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Paper No. 9
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME CORP.,

Petitioner

v.

WYETH LLC.,

Patent Owner

Case IPR2017-01194
Patent 8,895,024 B2

Before TONI R. SCHEINER, GRACE K. OBERMANN, and ULRIKE W. JENKS, Administrative Patent Judges.

OBERMANN, *Administrative Patent Judge.*

DECISION

Denying Institution of *Inter Partes* Review
35 U.S.C. § 314; 37 C.F.R. § 42.108

I. INTRODUCTION

Petitioner filed a Petition for *inter partes* review of claims 1–11 of U.S. Patent No. 8,895,024 B2 (Ex. 1001, "the '024 patent"). Paper 1 ("Pet."). Patent Owner filed a timely Preliminary Response. Paper 8 ("Prelim. Resp."). Based on the information presented in the Petition and the Preliminary Response, we hold that Petitioner has not demonstrated that it is reasonably likely to prevail at trial in showing that at least one challenged claim of the '024 patent is unpatentable.

Accordingly, we deny the Petition.

A. Related Proceedings

Petitioner identifies as related matters two Petitions that it filed for post grant review of U.S. Patent No. 9,399,060 ("the '060 patent"). Pet. 7 (citing Cases PGR2017-00016 and PGR2017-00017). The claims in the '060 patent are directed to formulations containing polysaccharide-protein conjugates. Concurrently herewith, we issue a consolidated decision in those proceedings.

Petitioner also identifies as related matters three prior Petitions for *inter partes* review of U.S. Patent No. 8,562,999 ("the '999 patent"). *Id*. at 7 (citing Cases IPR2017-00378, IPR2017-00380, and IPR2017-00390). The claims in the '999 patent are directed to formulations containing polysaccharide-protein conjugates. The Board instituted trial in those three proceedings on June 13, 2017.

Petitioner states that it "is unaware of any other judicial or administrative matter that would affect, or be affected by, a decision in this proceeding." Pet. 7. However, Petitioner filed three requests for *inter*

partes review of the ’060 patent. *See* Cases IPR2017-01211, IPR2017-01215, IPR2017-01223. Concurrently herewith, we issue decisions in those three related proceedings.

The ’024 Patent (Ex. 1001)

The ’024 patent issued from Application No. 12/357,853 (“the ’853 application”), filed on January 22, 2009. The ’853 application is a continuation of Application No. 11/395,593, filed March 31, 2006, now abandoned; which claims the benefit of the filing date of U.S. Provisional Patent Application No. 60/669,605 (“the ’605 application”), filed April 8, 2005. That history is important because the ground based on anticipation by Hausdorff 2006 turns on whether Petitioner establishes that claims 1–5 have an effective filing date that post-dates the applied reference. Pet. 39–49. We refer to the ’853 application and the ’605 application collectively in this decision as “the parent applications.”

The ’024 patent, entitled “Multivalent Pneumococcal Polysaccharide-Protein Conjugate Composition,” relates to an immunogenic composition comprising polysaccharide-protein conjugates containing capsular polysaccharides prepared from different *Streptococcus pneumoniae* serotypes. Ex. 1001, Abstract. The different serotypes represented in the immunogenic composition include serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F. *Id*. We adopt the parties’ convention and refer to the 13-valent pneumococcal conjugate as the “13vPnC” vaccine. *See, e.g.*, Pet. 1; Prelim. Resp. 10.

The polysaccharides are obtained from *S. pneumoniae* cell cultures that are harvested and then lysed to release cell-associated polysaccharides into the culture medium. *Id*. at 11:29–12:14. The polysaccharide containing lysate is clarified by continuous flow centrifugation followed by microfiltration. *Id*. at 12:28–30. The purification of the pneumococcal polysaccharide consists of several steps including: concentration/diafiltration operations, precipitation/elution, column chromatography, and depth filtration. *Id*. at 12:34–38. These steps are repeated for each individual serotype.

The ’024 patent explains that the purified polysaccharides are chemically activated with sodium periodate so that they are able to chemically interact with the carrier protein in order to form a glycoconjugate. *Id*. at 8:3–5. The ’024 patent explains that “different serotype saccharides follow different pathways for activation (hydrolysis or no hydrolysis prior to [sodium periodate] activation) and conjugation (aqueous or DMSO[1] reactions).” *Id*. at 24:9–12. For example, the ’024 patent explains that for the serotype 1 polysaccharide the chemical activation involves treating the purified polysaccharide with sodium carbonate to achieve partial deacetylation, followed by neutralization, and finally oxidation in the presence of sodium periodate. *Id*. at 13:53–60. For the serotype 3 polysaccharide the chemical activation process involves treating the purified polysaccharide with acetic acid to hydrolyze the polysaccharide, followed by adding sufficient magnesium chloride to achieve a final concentration of 0.1M, before proceeding to the oxidation step in the

[1] “DMSO” is dimethylsulfoxide. Ex. 1001, 19:15.

presence of sodium periodate. *Id*. at 16:40–48. The serotype 19A polysaccharide activation process involves adding sodium acetate before reaching the oxidation step with sodium periodate. *Id*. at 21:19–22.

The ’024 patent explains that the conjugation step involves lyophilizing the activated polysaccharide and then mixing in the lyophilized carrier CRM_{197} protein[2] and reconstituting the dried components before adding the crosslinking agent. *Id*. at 14:10–15. The lyophilized polysaccharide and lyophilized CRM_{197} protein are reconstituted in either DMSO or in an aqueous buffer before proceeding to the conjugation reaction with sodium cyanoborohydride to obtain the polysaccharide-protein conjugate. *Id*. at 25:1–52, 26:33–58; *see* 16:59–67 (Example 4: Preparation of Serotype 3 Pneumococcal Saccharide CRM_{197} Conjugate).

The ’024 patent specification explains that the final immunogenic composition is formulated by combining the individual polysaccharide-CRM_{197} protein conjugates. The formulation contains 2–2.2 µg of each saccharide, except for 6B at 4–4.4 µg, approximately 29 µg CRM_{197} carrier protein; 0.125 mg of elemental aluminum (0.5 mg aluminum phosphate) adjuvant, as well as sodium chloride and sodium succinate buffer as excipient. *Id*. at 3:6–10, 29:64–30:41.

[2] CRM_{197} (Wyeth, Sanford, N.C.) is a non-toxic variant (i.e., toxoid) of diphtheria toxin isolated from cultures of *Corynebacterium diphtheria* strain C7 (β197) grown in casamino acids and yeast extract-based medium. Ex. 1001, 8:21–24.

Illustrative Claim

Claim 1 is illustrative and is reproduced below:

> 1. A multivalent immunogenic composition comprising 13 distinct polysaccharide-protein conjugates and a physiologically acceptable vehicle, wherein each of the conjugates comprises a capsular polysaccharide from a different serotype of *Streptococcus pneumoniae* conjugated to a carrier protein, wherein the serotypes consist essentially of 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, and wherein the carrier protein is CRM_{197}.

Evidence Relied Upon

The Petition asserts the following references as prior art:

1. Hausdorff et al., U.S. Pat. Pub. 2006/0228380 A1 (Oct. 12, 2006) ("Hausdorff 2006") (Ex. 1018);[3]

2. Huebner et al., *Long-term antibody levels and booster responses in South African children immunized with nonavalent pneumococcal conjugate vaccine*, 22 Vaccine 2696–2700 (2004) ("Huebner 2004") (Ex. 1016);

3. Hausdorff et al., Multinational study of pneumococcal serotypes causing acute otitis media in children, 21 PEDIATR. INFECT. DIS. J. 1008–1016 (2002) ("Hausdorff 2002") (Ex. 1017);

4. Prevnar® entry from the 2001 (55th Edition) Physicians' Desk Reference ("Prevnar 2001") (Ex. 1011).

The Petition is supported by a declaration of Dennis L. Kasper, M.D. Ex. 1009. Based on Dr. Kasper's statement of qualifications and curriculum vitae, for the purposes of this decision, we hold that he is qualified to opine from the perspective of a person of ordinary skill at the time of the

[3] The parties refer to Hausdorff 2006 as "the '380 Publication." Pet. vii; Prelim. Resp. 20. We select a convention on par with the other asserted prior art references.

invention. *See* Ex. 1009 ¶¶ 4–12 (Dr. Kasper's statement of qualifications); *see also* Ex. 1009, Exhibit A (Dr. Kasper's curriculum vitae).

The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–11 of the '024 patent on the following grounds (Pet. 8):

Claims Challenged	**Basis**	**References**
1–5	§ 102(b)	Hausdorff 2006
1, 6, 11	§ 103(a)	Huebner 2004 and Hausdorff 2002
2–5, 7–10	§ 103(a)	Huebner 2004, Hausdorff 2002, and Prevnar 2001

II. ANALYSIS

In an *inter partes* review, the Board interprets claim terms in an unexpired patent according to the broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *In re Cuozzo Speed Techs., LLC*, 136 S. Ct. 2131, 2142 (2016). Under that standard, and absent any special definitions, we give claim terms their ordinary and customary meaning, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Broadest Reasonable Interpretation of "Immunogenic"

Each party proposes a specific construction for the term "immunogenic." Petitioner asserts that the term, which appears in the preamble of every claim, is limiting. Pet. 33–34[4] ("The fact that the preamble of every claim recites an 'immunogenic' composition underscores the intended limiting nature of the term"). "Patent Owner agrees with Petitioner that the term is a limitation notwithstanding that it appears in the preamble of the claim." Prelim. Resp. 7. We accept the uncontested proposition that "immunogenic" limits each challenged claim, because the proposition is consistent with the disclosure and prosecution history of the '024 patent. Pet. 33–34 (citing Ex. 1009 ¶¶ 102–110).

Petitioner proposes that the broadest reasonable interpretation of "immunogenic" is a composition "that 'elicits immunologic memory and/or functional antibody with respect to each serotype of the vaccine, including serotype 3.'" Pet. 37 (citing Ex. 1009 ¶ 112). Petitioner argues that Patent Owner "emphasized immunogenicity in the specification, and relied on it during prosecution history to gain allowance of the claims over a prior art vaccine." Pet. 33 (citing Ex. 1009 ¶¶ 103); *see id*. at 34 (citing Ex. 1001, 4:21–42; Ex. 1004, 147–148, 200, 201, 465–466) (disclosures in the '024 patent and its prosecution history).

[4] Except for citations to the Petition or Preliminary Response (which refer to the original page number), patents and patent publications (which refer to the originally published column and line numbers or paragraph number), and citations to the declaration of Dr. Kasper (which refers to paragraph numbers), this Decision cites to the page numbers added by Petitioner or Patent Owner at the bottom of each Exhibit.

Patent Owner counter argues that "immunogenic" means "eliciting 'higher serum IgG titers **and** overall greater functional antibody activity than seen with free polysaccharide alone or mixed with unconjugated CRM_{197}.'" Prelim. Resp. 7 (emphasis added) (citing Ex. 1001, 30:63–67). Patent Owner further contends that Petitioner "does not identify anything in the specification or prosecution history that supports [inserting] the '**and/or**' aspect" into the requirements of the immunogenic composition. *Id*. at 16 (emphasis added).

Patent Owner explains that "[n]either the specification nor the prosecution history supports including 'immunologic memory' within the definition of immunogenic. . . . While in some contexts a definition of immunogenicity can include memory, adding a test for memory that is not described or contemplated in the '024 patent is not reasonable." Prelim. Resp. 8–9. Instead, Patent Owner submits that "immunogenic" as recited in the claims "is based on two tests: antigen specific ELISA[5] for measuring serum IgG concentration and opsonophagocytic assay (OPA) for antibody function." *Id*. at 8 (citing Ex. 1001, 28:14–17, 30:43–47).

Patent Owner further explains that "[t]he OPA [response] is an important measure of functional immune response as opsonic activity has been shown to correlate with protection." Prelim. Resp. 10 (citing

[5] ELISA (acronym): (Biochemistry) enzyme-linked immunosorbent assay: an immunological technique for accurately measuring the amount of a substance, for example in a blood sample. The Free Dictionary, http://www.thefreedictionary.com/ELISA (last visited Oct. 8, 2017).

Ex. 2012,[6] 2; Ex. 2009,[7] 3; Ex. 2018,[8] 101). We are persuaded that measuring an OPA response is supported by the '024 specification, which compares "rabbit immune response to the polysaccharides contained in the vaccine, after immunization with the thirteen polysaccharide serotypes with or without conjugation to the carrier protein CRM_{197}." *Id*. at 11 (citing Ex. 1001, 29:64–30:36); *see* Ex. 1001, 30:36–39, 30:44–67, Tables 5 and 6 (relevant disclosures); Prelim. Resp. 11–12 (discussing import of those disclosures).

In an attempt to show that the applicants, during patent prosecution, invoked immunologic memory as a criterion for demonstrating immunogenicity, Petitioner directs us to a passage in Yeh 2010 (Ex. 1064[9]) but fails to show sufficiently that the passage was cited during prosecution. Pet. 36 (citing Ex. 1064, 1); Prelim. Resp. 13–14. Patent Owner, by contrast, identifies persuasive evidence that the applicants, during patent prosecution, expressly used the term "immunogenic" to describe the property of eliciting "higher serum IgG titers and overall greater functional antibody activity than seen with free polysaccharide alone or mixed with unconjugated CRM_{197}." Prelim. Resp. 14 (quoting Ex. 1005, 145). Based

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[6] J. Eskola, *Polysaccharide-based pneumococcal vaccines in the prevention of acute otitis media*, 19 VACCINE S78–S83 (2001).
[7] L. Jodar et al., *Serological criteria for evaluation and licensure of new pneumococcal conjugate vaccine formulations for use in infants*, 21 VACCINE 3265–3272 (2003).
[8] *WHO Expert Committee on Biological Standardization*, WHO, Geneva 2005.
[9] Yeh et al., *Immunogenicity and Safety of 13-Valent Pneumococcal Conjugate Vaccine in Infants and Toddlers*, 126 PEDIATRICS e493–e505 (2010).

on the information presented in the Petition and the Preliminary Response, we find that Petitioner directs us to no persuasive evidence that the applicants, during patent prosecution, equated "immunogenic" with the property of eliciting immunogenic memory alone. Pet. 33–37; Prelim Resp. 6–16 (and citations to the record therein).

On this record, Patent Owner's proposed interpretation of "immunogenic" is the broadest reasonable construction consistent with the specification of the '024 patent and its prosecution history. Based on the record before us, therefore, we accept Patent Owner's construction that "immunogenic," in the context of the challenged claims, means "eliciting 'higher serum IgG titers and overall greater functional antibody activity than seen with free polysaccharide alone or mixed with unconjugated CRM_{197}.'" Prelim. Resp. 7. No other claim terms require express construction for the purposes of this decision.

Claims 1–5 as Anticipated by Hausdorff 2006

Petitioner challenges claims 1–5 of the '024 patent as anticipated by Hausdorff 2006 (Ex. 1018). Pet. 49. We expressly decline to reach the merits of whether the disclosure of Hausdorff 2006 anticipates the invention of claims 1–5, because Petitioner fails to establish adequately that the applied reference qualifies as prior art.

The central dispute surrounds the effective filing date of claims 1–5, and whether it precedes the October 12, 2006, publication date of Hausdorff 2006. Petitioner asserts that the effective filing date is January 22, 2009—the actual filing date of the '853 application. *Id*. at 39–49. Patent Owner counters that claims 1–5 are entitled to claim priority through the parent

applications, which were filed as early as April 8, 2005. Prelim. Resp. 20–21 (citing Ex. 1001, 1:5–12 (claiming priority based on earlier filing dates of the parent applications)). For reasons that follow, we are not persuaded that Petitioner is reasonably likely to prevail at trial in showing that the effective filing date of claims 1–5 falls after the filing date of Hausdorff 2006. Given that circumstance, Petitioner cannot show sufficiently that Hausdorff 2006 qualifies as prior art with regard to the invention of claims 1–5. We deny the Petition as to the anticipation ground on that basis alone.

In Petitioner's view, the disclosures of the parent applications fail to enable claims 1–5; therefore, according to Petitioner, claims 1–5 are not entitled to claim priority through those applications. Pet. 39–49. That position, however, rests on a faulty assertion that claim 1 "is open-ended with respect to the number and identity of serotypes added to 13vPnC." Pet. 40 (heading). Petitioner ignores express language in claim 1, which also is incorporated into claims 4–5 that are dependent from claim 1, specifying serotypes "consisting essentially of 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F." Ex. 1001, claim 1. The Petition is deficient for failure to adequately analyze enablement in view of the "consisting essentially of" phrase. *Id*.

That failure of analysis persuades us to deny the Petition as to the ground based on anticipation by Hausdorff 2006. *See* Prelim. Resp. 21–22; *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998) ("Consist essentially of" is a phrase which "signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention."). Petitioner posits that claim 1 covers "1.7×10^{12} possible

combinations of serotypes" and, for that reason, is not enabled by the parent applications. Pet. 40. But "[c]onsist essentially of" is a phrase that "signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention." Prelim. Resp. 22 (quoting *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1354 (Fed. Cir. 1998)). Critically lacking in the Petition is analysis sufficient to show that the inclusion of any additional serotype would not materially affect the basic and novel characteristics of the claimed invention. Pet. 40–49. We agree with Patent Owner that the Petition incorrectly analyzes enablement as if the "consisting essentially of" term had been rewritten as "comprising." *Id*. at 21–22.

On this record, the evidence supports Patent Owner's contention that, at least with respect to the '593 application filed on March 31, 2006, Examples 1–16 provide adequate guidance enabling "the generation and characterization of a representative multivalent composition of the granted claims (and the specific 13-valent composition encompassed by claims 1–5)." *Id*. at 21; Ex. 1001[10], 11:25–28:67 (Examples 1–16). For reasons stated by Patent Owner, the Petition is deficient for failure "to show the effects of adding any unlisted serotype to 13vPnC." Prelim. Resp. 24.

We agree with Patent Owner, moreover, that the Petition is deficient for a second independent reason. The Petition fails "to address enablement

[10] For the purposes of this decision, we accept Petitioner's statement that the '593 application shares the same disclosure as the '024 patent, and that the '605 application shares a subset of that same disclosure. Pet. 2. For ease of reference, we cite to the '024 patent disclosure when assessing whether the disclosure of the '593 application enables claims 1–5.

and the level of skill in the art at the particular filing date of each" of the parent applications—and, in particular, neglects to assess the state of the art as of the March 31, 2006, filing date of the '593 application. *Id*. at 25–26. Even Petitioner acknowledges that the level of ordinary skill in this particular field of endeavor, including one's understanding of "the universe of clinically relevant serotypes," would not "remain static" during the relevant span of time. Pet. 45 (quoting Ex. 1009 ¶ 129). Yet the Petition does not clearly articulate the level of ordinary skill in the art applicable at the time of filing for each parent application. Instead, Petitioner focuses on the state of the art as of the earliest possible priority date of "April 8, 2005." Pet. 9 (heading "A"). The fact that Petitioner does not appropriately account for changes in the level of ordinary skill in the art, as of March 31, 2006, bolsters our holding that the Petition is deficient for failure to show sufficiently that Hausdorff 2006 qualifies as prior art—because no adequate showing is made that the '024 patent is not entitled to claim priority based on the March 31, 2006 filing date of the '593 application.

Accordingly, on this record, Petitioner has not shown a reasonable likelihood of prevailing at trial in showing that Hausdorff 2006 anticipates claims 1–5.

Claim 1, 6, and 11 as Obvious
Over Huebner 2004 and Hausdorff 2002

Petitioner also challenges claims 1, 6, and 11 as obvious over Huebner 2004 and Hausdorff 2002. Pet. 52–60. Patent Owner opposes the challenge. Prelim. Resp. 30–43. For reasons that follow, we agree with Patent Owner that the Petition is deficient because it analyzes obviousness in the context of

an overly broad construction of the term "immunogenic," which, as explained above, is a limitation of each challenged claim.

Huebner 2004

Huebner 2004 is a journal article reviewing response levels to a 9-valent pneumococcal conjugate vaccine containing serotypes 1, 4, 5, 6B, 9V, 14, 18C, 19F, and 23F. Ex. 1016, Abstract. The polysaccharides included in this 9-valent vaccine were conjugated to CRM_{197}-diptheria protein. *Id*. at 1. Huebner 2004 teaches that the majority of the vaccinated children had antibody levels of >0.15 μg/ml. *Id*. at 2. The study population included infants at 6, 10, and 14 weeks of age. *Id*. Boosting the children at 18 months with a polysaccharide vaccine resulted in a quick antibody response. *Id*. at 3.

Hausdorff 2002

Hausdorff 2002 is a journal article that is a retrospective study analyzing nine datasets collected between 1994 and 2000. Ex.1017, Abstract. The datasets relied on in the analysis are all listed in Table 1 of the article. *See* Ex.1017, 3. Figure 2, not shown here, is a graphic representation of pneumococcal serotypes circulating in the population and shows that the circulating serotypes vary from country to country. *Id*. at 6. The figure depicts the percentage of pneumococcal serotypes isolated from middle ear fluid that would be targeted the by the various vaccines formulations available at the date the article was published. *Id*. In other words, the figure shows the theoretical contributions PCV-9 and PCV-11 pneumococcal conjugate vaccines would have on preventing disease in each country. Figure 2 also shows that there are changes in pneumococcal

serotypes isolated from middle ear fluid based on the patient age group. *Id*. In the article, PCV-9 is an abbreviation for PCV-7 plus serotypes 1 and 5; PCV-11 is an abbreviation for PCV-9 plus serotype 3 and 7F. *Id*. at 2. The 7-valent pneumococcal conjugate vaccine (PCV-7) includes serotypes 4, 6B, 9V, 14, 18C, 19F, 23F). *Id*. The article indicates that the PCV-11 vaccines were in clinical trials at the time of the Hausdorff 2002 publication. *Id*. at 6.

Analysis

Petitioner asserts that the "9-valent pneumococcal CRM_{197}-conjugate vaccine [of Huebner 2004] . . . adds serotypes 1 and 5 to the 7 serotypes (4, 6B, 9V, 14, 18C, 19F and 23F) of Prevnar®, and demonstrates that the vaccine is immunogenic, as it elicits immunologic memory." Pet. 53 (citing Ex. 1009 ¶ 168). Petitioner further quotes Hausdorff 2002 for the observation "that '[i]t appears that the serotypes represented in PCV-11 [(representing serotypes 1, 3, 4, 5, 6B, 7F 9V, 14, 18C, 19F, 23F)], plus 6A and 19A, comprise all major serotypes in each age group studied.'" *Id*. at 54. Petitioner concludes that a person of ordinary skill in the art would have been led, with a reasonable expectation of success, to expand the 9-valent vaccine of Huebner 2004, given the disclosure in Hausdorff 2002 of an 11-valent conjugate vaccine suggesting the addition of serotypes 3 and 7F. *Id*. at 54 (citing Ex. 1009 ¶ 170). Petitioner further argues that, in view of Hausdorff 2002, a person of ordinary skill in the art would have been led to further add serotypes 6A and 19A, resulting in the immunogenic conjugate consisting essentially of the 13 serotypes specified in claim 1. *Id*. at 54–55 (citing Ex. 1009 ¶ 171).

Patent Owner counters that Huebner 2004 does not disclose an "immunogenic" conjugate as required by the challenged claims. Prelim.

Resp. 31. We agree with Patent Owner that "Huebner 2004 provides no data at all concerning functional antibody activity and certainly no data from an OPA" response. *Id.*; *see generally* Ex. 1016 (Huebner 2004). Patent Owner further argues, and we find persuasive on this record, that Hausdorff 2002 does not indicate that its conjugate is "immunogenic" as required by the challenged claims. In other words, the applied references do not disclose data that would have suggested a conjugate eliciting IgG as shown by ELISA and functional antibody as measured, for example, by an OPA response. *See generally* Ex. 1016 (Huebner 2004); *see also* Prelim. Resp. 32 ("Hausdorff 2002 does not point to any data showing that an 11-valent vaccine had in fact demonstrated immunogenicity" in terms of showing functional antibody); *see generally* Ex. 1017 (Hausdorff 2002).

Patent Owner also argues that the vaccines used in Hausdorff 2002 are not CRM_{197} conjugates as intimated by Petitioner. Prelim. Resp. 32. We agree. Patent Owner directs us to persuasive evidence that Hausdorff 2002 neither teaches nor suggests a vaccine that "used CRM_{197} as the carrier protein." *Id*. Specifically,

> Eskola 2001, the publication Hausdorff 2002 cites for support that the 11-valent conjugate is in "clinical trials" (*see* EX1017 at 6, reference "19"), mentions two 11-valent conjugates (neither of which used CRM_{197} as required by the claims): (1) an 11-valent mixed carrier (diphtheria toxoid/tetanus toxoid ("DT/TT")) conjugate by Aventis Pasteur; and (2) an 11-valent Hi Protein conjugate by SB Bio.

Id. In other words, the serotypes in Hausdorff 2002's vaccine were conjugated to a DT/TT mixed carrier, which is described in the '024 patent and prosecution history as being unsuccessful with respect to serotype 3. *Id*. at 32–33 (citing Ex. 1001, 4:18–42; Ex. 1002, 180–181).

We agree with Patent Owner, therefore, that "Hausdorff 2002 does not point to any data showing that an 11-valent vaccine had in fact demonstrated immunogenicity." *Id*. Nor does the combination of Hausdorff 2002 with Huebner 2004 teach or suggest a vaccine eliciting "immunogenicity" as required by the claims. *Id*. In that regard, for reasons stated by Patent Owner, we are persuaded that the Petition rests on background references that do not disclose or suggest a pneumococcal CRM_{197} conjugate vaccine at all, much less provide data establishing the immunogenicity of such a vaccine. Prelim. Resp. 33–34 (discussing Pet. 57–58 (citing Ex. 1013 (Overturf 2002), Ex. 1040 (O'Brien 2004))).

We agree with Patent Owner that neither reference asserted in this ground of the Petition "provides any data whatsoever establishing immunogenicity or confirming even the existence of the allegedly developed 11-valent pneumococcal CRM_{197}-conjugate vaccine." *Id*. at 33. For reasons explained above, we adopt Patent Owner's construction of the "immunogenic" composition of the invention as one that must produce an immune response that elicits *both* an IgG response as measured by ELISA and a functional antibody response as measured, for example, by an OPA response to the immunogen. We are not persuaded that Petitioner, in view of that construction, shows sufficiently that one of ordinary skill in the art would have had a reason to include serotype 3 in a multivalent CRM_{197}-conjugated vaccine, or would have had a reasonable expectation of success of accomplishing that task using CRM_{197} as the carrier protein. Pet. 54–55 (citing Ex. 1009 ¶¶ 170–171), 57 (citing Ex. 1009 ¶ 175)).

None of the arguments or evidence advanced in the Petition overcomes Patent Owner's supported proposition that "Huebner 2004

provides no data at all concerning functional antibody activity and certainly no data from an OPA" response. Prelim. Resp. 31. On that point, Patent Owner directs us to evidence that "[t]he 11-valent Hi Protein conjugate in Eskola 2001 is the 'protein D' conjugate described in the '024 patent and prosecution history as being unsuccessful with respect to serotype 3." Prelim Resp. 33 (citing Ex. 1001, 4:18–42; Ex. 1002, 180–181). That evidence sufficiently rebuts Petitioner's unsubstantiated position that, at the time of the invention, there was a reasonable expectation of success in producing a CRM_{197}-conjugated serotype 3 vaccine that elicits both an IgG immune response and an OPA response.

On this record, we hold that Petitioner has not established a reasonable likelihood it would prevail in showing that claims 1, 6, and 11 of the '024 patent are unpatentable under 35 U.S.C. § 103(a) as obvious over the combined disclosures of Huebner 2004 and Hausdorff 2002. Prelim. Resp. 30–43. Accordingly, we deny the Petition as it pertains to that ground.

Claims 2–5 and 7–10 as Obvious Over Huebner 2004, Hausdorff 2002, and Prevnar 2001

This ground of invalidity depends on the same arguments and evidence as the obviousness ground discussed above. Specifically, Petitioner argues that Huebner 2004 and Hausdorff 2002 would have led a person of ordinary skill in the art, with a reasonable expectation of success, to formulate a pneumococcal CRM_{197}-conjugate vaccine including serotype 3. Pet. 60. Our above analysis applies equally to this ground. Accordingly, for the reasons discussed above, we hold that Petitioner has not shown a reasonable likelihood of prevailing at trial in showing that claims 2–5 and 7–10 are unpatentable on this ground.

III. CONCLUSION

For the foregoing reasons, we are not persuaded that the Petition establishes a reasonable likelihood that Petitioner would prevail in showing that any claim of U.S. Patent 8,895,024 B2 is unpatentable.

IV. ORDER

It is

ORDERED that the Petition is *denied* and no trial is instituted.

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