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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME LLC
Petitioner,

v.

POGONA, LLC
Patent Owner.

Case IPR2026-00221
Patent 11,058,757

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

TABLE OF CONTENTS

I.	INTRODUCTION	1
II.	LEVEL OF ORDINARY SKILL	5
III.	BACKGROUND TECHNOLOGY AND OVERVIEW OF THE '757 INVENTION	5
IV.	CHALLENGED CLAIMS	12
V.	CLAIM CONSTRUCTION	12
VI.	STANDARD FOR GRANTING <i>INTER PARTES</i> REVIEW	12
VII.	IPR SHOULD NOT BE INSTITUTED	13
A.	Porro and Mekalanos's Disclosures of Thousands to Tens of Thousands of Options for Serotype Selection Do Not Anticipate the '757 Patent.....	13
1.	The Mathematical Scope of Porro and Mekalanos's Disclosures Renders Anticipation Impossible	14
a.	Porro Reference	15
b.	Mekalanos Reference	16
2.	Porro and Mekalanos Require Impermissible "Picking and Choosing".....	18
3.	Porro and Mekalanos Fail the Numerical Benchmarks that Limit Anticipation.....	22
B.	Porro and Mekalanos Fail to Disclose the "Immunogenic" Limitation	28
1.	Petitioner Provides No Evidence to Support its Conclusory Allegation that Porro Discloses "Immunogenic Saccharide- Polypeptide Conjugates"	29

2.	Petitioner Provides No Evidence to Support its Conclusory Allegation that Mekalanos Discloses “Immunogenic Saccharide-Polypeptide Conjugates”	31
C.	Porro Does Not Disclose “Conjugates, Each Comprising Individually a Capsular Polysaccharide Conjugated to a Polypeptide”	37
D.	Mekalanos Does Not Disclose “A Plurality of at Least Two...Conjugates, Each Comprising Individually a Capsular Polysaccharides [sic] Conjugated to a Polypeptide.”	45
E.	The Obviousness Grounds Fail for Many of the Same Reasons as the Anticipation Grounds	47
1.	Ground 3: the ’757 Patent is Not Obvious Over Mekalanos	47
2.	Ground 4: the ’757 Patent is Not Obvious Over Mekalanos in View of Porro and Siber	53
VIII.	CONCLUSION.....	59

TABLE OF AUTHORITIES

Cases

<i>Atofina v. Great Lakes Chem. Corp.</i> , 441 F.3d 991 (Fed. Cir. 2006)	19
<i>Bayer Pharma Aktiengesellschaft v. Mylan Pharms. Inc.</i> , 152 F.4th 1400 (Fed. Cir. 2025)	38
<i>Becton, Dickinson & Co. v. Tyco Healthcare Grp., LP</i> , 616 F.3d 1249 (Fed. Cir. 2010)	38
<i>Corephotonics, Ltd. v. Apple Inc.</i> , 84 F.4th 990 (Fed. Cir. 2023)	30
<i>Deeper, UAB v. Vexilar, Inc.</i> , IPR2018-01310, Paper 7 (PTAB Jan. 24, 2019)	13
<i>Ex parte Eckhardt</i> , 2020-003463 (PTAB Apr. 15, 2021)	27
<i>Ex parte Smith</i> , 2011-003337 (PTAB Feb. 28, 2012)	19, 20
<i>Grunenthal GMBH v. Alkem Lab 'ys Ltd.</i> , 919 F.3d 1333 (Fed. Cir. 2019)	52
<i>H. Lundbeck A/S v. Lupin Ltd.</i> , 87 F.4th 1361 (Fed. Cir. 2023)	44
<i>Hytera Commc'ns Co. v. Motorola Sols., Inc.</i> , 841 F. App'x 210 (Fed. Cir. 2021)	41
<i>Impax Lab 'ys, Inc. v. Aventis Pharms., Inc.</i> , 545 F.3d 1312 (Fed. Cir. 2008)	25, 27
<i>In re Arkley</i> , 455 F.2d 586 (C.C.P.A. 1972)	19
<i>In re Magnum Oil Tools Int'l, Ltd.</i> , 829 F.3d 1364 (Fed. Cir. 2016)	30

<i>In re Parameswar Sivaramakrishnan</i> , 673 F.2d 1383 (C.C.P.A. 1982)	17, 24
<i>In re Petering</i> , 301 F.2d 676 (C.C.P.A. 1962)	26
<i>In re Schaumann</i> , 572 F.2d 312 (C.C.P.A. 1978)	20
<i>Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.</i> , 821 F.3d 1359 (Fed. Cir. 2016)	29, 55
<i>Interconnect Planning Corp. v. Feil</i> , 774 F.2d 1132 (Fed. Cir. 1985)	21
<i>Kennametal, Inc. v. Ingersoll Cutting Tool Co.</i> , 780 F.3d 1376 (Fed. Cir. 2015)	23
<i>Maquet Cardiovascular LLC v. Abiomed Inc.</i> , 131 F.4th 1330 (Fed. Cir. 2025)	44
<i>MasterMine Software, Inc. v. Microsoft Corp.</i> , 874 F.3d 1307 (Fed. Cir. 2017)	42
<i>Merck Sharp & Dohme Corp. v. Wyeth LLC</i> , IPR2017-01223, Paper 8 (PTAB Oct. 20, 2017)	3, 33, 36
<i>Mylan Pharms. Inc. v. Merck Sharp & Dohme Corp.</i> , 50 F.4th 147 (Fed. Cir. 2022)	26
<i>Net MoneyIN, Inc. v. VeriSign, Inc.</i> , 545 F.3d 1359 (Fed. Cir. 2008)	14, 20
<i>Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.</i> , 851 F.3d 1270 (Fed. Cir. 2017)	23
<i>Ortho-McNeil Pharm., Inc. v. Mylan Lab'ys, Inc.</i> , 520 F.3d 1358 (Fed. Cir. 2008)	52
<i>Pfizer, Inc. v. Apotex, Inc.</i> , 480 F.3d 1348 (Fed. Cir. 2007)	52

<i>Procter & Gamble Co. v. Teva Pharms. USA, Inc.</i> , 566 F.3d 989 (Fed. Cir. 2009)	58
<i>Salazar v. Procter & Gamble Co.</i> , 414 F.3d 1342 (Fed. Cir. 2005)	44
<i>SAS Inst., Inc. v. Iancu</i> , 138 S. Ct. 1348 (2018).....	13
<i>Seachange Int’l, Inc. v. C-COR, Inc.</i> , 413 F.3d 1361 (Fed. Cir. 2005)	43
<i>Therasense, Inc. v. Becton, Dickinson & Co.</i> , 593 F.3d 1325 (Fed. Cir. 2010)	36, 46
<i>Virtek Vision Int’l ULC v. Assembly Guidance Sys., Inc.</i> , 97 F.4th 882 (Fed. Cir. 2024)	54
<i>Wasica Fin. GmbH v. Cont’l Auto. Sys., Inc.</i> , 853 F.3d 1272 (Fed. Cir. 2017)	14, 37
<i>Wm. Wrigley Jr. Co. v. Cadbury Adams USA LLC</i> , 683 F.3d 1356 (Fed. Cir. 2012)	23, 24, 25, 28
<i>Xerox Corp. v. Bytemark, Inc.</i> , IPR2022-00624, Paper 9 (PTAB Aug. 24, 2022).....	31, 32
Statutes	
35 U.S.C. § 102(b)	19
35 U.S.C. § 314(a)	12
Other Authorities	
<i>Office Patent Trial Practice Guide</i> , 77 Fed. Reg. 48756 (Aug. 14, 2012).....	12
Regulations	
37 C.F.R. § 42.100(b)	12
37 C.F.R. § 42.108(c).....	12

I. INTRODUCTION

On January 26, 2026, Petitioner Merck Sharp & Dohme LLC 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 (“Pogona”). The ’757 patent claims pneumococcal conjugate vaccine compositions comprising a plurality of individually conjugated polysaccharide-protein structures—specifically, compositions where each “immunogenic” conjugate comprises “individually” a capsular polysaccharide conjugated to a polypeptide from a *Streptococcus pneumoniae* serotype selected from the group consisting of serotypes 23A, 23B, and 35B, conjugated to a polypeptide. Each of these serotypes is absent from the composition of Pneumovax 23, the 23-valent pneumococcal polysaccharide vaccine (“PPSV23”) that has formed the basis for PCV development for decades. The ’757 patent embodies Pogona’s inventors’ novel insight—years ahead of the pharmaceutical industry—that the effectiveness of Prevnar 13, the 13-valent pneumococcal conjugate vaccine (“PCV13”), would elevate non-PPSV23 serotypes as the dominant drivers of invasive pneumococcal disease (“IPD”), and that a next-generation vaccine targeting those emerging serotypes, rather than additional PPSV23 serotypes, was both necessary and achievable.

Merck's Petition challenging Pogona's novel '757 patent fails to establish a reasonable likelihood of prevailing on any challenged claim, for multiple reasons.

First, Merck's anticipation grounds rest on two references—Porro and Mekalanos—that each disclose bare, undifferentiated lists of pneumococcal serotypes: 33 serotypes in Porro, and 85 serotypes in Mekalanos. Neither reference identifies which serotypes to select, how many to select, or which combinations satisfy the claimed invention. A straightforward mathematical analysis exposes the fatal flaw in Petitioner's theory: Porro's 33-serotype list yields over 8.5 billion possible vaccine formulations, and Mekalanos's 85-serotype list yields over 38 septillion. To arrive at the specific combination of at least two of serotypes 23A, 23B, and/or 35B recited in the '757 patent's claims, a person of ordinary skill in the art ("POSA") would be required to engage in precisely the impermissible "picking and choosing" that the Federal Circuit and the Board have long prohibited in the anticipation context. These combinatorial figures do not merely exceed the numerical thresholds that Federal Circuit precedent has found insufficient for anticipation—they exceed them by factors of millions to sextillions.

Second, Merck's anticipation grounds fail because neither Porro nor Mekalanos discloses the "immunogenic" limitation that every claim of the '757 patent recites. Petitioner offers no evidence—not a single data point, experimental result, or expert analysis—that any conjugate formed from serotypes 23A, 23B, or

35B would be immunogenic. The Board confronted precisely this gap in *Merck Sharp & Dohme Corp. v. Wyeth LLC*, IPR2017-01223, where it denied institution because the petitioner—who is the Petitioner here, as well—pointed to no evidence that compositions based on the claimed serotype had been tested for a functional antibody response. The prior art here is materially weaker than what the Board found insufficient in that proceeding: unlike the serotype-specific vaccine formulation at issue in *Merck v. Wyeth*, Porro and Mekalanos offer only generic, aspirational statements about immunogenicity with no working examples directed to the claimed serotypes.

Third, Merck’s anticipation ground based on Porro fails because Porro does not disclose the structural limitation that each conjugate comprise “individually” a capsular polysaccharide conjugated to a polypeptide. Porro teaches precisely the opposite architecture: multivalent molecular constructs in which a minimum of three carbohydrate structures are covalently bound to a single carrier protein. The applicant made this distinction explicit during prosecution of a related patent, and Petitioner’s attempt to read “individually” out of the claims by invoking the open-ended “comprising” transition cannot be reconciled with the Federal Circuit’s well-established prohibition on rendering claim terms meaningless.

Fourth, Merck’s anticipation ground based on Mekalanos fails because Mekalanos does not disclose a single pharmaceutical composition comprising a

plurality of individually formed conjugates directed to multiple serotypes.

Mekalanos's references to using conjugates "in combination" describe concurrent administration of separately formulated vaccines—not the unified multi-conjugate composition the claims require—and Petitioner's inherency argument cannot cure this absence.

Fifth, Merck's obviousness grounds fail for many of the same foundational reasons as its anticipation grounds, and for additional reasons as well. Petitioner's reasonable expectation of success analysis for each obviousness ground is conclusory, ignores the "immunogenic" limitation, and fails to account for the profound unpredictability of pneumococcal conjugate vaccine development. The vaccine epidemiology references Petitioner relies upon to justify its serotype selection—individually and in combination—leave a POSA with millions to septillions of possible serotype combinations and provide no direction toward the specific serotypes claimed in the '757 patent. Rather than reducing the universe of choices, Petitioner's references expand it.

For these reasons, explained in more detail below, the Board should deny institution of *inter partes* review.

II. LEVEL OF ORDINARY SKILL

For purposes of this Preliminary Response only, Patent Owner does not dispute Petitioner's definition of a person of ordinary skill in the art. Petition at 12–13.

III. BACKGROUND TECHNOLOGY AND OVERVIEW OF THE '757 INVENTION

Patent Owner Pogona is a biotechnology company advancing innovative discoveries and biotechnology that improve 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.

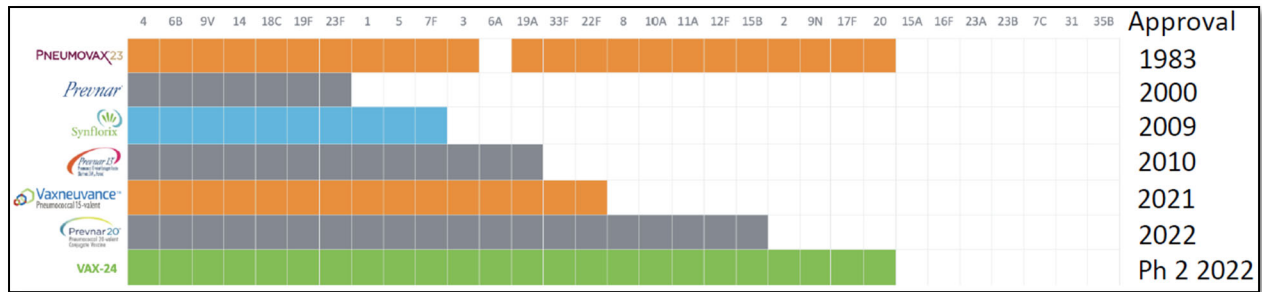
“*Streptococcus pneumoniae* (pneumococcus) can cause serious illness, including sepsis, meningitis, and pneumonia with bacteremia (invasive) or without bacteremia (noninvasive).” (Ex. 2007 at 1.) As of the priority date of the ’757 patent, there were two pneumococcal vaccines licensed for use in the 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 poorly 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 and prevalence 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 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 the majority of 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.

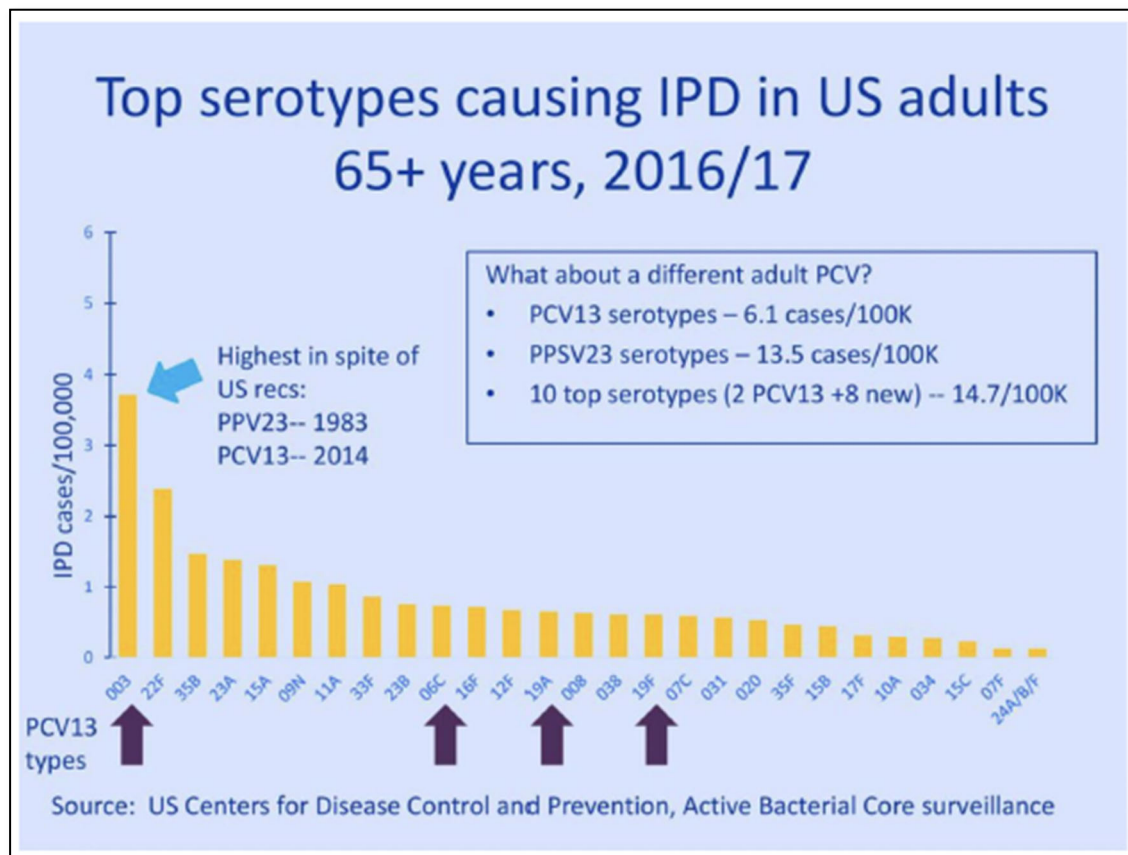
Claim 12: depending from claim 1 and reciting further selecting at least one additional serotype from the group of serotypes 6C, 8, 9N, 10A, 11A, 12F, 15A, 15B, 15C, 16F, 20A, 20B, 22F, and 34—of which 6C, 15A, 15C, 20A, 20B¹, and 34 are serotypes not included in PPSV23.

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

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

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:



(Ex. 2008 at 40.)

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. Porro and Mekalanos’s Disclosures of Thousands to Tens of Thousands 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). 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 Porro nor Mekalanos 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 21–22, 29–31.) 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.) Porro and Mekalanos 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 Porro and Mekalanos’s Disclosures Renders Anticipation Impossible

A straightforward mathematical analysis reveals the fundamental problem with Petitioner’s anticipation theories: both Porro and Mekalanos 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. Porro Reference

Petitioner alleges that “Porro discloses combining serotypes 23A and 35B in a conjugated vaccine,” and that “Porro discloses that these serotypes are ‘preferred.’” (Petition at 21–22.) Not so. Rather, Porro discloses that, “[a]ccording to preferred embodiments of the antigenic multivalent molecular construct of the invention the [sic] carried carbohydrate structures are selected among, but not limited to, P’s of” *thirty-three Streptococcus pneumoniae* serotypes and serogroups, as well as those from *Neisseria meningitidis*, *Haemophilus influenzae*, *Mycobacterium tuberculosis*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Escherichia coli*, and *Vibrio cholerae*. (Ex. 1005 at 14:26–15:8.) Indeed, far from identifying serotypes 23A and 35B as “preferred,” Porro proposed an 18-valent vaccine using his new invention, and omitted both serotypes 23A and 35B from this disclosure, 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.” (Ex. 1005 at 27:30–28:1.) Instead, he listed 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. 1005 at 65:7–67:9 (emphasis added).)

In light of Porro’s disclosure of ***thirty-three*** *S. pneumoniae* serotypes in its enumerated lists—without specifying a maximum number to be selected—meaning a POSA could select any subset of one or more serotypes, yielding **over 8.5 billion** possible serotype combinations ($2^{33} - 1 = 8,589,934,591$). Even applying Porro’s instruction that combinations of at least three serotypes are critical to its invention, directing a POSA to select any subset of three or more serotypes, the combinatorial space remains over 8.5 billion ($2^{33} - 1 - 33 - 528 = 8,589,934,030$). (See Petition at 20 (citing Ex. 1005 at 11:29–12:5 (acknowledging that “Porro discloses ‘a minimum of three carbohydrate structures’ covalently bound/conjugated to each ‘carrier protein’”))).) Of those over 8.5 billion possible combinations, only 31 combinations include both serotype 23A and serotype 35B as part of a 3-serotype formulation, representing a vanishingly small fraction of the total combinatorial space Porro presents to a POSA.

b. Mekalanos Reference

Petitioner relies on a 44-year-old case to argue that Mekalanos’s list of ***eighty-five*** *S. pneumoniae* serotypes anticipates the ’757 patent’s recitation of conjugates including at least two of serotypes 23A, 23B, and 35B, “despite Mekalanos listing 84 other serotypes because a POSITA would have had ‘no

difficulty in understanding or following [Mekalanos's] teachings' to include 23B and 35B. (Petition at 29–30 (citing *In re Parameswar Sivaramakrishnan*, 673 F.2d 1383, 1384–85 (C.C.P.A. 1982)).) As described in more detail in Sections VII.A.2. and VII.A.3., below, the Federal Circuit has spoken on this issue much more recently than Petitioner's CCPA case, and under Federal Circuit precedent, it is clear that Mekalanos's 85-serotype list does not anticipate.

In light of Mekalanos's disclosure of *eighty-five* *S. pneumoniae* serotypes in its enumerated list—without specifying a minimum or maximum number to be selected—meaning a POSA could select any subset of one or more serotypes, yielding over **38 septillion possible serotype combinations** ($2^{85} - 1 = 38,685,626,227,668,133,590,597,631$). Of those over 38 septillion possible combinations, only 83 three-serotype combinations include both 23B and 35B (necessary here since Mekalanos does not disclose serotype 23A), representing a vanishingly small fraction of the total combinatorial space Mekalanos presents to a POSA.

Both Porro's 8.5 billion possibilities and Mekalanos's 38 septillion combinations vastly exceed any acceptable threshold, requiring impermissible selection without guidance—a disclosure that falls well within the range the Board has found insufficient for anticipation, as discussed in Section VII.A.3., below. These numbers truly strain 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 **272 years** to examine all 8.5 billion combinations from Porro’s disclosure—longer than the United States has existed as a nation. The combinatorial space presented by Mekalanos is incomparably larger: at the same rate of one formulation per second, it would take approximately **1.2 quintillion years** to examine all 38 septillion possible serotype combinations—roughly **89 million times the age of the universe**. These figures underscore why the picking-and-choosing doctrine exists: no POSA working through either reference could arrive at the specific combination of glycoconjugates directed to serotypes 23A, 23B, and 35B through anything other than impermissible hindsight selection guided by knowledge of the claimed invention itself. The prior art does not disclose the claimed invention; it merely contains it, submerged beyond any practical possibility of recognition, within a combinatorial space of astronomical proportions.

2. Porro and Mekalanos 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 (C.C.P.A. 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 (C.C.P.A. 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)]’.”).

Both Porro and Mekalanos clearly require the impermissible “picking and choosing” that *Ex parte Smith* explicitly prohibits. Porro and Mekalanos provide bare lists of 33 and 85 serotypes, respectively, 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 21–22, 29–31; Ex. 1001 at claim 1.) A POSA must pick and choose among billions to septillions of possibilities, without any directional guidance, 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. *See Net MoneyIN*, 545 F.3d at 1371 (quotation omitted). Further, the references do 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, they present a selection problem requiring systematic enumeration and analysis to identify—with hindsight—which combinations satisfy the claims.

Petitioner attempts to justify its reliance on impermissible “picking and choosing” by arguing—without legal support—that the ’757 [p]atent itself does not provide any reason for why the serotypes 23A, 23B, and 35B would have been selected from its list of over 39 serotypes listed in its specification. This is both irrelevant and false. **First**, because it is impermissible to use the ’757 patent as a roadmap, a POSA would have to determine whether Mekalanos anticipated the ’757 patent’s claims without reference to what the ’757 patent’s inventors did. *See Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138 (Fed. Cir. 1985) (“The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time.”).

Second, the ’757 patent *does* explain the rationale for its serotype selection. For example, Figures 7–9 and their associated descriptions in columns 3–4 of the ’757 patent provide the epidemiological support for why 23A, 23B, and 35B were selected: they represent serotypes that cause IPD not covered by existing vaccines such as PCV13, and their inclusion in a supplemental vaccine is projected to substantially increase overall IPD coverage in the United States and Canada. Specifically, Figure 7 “illustrates the projected expanded coverage provided by a *Streptococcus pneumoniae* polypeptide conjugate vaccine comprising” 15 serotypes, three of which are 23A, 23B, and 35B—against IPD in the United States and Canada when administered in a vaccination regimen with Prevnar 13. (Ex.

1001 at 3:35–45.) The figure shows “an overall coverage of 90%,” as opposed to 46.1% with Prevnar 13 alone. (*Id.*) Similarly, Figure 8 “illustrates the projected expanded coverage provided by a *Streptococcus pneumoniae* polypeptide conjugate vaccine comprising” 8 serotypes, three of which are 23A, 23B, and 35B—against IPD in the United States and Canada when administered in a vaccine regimen with PCV13 (21% more coverage) or PCV20 (23% more coverage). (Ex. 1001 at 3:46–60.) Figure 9 also illustrates the “projected expanded coverage provided by a *Streptococcus pneumoniae* polypeptide conjugate vaccine comprising” 14 serotypes, three of which are 23A, 23B, and 35B—against IPD in the United States and Canada when administered in a vaccine regimen with PCV13 (21% more coverage) or PCV20 (29% more coverage). (Ex. 1001 at 3:61–4:9.)

3. Porro and Mekalanos 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 Porro’s and Mekalanos’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 that disclosed five binding agents and three coating techniques—creating fifteen

possible combinations—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, the only case Petitioner cites in support of its argument that Mekalanos’s 85-serotype list can anticipate the ’757 patent’s claimed serotypes (for Porro’s 33-serotype list, Petitioner cited no cases), is *In re Parameswar Sivaramakrishnan*. In that case, the prior art reference (Gable)

disclosed a two-component mixture—one resin combined with one salt—and specifically named cadmium laurate in a list of “approximately 70 other salts.” *In re Parameswar Sivaramakrishnan*, 673 F.2d at 1384. Thus, the total possible combinations that a POSA could try—one of which would meet the claim limitations—was approximately 70. At this number of combinations, the Court held that “one of ordinary skill informed by the teachings of Gable would not have had to choose judiciously from a genus of possible combinations of resin and salt to obtain the very subject matter to which appellant’s composition per se claims are directed.” *Id.* at 1385.

On a similar scale as *In re Parameswar Sivaramakrishnan*, in *Wrigley*, the Shahidi reference disclosed three “particularly preferred” cooling agents (WS–23 was one 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 Lab ’ys, 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* 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 (C.C.P.A. 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*, No. 71049US008, Appeal Br. at 9 (filed Nov. 4, 2019).) The Board agreed with the applicant that this required impermissible picking and choosing, holding that “Bartholomew’s disclosure is insufficient to establish anticipation of the compositional components” because “[t]he §102(a) rejections ... rely upon picking and choosing from various lists in Bartholomew.” (Ex. 2012, *Ex parte Eckhardt*, slip op. at 3.)

Porro and Mekalanos unquestionably fail these benchmarks and require picking and choosing on an unprecedented scale. Specifically, Porro’s 8.5 billion combinations exceed even “hundreds or thousands” (the maximum rejected in *Impax*) by a factor of approximately **8.5 million**, and Mekalanos’s 38 septillion combinations exceed that same maximum by a factor of approximately **38 sextillion**—a number so large it defies meaningful comparison to anything the *Impax* court could have contemplated. See *Impax*, 545 F.3d at 1315–16. Moreover, neither Porro nor Mekalanos provides any 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 1362. A POSA must engage in precisely the kind of extensive picking and choosing that *Smith* and *Eckhardt* prohibit.

Because the extensive serotype lists provided in Porro and Mekalanos cannot anticipate the '757 patent claims, Petitioner's Grounds 1 and 2 challenges must fail.

B. Porro and Mekalanos 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 “add[ing] only these routine serotype selections (without disclosure of any unique structure) to long-familiar conjugate vaccine constructs and methods.” (*See, e.g.*, 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,” even while acknowledging that the art before the Examiner “disclosed *S. pneumoniae* serotypes 23A, 23B, and/or 35B.” (*See, e.g.*, Petition at 2, 11–12, 14–15, 25, 42, 49 (emphasis omitted).) 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 Porro nor Mekalanos discloses this element, or even comes close.

1. Petitioner Provides No Evidence to Support its Conclusory Allegation that Porro Discloses “Immunogenic Saccharide-Polypeptide Conjugates”

With respect to Porro, Petitioner provides zero evidence that Porro discloses “*immunogenic* saccharide-polypeptide conjugates” as the claims recite.² *See Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1369 (Fed. Cir. 2016) (“It is of the utmost importance that petitioners in the IPR proceedings

² While Petitioner relies on an examiner’s rejection based on Porro in the ongoing prosecution of a related patent for other claim elements, Petitioner does not make any specific prosecution-based arguments with respect to the “immunogenic” limitation. (*See* Petition at 19–20.) Additionally, even if the Petitioner had relied on the related prosecution for the “immunogenic limitation,” the examiner’s rejection would have been insufficient evidence that Porro anticipates this limitation, because the applicant never acquiesced in the examiner’s characterization, as explained in more detail in Section VII.C., below.

adhere to the requirement that the initial petition identify ‘with particularity’ the ‘evidence that supports the grounds for the challenge to each claim’ ... [T]he expedited nature of IPRs bring[s] with it an obligation for petitioners to make their case in their petition to institute. While the Board’s requirements are strict ones, they are requirements of which petitioners are aware when they seek to institute an IPR.”). Indeed, the word “immunogenic” never appears in Petitioner’s analysis of claim 1 outside of the first sentence’s conclusory recitation of the claim language. (Petition at 19–20.) *See 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. The petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness.”). For this reason alone, Petitioner’s Porro-based grounds must fail. *See Corephotonics, Ltd. v. Apple Inc.*, 84 F.4th 990, 1001–02 (Fed. Cir. 2023) (“The IPR petition[] must provide an understandable explanation of the element-by-element specifics of the patentability challenges, including the identification of particular portions of prior art on which the petitioner is relying.”).

The expert declaration upon which Petitioner relies for its bare assertion—merely repeating the claim language—that “Porro discloses a pharmaceutical composition comprising a plurality of at least two unique immunogenic saccharide-polypeptide conjugates” fares no better. Notably, Petitioner’s expert

provides *no citation to any supporting evidence* for this assertion and offers *no technical reasoning* to support this conclusion. (See Ex. 1002 at ¶¶ 111–114.)

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.” *Xerox Corp. v. Bytemark, Inc.*, IPR2022-00624, Paper 9, 15 (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 Porro. (Petition at 19–20.) This is exactly the gap-filling that the Board rejected in *Xerox*.

2. Petitioner Provides No Evidence to Support its Conclusory Allegation that Mekalanos Discloses “Immunogenic Saccharide-Polypeptide Conjugates”

With respect to Mekalanos, Petitioner again provides zero evidence that Mekalanos discloses “*immunogenic* saccharide-polypeptide conjugates” as the claims recite. While Petitioner points to a handful of generic, conclusory

statements in Mekalanos about immunogenicity as a goal of its invention as a whole—without reference to any pneumococcal vaccine embodiment, much less with respect to the particular claimed combination of serotypes 23A, 23B, and/or 35B—Mekalanos fails to provide the specific, technical disclosure required for a POSA to make and use immunogenic conjugates of the claimed serotypes as anticipation requires. Specifically, Mekalanos provides zero experimental data, results, or specific guidance demonstrating that the particular combination of 23A, 23B, and/or 35B would elicit an immune response.

Petitioner’s expert—in his declaration that copies the relevant portion of the Petition almost verbatim—similarly fails to provide any evidence or analysis as to why Mekalanos’s conjugates, as applied to the combination of serotypes 23A, 23B, and/or 35B, would be immunogenic. (*See* Petition at 26 (citing Ex. 1002 at ¶¶ 130–133).) As described in Section VII.B.1., above, such 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.” *Xerox*, IPR2022-00624 at 15 (precedential.)

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 Sharp & Dohme Corp. v. Wyeth LLC*, IPR2017-01223, Paper 8, 11–14 (PTAB Oct. 20, 2017). In *Merck*, Petitioner sought to prove the 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 (emphasis added). 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.*

Mekalanos is materially weaker than the rejected prior art in *Merck v. Wyeth*. Mekalanos provides even less specific technical guidance than Overturf 2002, offering only generic lists of serotypes with conclusory statements about immunogenicity in general, without particularized disclosure tied to the claimed serotypes. Specifically, while Mekalanos provides two examples utilizing *S.*

pneumoniae serotypes, neither of these examples includes any of serotypes 23A, 23B, or 35B. Example 3 describes the “sortase-mediated immunogenic conjugation method [that] can be performed *in situ* on the surface of the polysaccharide-encapsulated organism, such as *Streptococcus pneumonia*,” and utilizes “23 *S. pneumoniae* serotypes”—none of which are among the set of 23A, 23B, and/or 35B claimed in the ’757 patent. (Ex. 1006 at 29:30–34.) Importantly, that example is purely about making the conjugate, and says nothing about testing its immunogenicity. Similarly, Example 4 purports to apply the invention to the “thirteen capsular types in the Wyeth product *Prevnar13*® (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F)” —again excluding any serotypes from the set of 23A, 23B, and/or 35B claimed in the ’757 patent. (Ex. 1006 at 30:3–11.) While this example acknowledges that immunogenicity testing is needed stating that these conjugates “can be assayed for their ability to induce IL-6 production by mouse macrophages,” it does not indicate any expectation or prior results showing that these conjugates, prepared according to Mekalanos, are immunogenic. Indeed, because Mekalanos provides for over 38 septillion possible *S. pneumoniae* serotype combinations, as described in Section VII.B.2., above, a POSA could never read Mekalanos as disclosing immunogenic conjugates; a POSA would view Mekalanos’s characterization of its conjugates as “immunogenic” as aspirational, at best. As the Board held in *Merck*, where the prior art reference in a vaccine trial

also had aspirations of immunogenicity, in this particular field, disclosures of immunogenicity require more than mere aspirations. *See Merck*, IPR2017-01223 at 11–14.

Because Mekalanos provides no 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, Inc. v. Becton, Dickinson & Co.*, 593 F.3d 1325, 1332 (Fed. Cir. 2010) (“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*. ‘[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.’” (cleaned up) (emphasis added)). And as the Board recognized in *Merck*, this is not the case here.

Because Petitioner fails to provide evidence to support its claims that Porro and Mekalanos disclose “immunogenic” conjugates as recited by the ’757 patent’s claim, Petitioner’s Grounds 1 and 2 challenges must fail.

C. Porro Does Not Disclose “Conjugates, Each Comprising Individually a Capsular Polysaccharide Conjugated to a Polypeptide”

Petitioner’s Ground 1 alleges that Porro anticipates claims 1, 3, and 12. (Petition at 17–24.) This ground fails because Porro does not disclose the claimed structure of individual conjugates where each comprises “individually” a capsular polysaccharide conjugated to a polypeptide.

Petitioner’s argument that “Porro discloses a pharmaceutical composition comprising a plurality of at least two unique immunogenic saccharide-polypeptide conjugates, each comprising individually a capsular polysaccharide conjugated to a polypeptide,” while utterly ignoring the term “immunogenic” as described in Section VII.B.1., above, reads the word “individually” out of the term “conjugates, each comprising individually a capsular polysaccharide conjugated to a polypeptide.” (See Petition at 19–21.) Petitioner’s argument fails, as “[i]t is highly disfavored to construe terms in a way that renders them void, meaningless, or superfluous.” *Wasica Fin. GmbH v. Cont’l Auto. Sys., Inc.*, 853 F.3d 1272, 1288 n.10 (Fed. Cir. 2017).

Petitioner argues that the use of “comprising” means that the claim “covers the structural elements recited plus additional elements,” including a structure with “a minimum of three carbohydrate structures covalently bound/conjugated to each carrier protein.” (Petition at 20 (quotation omitted).) But if “comprising” were read—as Petitioner argues—to permit structures with multiple polysaccharides on a single carrier protein, then the term “individually” would serve no purpose. But “[c]laims must be ‘interpreted with an eye toward giving effect to all terms in the claim.’” *Becton, Dickinson & Co. v. Tyco Healthcare Grp., LP*, 616 F.3d 1249, 1257 (Fed. Cir. 2010).

The interplay between “individually” and “comprising” is critical. While “comprising” certainly means that the conjugates are not limited to containing only “individually a capsular polysaccharide conjugated to a polypeptide,” it does not change the fact that the claims still require a structural element that cannot change or be read out of the claim—that “**each**” conjugate includes at least “**individually** a capsular polysaccharide conjugated to a polypeptide.” (Ex. 1001 at claim 1 (emphasis added).) See *Bayer Pharma Aktiengesellschaft v. Mylan Pharms. Inc.*, 152 F.4th 1400, 1406 (Fed. Cir. 2025) (where claims recite “administration of a **first product comprising** rivaroxaban and aspirin,” reversing “[t]he Board’s interpretation of ‘first product’ as encompassing separate dosage forms [that]

violates this basic claim construction principle by rendering ‘a first product comprising’ meaningless.”) (emphasis added)).

The term “individually” modifies how each conjugate is formed: each polysaccharide is individually (i.e., separately, one-by-one) conjugated to a polypeptide. This is the opposite of Porro’s teaching, as Petitioner acknowledges. (Petition at 20 (“Porro discloses ‘a minimum of three carbohydrate structures’ covalently bound/conjugated to each ‘carrier protein.’”).)

Petitioner never accounts for what “individually” means within the recited claim. (See Petition at 19–21.) This is likely because Petitioner’s argument conflicts with the plain and ordinary meaning of the term “conjugates, each comprising individually a capsular polysaccharide conjugated to a polypeptide,” wherein each conjugate is made up of at least a single capsular polysaccharide conjugated to a single polypeptide in a one-to-one relationship.

Indeed, elsewhere in the Petition—when it suits its argument—Petitioner seems to agree, arguing that Mekalanos discloses this element because **“each of these capsular polysaccharides is conjugated to a polypeptide.”** (Petition at 27 (emphasis added).) Similarly, Petitioner argues that Siber discloses this element because it “specifically teaches that ‘individual isolated antigens [i.e. **polysaccharides**] may be separately coupled to polypeptide carriers and then combined with one another after coupling,’” and also teaches including “7 to 11

serotypes individually conjugated to carrier proteins (i.e., at least two immunogenic saccharide-polypeptide conjugates) in a pharmaceutical composition.” (Petition at 52 (emphasis added).)

This is also the way the term is used in the ’757 patent’s specification. For instance, in Example 6, the ’757 specification states: “**Each** polysaccharide **serotype is individually conjugated to a CRM197** to produce the polysaccharide CRM197 conjugate. The polysaccharide-CRM197 conjugates for each serotype are combined into vaccine composition.” (Ex. 1001 at 60:13–26 (emphasis added); *see* Ex. 1001 at 62:12–16 (Example 8: “Each type of conjugate is separately sterilized and the appropriate volume of each **monovalent** bulk polysaccharide-CRM197 conjugate is added (volume is based on the polysaccharide concentration) to the formulation container **one at a time**.” (emphasis added).) Similarly, every working example in the ’757 patent that describes actual conjugation uses a 1:1 serotype-to-carrier architecture where each serotype’s polysaccharide is individually activated and individually conjugated to CRM197. (*See, e.g.*, Ex. 1001 at 59:61–60:3 (Example 5: “The isolated polysaccharide from serotype 8, serotype 10A, serotype 11A, serotype 12F, serotype 22F, **or** serotype 33F...were mixed with CDAP solution...A calculated amount of CRM197 was added to the activated polysaccharides. (emphasis added)”), 64:65–65:4 (Example 14: “A 6C serotype capsular polysaccharide is isolated from *S. pneumoniae*. The CRM197 is produced

and purified. The 6C polysaccharide is mixed with CDAP solution...A calculated amount of CRM197 is added to the activated 6C polysaccharides.”), 65:21–27 (Example 15: “A 20B serotype capsular polysaccharide is isolated from *S. pneumoniae*. The CRM197 is produced and purified. The 20B polysaccharide is mixed with CDAP solution...A calculated amount of CRM197 is added to the activated 20B polysaccharides.”). There is no example in the ’757 patent where two serotype polysaccharides are co-activated and co-conjugated to a single carrier in the same reaction. (See Ex. 1001, *passim*.) See *Hytera Commc’ns Co. v. Motorola Sols., Inc.*, 841 F. App’x 210, 219 (Fed. Cir. 2021) (where “the only embodiments are consistent with the plain meaning of the claim in the order that is written, [] we thus decline to construe the claim as allowing deviation from that order.”).

The plain and ordinary meaning of this term is confirmed by the applicant’s arguments during prosecution of a related patent that Porro does not anticipate a claim reciting—just as the ones at issue here—“conjugates, each comprising individually a capsular polysaccharide...conjugated to a polypeptide.” (Ex. 1015 at 1872.) Specifically, applicant argued:

Porro does not disclose immunogenic saccharide-polypeptide conjugates, **each** comprising a capsular polysaccharide...conjugated to a polypeptide. Instead, Porro relates to **multivalent** molecular constructs comprising **at least three** carbohydrate structures (*e.g.*,

capsular polysaccharides) all bound to a helper-T dependent carrier protein....Porro specifically explains that the **multivalent** construct structure is beneficial to address carrier protein-dependent immune-suppression and immune interference, noting that the ‘vaccine formulation encompassing as many as eighteen type-specific conjugate antigens, as an example, will be synthesized by using only one third (or 33%) of the amount of carrier protein needed in the nowadays available single-antigen-associated formulation, so that the immunogenic burden on the immune-system of the host will be significantly lower and, consequently, safer.’ [] Porro also indicates that the ‘new generation of conjugate antigens expressing **multiple specificities** or obtaining vaccines with an always broader spectrum of **protection against a variety of bacterial pathogens** while drastically reducing the amount of carrier protein’ will improve ‘the cost of production of the vaccines, production accuracy, safety, and the public utility of such conjugate vaccines’.”

(Ex. 1015 at 1873 (cleaned up) (emphasis in original).) Thus, by distinguishing Porro in this way, applicant made clear that the ’757 patent’s recitation of “conjugates, each comprising individually a capsular polysaccharide...conjugated to a polypeptide” does not include conjugates comprising multiple serotypes (capsular polysaccharides) to a single carrier protein (polypeptide), as Porro teaches. *See MasterMine Software, Inc. v. Microsoft Corp.*, 874 F.3d 1307, 1311–12 (Fed. Cir. 2017) (holding that where, “[d]uring prosecution of a related parent patent, the applicant, in an attempt to overcome prior art rejections, distinguished a

prior art reference,” the statement provides support for the district court’s claim construction because “this explanation presented by the inventor during patent examination is relevant to claim construction, for the role of claim construction is to ‘capture the scope of the actual invention’ that is disclosed, described, and patented.”) (quotation omitted)); *Seachange Int’l, Inc. v. C-COR, Inc.*, 413 F.3d 1361, 1372–73 (Fed. Cir. 2005) (“Where an applicant argues that a claim possesses a feature that the prior art does not possess in order to overcome a prior art rejection, the argument may serve to narrow the scope of otherwise broad claim language.”).

Petitioner ignores this argument from applicant during the related prosecution, instead focusing on the fact that applicant later amended the claim language to change from “conjugates, each comprising individually a capsular polysaccharide conjugated to a polypeptide” to “conjugates, each consisting of individually a capsular polysaccharide conjugated to a polypeptide.” Petitioner’s argument is a red herring. **First**, this amendment does not remove the word “individually,” from the ’757 claims, as Petitioner’s arguments require. (See Petition at 19–20.) **Second**, although the applicant amended its claims in a related application, it never abandoned its argument that, even without the amendment, Porro does not anticipate the original claims. Instead, the applicant explicitly stated that “[a]mendment or cancellation of the claims during

prosecution of this Application is not to be construed as acquiescence to any of the objections or rejections set forth in the Office Action and was done solely to expedite prosecution of the Application.” (Ex. 1015 at 1908.) In addition, in response to the Examiner’s statement that “it is the examiner’s position that Porro teach [sic] immune [sic] saccharide-polypeptide conjugates of the claims,” the applicant wrote that “[a]pplicant respectfully disagrees.” (*Id.*) See *H. Lundbeck A/S v. Lupin Ltd.*, 87 F.4th 1361, 1374 (Fed. Cir. 2023) (“In any event, there are no statements by the patentee during prosecution that limited the scope of ‘reacting,’ and ‘the examiner’s unilateral remarks alone do not affect the scope of the claim.’”) (quoting *Salazar v. Procter & Gamble Co.*, 414 F.3d 1342, 1347 (Fed. Cir. 2005)); *Maquet Cardiovascular LLC v. Abiomed Inc.*, 131 F.4th 1330, 1342 (Fed. Cir. 2025) (no disavowal of claim scope based on “acquiescence to statements made by the examiner” because “[a]n applicant’s silence in response to an examiner’s notice of allowance will generally not rise to a clear and unmistakable claim disavowal.”). Thus, Petitioner’s argument that Porro anticipates the ’757 patent claims—based on a misplaced reliance on applicant’s claim amendment in a different, ongoing prosecution—must fail.

D. Mekalanos Does Not Disclose “A Plurality of at Least Two...Conjugates, Each Comprising Individually a Capsular Polysaccharides [sic] Conjugated to a Polypeptide”

Petitioner’s argument that Mekalanos anticipates the “plurality of at least two...conjugates, each comprising individually a capsular polysaccharide conjugated to a polypeptide” limitation fails for at least two reasons.

First, Petitioner relies heavily on Mekalanos’s statement that its “immunogenic conjugates of the invention may be used in combination,’ including in pediatric immunizations.” (Petition at 27–28.) But this disclosure in Mekalanos does not describe a single pharmaceutical composition comprising a plurality of individually formed conjugates as the ’757 patent claims recite. Rather, it describes the practice of administering multiple separate vaccines concurrently—a common pediatric vaccination context in which distinct vaccines against different pathogens (e.g., influenza, pneumococcus, meningococcus) are administered during the same patient visit. (Ex. 1006 at 25:29–36.) The phrase “used in combination” simply means that different immunogenic conjugate products may be co-administered, not that multiple discrete polysaccharide-protein conjugates have been formulated together into a single composition. Mekalanos never states that the “combination” involves a unitary formulation comprising multiple individually formed conjugates directed to different serotypes, as would be required to anticipate the claim. Reading a multi-conjugate single composition into this

passage improperly equates co-administration of separate vaccines with the compositional structure demanded by the claim.

Second, Petitioner contends that Mekalanos's claim 44, which recites "a second antigen of interest," identifies "combinations involving more than one antigen and more than one carrier protein within a single composition." (Petition at 28.) Not so. Because Mekalanos does not actually disclose "combinations involving more than one antigen and more than one carrier protein within a single composition," as Petitioner acknowledges, Petitioner must rely on inherency for its argument. (See Petition at 28.) But "[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*, 593 F.3d at 1332) (cleaned up) (emphasis added).

Comprising "a second antigen of interest" does not necessarily disclose "combinations involving more than one antigen and more than one carrier protein within a single composition." (Petition at 28.) Indeed, Petitioner does not (and cannot) even argue this. (See Petition at 28 (arguing only that "a second antigen of interest" "**identif[ies]** combinations involving more than one antigen and more than one carrier protein within a single composition." (emphasis added).) For

example, as discussed above, Petitioner acknowledges that Porro discloses multiple antigens conjugated to a single carrier protein. (Petition at 20 (“Porro discloses ‘a minimum of three carbohydrate structures’ covalently bound/conjugated to each ‘carrier protein.’”).) Notably, Mekalanos itself explicitly teaches this possibility with respect to its disclosed invention, stating that “multiple antigenic polysaccharides can be coupled to a carrier protein....Thus, the method described herein enables multiplexing of the immunogenic conjugate, further reducing the cost of production.” (Ex. 1006 at 17:18–21.) Because Mekalanos’s disclosure of a composition incorporating a second antigen of interest does not necessarily disclose “multivalent conjugate vaccines comprised of a plurality of distinct saccharide-protein conjugates” as Petitioner argues, Petitioner’s inherency argument—and thus its Mekalanos anticipation Ground—must fail. (*See* Petition at 28–29.)

E. The Obviousness Grounds Fail for Many of the Same Reasons as the Anticipation Grounds

1. Ground 3: the ’757 Patent is Not Obvious Over Mekalanos

First, Petitioner alleges that Mekalanos “teaches “Element 1[a],” which is “a plurality of at least two unique immunogenic saccharide-polypeptide conjugates, each comprising individually a capsular polysaccharides [sic] conjugated to a polypeptide.” (Petition at 39–41.) While Petitioner incorporates its argument from its Mekalanos anticipation Ground, Petitioner provides no additional argument or

evidence to cure the fact that it provided no evidence to support its conclusory allegation that Mekalanos discloses “*immunogenic*” saccharide-polypeptide conjugates, as described in Section VII.B.2, above. Indeed, Petitioner’s case as to this element is worse with respect to obviousness, since obviousness requires that a POSA have a reasonable expectation of success. And yet, in its obviousness analysis for claim 1[a], Petitioner’s singular paragraph alleging a reasonable expectation of success fails to even mention the word “immunogenic,” much less any evidence that a POSA would have reasonably expected that each of the septillions of potential combinations—or at least those claimed in the ’757 patent—would be “immunogenic.” (*See* Petition at 41.)

As explained in detail in Section VII.B., above, 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. All Mekalanos provides for its over 38 septillion possible serotype combinations are generic statements of an intent that the conjugates are immunogenic, rather than any actual evidence of immunogenicity. (*See* Petition at 26–27.) Thus, Petitioner’s arguments that Mekalanos obviates claim element 1[a], which recites that the claimed conjugates are “immunogenic,” must fail for the same reasons as the prior art references in

Merck, which disclosed that the claimed serotype was in vaccine trials, but did not disclose any evidence of immunogenicity.

Second, Petitioner alleges that Mekalanos “teaches “Element 1[b],” which is “wherein each of the capsular polysaccharides is from a *Streptococcus pneumoniae* serotype selected from a group consisting of 23A, 23B, and 35B.” (Petition at 41–44.) As explained in detail in Section VII.A., above, Mekalanos’s disclosure of **eighty-five** *S. pneumoniae* serotypes in its enumerated list—without specifying a minimum or maximum number to be selected—meaning a POSA could select any subset of one or more serotypes, yields over **38 septillion possible serotype combinations**. Of those over 38 septillion possible combinations, only 83 three-serotype combinations include both 23B and 35B. Despite this incomprehensibly large number of combinations, Petitioner argues that a POSA would have “understood that each of the claimed serotypes—23A, 23B, and 35B—were known as potential targets for conjugated vaccines by 2016 and, therefore, would have found it obvious to select them from the finite lists of options taught by Mekalanos.” (Petition at 43.) However, Petitioner’s Ground—which alleges obviousness based on Mekalanos alone—does not point to a single disclosure in Mekalanos that indicates to a POSA that the claimed serotypes—23A, 23B, and 35B—should be greater candidates for selection than any other of the eighty-five

serotypes Mekalanos lists. (*See* Petition at 41–44.) Indeed, Mekalanos does not even include serotype 23A in its lists. (*See id.*)

For this reason, Petitioner relies on four other references that allegedly would have rendered obvious the selection of “the claimed serotypes—23A, 23B, and 35B” from Mekalanos’s lists.³ Putting aside the impropriety of relying on four additional references not included in Ground 3, Petitioner’s argument fails, because even relying just on these references—which Petitioner somehow cherry-picked over the voluminous other sero-epidemiological data that would have been known to a POSA—still leaves a POSA with over eight million possible combinations.

Specifically, Domenech lists 10 serotypes (11, 12, 15, 22F, 23A, 23B, 33F, 24, 34, and 35) that are “not included in PCV13” and “are rapidly increasing in prevalence worldwide.” (Ex. 1019 at 2.) Imohl lists 7 serotypes (3, 7F, 10A, 12F,

³ Petitioner once again incorrectly asserts: “Importantly, neither the ’757 Patent itself, nor the examiner who amended the claim, provided any reason for why the serotypes 23A, 23B, and 35B would have been selected from its list of over 39 serotypes that it mentions in the specification.” (Petition at 44.) As discussed in detail in Section VII.A.2., above, this is both irrelevant and false. (*See* Section VII.A.2.)

19A, 22F, and 23B) that “occurred most often” in the “post-PCV13 period,” which would be the current period with which a POSA would be concerned when considering future vaccines. (Ex. 1023 at 3.) Wagenvoort lists 11 serotypes (1, 6A, 6B, 7F, 10A, 15B, 18C, 23A, 23B, 23F, and 33F) that it states “could be considered if a new vaccine is designed to specifically target high risk groups.” (Ex. 1017 at 7.) Contrary to Petitioner’s allegation, Dransfield contains no sero-epidemiological data, but instead compares the effectiveness of the PPSV23 vaccine and PCV7 vaccine on 120 patients with COPD. In that limited context, the study indicated that offering “protection against cross-reactive serotypes (such as 23A/B and 9 L/N)” —which are merely serotypes known to cross-react with serotypes included in both PPSV23 and PCV7 (9V, 23F)—“then this could be extended to about two-thirds of exacerbation-associated isolates but this would still be inferior to PPSV23, which theoretically protects against 90% of serotypes.” (Ex. 1018 at 1, 2, 6.) Petitioner’s additional references include a total of 23 serotypes (1, 3, 6A, 6B, 7F, 9L, 9N, 10A, 11, 12, 12F, 15, 15B, 18C, 19A, 22F, 23A, 23B, 23F, 24, 33F, 34, and 35). This would provide a POSA with a total of **8,388,606** ($2^{23} - 1$) **possible combinations of serotypes**, even when improperly deriving the target serotypes from these references, rather than from Mekalanos—the only reference actually included in Petitioner’s Ground 3.

Neither the **38 septillion possible serotype combinations** from Mekalanos, nor the **8,388,606 possible combinations** from Petitioner’s additional four references constitute the “finite (and small in the context of the art) number of options easily traversed” by a POSA that the Federal Circuit requires for a selection among a list of options to be obvious. *See Ortho-McNeil Pharm., Inc. v. Mylan Lab’ys, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008) (affirming non-obviousness where the “invention, contrary to Mylan’s characterization, does not present a finite (and small in the context of the art) number of options easily traversed to show obviousness. The passage above in *KSR* posits a situation with a finite, and in the context of the art, small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness.”); *Grunenthal GMBH v. Alkem Lab’ys Ltd.*, 919 F.3d 1333, 1345 (Fed. Cir. 2019) (affirming **non-obviousness** where prior art “identified many variables for screening, i.e., a ‘**huge number of possible choices,**’ as opposed to a ‘**finite number,**’ as contemplated in *KSR*,” because “a conclusion of obviousness does not follow from merely ‘vary[ing] all parameters or try[ing] 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.’”) (quoting *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1365 (Fed. Cir. 2007) (“To be sure, ‘to have a reasonable

expectation of success, one must be motivated to do more than merely 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.””).

For this reason, whether using the list of serotypes in Mekalanos or in Petitioner’s additional references, the Petition has failed to demonstrate that it would have been obvious to a POSA to choose the serotypes recited in the ’757 claims. Petitioner’s Ground 3 therefore fails.

2. Ground 4: the ’757 Patent is Not Obvious Over Mekalanos in View of Porro and Siber

Petitioner’s Ground 4 fares no better. In this Ground, Petitioner attempts to combine Mekalanos with Porro and Siber to establish obviousness. (Petition at 49–55.) Petitioner’s Ground 4 fails for multiple reasons.

First, Petitioner has not established that a POSA would have been motivated to combine Mekalanos with Porro and Siber. Petitioner argues that a POSA “would have been motivated to combine Mekalanos, Porro, and Siber because they all relate to similarly structured pneumococcal conjugate vaccines and methods of administering them.” (Petition at 49–50.) Specifically, as Petitioner acknowledges, all three references teach different conjugation methods. (Petition at 14–16, 50.)

The Federal Circuit recently held that such a situation cannot, as a matter of law, support a finding of motivation to combine. Specifically, the Federal Circuit held:

We conclude that the Board erred as a matter of law with regard to the motivation to combine. **It does not suffice to meet the motivation to combine requirement to recognize that two alternative arrangements...were both known in the art...**The petition does not argue [the prior art] articulates any reason to substitute one for another or any advantages that would flow from doing so.

Virtek Vision Int’l ULC v. Assembly Guidance Sys., Inc., 97 F.4th 882, 886–87

(Fed. Cir. 2024) (emphasis added). Because Petitioner merely argues that Mekalanos, Porro, and Siber each provide methods for conjugating pneumococcal conjugate vaccines, without arguing that there is any advantage that would result from combining the references, Petitioner has failed to demonstrate that a POSA would have combined the references.

Second, Petitioner alleges that “Mekalanos-Porro-Siber teaches “Element 1[a],” which is “a plurality of at least two unique immunogenic saccharide-polypeptide conjugates, each comprising individually a capsular polysaccharides [sic] conjugated to a polypeptide.” (Petition at 52–53.) While Petitioner incorporates its argument from its Mekalanos anticipation and obviousness Grounds, Petitioner provides no additional argument or evidence to cure the fact that it provided no evidence to support its conclusory allegation that Mekalanos

discloses “*immunogenic*” saccharide-polypeptide conjugates, as described in Sections VII.B.2. and VII.E.1., above. Indeed, Petitioner’s case as to this element is worse with respect to obviousness than it was for anticipation, since obviousness requires that a POSA have a reasonable expectation of success. And yet, in its obviousness analysis for claim 1[a], Petitioner’s singular sentence alleging a reasonable expectation of success fails to even mention the word “immunogenic,” much less any evidence that a POSA would have reasonably expected that each of the septillions of potential combinations—or at least those claimed in the ’757 patent—would be “immunogenic.” (*See* Petition at 53.) Instead, Petitioner merely alleges that a POSA “would have a reasonable expectation of success in combining [the conjugate configurations taught in Siber and Mekalanos] because such configurations had been in use since the early 1990s and were viewed as an ‘outstanding success.’” (Petition at 53.) But Petitioner’s allegation that Siber’s conjugate configurations were an “outstanding success” is irrelevant, since this success is for Siber alone, and so has nothing to do with whether a POSA would reasonably expect Petitioner’s proposed Siber-Mekalanos combination to be successful. (*See id.*) *See Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016) (“The reasonable expectation of success requirement refers to the **likelihood of success in combining references to meet the limitations of the claimed invention.** [F]ailure to consider the appropriate

scope of the...patent's *claimed invention* in evaluating the reasonable expectation of success...constitutes a legal error that [is] review[ed] without deference.” (quotation omitted) (bold emphasis added)).

Further, far from supporting a reasonable expectation of success, the history of PCV vaccines 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 at least two new immunogenic conjugated serotypes as the claims require. Indeed, in contrast to its representations here regarding the “outstanding success” of prior pneumococcal vaccines, Petitioner has previously articulated some of the difficulties in expanding pneumococcal vaccine coverage to additional serotypes. (*See, e.g.*, Ex. 2014 at 2:9–12 (“[T]he prevalence of the pneumococci expressing serotypes not present in the vaccine has been increasing. The process conditions for novel serotypes has to be determined for each serotype for conjugation efficiency and for certain serotypes presented unique challenges.”), 2:24–32, 5:6–8, 24:54–25:4 (describing challenges in conjugating certain serotypes, including

23A), 2:33–43, 10:4–18, 32:29–43 (describing challenges in conjugating certain serotypes, including 35B); Ex. 2015 at 2:1–5 (“Other PCVs have covered 7, 10, 11, or 13 of the serotypes contained in PCV-15, but immune interference has been observed for some serotypes (e.g. lower protection for serotype 3 in GSK’s PCV-11) and lower response rates to serotype 6B in Pfizer’s PCV-13.”).) In addition, the Board’s decision in *Merck*, discussed in Section VII.B.2., above, also provides instructive guidance, particularly with respect to the unpredictability of the art.

Because Petitioner has not demonstrated that the Ground 4 references provide a reasonable expectation of success in achieving the claimed “*immunogenic*” saccharide-polypeptide conjugates, Petitioner’s Ground 4 challenge must fail.

Third, Petitioner alleges that “Mekalanos-Porro-Siber teaches Element 1[b],” which is “wherein each of the capsular polysaccharides is from a *Streptococcus pneumoniae* serotype selected from a group consisting of 23A, 23B, and 35B.” (Petition at 53–55.) Specifically, Petitioner incorporates its Mekalanos-based anticipation and obviousness arguments with respect to this claim element, and then also argues that Porro teaches this claim element—repeating its Porro-based anticipation arguments with respect to this element.

As explained in detail in Section VII.A., above, Mekalanos’s disclosure of *eighty-five S. pneumoniae* serotypes in its enumerated list yields over **38 septillion**

possible serotype combinations, and Porro’s disclosure of *thirty-three S. pneumoniae* serotypes in its enumerated lists yields **over 8.5 billion** possible serotype combinations. Because Porro includes 3 serotypes not in Mekalanos’s list (serotypes 6C, 6D, and 23A), combining the two references makes the total possible serotype combinations even larger (88), yielding over **309 septillion possible serotype combinations** ($2^{88}-1 = 309,485,009,821,345,068,724,781,055$). Thus, no matter what list Petitioner wants to use—Mekalanos, the additional 4 references in Ground 3, Porro, or any combination of these, for the reasons given in Sections VII.A., and VII.E.1., above, it would not have been obvious for a POSA to select at least two of the serotypes recited in claim 1 of the ’757 patent. *See Procter & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 996–97 (Fed. Cir. 2009) (affirming non-obviousness and holding that where “researchers can only vary all parameters or **try each of numerous possible choices** until one possibly arrives at a successful result, where the prior art gives either no indication of which parameters are critical or **no direction as to which of many possible choices is likely to be successful, ... courts should not succumb to hindsight claims of obviousness.**”(cleaned up) (quotations omitted) (emphasis added)).

Because it would not have been obvious for a POSA to select serotypes 23A, 23B, and/or 35B from any of the Ground 4 references, Petitioner’s Ground 4 arguments must fail.

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 29, 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 12,430 words, which is less than the 14,000 words allowed under 37 C.F.R. § 42.24(b)(1):

Dated: April 29, 2026

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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 29, 2026, by delivering a copy via electronic mail to the attorneys of record for Petitioner as follows:

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