Trials@uspto.gov
Tel: 571-272-7822

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME CORP.,
Petitioner,

v.

PFIZER INC.,
Patent Owner.

Case IPR2017-02136
Patent 9,492,559 B2

Before TONI R. SCHEINER, JEFFREY N. FREDMAN, and JACQUELINE T. HARLOW, *Administrative Patent Judges.*

FREDMAN, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

A. Background

Merck Sharp & Dohme Corp. ("Petitioner") filed a Petition (Paper 1, "Pet.") requesting an *inter partes* review of claims 11–15 and 20–37 (the "challenged claims") of U.S. Patent No. 9,492,559 B2 (Ex. 1001, "the '559 patent"). *See* 35 U.S.C. §§ 311–319. Pfizer Inc. ("Patent Owner") filed a Preliminary Response. Paper 6 ("Prelim. Resp.").

Institution of an *inter partes* review is authorized by statute when "the information presented in the petition . . . and any response . . . 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; *see* 37 C.F.R. §§ 42.4, 42.108. For the reasons set forth below, we conclude that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of at least one of the challenged claims of the '559 patent. Therefore, we institute an *inter partes* review for claims 11–15 and 20–37 of the '559 patent.

B. Related Proceedings

Petitioner indicates that three concurrent Petitions for *inter partes* review of the '559 patent were filed (IPR2017-02131, IPR2017-02132, IPR2017-02138), that IPR2017-00378, IPR2017-00380, and IPR2017-00390 were instituted with respect to US Patent 8,562,999, and that several PGR and IPR petitions were also filed with respect to US Patent 9,399,060 and 8,895,024. Pet. 5.

C. The '559 Patent (Ex. 1001)

The '559 patent "relates to vaccination of human subjects, in particular infants and elderly, against pneumoccocal infections. . . ." Ex.

1001, 1:21–22. "Pneumonia, febrile bacteraemia and meningitis are the most common manifestations of invasive pneumococcal disease, whereas bacterial spread within the respiratory tract may result in middle-ear infection, sinusitis or recurrent bronchitis." *Id.* at 1:28–32.

The '559 patent teaches the "etiological agent of pneumococcal diseases, *Streptococcus pneumoniae* (pneumococcus), is a Gram-positive encapsulated coccus,[1] surrounded by a polysaccharide capsule.[2] Differences in the composition of this capsule permit serological differentiation between about 91 capsular types." *Id.* at 1:49–53. "Pneumococcal conjugate vaccines (PCVs) are pneumococcal vaccines used to protect against disease caused by *S. pneumoniae* (pneumococcus)." *Id.* at 1:59–61. "There are currently three PCV vaccines[3] available on the global market: PREVNAR® (called PREVENAR® in some countries) (heptavalent vaccine), SYNFLORIX® (decavalent vaccine) and PREVNAR 13® (tridecavalent vaccine)." *Id*. at 1:61–64.

The '559 patent teaches "there is a need to address remaining unmet medical need for coverage of pneumococcal disease due to serotypes not

[1] A "coccus" is defined as "a spherical bacterium." *See* https://www.merriam-webster.com/dictionary/coccus.

[2] "Pneumococcus is encapsulated with a chemically linked polysaccharide which confers serotype specificity. There are 90 known serotypes of pneumococci, and the capsule is the principle virulence determinant for pneumococci, as the capsule not only protects the inner surface of the bacteria from complement, but is itself poorly immunogenic." Ex. 1007, 2:10–14.

[3] The valency of a vaccine refers to the number of different serotypes of bacteria to which the vaccine induces immune response (*e.g.* a heptavalent vaccine protects against seven different bacterial strains).

found in PREVNAR 13® and potential for serotype replacement over time." *Id*. at 2:3–6.

D. Illustrative Claims

All of the challenged claims 11–15 and 20–37 depend either directly or indirectly from independent claim 1 of the '559 patent.[4] Claims 1, 11, and 31 are illustrative of the challenged claims and recite:

> 1. An immunogenic composition comprising a *Streptococcus pneumoniae* serotype 22F glycoconjugate, wherein the glycoconjugate has a molecular weight of between 1000 kDa and 12,500 kDa and comprises an isolated capsular polysaccharide from *S. pneumo*niae serotype 22F and a carrier protein, and wherein a ratio (w/w) of the polysaccharide to the carrier protein is between 0.4 and 2.
>
> 11. The immunogenic composition of claim 1, wherein said immunogenic composition further comprises a buffer, a salt, a divalent cation, a non-ionic detergent, a cryoprotectant, an anti-oxidant, or a combination thereof.
>
> 31. A method of preventing an infection caused by *S. pneumoniae* in a subject comprising administering to the subject an effective amount of the immunogenic composition of claim 1.

Ex. 1001, 141:27–33, 142:26–29, 143:27–30.

E. The Asserted Grounds of Unpatentability

Petitioner contends that the challenged claims are unpatentable based on the following grounds. Pet. 6–7.

[4] Claims 1–10, 16–19, and 38–45 were not challenged in this proceeding, but were challenged in the related proceedings in IPR 2017-02131 and 2017-02132.

Reference	Basis	Claims Challenged
Merck 2011,[5] GSK 2008[6]	§ 103(a)	11–14, 23–33, 35–37
Merck 2011, GSK 2008, '787 Patent[7]	§ 103(a)	15
Merck 2011, GSK 2008, Obaro 2002[8]	§ 103(a)	20, 21
Merck 2011, GSK 2008, Sigurdardottir 2008[9]	§ 103(a)	22
Merck 2011, GSK 2008, MMWR 2012[10]	§ 103(a)	34

Petitioner relies on the Declaration of Dennis L. Kasper, M.D. Ex. 1087.

[5] Caulfield et al., WO 2011/100151 A1, published Aug. 18, 2011 ("Merck 2011," Ex. 1006).
[6] Biemans et al., WO 2009/000825 A2, published Dec. 31, 2008 ("GSK 2008," Ex. 1007).
[7] Khandke et al., US 7,935,787 B2, issued May 3, 2011 ("'787 Patent," Ex. 1010).
[8] Obaro et al., *Safety and immunogenicity of pneumococcal conjugate vaccine in combination with diphtheria, tetanus toxoid, pertussis and Haemophilus influenzae type b conjugate vaccine*, 21 PEDIATRIC INFECTIOUS DISEASE J. 940–6 (2002) ("Obaro 2002," Ex. 1040).
[9] Sigurdardottir et al., *Safety and immunogenicity of CRM_{197}-conjugated pneumococcal–meningococcal C combination vaccine (9vPnC–MnCC) whether given in two or three primary doses*, 26 VACCINE 4178–86 (2008) ("Sigurdardottir 2008," Ex. 1011).
[10] Bennett et al., *Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP)*, 61 MMWR 816–9 (2012) ("MMWR 2012," Ex. 1012).

II. ANALYSIS

A. Claim Interpretation

In an *inter partes* review, claim terms in an unexpired patent are given their broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b). Under the broadest reasonable interpretation approach, claim terms are given their ordinary and customary meaning as would be understood by one of ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Only terms which are in controversy need to be construed and only to the extent necessary to resolve the controversy. *See Wellman, Inc. v. Eastman Chem. Co.*, 642 F.3d 1355, 1361 (Fed. Cir. 2011); *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999).

We determine that the following claim term needs to be discussed.

1. *"immunogenic"*

Petitioner "submits that the broadest reasonable interpretation of the term 'immunogenic' is 'elicits functional antibody against at least pneumococcus serotype 22F.'" Pet. 30 (citing Ex. 1087 ¶ 67). Patent Owner "does not dispute . . . the aspect of Merck's proposal requiring that the 'immunogenic' composition 'elicits functional antibody.'" Prelim. Resp. 11. Patent Owner "disagrees, however, with the inclusion of 'at least pneumococcus serotype 22F' in Merck's proposal." *Id.* According to Patent Owner, "[t]he proper construction of 'immunogenic' is 'elicits functional antibody against each serotype in the claimed composition.'" *Id.*

We agree with the parties that the preamble language gives life and meaning to the claims by limiting the composition to require an antibody

response. *See* Ex. 1001 141:27–33, claim 1. *See Griffin v. Bertina*, 285 F.3d 1029, 1033 (Fed. Cir. 2002) ("Diagnosis is thus the essence of this invention; its appearance in the [claim] gives 'life and meaning' to the manipulative steps."). Furthermore, consistent with the interpretations advanced by the parties, we determine that the broadest reasonable interpretation of "immunogenic" requires a composition that "elicits functional antibody."

The parties incorporate into their proposed constructions of "immunogenic" arguments concerning the identity of the serotypes for which functional antibody must be elicited. In particular, Petitioner contends that the recited "immunogenic composition" must "elicit[] functional antibody against at least pneumococcus serotype 22F" (Pet. 30), whereas Patent Owner asserts that "term should be construed to require demonstration of immunogenicity against each serotype in the claimed composition" (Prelim. Resp. 12). We determine, based on the current record, that the claims, considered overall, require the "immunogenic" composition to elicit antibodies against serotype 22F glycoconjugate in claim 1. *See* Ex. 1001 141:47–49, claim 5. Independent claim 1 does not specifically require any additional glycoconjugates besides 22F and, therefore, reasonably need not include other immunogenic serotypes.

B. Principles of Law

A patent claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the claimed subject matter and the prior art are such that the subject matter, as a whole, would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 406

(2007). The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art;[11] and (4) where in evidence, objective indicia of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

In that regard, an obviousness analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR*, 550 U.S. at 418. In *KSR*, the Supreme Court also stated that an invention may be found obvious if trying a course of conduct would have been obvious to a person having ordinary skill:

> When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue

[11] Petitioner states that the level of skill in the art at the time of the invention "would have been an individual or team with Ph.D. degrees in the biological and chemical sciences and at least 3 years of work experience, or an M.D. degree and 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 protein (and analyzing the conjugates), and performing immunologic testing." Pet. 29 (citing Ex. 1087 ¶ 62). Patent Owner "does not dispute Merck's proposed level of skill for the person having ordinary skill in the art." Prelim. Resp. 11. We agree with both parties regarding the level of ordinary skill in the art. *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995). We also note that the applied prior art reflects the appropriate level of skill at the time of the claimed invention. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

> the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

KSR, 550 U.S. at 421. "*KSR* affirmed the logical inverse of this statement by stating that § 103 bars patentability unless 'the improvement is more than the predictable use of prior art elements according to their established functions.'" *In re Kubin*, 561 F.3d 1351, 1359–60 (Fed. Cir. 2009) (citing *KSR*, 550 U.S. at 417).

We analyze the asserted grounds of unpatentability in accordance with the above-stated principles.

C. Section 325(d) – Discretion to Decline to Institute

Patent Owner urges us to decline to institute the asserted grounds under 35 U.S.C. § 325(d) "because Merck 2011 and GSK 2008, which are at the center of Grounds 1-5 of the Petition, are cumulative of US 2013/0273098 ("Blue 2013"- EX2001) and WO 2009/000826 ("the WO '826 application"- EX2002), respectively, which were before the Patent Office during prosecution." Prelim. Resp. 12. Patent Owner contends that "Merck 2011 is substantially the same as Blue 2013" and that Petitioner "relies upon language in Merck 2011 that is identical to or nearly identical to language in Blue 2013." Prelim. Resp. 13–14. Patent Owner contends: "Although the Examiner did not explicitly rely on Blue 2013 in rejecting the claims, the Examiner's signature on the PTO/SB/429 form indicates that the Examiner did in fact consider the submission." Prelim. Resp. 15.

Similarly, Patent Owner contends "GSK 2008 is 'substantially the same' as the WO '826 application. The WO '826 application was

considered by the Examiner during prosecution of the ’488 application (which later issued as the ’559 patent), and is listed on the face of the ’559 patent.” Prelim. Resp. 16.

Patent Owner contends:

> The mailing of the Notice of Allowability confirms that the Examiner did not consider the ’559 patent claims to be obvious over Blue 2013 or the WO ’826 application. . . . Since the Examiner already considered and decided not to pursue the obviousness arguments based on prior art references substantially similar to those raised by the Petition, Pfizer requests the Board reject the Petition on this basis alone.

Prelim. Resp. 18.

Under § 325(d), we have discretion to “reject the petition or request because[] the same or substantially the same prior art or arguments previously were presented to the Office.” 35 U.S.C. § 325(d). While Blue 2013 and the WO ’826 application are similar to the currently relied upon Merck 2013 and GSK 2008, they are among numerous cited references listed on the front of the ’559 patent (Ex. 1001, references cited section) and were not cited by the Examiner or specifically relied upon by the Examiner during prosecution. *See* Prelim. Resp. 15. Petitioner also relies on a declaration from Dr. Kasper, which Patent Owner does not allege is duplicative of evidence previously presented to the Office. *See Tandus Flooring, Inc. v. Interface, Inc.*, Case IPR2013-00333, 2013 WL 8595289, at *2 (PTAB Dec. 9, 2013) (Paper 16) (declining to deny petition under § 325(d) where petitioner presented new declaration evidence). The Kasper Declaration presents the molecular weight and ratio evidence in a new light by explaining the underlying understanding of a person of ordinary skill in

the art regarding molecular weight ranges and ratios for polysaccharide conjugates. Ex. 1087 ¶¶ 111–115, 119–124.

Considering all of the relevant facts and circumstances, Patent Owner's argument is insufficient to persuade us to exercise our discretion to deny the Petition under 35 U.S.C. § 325(d).

D. Obviousness over Merck 2011 and GSK 2008

Petitioner contends that claims 11–14, 23–33, 35–37 are unpatentable under 35 U.S.C. § 103(a) as obvious over Merck 2011, GSK 2008, and the general knowledge of an ordinary artisan. Pet. 34. Patent Owner opposes this ground. Prelim. Resp. 21–24.

1. *Merck 2011 (Ex. 1006)*

Merck 2011 teaches "a multivalent immunogenic composition having 15 distinct polysaccharide-protein conjugates. Each conjugate consists of a capsular polysaccharide prepared from a different serotype of Streptococcus pneumoniae (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F or 33F) conjugated to a carrier protein, preferably CRM_{197}." Ex. 1006 1:7–11. Merck 2011 teaches "conjugates containing serotypes 22F and 33F provide[] robust antibody responses demonstrat[ing] the feasibility of expanding coverage of pneumococcal serotypes. . . ." Ex. 1006 4:2–3. Merck 2011 teaches the pneumococcal conjugate vaccine (PCV) with "induced high OPA[12] GMTs to each serotype and a 100% OPA response rate for all 15 serotypes contained in the vaccine." Ex. 1006, 23:3–4.

Merck 2011 teaches "purified polysaccharides are chemically activated to make the saccharides capable of reacting with the carrier

[12] Opsonophagocytosis.

protein. . . . Coupling to the protein carrier (*e.g.*, CRM_{197}) can be by reductive amination via direct amination to the lysyl groups of the protein." Ex. 1006, 6:11–23. Merck 2011 teaches the "concentrated saccharide was mixed with CRM_{197} carrier protein in a 0.2 – 2 to 1 charge ratio. The blended saccharide-CRM_{197} mixture was filtered through a 0.2 µm filter." Ex. 1006, 17:24–25. Table 1 of Merck 2011 shows a vaccine formulation comprising 32 µg of total polysaccharide and 32 µg of CRM_{197} carrier protein with the total polysaccharide being composed of 2 µg of 14 serotypes including 22F and 4 µg of serotype 6B. Ex. 1006, 19:5–9.

2. *GSK 2008*

GSK 2008 teaches a *Streptococcus pneumoniae* vaccine comprising "capsular saccharide antigens (preferably conjugated), wherein the saccharides are derived from at least ten serotypes of *S. pneumoniae*" that may include an "*S. pneumoniae* saccharide conjugate of 22F." Ex. 1007, 8:5–19. GSK 2008 teaches "*Streptococcus pneumoniae* capsular saccharides . . . may be conjugated to a carrier protein independently selected from the group consisting of . . . CRM197." Ex. 1007, 10:12–14. GSK 2008 teaches "saccharide conjugates present in the immunogenic compositions of the invention may be prepared by any known coupling technique" and specifically, conjugates "can also be prepared by direct reductive amination methods." Ex. 1007, 17:1–28. GSK 2008 teaches "22F-PhtD administered within the 13-valent conjugate vaccine formulation [was] shown immunogenic and induced opsono-phagocytic titers in young OF1 mice." Ex. 1007, 77:21–22.

GSK 2008 teaches: "Preferably the ratio of carrier protein to *S. pneumoniae* saccharide is between 1:5 and 5:1; e.g. between 1:0.5–4:1, 1:1–

3.5:1, 1.2:1–3:1, 1.5:1–2.5:1; e.g. between 1:2 and 2.5:1; 1:1 and 2:1 (w/w)." Ex. 1007, 20:24–26. Table 2 of GSK 2008 teaches fourteen different conjugates—the smallest conjugate size was PS4-PD of 1303 kDa and the largest conjugate size was PS9V-PD of 9572 kDa. Ex. 1007, 54–55, Table 2. GSK 2008 discloses a conjugate of serotype 22F, with a carrier/PS ratio of 2.17, but does not determine the conjugate size. Ex. 1007, 55, Table 2.

GSK 2008 claims a conjugate where "the average size (e.g. Mw) of the 22F saccharide is between 50 and 800 kDa. . . ." Ex. 1007, 93, claim 56. GSK 2008 further teaches in claim 61 an "immunogenic composition of any preceding claim wherein the average size (e.g. Mw) of the saccharides is above 50 kDa, e.g, 50–1600. . . ." Ex. 1007, 94.

GSK 2008 teaches "immunogenic conjugates prone to hydrolysis may be stabilised by the use of larger saccharides for conjugation. The use of larger polysaccharides can result in more cross-linking with the conjugate carrier and may lessen the liberation of free saccharide from the conjugate." Ex. 1007, 14:18–21. GSK 2008 teaches "that saccharide conjugate vaccines retaining a larger size of saccharide can provide a good immune response against pneumococcal disease." Ex. 1007, 14:23–25. GSK 2008 recommends optimization for larger size saccharide-protein conjugates, limited only by a requirement to be "filterable through a 0.2 micron filter. . . ." Ex. 1007, 14:34.

3. *Analysis*

Petitioner asserts "Merck 2011 and GSK 2011 disclose immunogenic compositions that include a conjugate of pneumococcal serotype 22F" and that "Merck 2011 demonstrates immunogenicity against serotype 22F by the generation of functional antibody against that serotype." Pet. 36 (citing Ex.

1087 ¶ 108, Ex. 1006 23:2–4). Petitioner asserts: "Based on the GSK 2008 disclosure of pneumococcal conjugates between 1,303-9,572 kDa, a POSITA would have been motivated with a reasonable expectation of success to construct the serotype 22F conjugate of Merck 2011/GSK 2008 in that approximate molecular weight range." Pet. 37 (citing Ex. 1087, ¶ 111). Petitioner also asserts "Merck 2011 and GSK 2008 both disclose the claimed range of conjugate polysaccharide to protein ratios (0.4 to 2), and reflect a POSITA's general understanding that conjugate polysaccharide to protein ratios in the claimed range are typical for immunogenic conjugates." Pet. 43 (citing Ex. 1087 ¶ 119).

Petitioner's Declarant, Dr. Kasper, states that a "POSITA would have considered the disclosure of pre-conjugation polysaccharide to CRM_{197} ratios in the range of 0.2 to 2 indicative of a final conjugate ratio in that range." Ex. 1087 ¶ 120 (citing Ex. 1006, 17:24–25). Dr. Kasper notes "the pre-conjugation ratios of Merck 2011 resulted in an average polysaccharide to protein ratio in the conjugates of approximately 1 (~32 μg of polysaccharide and ~32 μg of protein), squarely in the claimed range." Ex. 1087 ¶ 120 (citing Ex. 1006, 19:3–8). Dr. Kasper also notes "a POSITA's general understanding that conjugate polysaccharide to protein ratios in the claimed range (0.4 to 2) are typical for immunogenic conjugates" and cites a monograph disclosing ratios of saccharide to protein in a pneumococcal CRM_{197} conjugate vaccine with seven serotypes, concluding that each "disclosed ratio overlaps to a large extent with the claimed ratio of 0.4 to 2, consistent with the general understanding in the art as of January 21, 2014 that such ratios are typical for immunogenic conjugates." Ex. 1087 ¶¶ 123–124 (citing Ex. 1085, 20–24).

Dr. Kasper states "GSK 2008 discloses that '[p]referably the ratio of carrier protein to *S. pneumoniae* saccharide is . . . between 1:2 and 2.5:1 . . . (w/w),' which translates to a polysaccharide to protein ratio of 1:2.5 to 2:1, *i.e.*, the claimed polysaccharide to protein ratio of 0.4 to 2." Ex. 1087 ¶ 121, (citing Ex. 1007, 20:24–26). Dr. Kasper also states "Table 2 of GSK 2008 discloses an immunogenic serotype 22F conjugate (PS22F-PhtD) with a protein to polysaccharide ratio of 2.17, which translates to a polysaccharide to protein ratio of 1/2.17 or 0.46 - squarely within the claimed range." Ex. 1087 ¶ 121 (citing Ex. 1007, 54:27 to 55:1). Dr. Kasper also relies upon a monograph that "specifies the acceptable range of 'Saccharide content/protein ratio' (which a POSITA would have understood to be a w/w ratio)" and that "[e]ach disclosed ratio overlaps to a large extent with the claimed ratio of 0.4 to 2. . . ." Ex. 1087 ¶¶ 123–124 (citing Ex. 1085, 20–24).

Dr. Kasper states "the conjugate molecular weights that were determined (for every conjugate of the underlying 10-valent composition) ranged from 1,303-9,572 kDa, squarely within the claimed molecular weight range." Ex. 1087 ¶ 111. Dr. Kasper states "GSK 2008 discloses that the serotype 22F polysaccharide in its immunogenic conjugates can be, e.g., 'between 50 and 800 kDa.'" Ex. 1087 ¶ 112 (citing Ex. 1007, 93).

Dr. Kasper states the ordinary artisan would "have been motivated to stay roughly within the upper limit of molecular weights disclosed in GSK 2008, because 'excessive modifications to the PS or protein molecules can have an adverse impact on immunogenicity.'" Ex. 1087 ¶ 113 (citing Ex. 1035, 8). Dr. Kasper also notes that "both Merck 2011 and GSK 2008 disclose a sterile filtration step through a 0.2 μm filter, which sets an upper

limit on conjugate molecular weight." Ex. 1087 ¶ 113 (citing Ex. 1006 16:30–31, Ex. 1007 14:13–15).

Dr. Kasper states a "POSITA's motivation and reasonable expectation of success would have been further supported by the fact that Patent Owner disclosed in a scientific meeting in 2012 that the 'Typical Mass (kDa)' for a glycoconjugate is '500-5000,' largely overlapping with the range recited in GSK 2008 (and claim 1)." Ex. 1087 ¶ 114 (citing Ex. 1008, 6). Dr. Kasper states "Patent Owner even disclosed in a scientific meeting in 2007 that its own pneumococcal conjugates can be as large as ~7,000 to ~12,000 kDa, again overlapping with the range of GSK 2008 (and completely within the claimed range)." Ex. 1087 ¶ 114 (citing Ex. 1027, 21). Dr. Kasper states:

> Because the structure of serotype 22F capsular polysaccharide had been known to the art since 1989 (Ex. 1029), a POSITA would have required only routine experimentation to obtain a conjugate molecular weight within the desirable range disclosed in GSK 2008, e.g., by increasing or decreasing the amount of cross-linking in the conjugate.

Ex. 1087 ¶ 115 (citing Ex. 1030, 4:56–59).

We find that the current evidence of record in Merck 2011 and GSK 2008, as supported by Dr. Kasper, provides a reasonable likelihood that the references render the subject matter of claims 11–14, 23–33, and 35–37 obvious because the evidence currently of record supports Petitioner's position that an immunogenic composition comprising an *S. pneumoniae* serotype 22F glycoconjugate with a molecular weight within the range 1000 and 12,500 kDa and a polysaccharide to carrier protein ratio between 0.4 and 2 would have been obvious to the ordinary artisan at the time of invention.

In particular, we recognize that both Merck 2011 and GSK 2008 suggest multivalent immunogenic compositions comprising *S. pneumoniae*

serotype 22F conjugated to a carrier protein. Moreover, as Petitioner points out, Table 2 of GSK 2008 shows a range of conjugate sizes where the lowest reported value is 1303 kDa and the highest reported value is 9572 kDa, both values falling within the range of 1000 kDa to 12,500 kDa required by claim 1. Ex. 1007, 54–55; Ex. 1006, 1:7–11; Ex. 1007, 8:5–19.

a. "wherein the glycoconjugate has a molecular weight of between 1000 kDa and 12,500 kDa

Patent Owner asserts "[t]here is no motivation, however, to obtain a serotype 22F glycoconjugate having a molecular weight disclosed for the non-serotype 22F glycoconjugates in Table 2." Prelim. Resp. 21. Patent Owner asserts for "four of the six parameters for which data was provided for the serotype 19A and 22F glycoconjugates in Table 2 of GSK 2008, the data was almost entirely non-overlapping with the data provided for the other serotype glycoconjugates." Prelim. Resp. 22. Patent Owner concludes "a POSA would not have expected the serotype 19A and 22F glycoconjugates to have the same molecular weight parameters as the other glycoconjugates tested in Table 2." Patent Owner also asserts "neither the Petition nor Merck's expert, Dr. Kasper, provides any rationale as to why a POSA would have expected a serotype 22F glycoconjugate to have the same molecular weight as that of the other serotype glycoconjugates." Prelim. Resp. 23.

On the current record, we find this argument unpersuasive. While Table 2 in GSK 2008 shows that conjugate size for neither of the serotype 22F conjugates was determined, Table 2 shows a range of conjugate sizes where the lowest reported value is 1303 kDa and the highest reported value is 9572 kDa, both values falling within the range of 1000 kDa to 12,500 kDa

required by claim 1. Ex. 1007 54–55. Thus, we agree with Petitioner that GSK 2008 reasonably suggests that conjugate sizes between 1303 and 9572 kDa represent a desirable range because these conjugates may be used to generate multivalent vaccines. Pet. 38; Ex. 1007, 55:2–10.

"In cases involving overlapping ranges, we and our predecessor court have consistently held that even a slight overlap in range establishes a prima facie case of obviousness." *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003). Here, the range of conjugates disclosed within GSK 2008 all fall within the range recited in claim 1. While the standard for an issued patent in *inter partes* review is not "prima facie obviousness" because the burden is placed on Petitioner to demonstrate actual obviousness, we conclude the evidence of GSK 2008 supports a reasonable likelihood that the ordinary artisan would have had a reason to produce a serotype 22F glycoconjugate within the range of 1303 to 9572 kDa.

Patent Owner asserts Petitioner "does not provide any reason why reductive amination or CDAP conjugation chemistries would have resulted in serotype 22F glycoconjugates falling within the claimed molecular weight range." Prelim. Resp. 24. Patent Owner also asserts

> Merck has failed to explain why a POSA would not have elected to use a smaller serotype 22F polysaccharide (e.g., 50-100 kDa) and an average-sized protein carrier (e.g., CRM_{197} at ~58 kDa) in reductive amination or CDAP conjugation chemistries to generate a serotype 22F glycoconjugate well below the claimed molecular weight range in the '559 patent. Even if multiple 22F polysaccharides were cross-linked to multiple protein carriers, Merck has provided no evidence that the combination of these multiple polysaccharides or protein carriers would necessarily add up to a molecular weight within the claimed range.

Prelim. Resp. 25.

We find this argument unpersuasive because GSK 2008 specifically teaches a composition in claim 56 where "the average size (e.g. Mw) of the 22F saccharide is between 50 and 800 kDa. . . ." Ex. 1007, 93. GSK 2008 further teaches in claim 61 an "immunogenic composition of any preceding claim wherein the average size (e.g. Mw) of the saccharides is above 50 kDa, e.g, 50–1600. . . ." Ex. 1007, 94. Thus, GSK 2008 suggests that saccharides, including the 22F saccharide, may be as large as 1600 kDa, a value that falls squarely within the range required by claim 1, even excluding the addition 58 kDa added by the CRM_{197} protein carrier. Ex. 1007, 94; Ex. 1008, 20. "Such overlap itself provides sufficient motivation to optimize the ranges." *In re Applied Materials, Inc*., 692 F.3d 1289, 1295 (Fed. Cir. 2012).

GSK 2008 also provides more specific reasons to optimize the saccharide conjugates for larger sizes by teaching "immunogenic conjugates prone to hydrolysis may be stabilised by the use of larger saccharides for conjugation. The use of larger polysaccharides can result in more cross-linking with the conjugate carrier and may lessen the liberation of free saccharide from the conjugate." Ex. 1007, 14:18–21 (*cf*. Pet. 40, 45). GSK 2008 teaches "that saccharide conjugate vaccines retaining a larger size of saccharide can provide a good immune response against pneumococcal disease." Ex. 1007, 14:23–25. GSK 2008 recognizes optimization for larger size saccharide-protein conjugates, limited only by a requirement to be "filterable through a 0.2 micron filter." Ex. 1007, 14:34, *cf*. Pet. 40.

Therefore, GSK 2008 teaches that conjugate size is a results effective variable associated with improved stability of conjugates and good immune response, limited only by filter size, thereby rendering "optimization within

the grasp of one of ordinary skill in the art." *Applied Materials*, 692 F.3d at 1295. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456 (CCPA 1955). Patent Owner has, so far, provided no evidence demonstrating any secondary consideration regarding the conjugate sizes.

Patent Owner asserts "[w]hile Ground 1 appears to rely on just Merck 2011, GSK 2008 and general knowledge, the arguments in Ground 1 actually refer to numerous additional exhibits. Indeed . . . Merck actually refers to nearly *fifteen* additional documents." Prelim. Resp. 26. Patent Owner asserts "[t]his is improper. Pursuant to 37 C.F.R. § 42.104(b)(5), Merck is required to identify 'the relevance of the evidence' to its obviousness challenge, as well as the "specific portions of the evidence that support the challenge." Merck has not complied with the rule." Prelim. Resp. 26.

While Petitioner's obviousness position does not require the additional cited references, nor do we rely upon these additional references, Petitioner does not cite the additional references to establish limitations in the claims but rather to illustrate the understanding of the person of ordinary skill in the art.

Therefore, while Patent Owner contends that "[n]owhere in Pfizer 2012[13] is there any mention of pneumococcal glycoconjugates, much less a serotype 22F glycoconjugate" and that Pfizer 2012 "is not limited to

[13] Brown et al., *Characterization of Complex Prophylactic Vaccines with Protein and Glycoconjugate Components*, 9th CASSS Symposium (Sept. 12, 2012). The parties refers to Exhibit 1008 as "Pfizer 2012."

pneumococcal glycoconjugates and is only a statement about the general range of all glycoconjugates without respect to source," we understand the citation to Pfizer 2012 as evidencing that 500 to 5000 kDa was a known size range for glycoconjugates consistent with the disclosure of a range up to 1600 kDA disclosed by GSK 2008. *See* Prelim. Resp. 28–29, Ex. 1008, 6, Ex. 1007, 94 (*cf*. Pet. 19, 40).

Patent Owner similarly asserts that Jones 2005,[14] Wyeth 2007,[15] and Lees 2008[16] provide "no reason why molecular weight information for a glycoconjugate from one species would have informed a POSA how to make a glycoconjugate having a polysaccharide from a completely different species" and that "desirable characteristics of one serotype glycoconjugate may not be true for another serotype glycoconjugate." Prelim. Resp. 30–31, Pet. 40–41.

We find this argument unpersuasive because we understand Petitioner's citations to the disclosures in Jones 2005 of a 5000 kDa glycoconjugate, in Wyeth 2007 of pneumococcal serotype 7F glycoconjugates with sizes between 9202 and 11950 kDa, and in Lees 2008 of a multiple conjugate formation are provided to establish that the person of

[14] Jones, C., *Vaccines based on the cell surface carbohydrates of pathogenic bacteria*, 77 Anais da Academia Brasileira de Ciências 293324 (2005). The parties refer to Exhibit 1026 as "Jones 2005."
[15] Turula et al., *The Application of SEC-MALS in Vaccine Development*, International Light Scattering Colloquium 2007 1–48 (2007). The parties refer to Exhibit 1027 as "Wyeth 2007."
[16] Lees et al., *Conjugation Chemistry*, in Pneumococcal Vaccines: the Impact of Conjugate Vaccine 163–174 (2008). The parties refer to Exhibit 1035 as "Lees 2008."

ordinary skill in the art, at the time of invention, recognized how to generate glycoconjugates of varying sizes using known techniques and recognized that size was a known, optimizable variable. *See* Pet. 38, 40–41; Ex. 1026, 7; Ex 1027, 21; Ex. 1035, 7.

b. "ratio (w/w) of the polysaccharide to the carrier protein is between 0.4 and 2"

Patent Owner asserts the "ratio of the '559 patent claims and the ratio of Merck 2011 are presented in terms of two different units of measurement." Prelim Resp. 34. Patent Owner asserts the "terms 'w/w' and 'charge' are not the same, and Merck has therefore failed to demonstrate that Merck 2011 teaches or suggests the polysaccharide to protein ratio (w/w) limitation required of the '559 patent claims." Prelim. Resp. 34. Patent Owner also asserts

> neither Table 1 nor any other text in Merck 2011 states that all of the polysaccharides in the referenced formulation are actually conjugated to carrier protein. Table 1 merely indicates that the conjugate, polysaccharide and carrier protein components were mixed with each other to arrive at the total recited amounts. EX1006 at 19, Table 1. A POSA would have understood from prior art documents such as GSK 2008 that polysaccharides are not always conjugated to carrier proteins in a glycoconjugate formulation, and that some portion of the polysaccharides present in such a formulation is made up of "free" or unconjugated polysaccharides.

Prelim. Resp. 35–36.

While we agree with Patent Owner that Merck's teaching of a 0.2–2 to 1 charge ratio for polysaccharide and carrier protein does not necessarily teach the 0.4 to 2 w/w ratio required by claim 1, Merck's teaching does

suggest that the ratio of polysaccharide to carrier protein represents an optimizable variable.

We are not persuaded by Patent Owner's argument regarding Merck 2011 Table 1, because in that table Merck 2011 discloses an example that would reasonably have been expected to result in a 1:1 w/w ratio of the 22F polysaccharide to the CRM_{197} carrier protein. Ex. 1006, 19:5–9; Ex. 1087 ¶ 120. This expectation is supported by Dr. Kasper's statement that the ratios "resulted in an average polysaccharide to protein ratio in the conjugates of approximately 1. . . ." Ex. 1087 ¶ 120.

As this stage of the proceeding, Patent Owner provides no direct evidence that the pre-conjugation data disclosed in Table 1 of Merck 2011 would not have resulted in an approximately 1:1 w/w ratio for serotype 22F. However, Patent Owner points to GSK 2008 and asserts

> GSK 2008 demonstrates the opposite, *i.e*., the polysaccharide to protein ratios may differ substantially between pre-conjugation and final conjugation compositions. Tables 1 and 2 of GSK 2008 disclose pre-conjugation ratios that are 28% higher (2.5/1 up to 3.2/1 for serotype 19A) or 50% lower (1/1 down to 0.5/1 for serotype 23F) compared to the final conjugation ratios.

Prelim. Resp. 34–35 (citing Ex. 1007, 52–55).

Even crediting this indirect evidence related to other serotypes, we note that either a 50% reduction or a 28% increase in the 1:1 starting pre-conjugation ratio for serotype 22F disclosed in Merck 2011 would still result in a final conjugation composition that falls within the 0.4 to 2 w/w ratio range required by claim 1. Therefore, even fully accepting Patent Owner's position, the final conjugated composition of serotype 22F in Merck 2011 would have been expected to render claim 1 obvious. S*ee, e.g., Ineos USA LLC v. Berry Plastics Corp*., 783 F.3d 865, 869 (Fed. Cir. 2015) ("When a

patent claims a range, as in this case, that range is anticipated by a prior art reference if the reference discloses a point within the range.")

Patent Owner asserts "Merck points to a single range selected from one of several long lists in GSK 2008 that refers to a polysaccharide to protein range between 1:2 and 2.5:1. . . ." Prelim. Resp. 38. Patent Owner asserts "the referenced list includes several different ratio ranges generic to all *S. pneumoniae* polysaccharides, and nothing in this list specifies any particular range for a serotype 22F glycoconjugate." Prelim. Resp. 38. Patent Owner asserts "other sections of GSK 2008 refer to a variety of other polysaccharide to protein ratio ranges that fall well *outside* of the claimed range. For instance, GSK 2008 refers to protein to polysaccharide (without disclosing the specific serotype) ratio ranges of 6:1 to 3:1 (*i.e.*, a polysaccharide to protein ratio of 1:6 and 1:3, which translates to 0.17 to 0.33)." Prelim. Resp. 38.

We are not persuaded by this argument because GSK 2008 discloses a range of ratios of polysaccharide to carrier protein that includes and fully overlaps the range claimed. Ex. 1007, 20:24–28. *Peterson*, 315 F.3d at 1329. To the extent that GSK 2008 teaches ratios outside the ratio required by claim 1, the ordinary artisan would have found all of these ratios obvious, rather than discarding those that render claim 1 obvious. *Cf.* Merck & Co. v. Biocraft Labs., 874 F.2d 804, 807 (Fed. Cir. 1989) ("That the [prior art] discloses a multitude of effective combinations does not render any particular [composition] less obvious.")

Patent Owner asserts "Example 2 of GSK 2008 provides a specific protocol for generating a serotype 22F glycoconjugate . . . The GSK 2008 conjugation procedure therefore results in a polysaccharide to protein ratio

value *below* the '559 patent claimed range of 0.4 to 2.0." Prelim Resp. 39–40. Patent Owner acknowledges that "PS22F-PhtD in Table 2 of GSK 2008 has a protein to polysaccharide ratio of 2.17, which allegedly translates to a polysaccharide to protein ratio of 1:2.17, or 0.46" but asserts "data for a second glycoconjugate referred to as 'PS22F-AHPhtD'" shows the "polysaccharide to protein ratio for the PS22F-AHPhtD clearly falls *outside* of the '559 patent claimed range." Prelim. Resp. 41 (citing Ex. 1007, 54–55).

Patent Owner asserts "GSK 2008 states that the glycoconjugate having the ratio outside the claimed range, *i.e.*, PS22F-AH-PhtD, 'was shown [to be] much more immunogenic' than PS22F-PhtD (the glycoconjugate allegedly having a ratio within the claimed range) in terms of both IgG levels and opsonophagocytic titres." Prelim. Resp. 42.

We find this argument unpersuasive. Patent Owner acknowledges that GSK 2008 teaches a final conjugate of serotype 22F that has a polysaccharide to protein ratio of 0.46, within the range required by claim 1. To the extent that this conjugate with a 0.46 ratio had lower immunogenicity than a different conjugate of 22F with a lower polysaccharide to protein ratio, it is well settled that disclosed examples, and even preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments. *In re Susi*, 440 F.2d 442, 446 n.3 (CCPA 1971). *See also In re Fulton*, 391 F.3d 1195, 1201 (Fed.Cir.2004) ("The prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the [claimed] solution.").

We also note that GSK 2008 shows the immunogenicity for the two serotype 22F conjugates as either 37% or 28–31%, demonstrating similar results for both conjugates. Indeed, GSK 2008 teaches a "13 valent vaccine was made by further adding the serotypes 19A and 22F conjugates above (with 22F either directly linked to PhtD, or alternatively through an ADH linker)." Ex. 1007 55. Thus, GSK 2008 is reasonably understood as recognizing that either 22F conjugate may be used in the multivalent vaccine. Patent Owner points to no teaching in GSK 2008 that criticizes, discredits, or discourages the use of a ratio within the range required by claim 1.

Patent Owner asserts that Petitioner relies on a webpage from the Japanese National Institute of Infectious Diseases ("JNIID")[17] "to allege that a POSA would have considered the polysaccharide to carrier protein ratio of 0.4 to 2.0 to be 'typical for immunogenic compositions.'" Prelim. Resp. 43, citing Pet. 43, Ex. 1085, 23. Patent Owner asserts Petitioner "fails to provide any explanation as to why a POSA would have understood the ratio to be a w/w ratio" and that "JNIID is completely silent regarding serotype 22F glycoconjugates. A POSA would have understood from documents such as GSK 2008 that serotype 22F required special consideration with regard to polysaccharide to protein ratios." Prelim. Resp. 43 (citing Pet. 45–46).

[17] Japanese National Institute of Infectious Diseases, http://web.archive.org/web/20130105152418/http://www.nih.go.jp/niid/ja/mrbp.html (2012). The parties refers to Exhibit 1085 as "JNIID."

We understand JNIID is used by Petitioner to establish that the person of ordinary skill in the art, at the time of invention, recognized selection of saccharide content to protein ratios represents a known, optimizable variable. Dr. Kasper specifically states JNIID "specifies the acceptable range of 'Saccharide content/protein ratio' (which a POSITA would have understood to be a w/w ratio). . . ." Ex. 1087 ¶ 123; Pet. 45–46. As we balance this statement by an expert based on evidence in the record with Patent Owner's assertions without evidence, we find that the current record better supports Petitioner's position that JNIID supports the understanding of the ordinary artisan that saccharide to protein ratios generally range from as low as 0.3 to as high as 2.6 to 1. *See* Ex. 1085 23; Ex. 1087 ¶ 123.

At this stage of the proceeding, having considered the evidence and arguments of record, we determine that Petitioner has sufficiently shown a reasonable likelihood that it would prevail in demonstrating claims 11–14, 23–33, and 35–37 as obvious over Merck 2011 and GSK 2008.

E. Obviousness over Merck 2011, GSK 2008, and the '787 patent

Petitioner contends that claim 15 is unpatentable under 35 U.S.C. § 103(a) as obvious over Merck 2011, GSK 2008, and the '787 patent. Pet. 56–57. *See* Prelim Resp. 47–48.

Petitioner asserts "Merck 2011 discloses that '[t]he composition of the invention can be formulated as . . . pre-filled syringes.'" Pet. 56 (citing Ex. 1006, 13:1–2). Petitioner asserts "[t]he'787 Patent discloses pneumococcal polysaccharide-protein conjugate formulations in siliconized containers, including glass syringes; the formulations inhibit protein aggregation caused by the silicone oil." Pet. 56 (citing Ex. 1010, 13:34 –14:23). Petitioner asserts that a "POSITA designing a pneumococcal conjugate composition

based on Merck 2011/GSK 2008 would have considered the teachings of the '787 Patent relating to suitable containers for such compositions." Pet. 56 (citing Ex. 1087 ¶ 144).

Patent Owner asserts "[n]either Merck nor its expert, Dr. Kasper, has demonstrated that claim 1 is obvious over Merck 2011, GSK 2008, the '787 patent and the 'general knowledge.' Therefore, Merck has likewise not met its burden in showing that claim 15 is obvious." Prelim. Resp. 47. Patent Owner asserts

> the '787 patent is silent with regard to serotype 22F glycoconjugates. Moreover, the '787 patent does not refer to the molecular weight or polysaccharide to protein ratio for *any* glycoconjugates. As such, a POSA would not have had any motivation from the '787 Patent, whether viewed alone or in combination with Merck 2011, GSK 2008 or the "general knowledge," to generate an immunogenic composition comprising a serotype 22F glycoconjugate having a molecular weight or polysaccharide to protein ratio falling within the specific ranges recited in claim 1 (and dependent claim 15) of the '559 patent.

Prelim. Resp. 48.

We find Petitioner has the better position. Claim 15 depends from claim 1, and Patent Owner does not argue that claim 15 is independently patentable. As discussed above, on this record, Petitioner has established a reasonable likelihood that claim 1 would have been obvious over Merck 2011 and GSK 2008. The '787 patent teaches siliconization of conjugate holding containers including syringes as well as glass containers such as those taught by Merck 2011, and Petitioner provides cogent reasons supporting the use of such containers. Ex. 1006, 13:1–2; Ex. 1010, 13:44–49, 14:11.

At this stage of the proceeding, having considered the evidence and arguments of record, we determine that Petitioner has sufficiently shown a reasonable likelihood that it would prevail in demonstrating claim 15 as obvious over Merck 2011, GSK 2008, and the '787 patent.

F. Obviousness over Merck 2011, GSK 2008, and Obaro 2002

Petitioner contends that claims 20 and 21 are unpatentable under 35 U.S.C. § 103(a) as obvious over Merck 2011, GSK 2008, and Obaro 2002. Pet. 57–59. *See* Prelim Resp. 48–50.

Petitioner asserts "Obaro 2002 reports the safety and immunogenicity of Patent Owner's 9-valent pneumococcal CRM_{197}-conjugate vaccine ('PnCV') when given in combination with a vaccine ('TETRAMUNE') containing diphtheria toxoid, tetanus toxoid, whole cell pertussis, and CRM_{197}-conjugated *Haemophilus influenzae* type B oligosaccharide." Pet. 59 (citing Ex. 1040, 940–941). Petitioner asserts "a POSITA would have understood that combining distinct individual vaccines (e.g., pneumococcal and non-pneumococcal vaccinations) into a single composition is desirable, to enhance protection against disease and minimize the number of injections to a patient, particularly for infants." Pet. 58 (citing Ex. 1007 43:1–11).

Patent Owner asserts "[n]either Merck nor its expert, Dr. Kasper, has demonstrated that claim 1 is obvious over Merck 2011, GSK 2008, Obaro 2002 and the 'general knowledge.' Therefore, Merck has likewise not met its burden in showing that claims 20 and 21 are obvious." Prelim. Resp. 49. Patent Owner asserts

> The glycoconjugate vaccine compositions of Obaro 2002 comprise nine different, serotype glycoconjugates, *i.e.*, serotypes 1, 4, 5, 6B, 9V, 14, 18C, 19F and 23F. EX1040 at 2. None of the serotypes included in the compositions of Obaro 2002 is a

> serotype 22F glycoconjugate. In addition, Obaro 2002 does not refer to the molecular weight or polysaccharide to protein ratio for any of the glycoconjugates in its nine-valent composition.

Prelim. Resp. 49.

We find Petitioner has the better position. Claim 20 depends from claim 1 and claim 21 depends from claim 20. Patent Owner does not argue that claims 20 and 21 are independently patentable. As discussed above, on this record, Petitioner has established a reasonable likelihood that claim 1 would have been obvious over Merck 2011 and GSK 2008, and Obaro 2002 teaches combination vaccines, as does GSK 2008, and Petitioner provides cogent reasons supporting the use of such combination vaccines. Pet. 58, Ex. 1007, 43:1–11, Ex. 1040, 940–941.

At this stage of the proceeding, having considered the evidence and arguments of record, we determine that Petitioner has sufficiently shown a reasonable likelihood that it would prevail in demonstrating claims 20 and 21 as obvious over Merck 2011, GSK 2008, and Obaro 2002.

G. Obviousness over Merck 2011, GSK 2008, and Sigurdardottir 2008

Petitioner contends that claim 22 is unpatentable under 35 U.S.C. § 103(a) as obvious over Merck 2011, GSK 2008, and Sigurdardottir 2008. Pet. 57–59. *See* Prelim Resp. 50–52.

Petitioner asserts

> Sigurdardottir 2008 "evaluated safety and immunogenicity of a combined 9-valent pneumococcal and meningococcal C conjugate vaccine ['9vPnC-MnCC'], administered according to either a two- or a three-dose primary immunization schedule, followed by a booster dose." Ex. 1011 at 2. The authors conclude that, for both immunization schedules, 9vPnC-MnCC is safe and immunogenic.

Pet. 60 (citing Ex. 1011, 2, 8). Petitioner asserts "a POSITA would have understood that combining distinct individual vaccines (*e.g.*, pneumococcal and non-pneumococcal vaccinations) into a single composition is desirable, to enhance protection against disease and minimize the number of injections to a patient, particularly for infants." Pet. 60.

Patent Owner asserts "[n]either Merck nor its expert, Dr. Kasper, has demonstrated that claim 1 is obvious over Merck 2011, GSK 2008, Sigurdardottir 2008 and the 'general knowledge.' Therefore, Merck has likewise not met its burden in showing that claim 22 is obvious." Prelim. Resp. 50. Patent Owner asserts

> the pneumococcal glycoconjugates of Sigurdardottir 2008 comprise nine different, serotype glycoconjugates, *i.e.*, serotypes 1, 4, 5, 6B, 9V, 14, 18C, 19F and 23F. EX1011 at 2. None of the serotypes included in the glycoconjugate compositions of Sigurdardottir 2008 is serotype 22F. Sigurdardottir 2008 also does not refer to the molecular weight or polysaccharide to protein ratio for *any* of the glycoconjugates present in the nine-valent pneumococcal glycoconjugate vaccine.

Prelim. Resp. 51.

We find Petitioner has the better position. Claim 22 depends from claim 1. Patent Owner does not argue that claim 22 is independently patentable. As discussed above, on this record, Petitioner has established a reasonable likelihood that claim 1 would have been obvious over Merck 2011 and GSK 2008, and Sigurdardottir 2008 teaches combination vaccines, as does GSK 2008, and Petitioner provides cogent reasons supporting the use of such combination vaccines. Pet. 60, Ex. 1007, 43:1–11, Ex. 1011, 2, 8.

At this stage of the proceeding, having considered the evidence and arguments of record, we determine that Petitioner has sufficiently shown a reasonable likelihood that it would prevail in demonstrating claim 22 as obvious over Merck 2011, GSK 2008, and Sigurdardottir 2008.

H. Obviousness over Merck 2011, GSK 2008, and MMWR 2012

Petitioner contends that claim 34 is unpatentable under 35 U.S.C. § 103(a) as obvious over Merck 2011, GSK 2008, and MMWR 2012. Pet. 61–62. *See* Prelim Resp. 52–53.

Petitioner asserts "MMWR 2012 discloses the 'recommended routine use of 13-valent pneumococcal conjugate vaccine (PCV13; Prevnar 13, Wyeth Pharmaceuticals, Inc., a subsidiary of Pfizer, Inc.) for adults aged ≥ 19 years with immunocompromising conditions.'" Pet. 61 (citing Ex. 1012, 12). Petitioner asserts

> Based on MMWR 2012, as well as the demonstrated immunogenicity of the serotype 22F conjugates of Merck 2011 and GSK 2008, a POSITA would have been motivated with a reasonable expectation of success to practice the method of claim 30 (taught by the combination of Merck 2011 and GSK 2008) in an immunocompromised human.

Pet. 62.

Patent Owner asserts "[n]either Merck nor its expert, Dr. Kasper, has demonstrated that claim 1 is obvious over Merck 2011, GSK 2008, MMWR 2012 and the 'general knowledge.' Therefore, Merck has likewise not met its burden in showing that claim 34 is obvious." Prelim. Resp. 52. Patent Owner asserts

> MMWR 2012 discloses that an immunocompromised patient should be administered both Prevnar13® and Merck's 23-valent free polysaccharide pneumococcal vaccine, Pneumovax 23®.

> EX1012 at 12. As discussed above, Prevnar13® does not include a serotype 22F glycoconjugate. *See supra* at II.A. MMWR 2012 also does not refer to the molecular weight or polysaccharide to protein ratio for any of the glycoconjugates present in Prevnar13®.

Prelim. Resp. 52.

We find Petitioner has the better position. Claim 34 depends from claim 30 which depends from claim 1. Patent Owner does not argue that claim 34 is independently patentable. As discussed above, on this record, Petitioner has established a reasonable likelihood that claim 1 would have been obvious over Merck 2011 and GSK 2008, and MMWR suggests administration of multivalent pneumococcal conjugate vaccines to immunocompromised patients. Pet. 62, Ex. 1012, 479.

At this stage of the proceeding, having considered the evidence and arguments of record, we determine that Petitioner has sufficiently shown a reasonable likelihood that it would prevail in demonstrating claim 34 as obvious over Merck 2011, GSK 2008, and MMWR 2012.

III. CONCLUSION

After reviewing the information presented in the Petition and the Preliminary Response, as well as the evidence of record thus far, we determine that Petitioner has established a reasonable likelihood that it will prevail in showing that claims 11–15 and 20–37 of the ’559 patent are unpatentable.

IV. ORDER

Accordingly, it is

ORDERED that Pursuant to 35 U.S.C. § 314(a), an *inter partes* review is hereby instituted on the following grounds;

Reference	Basis	Claims Challenged
Merck 2011, GSK 2008	§ 103(a)	11–14, 23–33, 35–37
Merck 2011, GSK 2008, '787 Patent	§ 103(a)	15
Merck 2011, GSK 2008, Obaro 2002	§ 103(a)	20, 21
Merck 2011, GSK 2008, Sigurdardottir 2008	§ 103(a)	22
Merck 2011, GSK 2008, MMWR 2012	§ 103(a)	34

FURTHER ORDERED that pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial; the trial will commence on the entry date of this Decision.

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PETITIONER:
Arlene L. Chow
arlene.chow@hoganlovells.com

Ernest Yakob
ernest.yakob@hoganlovells.com
HOGAN LOVELLS US LLP

PATENT OWNER:

John Scheibeler
jscheibeler@whitecase.com

Dimitrios T. Drivas
ddrivas@whitecase.com

Anita Varma
anita.varma@whitecase.com
WHITE & CASE LLP