehension. To provide context: if a POSA could evaluate one vaccine formulation per second, working 24 hours per day, 365 days per year, it would take approximately **71 million years** to examine all 2.25 quadrillion combinations from Scenario 1, and approximately **1 billion years** to examine all 31.5 quadrillion combinations from Scenario 2.

b. Gu Reference

Gu discloses 8 total serotypes (including 23A, 23B, and 35B from the required group) with a selection range of 1-8 serotypes per formulation. (Petition at 42.) This creates **192 distinct vaccine combinations** that would satisfy the claim requirement of at least 2 serotypes “from a group consisting of 23A, 23B, and 35B.” (Ex. 1001 at claim 1.)

While substantially smaller than Alexander’s quadrillions of possibilities, Gu’s 192 combinations still represent a substantial universe of unchosen possibilities requiring impermissible selection without guidance—a disclosure that

-
- Remaining serotypes: $55 - 3 = 52$
 - Additional combinations: $2^{52} = 4,503,599,627,370,496$
 - Subtotal: $1 \times 4,503,599,627,370,496 = 4,503,599,627,370,496$

Total combinations: $27,021,597,764,222,976 + 4,503,599,627,370,496 = 31,525,197,391,593,472$

Result: 31.5 quadrillion combinations

falls well within the range the Board has found insufficient for anticipation, as discussed below.

2. Alexander and Gu Require Impermissible “Picking and Choosing”

The prohibition on “picking and choosing” from prior art lists is a foundational principle of anticipation law that explains why references disclosing large numbers of possibilities fail to anticipate specific claimed inventions. As the Board stated in an informative decision in *Ex parte Smith*, for anticipation:

[T]he [prior art] reference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing, and combining various disclosures.... Such picking and choosing may be entirely proper in the making of a 103, obviousness rejection, where the applicant must be afforded an opportunity to rebut with objective evidence any inference of obviousness..., but it has no place in the making of a 102, anticipation rejection.

(Ex. 2010 (No. 2011-003337, slip op. at 7 (PTAB Feb. 28, 2012) (informative), *aff’d* Ex. 2011 (*In re Smith*, No. 12-1344, slip op. at 2 (Fed. Cir. Nov. 20, 2012)) (quoting *In re Arkley*, 455 F.2d 586, 587–88 (CCPA 1972)) (emphasis in original).)

Applying this principle, the Board in *Ex parte Smith* reversed the prior anticipation finding because “[s]ome picking and choosing of ingredients from the

myriad of possible additives listed in [the prior art] depending on the application... is necessary to arrive at” the claimed composition “recited in claims 4 and 5.” *Id.*, 7–8. The Board further linked this principle to the specificity requirement of §102(b). *Id.* at 8 (citing *Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991, 999 (Fed. Cir. 2006) (“[w]hen a prior art reference teaches a large range (corresponding to a large genus) that encompasses, among other things, the claimed narrow range (corresponding to a few species), no reasonable fact finder could conclude that the prior art describes the claimed range [i.e., the claimed species,] with sufficient specificity to anticipate this limitation of the claim.”); *In re Schaumann*, 572 F.2d 312, 315 (CCPA 1978) (“The prior art reference must identify each and every element as set forth in the claim ‘with sufficient specificity to constitute a description thereof within the purview of 35 U.S.C. §102[(b)]’”).).

Alexander clearly requires the impermissible “picking and choosing” that *Ex parte Smith* explicitly prohibits. Alexander provides bare lists of 53-55 serotypes with no guidance on which combinations to select, no hierarchical preferences, no working examples, and no teaching about the claimed at least 2 serotypes “from a group consisting of 23A, 23B, and 35B.” (Petition at 24–25; Ex. 1001 at claim 1.) A POSA must pick and choose among quadrillions of possibilities to arrive at a combination satisfying this limitation. This is not a case where the reference

“clearly and unequivocally disclose[s] the claimed [combination]”—it is a case requiring extensive selection from vast alternatives.

Similarly, Gu requires impermissible picking and choosing. Gu provides a list of eight serotypes without teaching which specific combinations to form, which combinations are preferred, or how to identify combinations satisfying the claimed limitation. (Petition at 42.) A POSA must pick and choose from 192 possibilities without any directional guidance. The reference does not “direct those skilled in the art to the [claimed combination] without any need for picking, choosing, and combining various disclosures.” *Ex parte Smith*, slip op. at 7. Instead, it presents a selection problem requiring systematic enumeration and analysis to identify—with hindsight—which combinations satisfy the claims.

3. Alexander and Gu Fail the Numerical Benchmarks that Limit Anticipation

Federal Circuit precedent has established numerical benchmarks that apply the picking-and-choosing prohibition in practice. These benchmarks demonstrate that even relatively small numbers of combinations can fail to anticipate absent specific directional teaching, while Alexander’s and Gu’s vastly larger universes of possibilities catastrophically exceed any acceptable threshold.

At the lower end of the spectrum, in *Nidec*, the Federal Circuit explained that under a proper interpretation of *Kennametal*—a prior art reference disclosed five binding agents and three coating techniques, creating fifteen possible

combinations—the prior art in that case was anticipatory where the reference explicitly taught that any of the five binding agents could be used with any of the three coating techniques. *Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 851 F.3d 1270, 1274–75 (Fed. Cir. 2017) (citing *Kennametal, Inc. v. Ingersoll Cutting Tool Co.*, 780 F.3d 1376, 1382–83 (Fed. Cir. 2015)). The *Nidec* court further explained that in *Kennametal*, “the relevant question was ‘whether the number of categories and components disclosed in [the prior art reference] is so large that the combination ... would not be immediately apparent to one of ordinary skill in the art.’” *Id.* at 1274 (quoting *Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC*, 683 F.3d 1356, 1361 (Fed. Cir. 2012)). Critically, the *Nidec* court held that references cannot use the “at once envisage” standard “to fill in missing limitations simply because a skilled artisan would immediately envision them.” *Id.* at 1274–75. The reference itself must actually teach or disclose the combinations—POSA knowledge cannot supply missing teachings. *Id.* This reinforces the picking-and-choosing prohibition: if a reference requires a POSA to mentally fill in missing combinations, that constitutes impermissible selection.

Moving up the numerical scale, in *Wrigley*, the Shahidi reference disclosed three “particularly preferred” cooling agents (WS–3 and WS–23 were two of the three) and twenty-three flavoring agents (menthol was identified as among the “most suitable” flavoring ingredients). 683 F.3d at 1360–62. This created sixty-

nine possible combinations of cooling agents with flavoring agents. The Federal Circuit held that this number of combinations, coupled with critical additional features, was sufficiently limited that the specific combination of WS-23 and menthol would be “immediately apparent” to one of ordinary skill in the art. *Id.* at 1361.

The *Wrigley* court emphasized two features that made the sixty-nine combinations anticipatory and avoided the picking-and-choosing problem. **First**, Shahidi used strong preferential language, identifying WS-23 as one of only three “particularly preferred” cooling agents and menthol as among the “most suitable” flavoring ingredients. *Id.* at 1361. This hierarchical designation narrowed the universe of plausible combinations dramatically, directing a POSA to specific components rather than requiring selection from equally viable alternatives. **Second**, Shahidi explicitly “envisions using WS-23 and menthol in a single product,” disclosing “the use of both WS-23 and menthol in chewing gum.” *Id.* at 1361–62. Thus, the reference did not merely list ingredients—it affirmatively taught combining them, eliminating the need to pick and choose which combinations to form.

The court then distinguished Shahidi from *Impax*, which involved “hundreds or thousands of compounds” and was found not to be anticipatory. *Id.* at 1362 (citing *Impax Labs., Inc. v. Aventis Pharms. Inc.*, 545 F.3d 1312 (Fed. Cir. 2008)).

The *Wrigley* court explained that “[t]he question for purposes of anticipation is therefore whether the number of categories and components in [the prior art] was so large that the combination of WS–23 and menthol would not be immediately apparent to one of ordinary skill in the art.” *Id.* at 1361. Applying this standard while distinguishing *Impax* establishes that sixty-nine combinations approaches the upper limit of what can be “immediately apparent” without further direction, while “hundreds or thousands” clearly exceeds that limit and requires impermissible picking and choosing.

In the Federal Circuit’s most recent opinion on the issue, the Federal Circuit held that *In re Petering*—cited by Petitioner (Petition at 43, 47) stands for the proposition that a skilled artisan may “at once envisage each member of [a] *limited* class, even though the skilled person might not at once define in his mind the formal boundaries of the class.” *Mylan Pharms. Inc. v. Merck Sharp & Dohme Corp.*, 50 F.4th 147, 153 (Fed. Cir. 2022) (quoting *In re Petering*, 301 F.2d 676, 681 (CCPA 1962) (emphasis in original)). As the Federal Circuit explained, “[t]he key term here is ‘limited.’” *Id.* Specifically, the Federal Circuit noted that the prior art’s “list of 33 compounds, with no direction to select [the claimed element] from among them, plus the eight ‘pharmaceutically preferred’ acids and various stoichiometric possibilities, results in 957 salts, some of which may not exist. That is a far cry from the 20 compounds ‘envisaged’ by the narrow genus in *Petering* ...

We cannot provide a specific number defining a ‘limited class.’ It depends on the ‘class.’ But we agree...that a class of 957 predicted salts that may result from the 33 disclosed compounds and eight preferred acids, some of which may not even form under experimental conditions, is insufficient to meet the ‘at once envisage’ standard set forth in *Petering*.” *Id.* at 153–54.

The Board also applied this principle in *Ex parte Eckhardt* (Ex. 2012 (No. 2020-003463, slip op. at 3 (PTAB Apr. 15, 2021).) There, the applicant’s claims required a copolymer layer with four components chosen from lists of ten, eight, ten, and two options, respectively. As the applicant calculated in its Appeal Brief, the combination of these component lists created 1,600 possible polymer compositions. (See Ex. 2013, *Ex parte Eckhardt*, Appeal Br. at 9 (filed Nov. 4, 2019).) The Board agreed with applicant that this required impermissible picking and choosing, holding that “Bartholomew’s disclosure is insufficient to establish anticipation of the compositional components” because “the § 102(a) rejections... rely upon picking and choosing from various lists in Bartholomew.” (Ex. 2012, *Ex parte Eckhardt*, slip op. at 3.)

Alexander unquestionably fails these benchmarks and requires picking and choosing on an unprecedented scale. Specifically, Alexander’s 2.25 to 31.5 quadrillion combinations exceed even “hundreds or thousands” (the maximum rejected in *Impax*) by factors measured in trillions. Moreover, Alexander provides

none of the critical features that made smaller numbers acceptable in *Wrigley*—no “particularly preferred” or “most suitable” designations, no explicit envisioning of any combination, and no clear identification of the claimed serotypes. *See Wrigley*, 683 F.3d at 1361. A POSA must engage in precisely the kind of extensive picking and choosing that *Smith* and *Eckhardt* prohibit.

Gu similarly requires impermissible picking and choosing. Although Gu’s 192 combinations are numerically smaller than *Eckhardt*’s 1,600, Gu lacks all the directional features that made smaller numbers (sixty-nine) anticipatory in *Wrigley*. *See Wrigley*, 683 F.3d at 1361. Gu provides no preferential designations, no explicit envisioning of combinations, and no guidance distinguishing the claimed serotypes from the 191 other possibilities. Without these teachings, Gu requires impermissible picking and choosing, and thus fails anticipation, just as *Impax*’s similarly directionless “hundreds or thousands” of combinations also failed. *See Impax Lab ’ys, Inc. v. Aventis Pharms., Inc.*, 545 F.3d 1312, 1315–16 (Fed. Cir. 2008).

4. Alexander and Gu Are Readily Distinguished from Cases Finding Anticipation

Petitioner cites several Federal Circuit cases purportedly finding anticipation, but these cases are either not on point, or involved prior art with fewer possible combinations and/or substantially greater specificity and directional teaching than either Alexander or Gu provides. (*See* Petition at 25–26.)

Two of Petitioner’s cited cases—*3form* and *Purdue*—are simply irrelevant. (Petition at 25.)

In *3form*, although the prior art “discloses more than forty” objects, the claims required “compressible objects,” and **only one** of the “more than forty” objects was “compressible” and thus eligible for selection. *3form, Inc. v. Lumicor, Inc.*, 678 F. App’x 1002, 1009 (Fed. Cir. 2017). (*See* Ex. 2014 (*3form, Inc. v. Lumicor, Inc.*, Br. for Plaintiff-Appellant [Corrected] at 19, 43–44 (filed May 10, 2016)).) Thus, the issue was whether the named object was compressible, and not whether a POSA could identify which combination to select from the vast possibilities. *3form*, 678 F. App’x at 1009–10. Here, unlike *3form*’s prior art that contained a single viable option from a list of “over forty,” neither Alexander nor Gu explicitly discloses any single specific vaccine formulation matching the claimed serotype combination.

Petitioner’s citation to *Purdue* also misses the mark, as that case dealt with obviousness, not anticipation, and thus applied a standard not applicable here. *Purdue Pharma Prods. L.P. v. Par Pharm., Inc.*, 377 F. App’x 978, 981–82 (Fed. Cir. 2010). Even so, in that case, the Federal Circuit found it *obvious* (not anticipating) to select a single item from a list of fourteen—a drastically smaller number of available options than Alexander’s quadrillions or Gu’s 192. *Id.* at 982.

The simplest anticipation cases involve selecting a single, specifically-named element from a modest list. For instance, in *Perricone*, a POSA could move from the prior art to the claimed invention with only a single, straightforward selection decision—identifying one specifically-named ingredient from fourteen options—with no combinatorial complexity whatsoever. *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1376–77 (Fed. Cir. 2005). Alexander and Gu’s quadrillions and 192 possible combinations, respectively, fall far outside the range considered in *Perricone*. (See Petition at 25.) Additionally, the claimed invention here is not a single ingredient appearing in a list—it is a specific combination (“at least 2” serotypes “selected from a group consisting of 23A, 23B, and 35B”) that must be identified from among astronomical or substantial numbers of equally viable alternatives without any guidance. (Ex. 1001 at claims.)

Cases involving combinations of multiple elements establish numerical benchmarks and require directional teaching that Alexander and Gu lack. As discussed above, in *Wrigley*, the prior art contained sixty-nine combinations—still astronomically lower than Alexander and approximately one-third of Gu’s 192—but identified one of the two required selections as one of only three that was “particularly preferred” and identified the other required selection as one of the “most suitable” options. 683 F.3d at 1361. Moreover, the prior art in *Wrigley* “envision[s] using [both selections] in a single product,” discussing “the use of both

[selections] in a single product.” 683 F.3d at 1361–62. Thus, the reference did not merely provide a laundry list of ingredients as do Alexander and Gu—it affirmatively taught combining them, eliminating the need to pick and choose which combinations to form. Notably, *Wrigley* distinguished itself from *Impax*, which involved “hundreds or thousands of compounds”—the closest approximation to the numbers at issue here—and was found not anticipatory. *Id.* at 1362.

At the upper limit of anticipatory combinations, a district court in *Warner* found that approximately 336 combinations (14 bisphosphonates $\times$ 4 chelating agents $\times$ 6 delayed-release mechanisms) constituted a “defined and limited class” where the claimed combination would be “immediately apparent.” *Warner Chilcott Co., LLC v. Teva Pharms. USA, Inc.*, 89 F. Supp. 3d 641, 656–57 (D.N.J. 2015), *aff’d*, 642 F. App’x 996 (Fed. Cir. 2016). The court emphasized the fact that the prior art “disclosed a specific and limited number of bisphosphonates by name combined with a specific and limited number of chelating agents and delayed release mechanisms,” and directed a POSA to select one ingredient from each defined list such that it “combine[s] [the elements] in the same way as recited in the claim,” rather than a “random selection from unrelated elements.” *Id.* at 657. By contrast, Alexander’s quadrillions of combinations clearly do not present a “defined and limited class.” Even Gu’s 192 combinations, while numerically

smaller than *Warner Chilcott*'s 336 (though still nearly three times *Wrigley*'s sixty-nine), lacks the guidance that made *Warner Chilcott*'s disclosures anticipatory, such as the instruction to select one item from each of four defined categories, rather than Gu's free-for-all that—according to Petitioner's expert—would allow selecting from one to all eight of the serotypes in Gu's list with zero guidance as to the selection process. (*See* Ex. 1002, ¶ 195.)

Petitioner cites a lone case involving large numbers—although still nowhere in the universe of Alexander's possible combinations—*In re Gleave*, 560 F.3d 1331 (Fed. Cir. 2009). (Petition at 26–27.) But *Gleave* again presents distinguishing features absent from Alexander and Gu. In *Gleave*, the Wraight reference “expressly lists every possible fifteen-base-long oligodeoxynucleotide sequence in IGFBP-2,” totaling more than 1,400 sequences. *Id.* at 1338. The Federal Circuit held that this exhaustive list anticipated Gleave's claims, emphasizing two critical distinguishing facts.

First, Gleave admitted that “it is well within the skill of an ordinary person in the art to make any oligodeoxynucleotide sequence,” making enablement undisputed. *Id.* at 1336. Here, the alleged enablement of Alexander and Gu is both disputed and lacking. As demonstrated in Section VII.C., below, both Alexander and Gu fail to enable the “immunogenic” limitation—neither provides specific

conjugation protocols, working examples, immunogenicity data, or technical guidance for the claimed serotypes. (See Section VII.C., *infra*.)

Second, Gleave’s claims did not require the sequences to actually function as antisense inhibitors—they merely required sequences “of sufficient length to act as an antisense inhibitor,” and the claims “do not require antisense activity.” *Id.* The court emphasized that “evidence as to whether particular compounds work for their intended purpose is irrelevant to our § 102(b) analysis” when claims do not require actual functionality. *Id.* Here, by contrast, the claims require not just selection of the claimed serotypes, but that the conjugates produced from that selection are immunogenic—a functional limitation requiring at the very least that conjugates elicit immune responses. (See Petition at 30–31, 41, 45–46.) And as the Board held in *Merck*, discussed in more detail in Section VII.C., below, evidence that a conjugate is immunogenic requires data showing immunogenicity specific to the conjugated serotype. *Merck v. Wyeth*, IPR2017-01223 at 11–14 (PTAB Oct. 20, 2017). Under *Gleave*’s own reasoning, therefore, when claims include functional limitations requiring actual performance, “evidence as to whether particular compounds work for their intended purpose” becomes highly relevant. *In re Gleave*, 560 F.3d at 1336. Alexander and Gu provide no such evidence. (See, Section VII.C., *infra*.)

B. Gu Fails to Disclose the Claimed “Plurality of at Least Two Unique Immunogenic Saccharide-Polypeptide Conjugates”

1. Petitioner’s Argument that a POSA Would “At Once Envisage” this Limitation from Gu Is Contrary to Law

Petitioner acknowledges that Gu does not literally disclose the recited “plurality of at least two unique immunogenic saccharide-polypeptide conjugates.” This is why Petitioner argues that “the POSA would understand that Gu discloses compositions which comprise glycoconjugates with at least two of the three serotypes listed in limitation 1.c, and the POSA would **at once envisage** a vaccine composition involving glycoconjugates with at least two of the required serotypes.” (Petition at 42–43 (emphasis added).) This is directly contrary to Federal Circuit precedent. Specifically, the Federal Circuit has “previously rejected the proposition that ‘a reference missing a limitation can anticipate a claim if a skilled artisan viewing the reference would ‘at once envisage’ the missing limitation.’” *Galderma Lab'ys, L.P. v. Teva Pharms. USA, Inc.*, 799 F. App'x 838, 845 (Fed. Cir. 2020) (quoting *Nidec*, 851 F.3d at 1274–75)); *see UCB, Inc. v. Actavis Lab'ys UT, Inc.*, 65 F.4th 679, 688 (Fed. Cir. 2023) (reversing anticipation finding based on the argument that a POSA “would at once envisage” a claim element missing from the prior art’s disclosure). Consequently, in *Galderma*, the Federal Circuit reversed a finding of anticipation because the “court was not permitted ‘to fill in missing limitations simply because a skilled artisan would immediately envision them.’” *Id.* (quoting *Nidec*, 851 F.3d at 1274–75). Because controlling precedent does not allow the Board to find anticipation of this element

not disclosed in Gu, regardless of whether a “POSA would at once envisage” the limitation, Petitioner’s anticipation challenge as to Gu must fail.

2. “Multiple Glycoconjugates” Does Not Inherently Mean Multiple Serotypes

Because Petitioner acknowledges that Gu does not literally disclose the recited “plurality of at least two unique immunogenic saccharide-polypeptide conjugates,” Petitioner relies on an inherency argument based on Gu’s claim reciting “[a]n immunogenic composition comprising *at least one glycoconjugate*” (Petition at 41 (emphasis in Petition).) Specifically, Petitioner argues that “[b]y saying ‘at least’ Gu conveys to the POSA compositions that have multiple glycoconjugates....[T]he POSA would understand that a composition where all the glycoconjugates are the same serotype would not be described as having multiple glycoconjugates. (Petition at 41 (citing Ex. 1002, ¶ 153.)) This is incorrect. In fact, a composition with multiple glycoconjugates can refer to at least three different formulation approaches: (1) multiple serotypes conjugated to multiple carrier proteins; (2) multiple serotypes conjugated to a single carrier protein; or (3) a **single serotype conjugated to multiple carrier proteins**. Indeed, the Santiesteban-Lores study at Ex. 2015 demonstrates the use of this third approach—using multiple glycoconjugates wherein a single serotype (6B) is conjugated to

multiple carrier proteins—PspA1 and PspA3. (Ex. 2015 at 1–5.)⁴ Thus it is not the case that having multiple glycoconjugates ***necessarily*** means having glycoconjugates with at least two unique serotypes as Petitioner argues.

Notably, “[a]nticipation by inherent disclosure is appropriate only when the reference discloses prior art that ***must necessarily include the unstated limitation***. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” *Therasense, Inc. v. Becton, Dickinson & Co.*, 593 F.3d 1325, 1332 (Fed. Cir. 2010) (cleaned up) (emphasis added). Because having multiple glycoconjugates ***does not necessarily mean*** having glycoconjugates with at least two unique serotypes as Petitioner argues, Petitioner’s inherency argument must fail.

It is additionally worth noting that, despite carrying the burden of establishing that this limitation is necessarily present in Gu, Petitioner cited no

⁴ “Extrinsic evidence can be used to demonstrate what is ‘necessarily present’ in a prior art embodiment even if the extrinsic evidence is not itself prior art.” *Hospira, Inc. v. Fresenius Kabi USA, LLC*, 946 F.3d 1322, 1329 (Fed. Cir. 2020) (citing *Monsanto Tech. LLC v. E.I. DuPont de Nemours & Co.*, 878 F.3d 1336, 1345 (Fed. Cir. 2018) (allowing “non-prior art data” to be used to support inherency)).

evidence in support of its argument other than the conclusory declaration of its expert that, for this proposition, quotes the Petition verbatim. (Petition at 41 (citing Ex. 1002, ¶ 153.)) *See Crown Operations Int’l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1377–78 (Fed. Cir. 2002) (“In arguing inherent disclosure of the [controller] limitation in the [’383] patent, [Petitioner] bears an evidentiary burden to establish that the limitation was necessarily present.”). Specifically, in identical wording to the Petition, Petitioner’s expert asserts that “the POSA would understand that a composition where all the glycoconjugates are the same serotype would not be described as having multiple glycoconjugates.” (Ex. 1002, ¶ 153.) Notably, Dr. Musey provides *no citation to any supporting evidence* for this assertion and offers *no technical reasoning* to support this conclusion. Under the Board’s precedential decision in *Xerox*, expert testimony that “merely repeats, verbatim, the conclusory assertion for which it is offered to support” without citing “any additional supporting evidence or provid[ing] any technical reasoning” is “conclusory and unsupported, adds little to the conclusory assertion for which it is offered to support, and is entitled to little weight.” in *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9, 16 (PTAB Aug. 24, 2022) (precedential).

Petitioner’s expert’s unsupported opinion is “particularly problematic” under *Xerox* because it is “offered not simply to provide a motivation to combine prior-art teachings, but rather to supply a limitation missing from the prior art.” *Id.* Here,

Petitioner seeks to use its expert’s unsupported conclusion to supply the missing disclosure of a “plurality of at least two unique immunogenic saccharide-polypeptide conjugates” in Gu. (Petition at 40–41.) This is exactly the type of gap-filling that the Board rejected in *Xerox*.

3. Gu’s Disclosure Is Not “Arranged or Combined in the Same Way as Recited in the Claim”

Petitioner additionally argues that Gu discloses the recited “plurality of at least two unique immunogenic saccharide-polypeptide conjugates” based on three disclosures in Gu—a 137-page document—that are entirely separate from Gu’s disclosure on page 22 of a pneumococcal glycoconjugate. (Petition at 42–43) These disclosures are: (1) a disclosure on page 57 that “[t]he immunogenic compositions of the invention may [] comprise ... a plurality of capsular polysaccharide-protein conjugates”; (2) a disclosure on page 63 that “[t]he immunogenic amount of the different polysaccharide components in an immunogenic composition may diverge”; and (3) a claim including the language “[a]n immunogenic composition comprising *at least one* glycoconjugate.” (Petition at 40–41 (emphasis in Petition).) As discussed in Section VII.B.2., above, none of these disclosures necessarily indicate a disclosure of multiple **serotypes** as the claims require. Further, combining these three disparate disclosures with Gu’s disclosure on page 22 of a single pneumococcal glycoconjugate is forbidden in an anticipation analysis under Federal Circuit precedent.

Specifically, the Federal Circuit has repeatedly held that “[b]ecause the hallmark of anticipation is prior invention, the prior art reference—in order to anticipate under 35 U.S.C. § 102—must not only disclose all elements of the claim within the four corners of the document, but must also disclose those elements **‘arranged as in the claim.’**” *Net MoneyIN*, 545 F.3d at 1369 (emphasis added) (quoting *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983)). Thus, “unless a reference discloses within the four corners of the document not only all of the limitations claimed but *also all of the limitations arranged or combined in the same way as recited in the claim*, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate under 35 U.S.C. § 102.” *Net MoneyIN*, 545 F.3d at 1371 (emphasis added).

For these reasons, the Federal Circuit has repeatedly held that for anticipation, “it is not enough that the prior art reference discloses part of the claimed invention, which an ordinary artisan might supplement to make the whole, or that it includes multiple, distinct teachings that the artisan might somehow combine to achieve the claimed invention.” *Id.* (citing *In re Arkley*, 455 F.2d at 587 (“The prior art reference must clearly and unequivocally disclose the claimed invention or direct those skilled in the art to the invention without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference.” (cleaned up)))); *see, e.g., Net*

MoneyIN, 545 F.3d at 1370–71 (citing *Lindemann Maschinenfabrik GMBH v. Am. Hoist & Derrick Co.*, 730 F.2d 1452 (Fed. Cir. 1984) (“Because the district court had treated the claims as mere catalogs of separate parts, in disregard of the part-to-part relationships set forth in the claims and that give the claims their meaning, we reversed.” (quotation omitted)) and *Ecolochem, Inc. v. S. Cal. Edison Co.*, 227 F.3d 1361 (Fed. Cir. 2000) (finding no anticipation where, “although the reference taught all elements of the claim, it did not contain a discussion suggesting or linking hydrazine with the mixed bed in the figure, and thus did not show the invention arranged as in the claim.”)).

Contrary to Petitioner’s characterization, Gu’s disclosure of pneumococcal conjugates consistently uses singular language when describing serotype selection. Gu states:

In specific embodiments, **the** Pn capsular **polysaccharide** is selected from the group consisting of Pn-serotype 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F and 33F capsular polysaccharides. In other embodiments, **the** Pn capsular **polysaccharide** is selected from the group consisting of Pn-serotype 1, 2, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 9N, 10A, 11A, 12F, 14, 15A, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23A, 23B, 23F, 33F and 35B capsular polysaccharides.

(Ex. 1009 at 22:25–23:1 (emphasis added).) Gu’s specific embodiments further confirm this singular approach:

In one such embodiment, **the capsular polysaccharide is a Pn-33F capsular polysaccharide**. In another such embodiment, **the capsular polysaccharide is a Pn-22F capsular polysaccharide**. In another such embodiment, **the capsular polysaccharide is a Pn-10A capsular polysaccharide**. In yet another such embodiment, **the capsular polysaccharide is a Pn-11A capsular polysaccharide**.

(Ex. 1009 at 23:3–7 (emphasis added).) Indeed, every specific embodiment in Gu related to pneumococcal glycoconjugates describes selecting *one* serotype, not multiple serotypes.

There is also no language in Gu suggesting that the disparate passages upon which Petitioner relies would be combined with Gu’s serotype selection disclosure above. ***First***, Gu’s disclosure on page 57 states in full that “[t]he immunogenic compositions of the invention may further comprise one or more preservatives in addition to a plurality of capsular polysaccharide-protein conjugates.” (Ex. 1009 at 57:12–20.) Indeed, this entire paragraph is about the addition of preservatives to Gu’s invention, and has nothing to do with the selection of multiple serotypes in conjugate compositions. ***Second***, Gu’s disclosure on page 63 states in full that “[t]he immunogenic amount of a conjugate or immunogenic composition may vary **depending upon the bacterial serotype**. Generally, each dose will comprise 0.1 to 100 ug of **polysaccharide**...The immunogenic amount of the different polysaccharide components in an immunogenic composition may diverge and each

comprise 1 ug...or about 100 ug of any particular polysaccharide antigen.” (*Id.* at 63:6–12 (emphasis added).) Thus, this disclosure is about varying the weight or amount of any particular polysaccharide component, not about varying the number of serotypes selected. **Third**, Gu’s claim 25 recites in full “[a]n immunogenic composition comprising *at least one* glycoconjugate as defined in anyone [sic] of claims 1 to 24 and a pharmaceutically acceptable excipient, carrier, or diluents.” (*Id.* at 123:9–11.) However, only two claims from claims 1 to 24—claims 17 and 18 (which depends from and narrows the group from which the serotype may be selected)—claim a pneumococcal glycoconjugate, and, as with the remainder of Gu’s disclosures, both claims consistently use the singular: “[t]he glycoconjugate of anyone [sic] of claims 1 to 16, wherein the saccharide is a capsular polysaccharide derive from *S. pneumoniae*” (claim 17); “[t]he glycoconjugate of claim 17, wherein said capsular polysaccharide is selected from the group consisting of Pn-serotype 1, 2, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 9N, 10A, 11A, 12F, 14, 15A, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23A, 23B, 23F, 33F and 35B capsular polysaccharides” (claim 18).

Thus, these disclosures from Gu upon which Petitioner relies do not disclose the use of multiple glycoconjugates, but even if they did, they are far removed from Gu’s disclosure of a group of serotypes on page 22—as the Petition cites—and thus are not “*arranged or combined in the same way as recited in the claim*”

as anticipation requires. *Net MoneyIN*, 545 F.3d at 1371 (emphasis added).

Petitioner's anticipation argument must therefore fail with respect to Gu.

C. Alexander and Gu Fail to Disclose the “Immunogenic” Limitation

Throughout the Petition, Petitioner ignores the limitation, recited in every claim, that the claimed conjugates must be immunogenic. For example, Petitioner characterizes the claims as “merely claim[ing] including well-known serotypes in a PCV.” (Petition at 2.) Petitioner also repeatedly references the Examiner's supposed mistake in finding that the claimed serotypes “appear to be free of prior art” when the art before the Examiner “taught precisely the serotypes” at issue. (*See, e.g.*, Petition at 1, 10–12.) In interpreting the Examiner's statement as a repeated, blatant, error, Petitioner ignores the fact that the claims do not merely recite specific conjugated serotypes, but also require that these serotypes must be “immunogenic.” This is why the Examiner stated that the claimed immunogenic, conjugated serotypes “appear to be free of prior art.”

There is a good reason that Petitioner tries to hand-wave away the “immunogenic” limitation that the claims recite—neither Alexander nor Gu discloses this element, or even comes close. While both references make generic, conclusory statements about immunogenicity as a goal of their inventions as a whole—without reference to any pneumococcal vaccine embodiment, much less with respect to any particular serotype or combination of serotypes—neither

reference provides the specific, technical disclosure required for a POSA to make and use immunogenic conjugates of the claimed serotypes as anticipation requires.

The Board’s decision in *Merck* is directly on point and establishes that invalidating prior art references must provide actual evidence of immunogenicity, not merely generic statements of intent. *Merck v. Wyeth*, IPR2017-01223 at 11–14 (PTAB Oct. 20, 2017). In *Merck*, Petitioner sought to prove obviousness of a 13-valent pneumococcal conjugate vaccine based on the combination of Prevnar 2001 (a marketed 7-valent vaccine) and Overturf 2002. *Id.*

Overturf 2002 disclosed an 11-valent pneumococcal CRM197 conjugate vaccine containing serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F—an actual vaccine formulation in preclinical development. *Id.* at 13. It included a known serotype (serotype 3) recognized as causing serious disease, a proven carrier protein (CRM197) with established efficacy, and explicit reference to conjugation to that carrier. *Id.* at 11–16.

Despite these favorable factors, the Board denied institution because—just as Petitioner has done here—“Petitioner point[ed] to no evidence that the compositions relied upon by [their expert] were tested for the production of a functional antibody response.” *Id.* at 16. In *Merck*, the Board held that the use of the prior art compositions, even in a vaccine trial, “do not provide evidence for Petitioner’s assertion that any serotype 3 conjugated to a protein carrier is

immunogenic as claimed, i.e., showing higher serum IgG titers and overall greater functional antibody activity than seen with free polysaccharide alone or mixed with unconjugated CRM₁₉₇.” *Id.* at 16–17. In addition, the Board recognized that “[t]here is no indication in Overturf 2002 of how the individual polysaccharides are attached to the carrier protein, or that the composition had been tested.” *Id.* at 15 (emphasis added). The Board emphasized that “**different serotype saccharides follow different pathways for activation** (hydrolysis or no hydrolysis prior to [sodium periodate] activation) **and conjugation** (aqueous or DMSO reactions),” and that “the **same conjugation protocol does not work for every polysaccharide.**” *Id.* (emphasis added) In other words, generic statements about conjugation cannot substitute for serotype-specific technical disclosure.

In *Merck*, the Board declined institution where the prior art selected and tested the claimed serotypes in a conjugated vaccine, but had no evidence of immunogenicity (even though the goal, of course, was immunogenicity since the serotype was being tested in a vaccine). *Id.* at 15–17. The Board in *Merck* also rejected conclusory expert opinions—just like the one here—that the vaccine “would be immunogenic” as resting on “unsupported opinions” lacking “any objective proof.” *Id.*

Alexander and Gu are materially weaker than the rejected prior art in *Merck v. Wyeth*. Both references provide even less specific technical guidance than

Overturf 2002, offering only generic lists of serotypes with conclusory statements about immunogenicity in general. Neither reference provides any indication of how to conjugate serotypes 23A, 23B, or 35B to achieve immunogenicity or which conjugation pathways are appropriate for these serotypes.

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, ¶ 105.) This conclusory statement provides no the level of immune response that constitutes “Immunogenically effective” or on how to achieve it for serotypes 23A, 23B, or 35B. Alexander’s immunogenicity data is limited to ELISA and opsonophagocytic results for serotypes 6B, 14, and 9V, with no immunogenicity data for the claimed serotypes. (Ex. 1008, ¶¶ 134–41) Alexander provides no correlation data suggesting that results for the exemplified serotypes would predict success for the claimed serotypes. (*See, id.*)

Similarly, 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 page, (54), (57), 30:32–31:2.) Like Alexander, Gu’s disclosure provides no technical direction toward achieving immunogenicity for the claimed serotypes. Gu’s immunogenicity data is limited to

OPA titers for serotype 33F, with no immunogenicity data for serotypes 23A, 23B, or 35B. (Ex. 1009 at 86:23–87:14) Like Alexander, Gu provides no framework for determining what immune response level would enable the immunogenicity limitation for untested serotypes. (*See, id.*)

Because neither Alexander nor Gu provides any evidence that the claimed serotypes, when conjugated, would be immunogenic, Petitioner’s anticipation theory for the immunogenicity limitation must rest on inherency: the assertion that any polysaccharide-protein conjugate made from these serotypes would necessarily be immunogenic. But inherency requires that the missing limitation be *necessarily present* in every embodiment of the prior art disclosure—not merely possibly or probably present. *See Therasense*, 593 F.3d at 1332 (“The concept of ‘*inherent disclosure*’ *does not alter* the requirement that *all elements must be disclosed* in an anticipatory reference *in the same way as they are arranged or combined in the claim*. Anticipation by *inherent disclosure* is appropriate only when the reference discloses prior art that *must necessarily include the unstated limitation*.”)

Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.” (cleaned up) (emphasis added).). And as the Board recognized in *Merck*, this is not the case here.

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

Whether obviousness “is based on combining disclosures from multiple references, combining multiple embodiments from a single reference, or **selecting from large lists of elements in a single reference**, there must be a motivation to make the combination and a **reasonable expectation that such a combination would be successful, otherwise a skilled artisan would not arrive at the claimed combination.**” *In re Stepan Co.*, 868 F.3d 1342, 1346 n.1 (Fed. Cir. 2017) (emphasis added). Petitioner gives short shrift to its burden of demonstrating a reasonable expectation of success in each of its obviousness grounds.

1. Petitioner’s Reasonable Expectation of Success Analysis for Alexander Is a Single Conclusory Sentence Without Any Supporting Analysis

Petitioner argues that it would have been obvious for a POSA to select the claimed serotypes in light of Alexander. (Petition at 37.) But Petitioner’s entire showing on reasonable expectation of success consists of the second half of a single sentence: “The POSA...would have reasonably expected to succeed in making such a composition.” (*Id.* (citing Ex. 1002, ¶¶ 143–44).) This bare conclusion appears at the end of a paragraph focused entirely on *motivation to combine*—discussing serotype prevalence data, disease burden, and the desire to broaden vaccine coverage. (*Id.*) Petitioner’s citation to its expert’s declaration does not help, as it is focused almost entirely on the motivation to combine, and with respect to a reasonable expectation of success analysis, merely repeats the

Petitioner's sparse language, nearly verbatim. Specifically, Petitioner's expert asserts: "The POSA would also have reasonably expected, based on Alexander, to succeed in making such a composition." (Ex. 1002, ¶ 144.) Full stop. Despite the fact that "selecting from large lists of elements in a single reference" requires "a reasonable expectation that such a [selection] would be successful," that is the entirety of the reasonable expectation to combine analysis Petitioner and its expert set forth. *See In re Stepan*, 868 F.3d at 1346 n.1.

The law is clear: "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007); *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) ("To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements."). Because Petitioner has not provided this required "articulated reasoning with some rational underpinning," Petitioner's obviousness ground based on Alexander must fail. *See id.*

2. Gu: Petitioner Conflates Motivation with Reasonable Expectation of Success

Petitioner's argument that a POSA would select the claimed serotypes in light of Gu is similarly deficient. The entirety of the Petitioner's reasonable expectation of success analysis reads: "The POSA also would have reasonably

expected, based on this reference and the longstanding trend in the art toward including more serotypes, to succeed in making such a composition.” (Petition at 49 (citing Ex. 1002, ¶ 195).) Petitioner’s supporting expert declaration elaborates only slightly, adding without explanation or citation that including all eight serotypes disclosed in Gu—when the currently-available vaccine only targeted thirteen serotypes, “would have been manageable to do”:

Indeed, it would have been obvious to include all eight of the serotypes disclosed in one list in Gu, as the skilled artisan would have recognized as of the priority date that adding eight serotypes to prior art pneumococcal conjugate vaccines would have been manageable to do. The POSA would have reasonably expected, based on this reference and the longstanding trend in the art toward including more serotypes, to succeed in making such a composition.

(Ex. 1002, ¶ 195.)

In addition to failing as conclusory, for the reasons discussed with respect to Alexander in Section VII.D.1., above, this assertion wrongly conflates *motivation* with *reasonable expectation of success*—two distinct legal requirements that Petitioner must independently satisfy. *See Eli Lilly & Co. v. Teva Pharms. Int’l GmbH*, 8 F.4th 1331, 1344 (Fed. Cir. 2021) (“[W]e must first emphasize the clear distinction in our case law between a patent challenger’s burden to prove that a skilled artisan would have been motivated to combine prior art references and the additional requirement that the patent challenger also prove that the skilled artisan

would have had a reasonable expectation of successfully achieving the claimed invention from the combination.”).

The “longstanding trend in the art toward including more serotypes” is evidence of *motivation*—it explains *why* a POSA would *want* to add more serotypes (to broaden disease coverage), not the technical feasibility of achieving it. But motivation and reasonable expectation of success are separate requirements. *See id.* Indeed, the Federal Circuit has held that “to have a reasonable expectation of success, one must be motivated to **do more than** merely to vary all parameters or **try 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 is likely to be successful.**” *Medichem, S.A. v. Rolabo, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006). The fact that researchers *wanted* to include more serotypes in a pneumococcal vaccine says nothing about whether they could *successfully* select and conjugate the claimed serotypes and achieve immunogenicity. Petitioner has not explained—much less provided evidence showing—why a POSA would have expected to successfully add the claimed serotypes from among the 192 possible choices in Gu to a vaccine formulation.

3. The “Longstanding Trend in the Art” Contradicts Petitioner’s Conclusory Assertion of a Reasonable Expectation of Success

Far from supporting a reasonable expectation of success, the “longstanding trend in the art” demonstrates the substantial technical challenges and unpredictability inherent in pneumococcal conjugate vaccine development. Indeed, from the time the first PCV vaccine (Prevnar) was licensed in the United States in 2000 with 7 serotypes, by 2016—**sixteen years later**—only 6 additional serotypes had been successfully added (PCV13, licensed in 2010). (Petition at 6–7.) That represents an average of less than one serotype successfully added every two years. This is hardly a trend that promotes a reasonable expectation of success in creating three new immunogenic conjugated serotypes as the claims require.

Although Petitioner does not rely on obviousness for the “immunogenic” requirement, the Board’s decision in *Merck*, discussed in Section VII.C., above, still provides instructive guidance, particularly with respect to the unpredictability of the art. In addition, in other submissions to the Board, Wyeth “(acquired by Petitioner in 2009)” (Petition at 1) has specifically told the Board the opposite of what it alleges here. In an IPR challenging one of Wyeth’s patents, Wyeth’s expert argued to the Board:

A POSA would have had **significant concerns expanding the formulation of Prevnar 2005 because of the possible loss of immunogenicity due to ‘immune interference’** when developing a

13-valent conjugate vaccine, especially considering the highest valency present in a licensed conjugate vaccine was the 7-valent Prevnar® vaccine. **Immune interference is often seen when increasing vaccine valency due to the concomitant increase of carrier protein and polysaccharides.** The increased carrier protein and polysaccharide content increases the likelihood of interference with the immune response to other conjugated and/or co-administered antigens. There are numerous mechanisms by which immune interference may occur which include CIES, bystander interference, and interference between conjugated bacterial polysaccharides and their carrier protein.

(Ex. 2016, ¶ 26 (*Merck Sharp & Dohme Corp. v. Wyeth LLC*, IPR2017-00390, Ex. 2118 at 11–12) (citations omitted); *see id.* at ¶¶ 30, 32 (discussing a publication emphasizing that when developing a conjugate vaccine, “it will be **necessary to establish that the simultaneous administration of vaccines against several serotypes does not interfere** with the capsular polysaccharide-specific antibody response against the component polysaccharides.”), ¶ 34 (“It was well established that the protective level of pneumococcal polysaccharide antibodies is 0.35 ug/ml. The newly added conjugates should achieve this minimal level and at the same time it should not bring any of the Prevnar® components below this level. It would have been known that this balance should be maintained and managed with the addition of each new component. Since the **addition of new conjugates greatly increases the risk of one or more component of the combined vaccine will**

elicit a reduced immune response (below the 0.35 ug/ml) due to CIES, the **risk of failure is increased.**") (citation omitted); ¶ 36 ("On reading Pena 2004, a POSA would have understood that all Wyeth had done since the licensing of Prevenar® [sic] was conduct trials with a vaccine with two new serotypes. **This would not have led a POSA to conclude that the 7-valent conjugate vaccine of Prevnar®/Prevenar 2005 could be expanded to the 13-valent pneumococcal polysaccharide single-carrier CRM197 conjugate vaccine of claim 18 with a reasonable expectation of success.**"); ¶ 38 ("in the early 2000s, it was widely understood that the **addition of each new conjugate increases the risk of failure due to CIES.**".).)

In that same IPR, Wyeth told the Board:

Conjugate vaccine development, especially multivalent conjugate development, was an **unpredictable field characterized more by failures than successes....**Despite the need, only a handful of conjugate vaccines were licensed by the FDA as of April 26, 2006. Manufacturers encountered numerous problems regarding efficacy and stability in developing conjugate vaccines, **often resulting in failure.** For example, [Merck] abandoned development of a 7-valent pneumococcal-conjugate vaccine due to poor immunogenicity....Lack of immunogenicity observed in experimental multivalent vaccines gave rise to concerns of 'carrier induced epitope suppression' ('CIES')....**Increasing the amount of carrier protein in creating a higher multivalent conjugate vaccine would lead to a loss of**

immunogenicity to the targeted serotypes....Optimal formulation conditions for one polysaccharide serotype conjugate are not necessarily optimal for another. Formulation of a multivalent conjugate vaccine was a **challenging task requiring many parameters to be evaluated empirically for each conjugate separately**, and then for the composition as a whole. A formulation condition or combination of excipients that work for one conjugate may not be effective for another. One small change could potentially upset the careful balance between stabilities of very different conjugates in a composition.

Merck v. Wyeth, IPR2017-00390 at 5–8, 40 (PTAB Sept. 13, 2017) (citations omitted) (“The Petition offers no substantive explanation as to why a POSA would not have been steered away from the claimed invention in light of the known risks of and teachings in the art on addressing immune interference.”), 42–43 (“A POSA would have been aware of the risks of failure in multivalent conjugate vaccines caused by immune interference. Such a person would have been particularly concerned with immune interference in the context of a 13-valent conjugate vaccine – a higher valency than that for known vaccines which encountered issues with CIES.”).

Similarly, in yet another IPR, Pfizer wrote the following in a submission to the Board: “Different serotypes have varying chemical and immunological properties and these differences make the development of multivalent vaccines a

challenge. In developing multivalent polysaccharide-protein conjugate vaccines, developers have encountered issues such as immune interference between protein conjugates of serotypes and carrier induced epitopic suppression.” (*Sanofi Pasteur Inc. & SK Chemicals Co. v. Pfizer Inc.*, IPR2018-00188, Paper 8, 3 (PTAB Mar. 12, 2018); *see also Merck Sharp & Dohme Corp. v. Pfizer Inc.*, IPR2017-02132, Paper 39, 6 (PTAB Oct. 2, 2018) (“[o]ther PCVs have covered 7, 10, 11, or 13 of the serotypes contained in PCV-15, but immune interference has been observed for some serotypes.”).

Each of these prior statements from Petitioner to the Board directly refutes Petitioner’s unsupported assertion that the longstanding trend in the art toward including more serotypes would invoke a reasonable expectation of success. Each of Petitioner’s obviousness arguments must therefore fail.

4. Petitioner’s Combination Theories Based on Serotype Prevalence and Vaccine Recommendation References Fail to Demonstrate a Reasonable Expectation of Success

Petitioner attempts to salvage its obviousness case by combining either Alexander or Gu with “Serotype Prevalence References” and “Vaccine Recommendation References.” (Petition at 50–54.) This combination theory fails for the same fundamental reason that dooms Petitioner’s other obviousness theories: complete absence of evidence supporting a reasonable expectation of success. Indeed, Petitioner’s combination theory rests on a demonstrable

falsehood—the claim that there are “multiple teachings of PCVs that included these serotypes.” (Petition at 54.) As shown below, Petitioner has identified *zero* PCVs that included any of the claim 1 serotypes.

First, Petitioner’s entire showing on reasonable expectation of success once again consists of the second half of a single sentence, asserting that “the POSA would have had a reasonable expectation of success, as illustrated by the ***multiple teachings of PCVs that included these serotypes.***” (Petition at 54 (citing Ex. 1002, ¶ 204) (emphasis added).) This assertion is demonstrably false. Petitioner has identified **zero** prior art references disclosing actual PCVs that included any of the claim 1 serotypes—23A, 23B, or 35B. (See Petition at 52–54.) The Vaccine Recommendation References cited by Petitioner do not disclose or teach any such vaccines. Instead, at best, they *suggest* that these serotypes *might be considered* for *future* inclusion in vaccines. Speculation about future possibilities provides no basis whatsoever for a reasonable expectation that such vaccines would be successful.

Petitioner’s supporting expert declaration, while omitting the Petition’s false statement, elaborates only slightly, adding without explanation or citation an argument similar to the one he proffered with respect to Gu:

[G]iven the maturity of pneumococcal saccharide-polypeptide conjugate vaccine technology, the widespread recommendations to include additional serotypes, and the clear trend in the industry

towards inclusion of additional serotypes, the POSA would have had a reasonable expectation of success in being able to do so.

(Ex. 1002, ¶ 204.) Once again, Petitioner’s expert opinion is “conclusory and unsupported, [and so] adds little to the conclusory assertion for which it is offered to support, and is entitled to little weight.” *See Xerox*, IPR2022-00624 at 16.

As discussed in Section VII.D.3., above, the “widespread recommendations to include additional serotypes and the clear trend in the industry towards inclusion of additional serotypes” go to motivation to combine but say nothing about a reasonable expectation of success. In addition, while Petitioner’s expert does not explain what he believes makes the field “mature.” As discussed in Section VII.D.3., above, the state of the pneumococcal saccharide-polypeptide conjugate vaccine technology is one that, in Petitioner’s own words to the Board, is “an **unpredictable field characterized more by failures than successes.**” *Merck v. Wyeth*, IPR2017-00390, Paper 15 at 5–8, 40 (citations omitted) (emphasis added). This does not indicate a reasonable expectation of success, particularly in light of the absence of any explanation for Petitioner’s expert’s unsupported conclusion.

Second, the Serotype Prevalence References establish that the claim 1 serotypes—23A, 23B, and 35B—were known in the art and were prevalent causes of pneumococcal disease. However, knowledge of serotype existence and

prevalence is *not* sufficient to establish a reasonable expectation of success in achieving the immunogenic conjugates of the serotypes recited in claim 1.

This is demonstrated by the undisputed fact that roughly 100 pneumococcal serotypes were known in the art as of the priority date, yet by 2016, **only 13 serotypes** had been successfully included in a conjugate vaccine. (*See* Petition at 7.) If knowing the existence and prevalence of a serotype were sufficient motivation and provided a reasonable expectation of success, then all roughly 100 serotypes would have been included in vaccines. The fact that they were not—despite a known need, decades of research, and commercial incentives—demonstrates that *technical feasibility*, not mere knowledge or desire, is the rate-limiting factor in pneumococcal conjugate vaccine development.

The gap between the roughly 100 known serotypes and the 13 successfully incorporated into vaccines reflects the substantial technical challenges in conjugate vaccine development: serotype-specific conjugation chemistry, unpredictable immunogenicity, potential interference among serotypes, and formulation stability, as described in Section VII.D.3., above. Knowing that a serotype exists and causes disease provides no information about whether that serotype can be successfully conjugated, will generate protective immune responses, or can be combined with other serotypes without immunological interference.

5. The Vaccine Recommendation References Provide No Basis for Reasonable Expectation of Success

While Petitioner’s reasonable expectation analysis does not cite to the Vaccine Recommendation References (Petition at 54), a close examination of each Vaccine Recommendation Reference still reveals that none provides any basis for a reasonable expectation that vaccines including the claim 1 serotypes would be successful.

a. Porro: Wishful Thinking About “New Emerging Serotypes” for “Further Up-Dated” Vaccines

Porro provides no basis for a reasonable expectation of success in making vaccines with the claim 1 serotypes. To the contrary, Porro’s disclosure demonstrates why such vaccines would *not* have been expected to succeed.

Porro explained a fundamental problem with expanding pneumococcal conjugate vaccines beyond 13 serotypes—each new serotype conjugated to a carrier protein increased the amount of carrier protein in the whole conjugate formulation, which creates “an obvious stress on the immune system.” (Ex. 1010 at 2:22–4:5.) To address this problem, Porro invented a “new category of conjugate antigens” that would combine multiple serotypes in a single conjugate, thereby reducing total carrier protein load. (*Id.* at 4:6–18.) Porro disclosed an 18-valent vaccine using his new invention, stating that “any combination (triad or quartet) of the Ps type 1, 2, 3, 4, 5, 6A, 6B, 6C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F,

18C, 19A, 19F, 20, 22F, 23F, 33F of *S. pneumoniae* may be contemplated.” (*Id.* at 27:30–28:1.)

Notably absent from Porro’s list of serotypes that he believed would work with his invention is **any serotype recited in claim 1**. Porro did not include 23A, 23B, or 35B in his 18-valent formulation. Instead, he listed two of these serotypes—23A and 35B—in a separate category of eleven “[n]ew emerging serotypes” that “might be likely included in a *further up-dated* broad-spectrum vaccine formulation.” (Ex. 1010 at 65:7–67:9 (emphasis added).) Thus, Porro classified the claim 1 serotypes as aspirational additions for a hypothetical 25-valent future vaccine—not as serotypes expected to work with his current invention. This is wishful thinking, not a reasonable expectation of success.

b. Al-Sherikh: One Conclusory Sentence Based on Two Isolates from 78-Person Sample

Al-Sherikh provides even less support for Petitioner’s case. While Petitioner asserts that Al-Sherikh “expressly recommends the inclusion of serotype 23A in a future vaccine formulation,” this characterization grossly overstates what Al-Sherikh actually says. (Petition at 53.)

The entirety of Al-Sherikh’s “recommendation” consists of a single sentence in the last line of the Abstract’s conclusion: “Addition of 23A and 15 to the vaccine would improve the PCV performance in IPD prevention.” (Ex. 1011 at 1.) Full stop. The basis for this single-sentence conclusion is extraordinarily thin: Al-

Sherikh found serotype 23A in a grand total of **two isolates** from a **78-person sample** in Saudi Arabia. (Ex. 1011 at 4–5.) Drawing broad conclusions about vaccine development from two cases in a small regional study is not evidence of a reasonable expectation of success—it is speculation based on limited data.

Moreover, Al-Sherikh did *not* suggest including serotype 23B in a future vaccine, despite its appearance in the study. Petitioner’s assertion that Al-Sherikh identified 23B as “among the twenty most frequently occurring serotypes in pediatric pneumococcal diseases,” is misleading. (Petition at 53.) Serotype 23B appeared in only a single isolate in the 78-person sample—hardly evidence supporting a reasonable expectation of successful immunogenic conjugation of this serotype. (Ex. 1011 at 4–5.)

**c. Richter: Serotype 35B “May Warrant” Inclusion—
But No Expectation of Success and Excludes 23A**

Richter stated that its purpose was “to assess the impact of PCV13 on invasive and noninvasive pneumococcal disease by determining changes in serotype distribution in 2012-2013 with comparison to 2008-09...as a guide to future vaccine development,” and indicated that serotype 35B’s increase “may warrant its inclusion in future conjugate vaccines.” (Ex. 1013 at 1, 5.) Full stop. Richter provided **zero evidence** that such a vaccine would be expected to be successful. The phrase “may warrant its inclusion” is hedged speculation about future possibilities—not evidence of reasonable expectation of successful

immunogenic conjugation of this serotype. Moreover, despite listing serotype 23A among the serotypes increasing in prevalence, Richter **excluded** it from its suggested future vaccine inclusion. (*See id.* at 5.)

**d. Wagenvoort: Information “Could Be Considered”—
Not a Recommendation, Much Less Evidence of
Success**

Petitioner asserts that Wagenvoort “recommend[s] 23A and 23B for selection into future vaccines.” (Petition at 53–54.) This is false. Instead, Wagenvoort lists 9 serotypes (15B, 10A, 33F, 18C, 6A, 6B, 23A, 23B, and 23F) that impact high-risk patients, stating that “this information *could be considered* if a new vaccine is designed to specifically target high risk groups.” (Ex. 1014 at 6 (emphasis added).) This is not even a recommendation for inclusion of 23A and 23B into a future vaccine, much less evidence that a POSA should have a reasonable expectation of successful immunogenic conjugation of this serotype.

VIII. CONCLUSION

For the reasons discussed above, Patent Owner respectfully requests that the Board deny Petitioner’s request for *Inter Partes* Review of U.S. Patent No. 11,058,757.

Dated: April 6, 2026

Respectfully Submitted,

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CERTIFICATE OF WORD COUNT

Under the provisions of 37 CFR § 42.24(d), the undersigned hereby certifies that the Microsoft Office word count for the foregoing **PATENT OWNER'S PRELIMINARY RESPONSE UNDER 35 U.S.C. § 313 AND 37 C.F.R. § 42.107**, excluding the table of contents, table of authorities, certificate of word count, and certificate of service, totals 12,798 words, which is less than the 14,000 words allowed under 37 C.F.R. § 42.24(b)(1):

Dated: April 6, 2026

/Sarah E. Spires/

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Counsel for Patent Owner

CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e), the undersigned hereby certifies that a true and correct copy of the foregoing **PATENT OWNER'S PRELIMINARY RESPONSE UNDER 35 U.S.C. § 313 AND 37 C.F.R. § 42.107** was served on April 6, 2026, by delivering a copy via electronic mail to the attorneys of record for Petitioner as follows:

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Dated: April 6, 2026

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