Nos. 18-2133, -2134

IN THE

United States Court of Appeals

FOR THE FEDERAL CIRCUIT

MERCK SHARP & DOHME CORP.,

Appellant,

v.

WYETH LLC,

Appellee.

On Appeal from the United States Patent and Trademark Office,
Patent Trial and Appeal Board, in Nos. IPR2017-00378 and IPR2017-00380

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UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

MERCK SHARP & DOHME CORP. **v.** WYETH LLC

Case No. 2018-2133, -2134

CERTIFICATE OF INTEREST

Counsel for the:
☐ (petitioner) ■ (appellant) ☐ (respondent) ☐ (appellee) ☐ (amicus) ☐ (name of party)

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1. Full Name of Party Represented by me	2. Name of Real Party in interest (Please only include any real party in interest NOT identified in Question 3) represented by me is:	3. Parent corporations and publicly held companies that own 10% or more of stock in the party
Merck Sharp & Dohme Corp.	None	Merck & Co., Inc.

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court **(and who have not or will not enter an appearance in this case)** are:

From Hogan Lovells US LLP: Arlene L. Chow and Ernest Yakob.

From MoloLamken LLP: Jeffrey A. Lamken, Michael G. Pattillo, Jr., Sara E. Margolis, and Benjamin T. Sirolly.

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5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. *See* Fed. Cir. R. 47. 4(a)(5) and 47.5(b). (The parties should attach continuation pages as necessary).

None.

5/31/2019
Date

/s/ Jeffrey A. Lamken
Signature of counsel

Please Note: All questions must be answered

Jeffrey A. Lamken
Printed name of counsel

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INTRODUCTION

Wyeth attempts to defend the Board's decision to hold claim 18 non-obvious by invoking arguments the Board ***rejected*** when holding claims 1 and 17 obvious. There is a reason Wyeth cannot defend the Board's decision upholding claim 18 without attacking the Board's rationales for finding claims 1 and 17 unpatentable: The Board's opinion is self-contradictory. The Board never attempted to explain the internal inconsistency in its decision. Wyeth doesn't either.

The Supreme Court has explained that, "if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 417 (2007). The Board applied that rule to find claims 1 and 17 obvious. Claim 1 recites a stabilizing formulation for polysaccharide-protein conjugate compositions that inhibits protein aggregation induced by silicone oil. The Board found that a skilled artisan would have understood that Chiron teaches that stabilizing formulation. The Board then found claim 1 unpatentable because it was obvious to apply that known formulation to stabilize "one or more polysaccharide-protein conjugates" generally.

For claim 17, the Board found it obvious to apply claim 1's formulation to stabilize a polysaccharide-protein conjugate composition comprising 7 identified polysaccharide serotypes conjugated to a CRM_{197} protein. The identity of the poly-

saccharides, the Board found, would not have affected a skilled artisan's motivation to apply the formulation to inhibit silicone-induced protein aggregation. As the Board explained, it is the ***protein***, not the polysaccharides, that creates the aggregation problem. Likewise, it is the ***protein***, not the polysaccharides, that the stabilization formulation addresses. Accordingly, the specific polysaccharides that are conjugated to the protein do not render the claim non-obvious—skilled artisans would have reasonably expected Chiron's formulation to act on proteins, and to stabilize the polysaccharide-protein conjugate, regardless.

When the Board reached claim 18, however, it reversed course. Claims 17 and 18 recite applying ***the same*** stabilizing formulation to conjugate compositions with ***the same protein***. Claim 18 differs only by specifying additional polysaccharides. Yet the Board found no motivation to combine. The Board ignored its own explanation that—because aggregation and stabilization are a function of the protein—the identity of the polysaccharides is irrelevant. The Board's decision ignores that internal inconsistency. Wyeth ignores it as well. That unexplained inconsistency renders the Board's decision arbitrary and capricious.

The Board's decision fails for another reason: It fails to provide a reasoned basis for upholding claim 18, as required by the Administrative Procedure Act. That decision rests on the bare assertion that Merck failed to show that a skilled artisan would have been "motivated . . . to modify [the prior-art stabilizing

formulation] in a manner that yields the claimed invention with a reasonable expectation of successfully doing so." Appx40; *see* Appx39-44.

But the question is not whether a skilled artisan would ***modify*** a stabilizing formulation to include the polysaccharide-protein conjugates to be stabilized. It is whether a skilled artisan, knowing the formulation stabilizes polysaccharide-protein conjugates generally, would recognize that it would stabilize those recited in claim 18.

Moreover, when "the Board finds that there would have been no motivation to combine . . . , it must expressly say so ***with an adequate explanation***." *Vicor Corp. v. SynQor, Inc.*, 869 F.3d 1309, 1324 (Fed. Cir. 2017) (emphasis added). One cannot discern from the Board's opinion why a skilled artisan would not have been motivated to apply the formulation to the recited conjugate composition. Would she not have expected the formulation to stabilize the composition? Would she not have expected that the additional conjugates could be made? Would she not have conjugated the recited polysaccharides to a single-carrier CRM_{197} protein? The Board does not say.

Wyeth insists "[t]here is no ambiguity about what the Board meant." Wyeth Br. 50. Yet Wyeth refuses to commit to any explanation, offering only paraphrases as impenetrable as the Board's original conclusion: "Merck did not provide sufficient evidence to prove that a person skilled in the art would modify the asserted

prior art references to successfully yield the claimed invention in claim 18 – an immunogenic composition comprising a pH buffered saline solution with a particular pKa, aluminum salt, and thirteen specific pneumococcal conjugates that inhibits aggregation induced by a siliconized container." *Id.* Wyeth points to nothing in the Board's decision that explains ***which*** part was not proved, or ***why***. Likewise, while Wyeth insists the Board's findings "are supported by substantial evidence," *e.g.*, *id.* at 21, Wyeth cannot tie any supposed evidentiary finding to a coherent rationale in the Board's decision. Wyeth commits to no specific understanding of the Board's decision because none can be sustained on the Board's reasoning or this record.

Wyeth does argue—independent of the Board's reasoning—that the specific 13 polysaccharide-protein conjugates recited in claim 18 render the claim non-obvious. But the Board never said that. Nor does the argument make sense. The '999 Patent is directed to ***stabilizing formulations***—not to new vaccine compositions. And all the elements of the conjugates were known—and the motivation to combine apparent—regardless.

The fundamental problem is that Wyeth seeks to wield this stabilizing-formulation patent against competitors' novel vaccines. As an open-ended "comprising" claim, claim 18 purports to capture not merely application of the stabilizing formulation to the 13 recited conjugates, but also later-developed vaccines,

such as Merck's, that include additional conjugates with polysaccharides of 15 or more serotypes. Wyeth's efforts to use claim 18's obvious application of a stabilizing formulation to foreclose conjugate vaccine progress should be rejected—starting here.

ARGUMENT

I. THE BOARD'S MOTIVATION-TO-COMBINE ANALYSIS IS INTERNALLY INCONSISTENT AND CONTRARY TO LAW

A. The Board's Conclusion on Claim 18 Cannot Be Reconciled With Its Conclusions on Claims 1 and 17

The '999 Patent is directed to purportedly "novel formulations," Appx301, 2:53, that "improve the stability of immunogenic compositions such as polysaccharide-protein conjugates" by inhibiting protein "aggregation" induced by silicone oil, Appx290 (Abstract). The Summary of Invention declares that "[t]he present invention broadly relates to novel ***formulations which stabilize and inhibit precipitation*** of immunogenic compositions." Appx301, 2:53-55 (emphasis added). The Detailed Description of the Invention defines the "present invention" as "novel surfactant ***formulations*** and/or novel aluminum salt ***formulations which stabilize and inhibit precipitation*** of immunogenic compositions." Appx305, 10:2-5. The patent discusses applying that formulation to "stabilize[] a polysaccharide-protein conjugate" composition, *e.g.*, Appx306, 11:57-58, but ascribes no significance to any particular polysaccharide serotypes in the composition. The Board found the patent's supposedly novel "stabilizing formulation" was known.

And it found claims applying that formulation to polysaccharide-protein conjugate compositions—including claims 1 and 17—obvious.

As Merck explained (at 39-41, 51-53), the Board's express findings on motivation to apply the known formulation to polysaccharide-protein conjugate compositions for claims 1 and 17 should have rendered claim 18 obvious as well. The Board upheld claim 18 nonetheless. But it never reconciled those results. Nor does Wyeth—because they cannot be reconciled.

1. *The Board's Own Findings Foreclose Any Conclusion That a Skilled Artisan Would Not Have Expected Chiron's Formulation To Stabilize the Conjugates of Claim 18*

Claim 1, the sole independent claim, recites the supposedly inventive stabilizing formulation and its general application to "one or more polysaccharide-protein conjugates." Appx316, 31:7-12. The Board found that the prior art disclosed every element of the stabilizing formulation in a single reference—Chiron. Appx21. And the Board held it was obvious to use Chiron's formulation to inhibit protein aggregation of polysaccharide-protein conjugates caused by siliconized containers. Appx21. Wyeth did not cross-appeal. It accepted that finding and that claim 1 was unpatentable.

Dependent claim 17 recites the application of claim 1's formulation to stabilize a composition comprising ***7 specific*** polysaccharide serotypes, each conjugated to the CRM_{197} carrier protein. Appx316, 32:12-23. The Board found that

claim obvious as well. Appx36-38. Addressing motivation to combine, the Board was "not persuaded" by Wyeth's argument that the particular "seven valent" conjugate composition claim 17 recited would "alter [the formulation's] behavior" such that skilled artisans would "no longer reasonably expect" that "the formulation would inhibit any aggregation induced by" silicone oil. Appx37-38. To the contrary, a skilled artisan would have understood that the identity of the polysaccharides "'would not have affected [the formulation's] inhibition of silicone-induced protein aggregation.'" Appx38. That is true, the Board explained, because the "protein component"—not the polysaccharide—"is responsible for such aggregation." Appx38. Wyeth did not cross-appeal the Board's decision finding claim 17 obvious.

For claims 1 and 17, the Board followed the Supreme Court's mandate in *KSR*. *KSR* explains that, "if a technique has been used to improve one device," and a skilled artisan "would recognize that it would improve similar devices in the same way, using the technique is obvious." 550 U.S. at 417. The Board found that a skilled artisan would understand that Chiron disclosed a technique for improving the stability of vaccines—in particular, a formulation that inhibits silicone-induced protein aggregation in polysaccharide-protein conjugate compositions. Appx21-22. The Board further found that a skilled artisan would understand that the formulation would improve such compositions regardless of the particular polysac-

charide component. Appx38. Whether the artisan was considering the generic "one or more polysaccharide-protein conjugates" of claim 1, Appx316, 31:7-12, or the composition comprising 7 specific polysaccharide-protein conjugates in claim 17, Appx316, 32:12-23, she would have understood that the stabilizing formulation inhibits aggregation the same way—by preventing interaction between protein and silicone oil, Appx34, Appx37-38. Thus, the Board properly concluded that "using the technique is obvious." *KSR*, 550 U.S. at 417.

Yet on claim 18, the Board reversed course, holding that a skilled artisan would not have been motivated to apply Chiron's stabilizing formulation to another polysaccharide-protein conjugate composition. Appx38-40, 42-44. That makes no sense. Claim 18 differs from claim 17 ***only*** in that its recited polysaccharide-protein conjugate composition requires 6 additional ***polysaccharide*** serotypes. Appx38-40. Under the Board's own findings, that difference—altering the polysaccharide components of the conjugates—cannot affect the motivation-to-combine analysis: Because the "protein component," not the polysaccharide, "is responsible for . . . aggregation," skilled artisans would have understood that the particular "'polysaccharide molecules would not have affected [the formulation's] inhibition of silicone-induced protein aggregation.'" Appx38. The Board's failure to apply that finding to claim 18 cannot be reconciled with its application of that finding to claims 1 and 17. *See* Merck Br. 49-51. Wyeth never suggests other-

wise. That "'internal[] inconsistency'" renders the Board's decision on claim 18 "arbitrary and capricious," requiring reversal. *Nat. Res. Def. Council v. U.S. Nuclear Regulatory Comm'n*, 879 F.3d 1202, 1214 (D.C. Cir. 2018).

Separately, the Board was at least obligated to "provide a[] reasoned explanation for the inconsistent result." *Vicor*, 869 F.3d at 1323; *see* Merck Br. 39-41, 51-53. It did not. Nor could it. The scientific principles the Board invoked as informing a skilled artisan's motivations with respect to stabilizing the conjugates in claims 1 and 17 apply equally to stabilizing the conjugates in claim 18. For that reason, too, reversal is warranted.[1]

2. *Wyeth's Prior-Art, Inherency, and Surfactant Arguments Underscore the Inconsistency and Lack Merit*

Rather than reconcile that internal contradiction, Wyeth changes the subject. It offers a series of barred and erroneous arguments the Board did not accept—and often expressly rejected.

Prior Art. Wyeth accuses Merck of improperly "wield[ing]" "claim 17 . . . as prior art." Wyeth Br. 51; *see id.* at 3, 40. But Merck is not invoking claim 17, or claim 1, as prior art. The point is that the Board's findings for claims 1 and 17 prove that claim 18 is obvious as well. *See* pp. 6-9, *supra*. Simply put, if one

[1] Wyeth urges that Merck "does not challenge the Board's explanations regarding claim 18" in the 380 Proceeding. Wyeth Br. 46. But Merck made clear that the Board's decision in the 380 Proceeding fails for the same reasons as its decision in the 378 Proceeding. *See* Merck Br. 17 n.2. "[F]or simplicity[]," Merck explained, it would "cite only the Board's decisions in the 378 Proceeding." *Id.*

accepts the Board's findings with respect to claim 1 and 17, the Board's conclusion on claim 18 cannot be right.

Inherency. Wyeth attempts to dismiss Merck's arguments as improperly "relying on inherency of [prior-art] disclosures to meet the limitation of inhibiting silicone-induced aggregation" because, according to Wyeth, "Chiron, Prevenar 2005, and Peña are silent on silicone-induced aggregation." Wyeth Br. 29-30. That cannot salvage the decision in the 378 Proceeding. In that proceeding, Merck never relied on inherency in connection with Chiron's formulation. The use of Chiron's surfactant to inhibit silicone-induced protein aggregation is taught in Elan, which Merck invoked in the IPR. *See* Appx29-35. Merck's argument in this appeal is that the Board's findings for claims 1 and 17—which acknowledge Elan's teachings, Appx34—contradict its decision on claim 18.

In the separate 380 Proceeding (where Merck did rely on inherency), the Board rejected Wyeth's argument. *See* Appx75-77 (rejecting argument that Merck had not shown prior-art formulations "inherently possessed" protein-aggregation inhibiting "properties of the claimed invention"); Appx76 ("inhibition of silicone-induce[d] aggregation is the natural result of the combination of elements disclosed in the prior art"); Appx77 (prior art "yields the formulation of claim 1, wherein the recited aggregation inhibition property . . . must be present"). Wyeth never explains why the Board's findings on inherency, which undergirded its decision

finding claims 1 and 17 obvious, do not operate for claim 18 as well. *Cf. Max-Linear, Inc. v. CF CRESPE LLC*, 880 F.3d 1373, 1377 (Fed. Cir. 2018). Wyeth's inability to defend the Board's conclusion of non-obviousness for claim 18 without attacking the inherency determinations underlying the Board's invalidation of claims 1 and 17 confirms the contradiction in the Board's reasoning.

Wyeth's effort to inject inherency objections into this appeal is also foreclosed by waiver. Wyeth claims "it was ***unexpected***" that the formulation would "inhibit[ ] silicone-induced aggregation" in "the composition of claim 18." Wyeth Br. 30. Wyeth never made that argument in either proceeding below. In the 380 Proceeding, the Board specifically ruled that Wyeth "has not alleged, or provided any evidence demonstrating that the claimed formulations ***unexpectedly inhibit*** silicone-induced aggregation." Appx76 (emphasis added). Wyeth cannot raise new arguments on appeal. *Monsanto Tech. LLC v. E.I. DuPont de Nemours & Co.*, 878 F.3d 1336, 1342 n.8 (Fed. Cir. 2018).

Surfactant. Wyeth asserts that Merck cannot rely on Chiron's surfactant in establishing obviousness because "[c]laim 18 does not claim a surfactant as a necessary component." Wyeth Br. 29-30. The Board's reasoning on claims 1 and 17 forecloses that argument, too. The Board held that, because claim 1 (like claims 17 and 18) is a comprising claim, it "includes formulations comprising additional, unrecited ingredients"—such as a surfactant—and that "such additional ingredi-

ent(s) may contribute to the required aggregation inhibition." Appx13. The Board concluded that "Chiron's formulation" (which includes a surfactant) "may read on the functional claim requirement" of "inhibit[ing] silicone-induced aggregation." Appx33. The Board rejected the argument Wyeth now presses.

3. *Wyeth's Prior-Art, Inherency, and Surfactant Arguments Are Barred by* Chenery

One final deficiency unites Wyeth's prior art, inherency, and surfactant arguments: Each is barred by *Securities and Exchange Commission v. Chenery Corp.*, 318 U.S. 80 (1943). Under *Chenery*, an agency decision "must be measured by what the [agency] did, not by what it might have done." *Id.* at 93-94. Thus, "an administrative order cannot be upheld" on grounds other than those "upon which the agency acted." *Id.* at 95; *see also Power Integrations, Inc. v. Lee*, 797 F.3d 1318, 1326 (Fed. Cir. 2015) ("patentability determination is confined to 'the grounds upon which the Board actually relied'").

Here, the Board did not invoke the rationales Wyeth asserts. Wyeth never asserted its present inherency objection, and the Board never adopted it, in either the 378 or 380 Proceeding. *See* pp. 10-11, *supra*. The Board rejected Wyeth's argument regarding surfactants. Appx32-33. The Board nowhere mentioned Wyeth's "claim-as-prior-art" argument. This Court may not affirm on a ground different from the one the Board adopted. *Chenery*, 318 U.S. at 94; *Ariosa Diagnostics v. Verinata Health, Inc.*, 805 F.3d 1359, 1365 (Fed. Cir. 2015). If the

Board's decision can be defended only by inventing new rationales—or attacking the Board's reasoning—the decision must be reversed.

B. The Board's Motivation-To-Combine Analysis Defies *KSR* and *Belden*

1. *The Board Applied the Wrong Test*

The Board reached the wrong result on claim 18 because it applied the wrong legal test. In *KSR*, the Supreme Court explained that, if "a technique has been used to improve one device," and an artisan would recognize that it "would improve similar devices in the same way," then "using the technique is obvious." 550 U.S. at 417. For claim 18, *KSR* required the Board to ask if a skilled artisan would recognize that Chiron's formulation—which an artisan would understand inhibits silicone-induced protein aggregation in polysaccharide-protein conjugates generally—would inhibit such aggregation in the particular 13 polysaccharide-protein conjugates recited in claim 18. *See* Merck Br. 43-44. Wyeth does not dispute that the Board failed to apply that standard.

The Board instead asked whether a skilled artisan "would have ***modified Chiron's formulation*** to comprise a thirteen valent conjugate." Appx39 (emphasis added). As Merck explained (at 43-44), that is the wrong question. It erroneously asks whether there was a reason to change ***Chiron's successful stabilizing formulation***. But the proper question is whether there was a reason ***to use*** that successful formulation to address the same problem, in the same way, for a similar conjugate

composition. The Board's failure to apply the correct legal standard alone warrants reversal. *See E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 999 (Fed. Cir. 2018).

Wyeth never defends the Board's framing of the issue as correct. Wyeth argues instead that "Merck framed the issue in exactly the same order." Wyeth Br. 42. That is not true. As Wyeth acknowledges, the Board began with Chiron, asking whether a skilled artisan "'would have modified Chiron's formulation to comprise a thirteen valent conjugate.'" *Id.* (emphasis omitted). And Wyeth's quote shows that Merck framed the issue the other way: Merck asked whether "'[i]t would have been obvious ***to use*** the claimed pneumococcal polysaccharide-protein antigens ***in the formulations of Chiron 2003***, and that ***such formulations would still inhibit silicone-induced aggregation***.'" *Id.* (quoting Appx272) (emphasis added). That applies *KSR*. Unlike the Board's framing, it asks whether an artisan would have understood that Chiron's formulation would stabilize the conjugates of claim 18—just as it stabilizes other polysaccharide-protein conjugates.[2]

[2] Wyeth faults Merck (at 42-43) for "assert[ing] obviousness from multiple directions and combinations of prior art," urging that Merck listed references in "the same order" as the Board. But obviousness depends on those references' ***teachings***. *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1076 (Fed. Cir. 2015). Nothing suggests that the motivation-to-combine question depends on which reference is listed as primary and which as secondary.

2. *Wyeth's Efforts To Distinguish* Belden *Fail*

This Court's decision in *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064 (Fed. Cir. 2015), confirms the Board's error. Merck Br. 44-49.

a. Wyeth does not dispute that the purported invention in *Belden*—like the one here—was an improvement technique. In *Belden*, it was a method of aligning transmission wires around a core to prevent "twisting" during manufacture. 805 F.3d at 1068. Here, it is a formulation for stabilizing polysaccharide-protein conjugates against protein aggregation. In *Belden*, the challenged claim applied the improvement technique to a particular item. In particular, the claim applied the alignment method to "'twisted pairs of insulated conductors.'" *Id.* Here, too, the claim applies the improvement technique to a particular item. In particular, it applies the stabilizing formulation to a composition comprising 13 specific polysaccharide-protein conjugates.

In *Belden*, the Board found that the improvement technique was disclosed in a prior-art reference. The question thus concerned a skilled artisan's motivation to combine the obvious technique with the particular element recited in the claim. *Belden*, 805 F.3d at 1075. The Board, however, framed the issue as "whether a skilled artisan would substitute the twisted pairs" of insulated conductors recited in the claim "into the [alignment] method" of the prior-art reference, *id.* at 1075, which had applied the improvement technique only to "bare metal conductors," *id.*

at 1076. That is, the Board focused on whether a skilled artisan would have been motivated to ***modify the improvement technique*** by adding the particular item to be improved.

This Court rejected that framing of the motivation-to-combine inquiry as "legal error[]." *Belden*, 805 F.3d at 1075. The Board had improperly focused on whether an artisan would have modified "'the particular ***invention***'" of the prior-art reference. *Id.* at 1076. The "proper question" was whether the prior-art reference "taught a solution to the problem of aligning cable components that a skilled artisan would have been motivated to use in making" the twisted-pair cables recited in the claim. *Id.* at 1077.

The Board made the same error here. It asked whether a skilled artisan "would have modified Chiron's [stabilizing] formulation to comprise a thirteen valent conjugate." Appx39. It thus erroneously focused on whether an artisan would have "modified" the "particular [stabilizing] invention" Chiron "describ[ed]" by adding the composition to be stabilized. But the "proper question" is whether Chiron, as understood by a skilled artisan, "taught a solution to the problem" of silicone-induced protein aggregation that the artisan "would have been motivated to use" with the 13 conjugates recited in claim 18. As in *Belden*, the Board's failure to ask the right question is "legal error."

b. Wyeth argues that the "facts here differ" because the "pieces of prior art" in *Belden* "in combination taught or suggested all elements of the particular claims." Wyeth Br. 44. But that was not the Board's rationale, *see Chenery*, 318 U.S. at 94, and it is incorrect for the reasons given below, *see* p. 23, *infra*. More fundamentally, it fails to address *Belden*'s logic—and *KSR*'s.

Under those precedents, the proper question is whether the skilled artisan would have understood that applying the claimed improvement technique—here a stabilizing formulation—to the particular recited context would yield a similar improvement in the same fashion. For example, if the invention here concerned styrofoam packing material—long used to inhibit breakage in shipping by stabilizing goods and absorbing impact—no one would ask whether artisans would "modify" styrofoam "to comprise" different items being shipped (*e.g.*, vases or glassware). The question would be whether skilled artisans would understand that styrofoam, because it stabilizes other goods, would stabilize those different items in shipping in the same way. The question is no different if one substitutes "stabilizing formulation" for styrofoam and "polysaccharide-protein conjugate" for vase.

Wyeth next urges that *Belden*'s analysis applies only to common problems or "predictable art[s]." Wyeth Br. 44-45. There is no such restriction in *Belden*'s holding or logic. Regardless, whether or not "vaccine development" is "highly unpredictable," Wyeth Br. 44, the ***stabilization*** of protein-based vaccines—the sub-

ject of the '999 Patent—is not. The Board found that skilled artisans would not "reasonably expect" that Chiron's "'inhibition of silicone-induced protein aggregation'" would vary based on "modifying the polysaccharide-protein conjugate." Appx37-38. And, insofar as Wyeth suggests (at 45) that prior-art references disclosing the polysaccharide-protein conjugates are too far afield from prior-art references addressing the stabilization of such conjugates—that nothing "would motivate a skilled artisan" to combine them—that defies both common sense and the Board's findings on claim 17. *See* pp. 6-9, *supra*.

Finally, Wyeth urges that, "[u]nlike the facts in *Belden*, the Board here did not read an artificial constraint into the asserted prior art." Wyeth Br. 46. But the Board did impose an "artificial constraint" on Chiron: It erroneously limited Chiron by asking whether an artisan would have modified "'the particular ***invention*** [Chiron] is describing,'" rather than considering Chiron "'for everything it ***teaches***'" about stabilizing polysaccharide-protein conjugate compositions. *Belden*, 805 F.3d at 1076. *Belden* is on point—and points to reversal.

II. THE APA, THE PATENT, AND THE RECORD FORECLOSE EFFORTS TO SUSTAIN CLAIM 18 BASED ON THE RECITED 13-VALENT CONJUGATE COMPOSITION

It is unclear what, exactly, the Board meant when it concluded that Merck failed to show that a skilled artisan would have been "motivated . . . to modify" the prior-art stabilizing formulation "in a manner that yields the claimed invention" in

claim 18 "with a reasonable expectation of successfully doing so." Appx40. Time and again, Wyeth paraphrases that assertion. Wyeth Br. 2, 21-22, 26-28, 31, 40-41, 43, 50-51, 57-58. But Wyeth never commits to ***what*** that assertion means. At times, Wyeth appears to argue that the 13 polysaccharide-protein conjugates themselves were not obvious. *See*, *e.g.*, *id.* at 28-30. But it fails to locate that theory within the Board's decision. Wyeth will not say whether the Board meant that artisans would not have expected that the six additional conjugates in claim 18 could be produced successfully, *but see* Merck Br. 54-61, that an artisan would not have conjugated those polysaccharides to a single-carrier CRM_{197} protein, *but see* Merck Br. 56-65, or something else entirely.

Wyeth instead invokes *Chenery* for the proposition that it is "improper" to "speculate as to what rationale the Board may have employed." Wyeth Br. 49. But the necessity of speculating here is exactly why the Board's decision fails. If one cannot discern the Board's rationale, reversal is required. *See Vicor*, 869 F.3d at 1323. Moreover, "[i]f the Board finds that there would have been no motivation to combine . . . , it must expressly say so ***with an adequate explanation***." *Id.* at 1324 (emphasis added). And this Court is restricted to the rationale the agency actually gave. *Chenery*, 318 U.S. at 93-94. Regardless, ***each*** potential interpretation of the Board's decision fails on this record. Wyeth can defend none of them.

A. Wyeth Cannot Recast the Invention as a 13-Valent Conjugate Composition

Initially, Wyeth acknowledges that the purported "invention of claim 18" is directed to "solv[ing]" the "problem[]" of "***aggregation induced by silicone*** when the thirteen-valent pneumococcal conjugate recited in the claim is packaged in siliconized containers." Wyeth Br. 1 (emphasis added). But Wyeth promptly pivots, recasting the purported invention as the 13-valent conjugate ***composition***, rather than the ***formulation*** used to stabilize it. Wyeth devotes pages to its Prevnar13® vaccine's development (describing it as claim 18's "commercial embodiment"). *Id.* at 10; *see id.* at 5-7, 9-10. Wyeth asserts "a long-felt but unmet need" for "conjugate vaccines with higher valency." *Id.* at 1. And it urges that the "successful development of a multivalent conjugate vaccine of higher valency was not a foregone conclusion." *Id.* at 6; *see id.* at 34.

Wyeth has obtained numerous patents for the multivalent compositions in its conjugate vaccines, including an immunogenic composition comprising the 13 polysaccharide-protein conjugates recited in claim 18. *See* Merck Br. 14 (listing patents). But the '999 formulation patent is not one of those patents. As the Board acknowledged, the claimed invention concerns "'***stabili[zing] and inhibit[ing] precipitation*** of immunogenic compositions.'" Appx10 (quoting Appx301, 2:53-55) (emphasis added). There is ***no*** indication in the '999 Patent that the invention is a particular immunogenic composition.

To the contrary, from start to finish, the patent identifies the invention as a "formulation" for inhibiting silicone-induced protein aggregation. The patent's title is "Formulations Which ***Stabilize and Inhibit Precipitation*** of Immunogenic Compositions." Appx290 (emphasis added). The Abstract states that "the invention . . . addresses a need in the art for ***formulations which stabilize and inhibit*** particulate formation (e.g., ***aggregation***, ***precipitation***) of immunogenic compositions" that are "stored in container[s]" with silicone oil. Appx290 (emphasis added). The Field of the Invention (Appx301, 1:22-24), Background of the Invention (Appx301, 1:28-31), Summary of the Invention (Appx301, 2:53-55), and Detailed Description of the Invention (Appx305, 9:66-10:2), ***all*** describe the purported invention the same way. *See* Merck Br. 54-55.

Nowhere does the patent describe the invention as "a multivalent conjugate vaccine of higher valency." Wyeth Br. 6. Nor does the specification suggest the 13-valent conjugate composition is a breakthrough. That composition is matter-of-factly described as an ***example*** of a composition that could be stabilized by the patent's purportedly inventive formulation. *See* Appx305-306, 10:47-11:5 (describing "stability study of the 13vPnC"). The patent does not even disclose how to make the 13 conjugates. It explains only that the "polysaccharides were prepared by standard techniques." Appx310, 19:29-30. And conjugation of the 13

polysaccharides to CRM_{197} was "achieved by conventional means." Appx310, 19:40-41.

Indeed, the Board twice ruled that the patent's claimed "polysaccharide-protein conjugate[s]" do not require any level of immunogenicity—*i.e.*, immune response in the body. Appx4204-4205 (Institution Decision); Appx7-11 (Final Written Decision). It makes no sense to read claim 18 as covering a novel vaccine where the claim does not require that the conjugates be effective as a vaccine. Merck pointed all that out in its opening brief (at 54-55). Wyeth offers no response.

Wyeth seeks to re-characterize the invention as the conjugate composition because it seeks to wield its '999 Patent—which is directed to a stabilizing formulation found to have been obvious—against competitors' novel ***conjugate vaccines***. Claim 18 is an open-ended comprising claim. Appx316, 32:25. It reaches beyond a composition of the recited 13 conjugates, to compositions that add additional conjugates with other polysaccharide serotypes, *see Exergen Corp. v. Wal-Mart Stores, Inc.*, 575 F.3d 1312, 1319 (Fed. Cir. 2009)—such as Merck's 15-valent composition, with serotypes nowhere mentioned in the '999 Patent. Wyeth should not be permitted to block competitors' novel vaccines by rewriting claim 18's obvious application of a known stabilizing formulation.

B. No Reading of the Board's Decision Supports Wyeth's 13-Valent Conjugate Theory

In any event, no reading of the Board's decision will support non-obviousness based on the 13-valent conjugate composition recited in claim 18. Wyeth's arguments confirm that.

1. *Wyeth's Argument That Not All Elements of Claim 18 Are in the Prior Art*

Wyeth urges that "the prior art does not disclose the thirteen-valent conjugate of claim 18." Wyeth Br. 28; *see id.* at 46 ("no disclosure of all elements of claim 18"). That was not the basis of the Board's decision. The decision rests on the assertion that Merck failed to show that a skilled artisan would have been "motivated . . . ***to modify Chiron*** in a manner that yields the claimed invention with a reasonable expectation of successfully doing so." Appx40 (emphasis added). The Court cannot affirm based on a "substitut[e]" rationale the Board never identified. *In re Lee*, 277 F.3d 1338, 1345-46 (Fed. Cir. 2002); *see* pp. 12-13, *supra*. Besides, as Merck explained (at 35), the elements—the 13 polysaccharide serotypes and the CRM_{197} protein—were well known in the prior art. Wyeth's assertion (at 46) that the "elements" of the conjugates cannot be found in "any combination of the prior art" is false.

2. *Performing the Conjugation Was Routine*

Merck explained (at 60-61) that the Board's decision cannot be sustained on the theory that skilled artisans would not reasonably expect to successfully ***make***

the 13 polysaccharide-protein conjugates recited in claim 18. The '999 Patent's specification explains that the "polysaccharides were prepared by standard techniques known to those skilled in the art." Appx310, 19:29-30. And the conjugation of the 13 polysaccharides to CRM_{197} likewise was "achieved by conventional means." Appx310, 19:40-41.

Wyeth objects to using "an applicant's own disclosure against the claimed invention." Wyeth Br. 28. That misses the point. While "[t]he inventor's own path itself never leads to a conclusion of obviousness," *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012), the '999 Patent does not disclose "the inventor's own path" to making the conjugates. It directs skilled artisans to use "standard techniques" already "known" to them. Appx310, 19:29-30.

If the specification states that a technique is standard, the inventor has conceded that the technique is standard. *See PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1362 (Fed. Cir. 2007). In any event, if the Board's rationale was that a skilled artisan who "endeavored" to make the recited conjugate composition would not have had a reasonable expectation of successfully making the conjugates, the Board offered no reasoning and no facts to support that conclusion. Appx44.

3. *The Particular 13 Recited Serotypes Do Not Support Non-Obviousness*

Wyeth appears to invoke the identity of the "thirteen serotypes" recited in claim 18, when "[t]here were more than 90 known serotypes to choose from" at the patent's priority date. Wyeth Br. 33. But the Board nowhere suggested that its decision rested on the choice of serotypes. And the Board acknowledged that Peña expressly discloses "a 13-valent pneumococcal conjugate vaccine with the same serotypes recited by claim 18." Appx44; *see* Merck Br. 56-57 (targeting 13 most common serotypes obvious).

Nor is claim 18 ***limited*** to a composition with those 13 serotypes. As explained above (at 22), claim 18 is an open-ended "compris[ing]" claim, Appx316, 32:25, and thus includes any composition with the recited 13 conjugates, even if it also includes conjugates with additional serotypes, *see Exergen*, 575 F.3d at 1319. Wyeth cannot invoke the choice of 13 particular serotypes to avoid obviousness when the claim is not so limited.

4. *Wyeth's Reliance on the CRM_{197} Carrier Protein*

Wyeth argues that "the thirteen pneumococcal serotype-CRM_{197} conjugates required in claim 18" are not in the prior art because the "individual, unconjugated polysaccharide serotypes," and "the CRM_{197} protein," were in the art "separately." Wyeth Br. 28. But an obviousness challenge permits "combination of elements of prior art." *KSR*, 550 U.S. at 417.

The Board, however, never expressly analyzed whether skilled artisans would have been motivated to conjugate the 13 known polysaccharide serotypes to the known CRM_{197} carrier protein. *See* Merck Br. 57-60. Nor did it address the long history of using CRM_{197} as a single-carrier protein, including with higher-valent vaccine compositions. CRM_{197} had been used as a carrier for polysaccharide-protein conjugate vaccines as early as 1987—nearly two decades before the '999 Patent's 2006 priority date. Appx1113-1119. Chiron teaches that CRM_{197} is "particularly preferred" when conjugating pneumococcal serotypes. Appx901, 3:23-24. The Board offered no reason why a skilled artisan would not have been motivated to use that "particularly preferred" protein.

Again departing from the Board's rationale, Wyeth urges that "the text of Chiron" does not suggest that CRM_{197} is particularly preferred when conjugating pneumococcal serotypes. Wyeth Br. 54; *see id.* at 22-23. That is baffling. Chiron declares that its formulation is "preferably" used for prevention of disease caused by "pneumococcus." Appx904, 3:32-35. It continues: "Where a saccharide . . . antigen is used, it is preferably conjugated to a carrier protein in order to enhance immunogenicity . . . . The ***CRM_{197}*** diphtheria toxoid ***is particularly preferred***." Appx901, 3:20-23 (emphasis added).[3] Chiron is clear that CRM_{197} is particularly preferred when conjugating pneumococcal serotypes.

[3] Pneumococcal serotypes are saccharide antigens. *See* Appx900, 2:15.

Wyeth argues that "the prior art was trending toward a mixed carrier approach." Wyeth Br. 24, 35. But the Board did not offer that as a rationale. *See Power Integrations*, 797 F.3d at 1326. Regardless, Merck did not bear the burden to show that a single-carrier approach with CRM_{197} was "'the ***best*** option, only that it [was] a ***suitable*** option from which the prior art did not teach away.'" *Bayer Pharma AG v. Watson Labs., Inc.*, 874 F.3d 1316, 1328 (Fed. Cir. 2017) (quoting *Par Pharm., Inc. v. TWi Pharm., Inc.*, 773 F.3d 1186, 1197-98 (Fed Cir. 2014)) (emphasis in original). Conjugating the polysaccharides to CRM_{197} was at least a "***suitable*** option."

As Merck pointed out (at 58-61), the prior art clearly reflects that ***Wyeth*** was pursuing CRM_{197} as a single-carrier protein. Each of the 7 pneumococcal serotypes in Wyeth's Prevnar® are "conjugated to the CRM_{197} carrier protein." Appx695-696. Chiron and Peña disclose that Wyeth's 9-valent vaccine uses CRM_{197} as its sole carrier protein. Appx901, 2:15 (citing Appx1894 (Rubin 2000)); Appx995. Other sources disclose that Wyeth's 9- and 11-valent vaccines used CRM_{197} as the sole carrier protein. *See* Appx1223 (Obaro 2002) ("[e]ach polysaccharide" in Wyeth's 9-valent vaccine "was coupled independently to CRM_{197}"); Appx1232 (Overturf 2002) ("polysaccharides conjugated to . . . CRM_{197}" in Wyeth's "11-valent" vaccine); Appx1243 (O'Brien 2004) (same). Wyeth does not contest that.

Wyeth argues that "Merck offered no evidence as to whether Rubin was properly incorporated by reference into the Chiron disclosure." Wyeth Br. 23. And Wyeth objects to consideration of Obaro, Overturf, and O'Brien on the theory that they "were not part of any of the grounds in either IPR." *Id.* Wyeth made no such arguments below. "[B]y failing to present them to the Board," Wyeth has "waived them." *Bradium Techs. LLC v. Iancu*, 923 F.3d 1032, 2019 WL 2079174, at *11 (Fed. Cir. May 13, 2019).

Regardless, prior art "can legitimately serve" as background "to document the knowledge that skilled artisans would bring to bear in reading the prior art identified as producing obviousness," whether or not the reference had "been identified at the petition stage as one of the pieces of prior art defining a combination for obviousness." *Ariosa*, 805 F.3d at 1365. That is how the challenged references were used here. Merck's expert explained that, based on Rubin, a skilled artisan would have understood that Wyeth's 9-valent vaccine was "conjugated to only the single CRM_{197} carrier." Appx697 (Kasper ¶45). He explained, based on Obaro, Overturf, and O'Brien, that the "literature" reported that "Wyeth's 9- and 11-valent conjugate vaccines used only CRM_{197} as a carrier protein." *Id.* The Board was required to consider those disclosures and explain why, if ***Wyeth itself*** was pursuing 9- and 11-valent vaccines using CRM_{197} alone, skilled artisans would not have been motivated to do so for a 13-valent vaccine. Dismissing that as a "'natural

progression'" that "resembles" hindsight, Appx40; Wyeth Br. 23-24, does not excuse the Board from explaining why skilled artisans would think that CRM_{197} works for 7-, 9-, and 11-valent conjugates but not for 13.

But even that does not matter: It was known that ***Wyeth's 13-valent vaccine***—which Wyeth claims is the commercial embodiment of claim 18, Wyeth Br. 9—***used CRM_{197}*** as a single-carrier protein. Merck's expert explained that, "when Wyeth applied for a facility license to produce the 13-valent conjugate vaccine in around ***2003***," Ireland's Environmental Protection Agency ("EPA") "noted that ***CRM_{197}*** would be the ***only carrier protein*** for the 7-, 9- and ***13-valent*** versions." Appx697-698 (Kasper Decl.) (emphasis added); *see also* Appx10296.

Wyeth does not dispute that disclosure's contents. It characterizes reliance on the Ireland EPA document as "a new argument on appeal." Wyeth Br. 55. But Merck made that very argument below. Appx248; *see generally* Appx17567-17571. ***Wyeth*** "challenged the admissibility" of the Ireland EPA document before the Board, complaining about "[c]haracteristics of the document," such as lack of a date or signature page. Wyeth Br. 55. But the document is ***Wyeth's own application*** for a license to manufacture the 13-valent version of its Prevnar® vaccine. Wyeth does not deny the document's accuracy or authenticity. And the document is posted on an Irish government website. *See* Appx17568. The Board could not have concluded that using CRM_{197} as a single-carrier protein for the 13

serotypes in claim 18 made the combination non-obvious without addressing a document that disclosed precisely that combination.[4]

III. THE COURT CANNOT AFFIRM THE BOARD'S DECISION BASED ON WYETH'S NEW ARGUMENTS

Wyeth posits two additional non-obviousness theories: (1) that concerns about "immune interference," or "CIES," weighed against using CRM_{197} as a single-carrier protein; and (2) that secondary considerations (*e.g.*, "long-felt but unmet need," "commercial success") support non-obviousness. Wyeth Br. 35-39. But Wyeth concedes that "[t]he Board did not reach Wyeth's argument regarding immune interference," and likewise admits that the Board issued its decision "without addressing secondary considerations." *Id.* at 36, 56-57. Because the Board did not reach those issues, this Court cannot affirm on either ground. *Chenery*, 318 U.S. at 93-94. Wyeth thus asks for a "remand" for "factual findings that were not made by the PTAB below." Wyeth Br. 58-59.

Wyeth nonetheless appears to argue that the "Court may consider" its alternative theories because the Board's decision "'can be defended . . . on any ground that is supported by the record.'" Wyeth Br. 36-37 (quoting *Rexnord*

[4] The Board did not exclude the Ireland EPA document. It declined to rely on the document as "cumulative to previously submitted evidence, or related to issues disposed upon other bases." Appx48. But the document would not have been "cumulative" on whether skilled artisans would have selected CRM_{197} as a single-carrier for the 13 recited polysaccharides in claim 18—it was the clearest disclosure of that combination. That suggests the Board's decision rested "upon other bases." Appx48.

Indus., LLC v. Kappos, 705 F.3d 1347, 1356 (Fed. Cir. 2013)). That contradicts *Chenery* and this Court's precedent applying it. *See* pp. 12-13, *supra*. Although Wyeth invokes *Rexnord*, that case concerns the standards for internal PTO review of patent-examiner decisions. 705 F.3d at 1347, 1355-56. Relying on the standard for appellate review of district court decisions, this Court allows the appellee ***before the Board*** to defend an examiner decision on any ground supported by the record. *Id.* at 1356. But that rule does not apply to judicial review of final agency decisions. For this Court's review of agency decisions, *Chenery* is binding. And *Chenery* precludes affirming on grounds the agency itself did not rely upon. 318 U.S. at 93-94.

Merck has already explained at length (at 62-65) why Wyeth's arguments regarding immune interference fail regardless. That includes Wyeth's expert's admission that "CIES is not something that will prevent you from developing any vaccine with any valency." Appx7159-7160, 77:25-78:21. And it is hard to see how the purported desire to avoid some degree of immune interference could justify upholding a patent that requires no particular degree of immunogenicity. Appx7-11; Merck Br. 63-64. Likewise, Wyeth's arguments about secondary considerations are unrelated to the '999 Patent. "For objective evidence of secondary considerations to be accorded substantial weight, its proponent must establish a nexus between the evidence and the merits of the claimed invention." *In re Huai-*

Hung Kao, 639 F.3d 1057, 1068 (Fed. Cir. 2011) (quotation marks and emphasis omitted). The secondary considerations Wyeth invokes relate to the success of its Prevnar13® vaccine, *see* Wyeth Br. 37, not the stabilizing formulation that is the '999 Patent's purported invention, *see* pp. 20-22, *supra*.

CONCLUSION

The Board's decision upholding claim 18 of the '999 Patent should be reversed.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I certify that today, May 31, 2019, I electronically filed the foregoing Reply Brief for Appellant Merck Sharp & Dohme Corp. with the Clerk of the Court for the U.S. Court of Appeals for the Federal Circuit using the appellate CM/ECF system. All participants in the case are registered CM/ECF users and will be served by the appellate CM/ECF system.

May 31, 2019 /s/ Jeffrey A. Lamken

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