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Paper 10
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SANOFI PASTEUR INC. AND SK CHEMICALS CO., LTD.,
Petitioner,

v.

PFIZER INC.,
Patent Owner.

Case IPR2018-00188
Patent 9,492,559 B2

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

FREDMAN, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
35 U.S.C. § 314(a)

I. INTRODUCTION

A. Background

Sanofi Pasteur Inc. and SK Chemicals Co., Ltd. ("Petitioner") filed a Petition (Paper 3, "Pet.") requesting an *inter partes* review of claims 1–45 (the "challenged claims") of U.S. Patent No. 9,492,559 B2 (Ex. 1001, "the '559 patent") that claims benefit of priority to U.S. Provisional 61/929,547 (Ex. 1002, "the '547 provisional"). *See* 35 U.S.C. §§ 311–319. Pfizer Inc. ("Patent Owner") filed a Preliminary Response. Paper 8 ("Prelim. Resp."). The Board, acting on behalf of the Director, has jurisdiction under 35 U.S.C. § 314.

For the reasons that follow, the Board determines that the prior art relied upon by Petitioner is excluded because the '559 patent receives benefit of priority to the '547 provisional and, further, that the cited references do not qualify as prior art under AIA 35 U.S.C. § 102(a)(2). Therefore, the Board declines to institute an *inter partes* review.

B. Related Proceedings

Petitioner indicates that a concurrent Petition for *inter partes* review of the '559 patent was filed (IPR2018-00187) and that several IPRs were filed by a different petitioner (IPR2017-02131, IPR2017-02132, IPR2017-02136, IPR2017-02138). Pet. 2.

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 available on the global market: PREVNAR® (called PREVENAR® in some countries) (heptavalent[3] vaccine), SYNFLORIX® (a decavalent vaccine) and PREVNAR 13® (tridecavalent vaccine)." *Id*. at 1:61–65.

The '559 patent teaches "there is a need to address remaining unmet medical need for coverage of pneumococcal disease due to serotypes not found in PREVNAR 13® and potential for serotype replacement over time." *Id*. at 2:3–6.

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[1] A "coccus" is defined as "a spherical bacterium." *See Coccus Definition*, Merriam-Webster.com, https://www.merriam-webster.com/dictionary/coccus (last visited May 21, 2017).

[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).

D. Illustrative Claims

Claim 1, the sole independent claim of the '559 patent, is illustrative of the challenged claims and recites:

> 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. pneumoniae* 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.

Ex. 1001, 141:28–34. Each of the remaining claims 2–45 depends directly or indirectly from claim 1.

E. The Asserted Grounds of Unpatentability

Petitioner contends that the challenged claims are unpatentable based on the following grounds. Pet. 4, 15, 17.

Reference	Basis	Claims Challenged
Pfizer-302[4]	§ 102(a)	1–18, 20, 22–27, 29–32, 35–45
Pfizer-302, GSK-711,[5] Merck-086,[6] GSK-531[7]	§ 103	3–9, 19, 21, 28, 33, 34

[4] Gu et al., WO 2014/027302 A1, published Feb. 20, 2014 ("Pfizer-302," Ex. 1009).
[5] Biemans et al., WO 2007/071711 A2, published June 28, 2007 ("GSK-711," Ex. 1007).
[6] Caulfield et al., US 2011/0195086 A1, published Aug. 11, 2011 ("Merck-086," Ex. 1008).
[7] Biemans et al., WO 2011/110531 A2, published Sept. 15, 2011 ("GSK-531," Ex. 1014).

Pfizer-099[8]	§ 102(a)	1, 3–14, 16–18, 20–32, 35–37, 39, 41, 42, 45
Pfizer-099, GSK-711, Merck-086, GSK-531, Lees-2008,[9] PVP 2013,[10] Pfizer-605,[11] Hsieh 2000[12]	§ 103	2, 3–9, 15, 19, 33, 34, 38, 40, 43, 44

Petitioner relies on the Declaration of Andrew Lees, Ph.D. Ex. 1006.

I. ANALYSIS

A. Priority and AIA 35 U.S.C. § 102(a)(1)

Petitioner asserts the '559 patent is not entitled to the priority date of its provisional application, US 61/929,547, because the provisional does not describe a polysaccharide to carrier protein ratio range "between 0.4 and 2," fails to describe sufficient species to support the molecular weight range between 1000 and 12,500 kDa, and only exemplifies a single CRM_{197} carrier protein that "cannot represent the entire genus of any carrier proteins." Pet. 15, 21, 23, 24, 26. Petitioner therefore asserts that Pfizer-099 and Pfizer-302

[8] Han et al., WO 2014/097099 A2, published June 26, 2014 ("Pfizer-099," Ex. 1010).
[9] Lees et al., "Chapter 11. Conjugation Chemistry," In: Pneumococcal Vaccines: The Impact of Conjugate Vaccine (Ed. George R. Siber et al.); pp. 163–174 (2008) ("Lees-2008," Ex. 1011).
[10] "Pneumococcal Vaccine Polyvalent" revision to Japan's "Minimum Requirements for Biological Products" published on the website of Japan's National Institute of Infectious Diseases (as of March 2, 2013) ("PVP 2013," Ex. 1012).
[11] Prasad, A.K., US 7,955,605 B2, issued June 7, 2011 ("Pfizer-605," Ex. 1013).
[12] Hsieh, *Characterization of Saccharide-CRM_{197} Conjugate Vaccines*, In: *Physico-Chemical Procedures for the Characterization of Vaccines* (Eds. Brown F., Corbel M., and Griffths E.); Vol. 103, pp. 93–104; Basel; Karger, 2000 ("Hsieh 2000," Ex. 1015).

are prior art to the '559 patent under AIA 35 U.S.C. § 102(a)(1) or 35 U.S.C. § 102(a)(2). Pet. 15, 17.

Patent Owner asserts the "'559 patent is entitled to its priority date." Prelim. Resp. 16. Patent Owner relies on *Wertheim* for the proposition that "a claimed range may be supported by the combination of a generic range and specific embodiments disclosed in a patent application." Prelim. Resp. 29 (*citing In re Wertheim*, 541 F.2d 257, 265 (CCPA 1976)). Patent Owner asserts both the '547 provisional and the '559 patent show a Table 16 with glycoconjugate batches with polysaccharide to protein ratios of 0.4 and 2, providing descriptive support for the claimed range of a "polysaccharide to the carrier protein [that] is between 0.4 and 2." Prelim. Resp. 29–30, 33–34. Patent Owner notes Table 16 shows "numerous ratios falling within the claimed range (0.75, 0.87, 0.8, 0.8, 1.9, 0.8, 0.65 and 1.0)." Prelim. Resp. 33−34 (citing Ex. 1002, 16).

Patent Owner asserts, regarding the molecular weight range of 1000 kDa to 12,500 kDa in claim 1 of the '559 patent, that the "'547 application teaches the generation and characterization of sufficient representative species encompassed by the '559 patent claims." Prelim. Resp. 35–36. Patent Owner asserts, regarding the breadth of carrier proteins encompassed by claim 1 of the '559 patent, that "the '547 application discloses a number of possible specific carrier proteins" and that "[b]y listing these carrier proteins, the '547 application adequately describes numerous carrier proteins, not just one as contested by Sanofi, for potential inclusion in the claimed compositions." Prelim. Resp. 39.

Benefit of priority depends upon whether there is descriptive support for claim 1 of the '559 patent in the '547 provisional. "A reference patent is only entitled to claim the benefit of the filing date of its provisional application if the disclosure of the provisional application provides support for the claims in the reference patent in compliance with § 112, ¶ 1." *Dynamic Drinkware, LLC v. National Graphics, Inc.*, 800 F.3d 1375, 1381 (Fed. Cir. 2015).

We are persuaded that the '547 provisional supports the immunogenic composition recitation in claim 1 because it teaches the "present invention relates to new immunogenic compositions . . . [that] typically comprise conjugated capsular saccharide antigens . . . derived from serotypes of *S. pneumoniae*." Ex. 1002, 17. We are also persuaded that the '547 provisional supports the serotype 22F molecular weight recitation in claim 1 because it teaches embodiments where "the serotype 22F glycoconjugate has a molecular weight of . . . between 1,000 kDa and 12,500 kDa." Ex. 1002, 38. The '547 provisional also provides ten examples of conjugated serotype 22F molecular weights ranging from 1419 kDa to 10,450 kDa, further demonstrating examples within the claimed range. *See* Ex. 1002, 116.

We are persuaded that the '547 provisional supports the recitation in claim 1 of the '559 patent requiring a "ratio (w/w) of the polysaccharide to the carrier protein [that] is between 0.4 and 2." Ex. 1001, 89. The '547 provisional teaches "the ratio of serotype 22F polysaccharide to carrier protein in the glycoconjugate (w/w) is between 0.5 and 3 (e.g. about 0.5 . . . [)] . . . . In other embodiments, the saccharide to carrier protein ratio (w/w) is between 0.5 and 2." Ex. 1002, 39. In addition to these general range teachings, the '547 provisional provides ten specific examples of

saccharide/protein ratios within the range of 0.4 and 2, including batch 6 with a saccharide/protein ratio of 0.4 and batch 3 with a saccharide/protein ratio of 2. *See* Ex. 1002, 116.

We are not persuaded by Petitioner's argument that the disclosure of a range and the exemplary batches "is not a description for the range of 'between 0.4 and 2.0' in full, clear, concise, and exact terms, even if the ratio of Batch 6 in Table 16 is combined with the range of 'between 0.5 and 2' disclosed in the specification." Pet. 22.

In *Wertheim*, the predecessor to our reviewing court explains that "in light of the description of the invention as employing solids contents within the range of 25-60% along with specific embodiments of 36% and 50%, we are of the opinion that, as a factual matter, persons skilled in the art would consider processes employing a 35-60% solids content range to be part of appellants' invention." *In re Wertheim*, 541 F.2d 257, 265 (CCPA 1976). Similarly, the disclosure in the '547 provisional of both a range for the polysaccharide/protein ratio of between "0.5 and 2" along with a ratio "about 0.5" and specific embodiments of 0.4 and 2 reasonably provide descriptive support for a polysaccharide/protein ratio range between 0.4 and 2 as recited in claim 1 of the '559 patent. *See* Ex. 1002, 39, 116.

The fact pattern in this case is different than the facts in the cases relied upon by Petitioner. *See* Pet. 22. In *Ahlbrecht*, there was "nothing in the original specification to indicate that any other esters (i.e., those where m is 2 or greater than 12) may be made by the methods disclosed." *In re Ahlbrecht*, 435 F.2d 908, 911 (CCPA 1971). In the instant case, both the "about 0.5" language, which suggests the adjacent range value of 0.4, and

the specific exemplification of a polysaccharide/protein ratio of 0.4 demonstrate that this embodiment was described and enabled by the '547 provisional. *See* Ex. 1002, 39, 116. In *Blaser*, there was no description of the value at issue in the Specification of the priority document, unlike the current situation where there is a specific example of a 0.4 ratio of polysaccharide/protein. *See In re Blaser*, 556 F.2d 534, 538 (CCPA 1977); Ex. 1002, 116. Similarly, in *Lukach*, the court explained that a "single example [of an Mw/Mn ratio of 2.6] does not alone provide support for the recited range from 2.0 to 3.0, and nothing has been brought to our attention to show that any other language in the grandparent application, taken together with the knowledge of persons skilled in the art, points to the recited range." *In re Lukach*, 442 F.2d 967, 969 (CCPA 1971). However, in the '547 provisional, in addition to the disclosure of a range for the polysaccharide/protein of between 0.5 and 2, and a disclosure of a value of about 0.5, the '547 provisional has ten examples of 22F polysaccharide/protein ratios that range from 0.4 to 2. *See* Ex. 1002, 39, 116. These disclosures in the '547 provisional reasonably satisfy the written description requirement and provide descriptive support for the range in claim 1 of the '559 patent of a "ratio (w/w) of the polysaccharide to the carrier protein [that] is between 0.4 and 2." Ex. 1001, 89.

We are not persuaded by Petitioner's argument that "out of the whole range span of the claimed genus (from 0.4 to 2, which is 1.6), there is no description of more than half of the claimed range (from 1 to 1.9, which is 56% of the whole genus (i.e., 0.9/1.6))." Pet. 23. Nor are we persuaded by Petitioner's argument that the "vast majority of variations with respect to

this combination are not represented by the examples disclosed in the provisional application." Pet. 25.

"An adequate written description must contain enough information about the actual makeup of the claimed products—'a precise definition, such as by structure, formula, chemical name, physical properties, or other properties, of species falling within the genus sufficient to distinguish the genus from other materials.'" *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1378 (Fed. Cir. 2017) (*citing Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350 (Fed. Cir. 2010) (*en banc*)). Both the '547 provisional and claim 1 of the '559 patent provide a structural formula composed of a ratio between the polysaccharide and the carrier protein, with the '547 provisional expressly disclosing a range between 0.5 and 2, a specific value of about 0.5, and ten examples of serotype 22F polysaccharide/protein ratios including ratios from 0.4 to 2. *See* Ex. 1002, 39, 116. The '547 provisional further provides chemical names and structural information for both the carrier proteins and the serotype 22F polysaccharides. See Ex. 1002, 20–21, 29. Thus, the '547 provisional provides enough information about the actual makeup of the range of serotype 22F glycoconjugates to distinguish the genus from materials not falling within the scope of claim 1 of the '559 patent and providing descriptive support for that claim.

We are not persuaded by Petitioner's argument that:

> The genus of carrier proteins is vast. Lees ¶135. The provisional application itself discloses at least 55 different possible carrier proteins that can be used to conjugate to each individual serotype. Ex. 1002, 20:12–21:2; Lees ¶135. These carrier proteins share no common structural features and are derived from completely different sources. Lees ¶135.

> Therefore, a single example of CRM_{197} cannot represent the entire genus of any carrier proteins. Lees ¶ 135.

Pet. 26.

We are persuaded that the '547 provisional provides support for the genus of carrier proteins because it teaches a large number of different carrier proteins, while recognizing that "[c]arrier proteins should be amenable to standard conjugation procedures." Ex. 1002, 20–21. "[T]he determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter." *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005). The '547 provisional cites literature sources for each of the many different cited carrier proteins, including both patent and non-patent references, demonstrating that selection of carrier proteins was a predictable choice made based on the extensive knowledge in the field of vaccine production. *See* Ex. 1002, 20–21.

Dr. Lees provides no evidentiary support for the position that a "single example of CRM_{197} cannot adequately represent the entire genus of any carrier protein." Ex. 1006 ¶ 135. Indeed, Dr. Lees cites other prior art that demonstrates the predictability of conjugation of pneumococcal saccharides to other carrier proteins specifically "GSK-711 also discloses that the saccharides present in the immunogenic composition (such as 22F) may be conjugated to a carrier protein independently selected from CRM197, diphtheria toxoid (DT), tetanus toxoid (TT), pneumococcal pneumolysis (Ply), polyhistidine triad proteins (PhtX proteins such as PhtD proteins), or

Haemophilus influenzae protein D (PD)." Ex. 1006 ¶ 90 (citing Ex. 1007, 9, 11).

> We are not persuaded by Petitioner's argument that:
>
> > Pfizer itself has admitted that other carrier proteins are not always substitutable and that CRM_{197} is unique because it unexpectedly solved the immunogenicity problem in a 13-valent PCV composition while other carrier proteins cannot. *E.g.*, *Merck Sharp & Dohme Corp. v. Wyeth LLC*, 2017 WL 3160412, IPR2017-01215 paper 8 at 28–36 (PTAB July 25, 2017).

Pet. 27. In Paper 8 of IPR 2017-01215, Patent Owner states that the prior art "directed a POSA to utilize multiple carriers in a conjugate-based vaccine" due to a concern over carrier-induced epitopic suppression (CIES). *Merck Sharp & Dohme Corp. v. Wyeth LLC*, IPR2017-01215 paper 8 at 30 (PTAB July 25, 2017). Moreover, Patent Owner noted a prior art "mixed carrier vaccine comprising use of protein D, tetanus toxoid, and diphtheria toxoid." *Id*. at 31. Thus, this evidence tends to support, rather than rebut, the expectation that a general description of carrier proteins for use in vaccines provides descriptive support because these carrier proteins are routinely and predictably used for vaccine formulations. *Id*. at 30–31. That unexpected improvements may be identified for specific carrier proteins does not undermine descriptive support based on the '547 provisional's recitation of the chemical names and prior art related to a large number of known carrier proteins. Ex. 1002, 20–21. Therefore, the evidence currently of record does not provide a reasonable likelihood that there is any unpredictability or lack of knowledge in the mature field of conjugating carrier proteins to saccharides to form polysaccharide conjugate vaccines.

Because we find that the '559 patent receives benefit of priority to the '547 provisional with a priority date of January 21, 2014, neither Pfizer-302 nor Pfizer-099 are prior art under AIA 35 U.S.C. §102(a)(1) and cannot serve as the basis for either anticipation or obviousness under that section.

B. AIA 35 U.S.C. § 102(a)(2) [13]

Petitioner asserts: "In the event the Board determines that the '559 patent is entitled to the priority date, Pfizer-302 is prior art to the '559 patent under AIA 35 U.S.C. § 102(a)(2)" and "Pfizer-099 is prior art to the '559 patent under AIA 35 U.S.C. § 102(a)(2)." Pet. 15, 17.

Patent Owner asserts "Pfizer-302 and Pfizer-099 [] are not prior art pursuant to AIA 35 U.S.C. § 102(b)(2)(C) because the references and the claimed invention were, as of the effective filing date of the claimed invention, commonly owned by and subject to an obligation to assignment to Pfizer." Prelim. Resp. 24. Patent Owner:

> submits assignment documents[] and declarations[] from PCT request forms[] confirming that all of the inventors listed on Pfizer-302, Pfizer-099, the '547 application and the '559 patent assigned, and had an obligation to assign, these patent application filings to Pfizer. EX2005 at 3−12; EX2006 at 3−16; EX2007 at 5−7; EX2008 at 3−5; EX2009 at 5−7; EX2010 at 5−7. Further, Sanofi has not provided any evidence that raises a material doubt as to Pfizer's claim of common ownership.

Prelim. Resp. 25.

[13] We note that MPEP § 2152.04 states "the Office is treating the term 'disclosure' as a generic expression intended to encompass . . . WIPO published application[s]." We note that both Pfizer-302 and Pfizer-099 are WIPO published applications and therefore included as prior art under AIA 35 U.S.C. § 102(a)(2).

"A disclosure shall not be prior art to a claimed invention under subsection (a)(2) if— . . . (C) the subject matter disclosed and the claimed invention, not later than the effective filing date of the claimed invention, were owned by the same person or subject to an obligation of assignment to the same person." AIA 35 U.S.C. § 102(b)(2)(C).

We are persuaded that Pfizer-302 and Pfizer-099 are not prior art to the '559 patent under AIA 35 U.S.C. § 102(a)(2) because they fall within the exception to that provision articulated in AIA 35 U.S.C. § 102(b)(2)(C). In particular, we find that Patent Owner provided evidence that these publications were subject to assignment to Patent Owner as of the effective filing date of the '559 patent.[14] The assignments were recorded in the '547 provisional by February 11, 2014, prior to the February 20, 2014 publication of Pfizer-302 and the June 26, 2014 publication of Pfizer-099. Ex. 2005, 1–2; Ex. 1009, 1; Ex. 1010, 1. Both Pfizer-302 and Pfizer-099 were also subject to assignment to Patent Owner. *See* Ex. 2009, 1–9; Ex. 2010 1–9. Additionally, Patent Owner submits assignment to Patent Owner of the U.S. 14/597,488 application to leading to the '559 patent as well. Ex. 2006, 1–2.

Therefore, Pfizer-302 and Pfizer-099 are not prior art to the '559 patent under AIA 35 U.S.C. § 102(a)(2) because they are excluded under AIA 35 U.S.C. § 102(b)(2)(C) as subject to an obligation of assignment to the same person, here Patent Owner.

[14] We note that MPEP § 2154.02(c) states: "If the provisions of AIA 35 U.S.C. 102(b)(2)(C) are met, a U.S. patent document that might otherwise qualify as prior art under AIA 35 U.S.C. 102(a)(2) is not available as prior art under either AIA 35 U.S.C. 102 or 103."

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 not established a reasonable likelihood that it will prevail in showing that claims 1–45 of the '559 patent are unpatentable.

IV. ORDER

Accordingly, it is

ORDERED that Pursuant to 35 U.S.C. § 314(a), the petition for *inter partes* review is hereby denied as to all challenged claims and no trial is instituted.

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