United States Court of Appeals for the Federal Circuit

PFIZER INC.,
Appellant

v.

SANOFI PASTEUR INC., SK CHEMICALS CO., LTD.,
Appellees

KATHERINE K. VIDAL, UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE,
Intervenor

2019-1871, 2019-1873, 2019-1875, 2019-1876, 2019-2224

Appeals from the United States Patent and Trademark Office, Patent Trial and Appeal Board in Nos. IPR2017-02131, IPR2017-02132, IPR2017-02136, IPR2017-02138, IPR2018-00187.

Decided: March 5, 2024

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Before LOURIE, BRYSON, and STARK, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Pfizer Inc. appeals from five final written decisions of the U.S. Patent and Trademark Office Patent Trial and Appeal Board ("the Board") concluding that claims 1–45 of U.S. Patent 9,492,559 ("the '559 patent") are unpatentable. *Merck Sharp & Dohme Corp. v. Pfizer Inc.*, No. IPR2017-02131, 2019 WL 1222935 (P.T.A.B. Mar. 13, 2019) (holding claims 1–10, 16–19, and 38–45 unpatentable) ("*'131 Decision*"), J.A. 1–81; *Merck Sharp & Dohme Corp. v. Pfizer Inc.*, No. IPR2017-02132, 2019 WL 1220899 (P.T.A.B. Mar. 13, 2019) (same) ("*'132 Decision*"), J.A. 82–160; *Merck Sharp & Dohme Corp. v. Pfizer Inc.*, No. IPR2017-02136, 2019 WL 1222965 (P.T.A.B. Mar. 13, 2019) (holding claims 11–15 and 20–37 unpatentable) ("*'136 Decision*"), J.A. 161–216; *Merck Sharp & Dohme Corp. v. Pfizer Inc.*, No. IPR2017-02138, 2019 WL 1220900 (P.T.A.B. Mar. 13, 2019) (same) ("*'138 Decision*"), J.A. 217–71; *Sanofi Pasteur Inc. v. Pfizer Inc.*, No. IPR2018-00187, 2019 WL 2352182 (P.T.A.B. June 3, 2019) (holding claims 1–45 unpatentable) ("*Sanofi*

Decision"), J.A. 272–360.[1] The Board also denied Pfizer's contingent motions to amend the claims filed in three of the five IPRs, concluding that proposed claims 46–52, which Pfizer proposed to substitute for claims 1–4, 9, 41, and 42, respectively, were not independently patentable. *Sanofi Decision* at *27–37; *'131 Decision* at *24–33; *'132 Decision* at *23–32.

For the following reasons, we affirm the Board's conclusions that claims 1–45 are unpatentable. We further affirm the Board's denials of Pfizer's motions to amend by adding proposed claims 46, 47, and 50–52. But we vacate those denials as to proposed claims 48 and 49, and remand to the Board for further consideration of those claims.

BACKGROUND

Pfizer owns the '559 patent, which is directed to immunogenic compositions comprising conjugated *Streptococcus pneumoniae* capsular saccharide antigens (*i.e.*, glycoconjugates) for use in pneumococcal vaccines. *See* '559 Patent at Abstract, J.A. 845. As the '559 patent explains, *S. pneumoniae* "is a Gram-positive encapsulated coccus, surrounded by a polysaccharide capsule." *Id.* at col. 1, ll. 50–52, J.A. 863. There are over 91 different pneumococcus serotypes, some of which cause diseases such as pneumonia, febrile bacteremia, and meningitis. *See id.* at col. 1, ll. 52–58, J.A. 863. Claim 1 is the only independent claim. It reads as follows:

> 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

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[1] The final written decisions consolidated in this appeal share similar analyses of the issues relevant to the parties' disputes. Unless otherwise indicated, we cite the *Sanofi Decision* as representative.

> 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.

Id. at col. 141, ll. 28–34, J.A. 933. As relevant here, dependent claims 3 and 4 recite that the composition further includes various additional glycoconjugates. Those claims read as follows:

> 3. The immunogenic composition of claim 1, wherein the composition further comprises a *S. pneumoniae* serotype 15B glycoconjugate and a *S. pneumoniae* serotype 33F glycoconjugate.
>
> 4. The immunogenic composition of claim 3, wherein the composition further comprises a *S. pneumoniae* serotype 12F glycoconjugate, a *S. pneumoniae* serotype 10A glycoconjugate, a *S. pneumoniae* serotype 11A glycoconjugate and a *S. pneumoniae* serotype 8 glycoconjugate.

Id. at col. 141, ll. 38–46, J.A. 933.

Across five IPR petitions, Merck Sharp & Dohme Corp. ("Merck") and Sanofi Pasteur Inc. and SK Chemicals Co., Ltd. (collectively, "Sanofi") separately challenged all claims of the '559 patent, arguing that they would have been obvious over, *inter alia*, PCT Patent Application Publication 2007/071711 ("GSK-711") and U.S. Patent Application Publication 2011/0195086 ("Merck-086").[2] GSK-711 is

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[2] Sanofi asserted that the claims would have been obvious over GSK-711 and Merck-086, while Merck asserted that the claims would have been obvious over International Patent Application Publication 2011/100151 ("Merck 2011") and International Patent Application Publication 2009/000825 ("GSK 2008"). Merck-086 is the U.S. counterpart to Merck 2011, while GSK-711 and GSK 2008

directed to *S. pneumoniae* vaccines comprising "capsular saccharide antigens (preferably conjugated), wherein the saccharides are derived from at least ten serotypes of *S. pneumoniae*," which may include an "*S. pneumoniae* saccharide conjugate of 22F." GSK-711 at p. 6, ll. 4, 24–26, J.A. 4578. Merck-086 is directed to "multivalent immunogenic composition[s] having 15 distinct polysaccharide-protein conjugates" in which an *S. pneumoniae* serotype, including 22F, is conjugated to a carrier protein. Merck-086 at Abstract, J.A. 4667.

The Board instituted review based on each petition and issued final written decisions which, taken together, found all claims unpatentable. *See, e.g.*, *Sanofi Decision* at *39. The Board also rejected Pfizer's contingent motions to amend, finding that Merck and Sanofi had each demonstrated that the proposed substitute claims were unpatentable. *Id.* at *27; *'131 Decision* at *24; *'132 Decision* at *23.

Pfizer timely appealed. After a stay pending the Supreme Court's decision in *United States v. Arthrex, Inc.*, 141 S. Ct. 1970 (2021), we remanded for the limited purpose of allowing Pfizer the opportunity to request Director Review of the Board's decisions. *See, e.g.*, Appeal 2019-1871, ECF No. 82. The Director denied those requests on February 4, 2022, *see id.*, ECF No. 85, so the Board's final written decisions are now ripe for our review. We have jurisdiction under 28 U.S.C. § 1295(a)(4)(A) and 35 U.S.C. § 141(c).

DISCUSSION

Pfizer raises four challenges on appeal. First, it argues that the Board erred in determining that GSK-711 and

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are related international applications with substantively identical disclosures. For clarity, we will refer only to the Sanofi-asserted references, GSK-711 and Merck-086, in this opinion.

Merck-086 would have rendered obvious the claimed immunogenic composition comprising a *S. pneumoniae* serotype 22F glycoconjugate, wherein the glycoconjugate has a molecular weight of between 1000 kDa and 12,500 kDa. Second, it argues that the Board erred in finding that the compositions of claims 3 and 4, which comprise a total of three and seven distinct *S. pneumoniae* serotype glycoconjugates, respectively, would have been obvious over GSK-711 and Merck-086. Third, it contends that the Board abused its discretion in denying its contingent motions to amend. And finally, it challenges the Patent and Trademark Office's ("PTO's") Director Review procedure, arguing that it violates the Administrative Procedure Act ("APA"). We address each argument in turn.

I

Pfizer's first two challenges relate to the Board's obviousness determinations. "Obviousness is a question of law that we review de novo, but the Board's underlying findings of fact are reviewed for substantial evidence." *Liqwd, Inc. v. L'Oreal USA, Inc.*, 941 F.3d 1133, 1136 (Fed. Cir. 2019). "An obviousness determination requires finding that a person of ordinary skill in the art would have been motivated to combine or modify the teachings in the prior art and would have had a reasonable expectation of success in doing so." *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1382 (Fed. Cir. 2019) (quoting *Regents of Univ. of Cal. v. Broad Inst., Inc.*, 903 F.3d 1286, 1291 (Fed. Cir. 2018)). Whether or not a person of ordinary skill would have had the requisite motivation to combine references, and whether or not she would have had a reasonable expectation of success in doing so, are questions of fact we review for substantial evidence. *Id.* A finding is supported by substantial evidence if a reasonable mind might accept the evidence as adequate to support the finding. *Consol. Edison Co. v. NLRB*, 305 U.S. 197, 229 (1938).

A

Claim 1 of the '559 patent recites that the *S. pneumoniae* serotype 22F glycoconjugate has a molecular weight of between 1000 kDa and 12,500 kDa. '559 patent at col. 141, ll. 30–31, J.A. 933. As the Board recognized, and Sanofi concedes, neither GSK-711 nor Merck-086 discloses any molecular weight for a *S. pneumoniae* serotype 22F glycoconjugate. *See Sanofi Decision* at *5; Sanofi Resp. Br. at 26. The Board nevertheless concluded that, based on the evidence of record, glycoconjugate molecular weight is a result-effective variable that a person of ordinary skill in the art would have been motivated to optimize to provide a conjugate having improved stability and good immune response. *Sanofi Decision* at *13. The Board therefore concluded that claim 1 would have been obvious over the references.

Pfizer first contends that the Board erred in applying the "result-effective variable doctrine," arguing that it is only appropriate in circumstances where there is actual overlap between a range in the prior art and a claimed range. *See* Pfizer Br. at 27. In Pfizer's view, because it is undisputed that the prior art does not disclose any molecular weight for the claimed serotype 22F glycoconjugate, there could be no presumption of obviousness, and it was error for the Board to consider whether that variable was result-effective. *Id.* We disagree.

We begin by stating that the determination whether or not a claimed parameter is a result-effective variable is merely one aspect of a broader routine optimization analysis. That analysis is rooted in the decades-old legal principle that "where 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); *see E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1006 (Fed. Cir. 2018) (collecting cases). In the context of claimed

numerical ranges, such as the molecular weight here, we have explained that an overlap between a claimed range and a prior art range creates a presumption of obviousness that can be rebutted with evidence that the given parameter was *not* recognized as result-effective. *See Genentech, Inc. v. Hospira, Inc.*, 946 F.3d 1333, 1341 (Fed. Cir. 2020) (citing *E.I. DuPont*, 904 F.3d at 1006); *In re Applied Materials, Inc.*, 692 F.3d 1289, 1295 (Fed. Cir. 2012). That does not mean, however, that the determination whether or not a variable is result-effective is *only* appropriate when there is such an overlap. A routine optimization analysis generally requires consideration whether a person of ordinary skill in the art would have been motivated, with a reasonable expectation of success, to bridge any gaps in the prior art to arrive at a claimed invention. Where that gap includes a parameter not necessarily disclosed in the prior art, it is not improper to consider whether or not it would have been recognized as result-effective. If so, then the optimization of that parameter is "normally obvious." *In re Antonie*, 559 F.2d 618, 620 (CCPA 1977). The Board therefore did not err in considering, as part of its obviousness analysis, whether or not the claimed molecular weight of a *S. pneumoniae* serotype 22F glycoconjugate was a result-effective variable.

Substantial evidence supports the Board's conclusion that the molecular weight recited in claim 1 would have been obvious over the references. Although it is undisputed that no reference teaches a molecular weight for the particularly claimed serotype 22F glycoconjugate, it is similarly undisputed that GSK-711 discloses both a serotype 22F glycoconjugate and the molecular weights for fourteen other *S. pneumoniae* serotype glycoconjugates. As the Board observed, those molecular weights, ranging from 1303 kDa to 9572 kDa, overlap with the claimed range (*i.e.*, 1000 kDa to 12,500 kDa). *Sanofi Decision* at *5; GSK-711 at Table 2, J.A. 25056. The Board further explained that GSK-711 discloses that "saccharide conjugate vaccines

retaining a larger size of saccharide can provide a good immune response against pneumococcal disease," and that both GSK-711 and Merck-086 disclose that known methods and techniques could be used to isolate the polysaccharide from the bacteria and to couple it to a carrier protein. *Sanofi Decision* at *9–10. For example, both GSK-711 and Merck-086 disclose methods for preparing *S. pneumoniae* glycoconjugates and teach that the polysaccharides can be sized to improve the filterability of the conjugated product. *Id.* at *6, *10. Expert testimony further supported the notion that, at the time of the invention, conjugation techniques and conditions were routine such that a person of ordinary skill in the art would have understood the claimed molecular weight to be "typical of immunogenic conjugates." *Id.* at *11. That evidence therefore supports the Board's conclusion that "conjugate size is a result[-]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.'" *Sanofi Decision* at *13 (quoting *Applied Materials*, 692 F.3d at 1295).

We are unpersuaded by Pfizer's argument that the Board disregarded contrary evidence showing that glycoconjugate molecular weight would have been unpredictable because it required "case-by-case experimentation" or "individualized design and testing." *See* Pfizer Br. at 36. Not only does Pfizer's argument call on us to reweigh evidence presented to the Board—which is not the role of this court, *see In re NTP, Inc.*, 654 F.3d 1279, 1292 (Fed. Cir. 2011)—but it relies on the faulty premise that where optimization requires case-specific considerations, then the results must be unexpected. Although that could be the case under some circumstances, it is not the case here where the methods and conditions for creating the glycoconjugates of the invention were generally recognized as routine. As Pfizer's own expert explained, "[c]hemists have all kind of tricks to control . . . to come up with the desired product,"

such that conjugation conditions could be easily controlled. *Sanofi Decision* at *11; *see* J.A. 30375–78.

Accordingly, we conclude that the Board's determination that claim 1 would have been obvious over the references was supported by substantial evidence.

B

Claims 3 and 4 of the '559 patent depend from claim 1 and recite that the claimed immunogenic composition further comprises glycoconjugates from *S. pneumoniae* serotypes 15B, 33F, 12F, 10A, 11A, and 8. '559 patent at col. 141, ll. 38–46, J.A. 933. As with claim 1, the Board concluded that the compositions of those claims would have been obvious over the combination of GSK-711 and Merck-086. Specifically, the Board concluded that, because GSK-711 expressly discloses multivalent immunogenic *S. pneumoniae* glycoconjugate compositions that can include serotypes 1, 2, 3, 4, 5, 6A, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F, it would have been obvious to incorporate the claimed glycoconjugates into an immunogenic composition containing an *S. pneumoniae* serotype 22F glycoconjugate to arrive at the claimed invention. *Sanofi Decision* at *21–22.

Pfizer argues that the Board's conclusion was not supported by substantial evidence because the record does not support a finding that "there would have been a reasonable expectation of success in formulating *immunogenic* conjugates for the claimed serotypes." Pfizer Br. at 40. In Pfizer's view, because none of the prior art discloses that any of the claimed glycoconjugates were actually made or tested, there was insufficient evidence to support the Board's finding that the glycoconjugates would have each been expected to "elicit functional antibody," as the term "immunogenic" was construed to mean. *Id.* at 42–43; *see Sanofi Decision* at *3–4. Pfizer argues that, because the unpredictability of the art is high, without examples showing that the claimed glycoconjugates would have each been

immunogenic, there would have been no reasonable expectation of success. We disagree.

As an initial matter, Pfizer's position that the claims could not have been obvious because no prior art reference *exemplifies* each of the claimed serotype glycoconjugates is unavailing. That argument was considered, and rejected, by the Board. The Board correctly explained that a prior art reference is not limited to its specific working examples. *Sanofi Decision* at *21 (citing *In re Mills*, 470 F.2d 649, 651 (CCPA 1972)). And the fact that the art of pneumococcal glycoconjugate vaccines is unpredictable does not affect our analysis. We have previously explained that "a rule of law equating unpredictability to patentability . . . . cannot be the proper standard since the expectation of success need only be reasonable, not absolute." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007) (collecting cases and explaining that "obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success"). As we explain next, the Board's conclusion that a person of ordinary skill in the art would have had a *reasonable* expectation of success in arriving at the immunogenic compositions of claims 3 and 4 was supported by substantial evidence.

The Board found that GSK-711 teaches the incorporation of glycoconjugates of the claimed serotypes, specifically 15B, 33F, 12F, 10A, 11A, and 8, into a pneumococcal vaccine. *Sanofi Decision* at *21–22. The Board also observed that, like the '559 patent, GSK-711 refers to its compositions as "immunogenic." *Id.* The Board therefore concluded that each of the glycoconjugates of GSK-711 must be taken to be immunogenic (*i.e.*, elicit functional antibody) because "otherwise there would be no need to include a serotype unable to induce such a response." *Id.* at *21. That conclusion is not unreasonable, particularly where the specifically claimed serotypes have long been recognized as immunogenic. Since 1983, free (*i.e.*,

unconjugated) polysaccharides from the claimed *S. pneumoniae* serotypes have been formulated into a commercial pneumococcal vaccine, PNEUMOVAX® 23. *Id.* And, as the '559 patent itself explains, at the time of the invention, there were three other commercial pneumococcal vaccines that incorporated glycoconjugates of other, unclaimed *S. pneumoniae* serotypes. *See id.* at *1. The Board therefore accepted Sanofi's expert's testimony that, because the claimed serotypes had already been included in commercial multivalent vaccines (albeit in "free," not "conjugated," form), and because multivalent glycoconjugate vaccines were generally known to be effective, the person of ordinary skill in the art would have reasonably expected that the claimed glycoconjugates could be incorporated into a vaccine "while maintaining the immunogenicity to all serotypes in the composition." *Id.* at *22. Substantial evidence therefore supports the Board's conclusion that the subject matter of claims 3 and 4 "would have been obvious in order to increase the coverage of serotypes of pneumococcal vaccines." *Id.*

Because all of the remaining claims of the '559 patent depend from claim 1, they are subject to the obviousness reasoning that we have affirmed. Pfizer has not argued otherwise.

II

Pfizer next challenges the Board's denials of its motions to amend, which Pfizer filed in three of the five IPRs. We review the Board's decision to deny a motion to amend under the APA and must set aside the Board's action if it is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A); *Fleming v. Cirrus Design Corp.*, 28 F.4th 1214, 1225 (Fed. Cir. 2022). We will uphold a decision of less than ideal clarity if the agency's path can reasonably be discerned, but "we may not supply a reasoned basis for the agency's action that the agency itself has not given." *Bowman Transp.,*

Inc. v. Ark.-Best Freight Sys., Inc., 419 U.S. 281, 285–86 (1974); *see also SEC v. Chenery Corp.*, 318 U.S. 80, 94 (1943). Accordingly, "the Board must, as to issues made material by the governing law, set forth a sufficiently detailed explanation of its determinations both to enable meaningful judicial review and to prevent judicial intrusion on agency authority." *Rovalma, S.A. v. Bohler-Edelstahl GmbH & Co. KG*, 856 F.3d 1019, 1024 (Fed. Cir. 2017) (collecting cases).

In each of IPR2017-02131, IPR2017-02132, and IPR2018-00187, Pfizer submitted, pursuant to 35 U.S.C. § 316(d) and 37 C.F.R. § 42.121, a motion to amend that proposed to substitute claims 46–52 for claims 1–4, 9, 41, and 42, respectively, should those claims be deemed unpatentable. *See Sanofi Decision* at *27; *'131 Decision* at *24; *'132 Decision* at *23. Relevant here, proposed claims 46, 48, and 49 recite:

> 46. An immunogenic composition comprising:
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> a *Streptococcus pneumoniae* serotype 22F glycoconjugate, wherein the 22F 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 CRM_{197} carrier protein, and wherein a ratio (w/w) of the polysaccharide to the carrier protein is between 0.4 and 2;
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> glycoconjugates from *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F all individually conjugated to CRM_{197};
>
> an aluminum salt adjuvant; and
>
> wherein the composition exhibits more than a 2-log increase above baseline in serum IgG levels in New Zealand White Rabbits across all serotypes in the composition following administration of two

> equal doses of the composition in the form of an initial dose and a booster dose.
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> 48. The immunogenic composition of claim ~~1~~ 46, wherein the composition further comprises a *S. pneumoniae* serotype 15B glycoconjugate and a *S. pneumoniae* serotype 33F glycoconjugate, wherein said serotypes 15B and 33F are all individually conjugated to CRM_{197}.
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> 49. The immunogenic composition of claim ~~3~~ 48, wherein the composition further comprises a *S. pneumoniae* serotype 12F glycoconjugate, a *S. pneumoniae* serotype 10A glycoconjugate, a *S. pneumoniae* serotype 11A glycoconjugate and a *S. pneumoniae* serotype 8 glycoconjugate, wherein said serotypes 12F, 10A, 11A and 8 are all individually conjugated to CRM_{197}.

E.g., J.A. 28091–92 (additions underlined and deletions struck through).[3]

The Board denied each of Pfizer's motions to amend on the basis that the claimed subject matter would have been obvious over a combination of various references, including U.S. Patent Application Publication 2012/0237542 ("Hausdorff"), Merck-086, GSK-711, and the knowledge of a person of ordinary skill in the art. *See Sanofi Decision* at *31.

A

We begin with the Board's treatment of proposed claim 46. As amended, that claim recites, in part, a 14-valent

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[3] Pfizer has not independently challenged on appeal the Board's treatment of proposed claims 47 and 50–52, so any challenge as to those claims is waived. *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1319 (Fed. Cir. 2006).

immunogenic composition that exhibits a 2-log (*i.e.*, 100-fold) increase above baseline in serum IgG levels across *all* serotypes according to a particular dosing regimen. The Board's conclusion that, based on the prior art, it would have been obvious to arrive at the claimed composition with a reasonable expectation of success in obtaining a 2-log increase above baseline in serum IgG levels across all serotypes was supported by substantial evidence.

As the Board observed, each of Merck-086 and GSK-711 provides specific reasons why a person of ordinary skill in the art would have been motivated to incorporate a serotype 22F glycoconjugate into a multivalent vaccine; for example, to provide "expand[ed] coverage of pneumococcal serotypes not covered by existing pneumococcal vaccines." *Sanofi Decision* at *34 (quoting Merck-086 at ¶ 15, J.A. 4672). Merck-086 further shows that, in two of four studies, a multivalent pneumococcal vaccine comprising a serotype 22F glycoconjugate exhibited a greater than 2-log increase above baseline serum IgG levels as to the 22F serotype. *Id.* at *32 (citing Merck-086 at ¶ 117, Table 4, J.A. 4680). Moreover, the Board observed that Hausdorff discloses a 13-valent glycoconjugate vaccine comprising the same thirteen serotypes added in proposed claim 46. *See Sanofi Decision* at *31, *34. That multivalent vaccine showed a greater than 2-log increase above baseline in serum IgG levels "for every single serotype tested." *Id.* at *31 (citing Hausdorff at Table 3, J.A. 28170). The Board therefore concluded that it would have been obvious to incorporate the serotype 22F glycoconjugate as rendered obvious by Merck-086 and GSK-711 "into a pneumococcal vaccine with the 13 serotypes . . . disclosed by Hausdorff with a reasonable expectation of success in obtaining a 2-log increase above baseline in serum IgG levels as required by claim 46." *Sanofi Decision* at *34.

On appeal, Pfizer argues that the Board's conclusion was error because the data in Merck-086 provide "clear evidence that the claimed 2-log increase across all serotypes

would *not* have been obvious, notwithstanding the immunogenicity data in Hausdorff." Pfizer Reply Br. at 24. Pfizer argues that "where the prior art contains evidence directly showing that others failed to achieve the claimed invention (as here), there can be no finding of obviousness." *Id.* at 25 (citing *Univ. of Strathclyde v. Clear-Vu Lighting LLC*, 17 F.4th 155, 165–66 (Fed. Cir. 2021)). We disagree that that is the case here. As explained, Merck-086 discloses the claimed 2-log IgG increase for a 22F glycoconjugate within a multivalent vaccine, and Hausdorff discloses that result for the remaining thirteen claimed glycoconjugates. While neither Merck-086 nor Hausdorff discloses the claimed result across *all* fourteen claimed serotypes, a finding of obviousness does not require a guarantee of success. As we have already noted, an expectation of success need only be *reasonable*, not absolute. *Pfizer*, 480 F.3d at 1364; *Univ. of Strathclyde*, 17 F.4th at 165.

Pfizer's reliance on Merck-086, alone, ignores other evidence in the record that suggests that achieving a 2-log IgG increase would have been reasonably expected. Moreover, unlike in *University of Strathclyde*, the prior art here does not evidence "*only failures* to achieve that at which the inventors succeeded." 17 F.4th at 165 (emphasis added). Indeed, each of Merck-086 and Hausdorff clearly demonstrated that the claimed 2-log IgG increase could be achieved across various serotypes in a multivalent composition, which is consistent with the disclosure in the prior art that new glycoconjugates could be added to multivalent compositions without negatively affecting the components already within the vaccine. *Id.* at *36.

Accordingly, substantial evidence supports the Board's conclusion that a person of ordinary skill in the art would have had a reasonable expectation of success in arriving at the composition claimed in proposed claim 46. Therefore, the Board did not abuse its discretion in denying Pfizer's motions to amend as to that claim.

B

We now turn to the Board's treatment of proposed claims 48 and 49. Those claims mirror claims 3 and 4 but further require the limitation from proposed claim 46 that the compositions exhibit more than a 2-log increase above baseline in serum IgG levels across *all* serotypes within the claimed composition. That is, proposed claims 48 and 49 require that, in addition to the 2-log IgG increase across all 14 serotypes of claim 46, the composition must also exhibit that increase with respect to serotypes 15B and 33F for claim 48 and with respect to 15B, 33F, 12F, 10A, 11A and 8 for claim 49.

The *Sanofi Decision* is silent as to why proposed claims 48 and 49 would have been obvious over the references. The only mention of those claims in that decision is a conclusory statement, prior to any analysis, that the Board determined that "claims 46 and 48–52 would have been obvious over the combination of Hausdorff, Merck-086, GSK-711, and the knowledge of the skilled artisan." *Sanofi Decision* at *31. The ensuing analysis, however, focuses only on the elements of claim 46, and fails to consider whether the incorporation of the glycoconjugates recited in proposed claims 48 and 49 would have been expected to exhibit the claimed 2-log IgG increase. *See generally id.* at *31–37.

The *'131 Decision* and *'132 Decision* fare no better. Unlike the *Sanofi Decision*, each of those decisions has a separate analysis as to proposed claims 48 and 49. *'131 Decision* at *32–33; *'132 Decision* at *31–32. But those analyses merely consider whether it "would have been obvious to *incorporate*" the claimed glycoconjugates into a pneumococcal vaccine. *'131 Decision* at *33 (emphasis added); *'132 Decision* at *32. It does not appear that the Board considered whether, once incorporated, it would have been reasonably expected that the compositions

exhibit the claimed 2-log IgG increase across all serotypes recited in proposed claims 48 and 49.

Sanofi and the PTO argue that the Board's conclusion that proposed claims 48 and 49 would have been obvious is supported by the same evidence that supported the obviousness of claim 46, as well as the evidence that supported the obviousness of claims 3 and 4. Sanofi Br. at 61; PTO Br. at 57–58. But we cannot say, with any modicum of certainty, that that is the case. It is hornbook law that administrative agencies must provide a "reasoned basis" for their actions that is sufficient to permit meaningful judicial review. *See Bowman Transp.*, 419 U.S. at 285. The Board's decisions, which fail to consider, let alone recognize, that the compositions of proposed claims 48 and 49 must satisfy the recited 2-log IgG increase, do not meet that standard.

Accordingly, because the Board's determination that proposed claims 48 and 49 would have been obvious was not supported by substantial evidence, it abused its discretion in denying Pfizer's motions to amend as to those claims. We therefore remand for the Board to further consider Pfizer's motions.

III

Finally, we address Pfizer's argument that the PTO's Director Review procedure violates the APA because it was not promulgated through notice-and-comment rulemaking. We review *de novo* whether or not an agency action complied with the APA, and we must "hold unlawful and set aside agency action, findings, and conclusions found to be . . . arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law . . . [or] without observance of procedure required by law." 5 U.S.C. § 706(2)(A), (D); *EmeraChem Holdings, LLC v. Volkswagen Grp. of Am., Inc.*, 859 F.3d 1341, 1345 (Fed. Cir. 2017).

Pfizer contends that "[t]he PTO has unpredictably changed the [Director Review] Q&A webpages [sic]

multiple times since it was created," which has therefore provided "insufficient notice to the public and patent owners" as to the Director Review process post-*Arthrex*. Pfizer Br. at 57–58. Pfizer further argues that the PTO has never provided any reason or evidence as to why its practices with respect to Director Review qualify for any of the exceptions to notice-and-comment rulemaking in 5 U.S.C. § 553(b)(B). *Id.* at 58.

This is not the first time this court has addressed Pfizer's precise argument. As Sanofi and the PTO explained in their respective citations of supplemental authority, *see, e.g.*, Appeal 2019-1871, ECF Nos. 142, 143, we recently held, nonprecedentially, that even if the PTO's guidance governing Director Review was not exempt from notice-and-comment rulemaking, any error by the PTO in that regard would be harmless absent a showing of prejudice by the party challenging the agency action. *Carucel Invs. L.P. v. Vidal*, No. 2021-1731, 2023 WL 8888644, at *9 (Fed. Cir. Dec. 26, 2023) (nonprecedential) ("[W]e must take 'due account . . . of the rule of prejudicial error.'" (quoting 5 U.S.C. § 706)); *Jicarilla Apache Nation v. U.S. Dep't of Interior*, 613 F.3d 1112, 1121 (D.C. Cir. 2010) ("The burden to demonstrate prejudicial error is on the party challenging agency action."). Pfizer has not shown such prejudice here. As in *Carucel*, Pfizer "does not contend it was unaware of the relevant procedural requirements for filing a request for Director Review; nor does it identify any way in which it was prejudiced by the manner in which the PTO distributed its guidance." *Id.* Rather, Pfizer timely and properly filed each of its requests, none of which was denied for a failure to abide by the PTO's procedural requirements.

Because we can find no prejudice to Pfizer, any APA violation by the PTO was harmless and cannot serve as a basis to reverse or vacate the Board's decisions.

CONCLUSION

We have considered Pfizer's remaining arguments and find them unpersuasive. Accordingly, we affirm *in toto* the Board's decision at issue in Appeals 2019-1875 and 2019-1876. We further affirm the Board's decisions at issue in Appeals 2019-1871, 2019-1873, and 2019-2224 as to claims 1–45 and proposed substitute claims 46, 47, and 50–52. Claims 1–45 are therefore unpatentable. But we vacate the Board's denials of Pfizer's motions to amend in those decisions as to proposed substitute claims 48 and 49 and remand for further proceedings consistent with this opinion.

AFFIRMED-IN-PART, VACATED-IN-PART, AND REMANDED-IN-PART

COSTS

Costs to Sanofi.