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Paper 12
Entered: September 9, 2019

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. REDDY'S LABORATORIES, INC.,[1]
Petitioner

v.

HORIZON PHARMA USA, INC. and NUVO PHARMACEUTICALS (IRELAND) DESIGNATED ACTIVITY COMPANY,
Patent Owners.

Case IPR2018-00272
Patent 9,393,208 B2

Before MICHELLE N. ANKENBRAND, *Acting Vice Chief Administrative Patent Judge*, TONI R. SCHEINER, and DEBRA L. DENNETT, *Administrative Patent Judges.*

DENNETT, *Administrative Patent Judge*.

FINAL WRITTEN DECISION

[1] We terminated the proceeding between Petitioner Mylan Pharmaceuticals Inc. and Patent Owners by Order on August 12, 2019. Paper 73. Petitioner Dr. Reddy's Laboratories, Inc. ("Dr. Reddy's") from IPR2018-01341 was joined as Petitioner to this proceeding on April 1, 2019. Paper 36. Dr. Reddy's remains as a Petitioner in this case.

Finding Claims 1–7 Unpatentable
35 U.S.C. § 318(a); 37 C.F.R. § 42.73

Denying as Moot Petitioner's Motion to Exclude
and Dismissing-in-part as Moot and Denying-in-part
Patent Owners' Motion to Exclude
37 C.F.R. § 42.64(c)

I. INTRODUCTION

This is a Final Written Decision in an *inter partes* review challenging the patentability of claims 1–7 (collectively, the "challenged claims") of U.S. Patent No. 9,393,208 B2 (Ex. 1001, "the '208 patent"). We have jurisdiction under 35 U.S.C. § 6. For the reasons that follow, we determine that Petitioner Dr. Reddy's Laboratories, Inc. ("Dr. Reddy's" or "Petitioner") demonstrates, by a preponderance of the evidence, that the challenged claims are unpatentable.

A. Procedural History

The procedural history of this proceeding is unusually complex, involving joinder; bankruptcy; change in ownership of the patent; settlement between the original Petitioner, Mylan Pharmaceuticals, Inc. ("Mylan") and Patent Owners; and a decision on the merits in the trial between the remaining Petitioner after joinder, Dr. Reddy's, and Patent Owners.

Mylan filed a Petition (Paper 2, "Pet.") requesting an *inter partes* review of claims 1–7 of the '208 patent under 35 U.S.C. § 311. Mylan supported its Petition with the testimony of David C. Metz, M.D. (Ex. 1002) and Michael Mayersohn, Ph.D. (Ex. 1003). We instituted trial on June 14, 2018, to determine whether:

1. Claims 1–7 of the '208 patent are unpatentable under 35 U.S.C. § 102 as anticipated by the '285 patent[2];

2. Claims 1–7 of the '208 patent are unpatentable under 35 U.S.C. § 103 as obvious over the '285 patent; and

3. Claims 1–7 of the '208 patent are unpatentable under 35 U.S.C. § 103 as obvious over the combination of the '285 patent with the EC-Naprosyn label[3] and Howden 2005.[4]

Paper 9 ("Institution Decision" or "Inst. Dec."), 24.

On July 2, 2018, Dr. Reddy's filed a Petition requesting an *inter partes* review of claims 1–7 of the '208 patent in IPR2018-01341 ("1341 IPR") and filed a Motion for Joinder to this proceeding. 1341 IPR, Papers 2, 3. In its motion requesting joinder, Dr. Reddy's represented that it had filed substantively the same Petition as Mylan and agreed to take an "understudy" role to Mylan, accepting Mylan's arguments and experts, and agreeing to take an active role only if Mylan dropped out of the proceedings. 1341 IPR, Paper 3, 1, 7.

Shortly thereafter, on August 28, 2018, Patent Owner Pozen Inc. ("Pozen") filed a Suggestion of Bankruptcy in this case, the effect of which automatically stayed this proceeding pursuant to 11 U.S.C. § 362. Paper 12. We suspended all deadlines in this proceeding on August 31, 2018. Paper 13.

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[2] U.S. Patent 8,557,285 B2, filed Aug. 23, 2011, issued Oct. 15, 2013, to John R. Plachetka (Ex. 1005, "the '285 patent").

[3] Prescription Drug Label for EC-Naprosyn® and other Naprosyn® formulations (Ex. 1009, "EC-Naprosyn label").

[4] C.W. Howden, *Review article: immediate-release proton-pump inhibitor therapy–potential advantages*, 22 ALIMENT. PHARMACOL. THER. 25–30 (2005) (Ex. 1006, "Howden 2005").

On January 4, 2019, Mylan filed an order from the bankruptcy court approving the sale of certain of Pozen's assets, including the '208 patent, to Nuvo Pharmaceuticals (Ireland) Designated Activity Company ("Nuvo"), which lifted the automatic stay of this proceeding. Ex. 1051, 1, 19 (identifying Nuvo as the purchaser). On January 16, 2019, we received Mandatory Notices identifying Nuvo as a real party-in-interest in this proceeding. Paper 16. On January 25, 2019, we issued an order modifying the schedule and the case caption to reflect the change in ownership of the '208 patent to Horizon Pharma USA, Inc. ("Horizon") and Nuvo (collectively, "Patent Owners"). Paper 20.

Patent Owners filed a Response on March 1, 2019.[5] Paper 32 ("PO Resp."). We granted Dr. Reddy's motion to join this proceeding on April 1, 2019. Paper 36. Mylan and Dr. Reddy's filed a Reply on May 8, 2019 (Paper 49, "Pet. Reply"), and Patent Owners filed a Sur-reply on May 20, 2019 (Paper 52, "PO Sur-reply"). On June 3, 2019, pursuant to 37 C.F.R. § 42.100(c), we adjusted the one-year pendency of this proceeding due to joinder. Paper 60.

Patent Owners filed a motion to seal certain exhibits. Paper 31 ("PO Motion to Seal"). Both parties also filed motions to exclude, which have been fully briefed. *See* Papers 56, 57, 66 (briefing related to Petitioner's Motion to Exclude); Papers 55, 58, 65 (briefing related to Patent Owners' Motion to Exclude).

We held a hearing on June 14, 2019, and entered the transcript of the hearing into the record. Paper 70 ("Tr."). On July 29, 2019, Mylan and Patent Owners filed a Joint Motion to Terminate Petitioner Mylan from the proceeding. Paper 71.

[5] Patent Owners' rely on the expert testimony of Dr. David R. Taft (Ex. 2025) and Dr. David A. Johnson (Ex. 2026) to support the Response.

We granted the motion and terminated Mylan from this proceeding on August 12, 2019. Paper 73.

B. Related Matters

Mylan previously filed a petition requesting an *inter partes* review of U.S. Patent No. 9,220,698 ("the '698 patent"), case IPR2017-01995 ("1995 IPR"). 1995 IPR Petition 2. Mylan asserted that the '698 patent and '208 patent are "related" (*id.*), and Patent Owners acknowledged that the '208 patent "claims, or may claim, the benefit of priority" to the same application to which the '698 patent claims priority (1995 IPR Paper 4, 2). On March 8, 2018, we instituted an *inter partes* review of all claims challenged on all asserted grounds in the 1995 IPR. *See* 1995 IPR, Paper 18. On August 14, 2018, we joined Dr. Reddy's to the 1995 IPR. We terminated the 1995 IPR on March 27, 2019 (1995 IPR Paper 71), and denied Dr. Reddy's Request for Rehearing of our termination decision on August 12, 2019 (1995 IPR Paper 77).

C. The '208 Patent (Ex. 1001)

The '208 patent, titled "Method for Delivering a Pharmaceutical Composition to Patient in Need Thereof," issued July 19, 2016. Ex. 1001. The '208 patent relates to methods for delivering a pharmaceutical composition of naproxen and esomeprazole in a unit dose form. *Id.* at col. 1, ll. 13–18.

Nonsteroidal anti-inflammatory drugs (NSAIDs) such as naproxen are used widely to treat pain and inflammation, but many NSAIDs are associated with gastrointestinal complications. *Id.* at col. 1, ll. 19–24. The presence of acid in the stomach and upper small intestine is a major factor in development of gastrointestinal disease in patients taking NSAIDs. *Id.* at col. 1, ll. 24–26.

Esomeprazole is a proton pump inhibitor ("PPI"). PPIs inhibit gastric acid secretion, and thus raise the gastrointestinal tract pH. *Id*. at col. 1, ll. 30–33. PPIs

used in conjunction with NSAIDs reduce the risk of gastrointestinal injury. *Id.* at col. 1, ll. 27–30.

The specification explains that administering formulations providing certain unit dosages of PPIs and naproxen may produce desired pharmacodynamic ("PD") responses and pharmacokinetic ("PK") values, such as an intragastric pH of about 4 or greater, and a plasma level of naproxen that is efficacious. *Id.* at col. 1, ll. 34–37, ll. 46–48. The specification discloses the results of a clinical trial comparing PD responses and PK values resulting from twice daily orally-administered formulations of enteric coated naproxen 500 mg combined with non-enteric coated esomeprazole in dosages of 10, 20, and 30 mg, with twice daily orally-administered 500 mg non-enteric coated naproxen and once daily orally-administered enteric coated esomeprazole. *Id.* at col. 24, l. 5–col. 46, l. 30.

The claims recite targeting naproxen and esomeprazole PK profile ranges for C_{max}, T_{max}, and AUC.[6]

D. Illustrative Claim

Petitioner challenges claims 1–7 of the '208 patent. Claim 1, the sole independent claim, is illustrative of the claimed subject matter and recites:

> 1. A method for delivering a pharmaceutical composition to a patient in need thereof, comprising:
>
> orally administering to a patient an AM unit dose form and, 10 hours (±20%) later, a PM unit dose form, wherein:
>
> the AM and PM unit dose forms each comprises:

[6] C_{max} refers to the maximum plasma concentration of the drug administered, T_{max} (or t_{max}) refers to the time to the maximum plasma concentration of the drug administered, and AUC refers to the area under the plasma-concentration time curve from time zero to a specified time after drug administration. Ex. 1001, Table 1.

i) naproxen, or a pharmaceutically acceptable salt thereof, in an amount to provide 500 mg of naproxen, and

ii) esomeprazole, or a pharmaceutically acceptable salt thereof, in an amount to provide 20 mg of esomeprazole;

said esomeprazole, or pharmaceutically acceptable salt thereof, is released from said AM and PM unit dose forms at a pH of 0 or greater,

the AM and PM unit dose forms target:

i) a pharmacokinetic (pk) profile for naproxen where:

a) for the AM dose of naproxen, the mean C_{max} is 86.2 μg/mL (±20%) and the median T_{max} is 3.0 hours (±20%); and

b) for the PM dose of naproxen, the mean C_{max} is 76.8 μg/mL (±20%) and the median T_{max} is 10 hours (±20%); and

ii) a pharmacokinetic (pk) profile for esomeprazole where:

a) for the AM dose of esomeprazole, the mean area under the plasma concentration-time curve from when the AM dose is administered to 10 hours (±20%) after the AM dose is administered ($AUC_{0\text{-}10,am}$) is 1216 hr*ng/mL (±20%),

b) for the PM dose of esomeprazole, the mean area under the plasma concentration-time curve from when the PM dose is administered to 14 hours (±20%) after the PM dose is administered ($AUC_{0\text{-}14,pm}$) is 919 hr*ng/mL (±20%), and

c) the total mean area under the plasma concentration-time curve for esomeprazole from when the AM dose is administered to 24 hours (±20%) after the AM dose is

> administered (AUC_{0-24}) is 2000 hr*ng/mL (±20%); and
>
> the AM and PM unit dose forms further target a mean % time at which intragastric pH remains at about 4.0 or greater for about a 24 hour period after reaching steady state that is at least about 60%.

Ex. 1001, col. 46, l. 33–col. 47, l. 9.

II. DISCUSSION

Petitioner Dr. Reddy's bears the burden of proving unpatentability of the challenged claims, and that burden of persuasion never shifts to Patent Owners. *Dynamic Drinkware, LLC v. Nat'l Graphics, Inc.*, 800 F.3d 1375, 1378 (Fed. Cir. 2015). To prevail, Petitioner must establish the facts supporting its challenge by a preponderance of the evidence. 35 U.S.C. § 316(e); 37 C.F.R. § 42.1(d). Below, we explain how Petitioner has met its burden with respect to the challenged claims.

A. Principles of Law

A claim is unpatentable under 35 U.S.C. § 103(a) if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). Obviousness is a question of law based on underlying determinations of fact. *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966); *Richardson-Vicks, Inc. v. Upjohn Co.*, 122 F.3d 1476, 1479 (Fed. Cir. 1997). The underlying factual determinations include: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level of skill in the art; and (4) objective evidence of nonobviousness, i.e., secondary considerations. *See Graham*, 383 U.S. at 17–18. Subsumed within the *Graham* factors are the requirements that all claim limitations

be found in the prior art references and that the skilled artisan would have had a reasonable expectation of success in combining the prior art references to achieve the claimed invention. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361 (Fed. Cir. 2007). "Obviousness does not require absolute predictability of success . . . all that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903–4 (Fed. Cir. 1988).

Moreover, "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR*, 550 U.S. at 416. "If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability." *Id.* at 417.

B. Level of Ordinary Skill in the Art

We consider each asserted ground of unpatentability in view of the understanding of a person of ordinary skill in the art. Petitioner's declarants, Dr. Metz and Dr. Mayersohn, testify that a person of ordinary skill in the art would have had the knowledge of a collaboration of a pharmacologist or pharmacokineticist having a Ph.D. degree or equivalent training, or a M.S. degree with at least 2 years of some experience in dosage form design and in *in vitro* and *in vivo* evaluation of dosage form performance, and a medical doctor having at least 2 years of practical experience treating patients in the gastroenterology field. Ex. 1002 (Metz Decl.) ¶ 24, and Ex. 1003 (Mayersohn Decl.) ¶ 19. Dr. Metz offers his opinion from the perspective of a medical doctor in the field of gastroenterology with at least 2 years of experience treating patients as of September 9, 2008. Ex. 1002 ¶ 24. Dr. Mayersohn offers his opinion from the perspective of a pharmacologist with the training described above. Ex. 1003 ¶¶ 19–20.

We adopted Petitioner's definition of the person of ordinary skill in the art in our Institution Decision, and Patent Owners' experts apply that definition. *See* Ex. 2025 ¶ 34; Ex. 2026 ¶ 53.

Patent Owners contend that Petitioner's declarants do not meet Petitioner's hypothetical construct of a person of ordinary skill in the art because they did not consult with each other in providing their opinions on the patentability of the '208 patent. Paper 32 ¶¶ 20–21. Dr. Metz, a medical doctor, testifies that he collaborated with Dr. Mayersohn, a pharmacologist, by providing an opinion which, when combined with that of Dr. Mayersohn, concludes that the challenged claims are unpatentable. Ex. 1059 (Metz Reply Decl.) ¶ 8. Dr. Mayersohn testifies that Patent Owners take an overly formalistic reading of the proposed definition of a person of ordinary skill in the art, and that the definition simply means that both a medical doctor and a pharmacologist or pharmacokineticist "have a contribution to make in understanding the claimed subject matter." Ex. 1074 (Mayersohn Reply Dec. ¶ 9.

We adopt the following as the level of ordinary skill in the art: person(s) having the knowledge of a collaboration of a pharmacologist or pharmacokineticist having a Ph.D. degree or equivalent training, or a M.S. degree with at least 2 years of some experience in dosage form design and in *in vitro* and *in vivo* evaluation of dosage form performance, and a medical doctor having at least 2 years of practical experience treating patients in the gastroenterology field. We do not find that one individual would be required to satisfy all of the above requirements or necessarily would have to consult with a counterpart before forming an opinion, as the art involved represents two different areas of study, yet reflects the skill in the art. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001).

Based on their stated qualifications, we find: (1) Dr. Mayersohn is qualified to opine from the perspective of the pharmacologist or pharmacokineticist at the time of the invention (*see* Ex. 1003 ¶¶ 2–9 (Dr. Mayersohn's statement of qualifications) and Exhibit A (curriculum vitae)), and (2) Dr. Metz is qualified to opine from the perspective of a medical doctor with at least two years of practical experience treating patients in the gastroenterology field at the time of the invention (*see* Ex. 1002 ¶¶ 2–10 (Dr. Metz's statement of qualifications) and Exhibit A (curriculum vitae)); (3) Dr. Taft is qualified to opine from the perspective of the pharmacologist or pharmacokineticist at the time of the invention (*see* Ex. 2025 ¶¶ 2–12 (Dr. Taft's statement of qualifications) and Exhibit 1 (curriculum vitae)); and (4) Dr. Johnson is qualified to opine from the perspective of a medical doctor with at least two years of practical experience treating patients in the gastroenterology field at the time of the invention (*see* Ex. 2026 ¶¶ 1–15 (Dr. Johnson's statement of qualifications) and Exhibit A (curriculum vitae)).

C. Claim Construction

The Board interprets claims in an unexpired patent using the "broadest reasonable construction in light of the specification of the patent." 37 C.F.R. § 42.100(b) (2016)[7]; *Cuozzo Speed Techs., LLC v. Lee*, 136 S. Ct. 2131, 2144–46

[7] The Office recently changed the claim construction standard applicable to an *inter partes* review. *See* Changes to the Claim Construction Standard for Interpreting Claims in Trial Proceedings Before the Patent Trial and Appeal Board, 83 Fed. Reg. 51,340 (Oct. 11, 2018). The rule changing the claim construction standard, however, does not apply to this proceeding because Petitioner filed its Petition before the effective date of the final rule, i.e., November 13, 2018. *Id.* at 51,340 (rule effective date and applicability date), 51,344 (explaining how the Office will implement the rule).

(2016). Under that standard, claim terms are given their ordinary and customary meaning in view of the specification, as would be understood by one of ordinary skill in the art at the time of the invention. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Any special definitions for claim terms must be set forth in the specification with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994).

Petitioner proposes construction of the claim limitation "target," contending that the broadest reasonable construction of "target" is "with the goal of obtaining," which follows from the term's plain meaning. Pet. 13–14. According to Petitioner, the intrinsic evidence does not expressly ascribe any particular meaning to "target," and the term is not a term of art in the patent's field. *Id.* at 15 (citing Ex. 1003 ¶¶ 66, 74–78).

In the Institution Decision, we generally adopted Petitioner's proposed construction of the "target," limitation, but altered the meaning for grammatical purposes, determining that "target" means to "have or set the goal of obtaining." Inst. Dec. 9–10.

Patent Owners do not offer a construction of "target." *See generally* PO Resp. Rather, Patent Owners argue that in the related district court litigation, the court granted Petitioner's motion for summary judgment that the '208 patent is invalid as indefinite in its use of the term "target." *Id.* at 16. Patent Owners argue that the Board, therefore, should not consider the prior art challenges made here. *Id.* at 19.

We do not agree. Indeed, we previously addressed Patent Owners' argument in this regard in a decision denying a motion to terminate that we permitted Patent Owners to file after the district court's grant of summary judgment. *See* Paper 35.

As we explained in that decision, indefiniteness under 35 U.S.C. § 112 is outside our statutory authority in an *inter partes* review. *Id.* at 5.[8]

We remain persuaded that our construction in the Institution Decision is the broadest reasonable construction of the term "target" consistent with the specification of the '208 patent and its file history. Thus, we determine that the term "target" means to "have or set the goal of obtaining."

No other claim term requires express construction. *See Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999) ("only those terms need be construed that are in controversy, and only to the extent necessary to resolve the controversy").

D. Obviousness of the Challenged Claims Over the '285 Patent

Petitioner asserts that the subject matter of claims 1–7 of the '285 patent would have been obvious over the '285 patent. Pet. 43–48. Patent Owners disagree. Resp. 34–40. Before turning to Petitioner's challenge, we provide a brief background of the '285 patent and address several preliminary issues that the parties raise, including whether the '285 patent qualifies as prior art.

1. The '285 Patent (Ex. 1005)

The '285 patent is directed generally to a pharmaceutical composition in unit dosage form suitable for oral administration to a patient. Ex. 1005, col. 3, ll. 27–29. The '285 patent refers to a "unit dosage form" as a single entity for drug administration, such as a tablet or capsule combing both an acid inhibitor and an NSAID. *Id.* at col. 4, ll. 42–45. The composition contains an acid inhibitor in an

[8] Patent Owners did not request rehearing of that decision. Tr. 19:21–20:7. Having already decided the issue, we do not further address Patent Owners' argument here.

amount effective to raise the gastric pH of a patient to at least 3.5, preferably to at least 4, and more preferably to at least 5. *Id.* at col. 3, ll. 29–32. The '285 patent identifies esomeprazole and omeprazole as among the preferred PPIs that may be used effectively as acid inhibitors. *Id.* at col. 3, ll. 44–50. The '285 patent also identifies naproxen and naproxen sodium as long-acting NSAIDs useful in the invention, having half-lives of about 12 to 15 hours. *Id.* at col. 6, ll. 29–33.

Example 6 discloses a multi-layer tablet dosage form comprising 500 mg naproxen sodium, an enteric film coat that dissolves only when the local pH is above 4, and 5 mg immediate-release omeprazole. *Id.* at col. 16, ll. 1–54, col. 17, l. 36. Examples 7 and 8 disclose coordinated delivery dosage forms containing, respectively, 20 mg immediate release omeprazole and 250 mg delayed release naproxen, and 10 mg immediate release omeprazole and 250 mg delayed release naproxen. *Id.* at col. 17, l. 49–col. 20, l. 36. Example 9 discloses a clinical study in which one group of participants received twice daily 20 mg omeprazole followed by 550 mg naproxen sodium. *Id.* at col. 20, ll. 45–50.

In addition, the '285 patent claims pharmaceutical compositions in unit dosage form comprising therapeutically effective amounts of esomeprazole, wherein at least a portion of the esomeprazole is not surrounded by an enteric coating, and enteric coated naproxen. *Id.* at col. 22, ll. 8–29.

2. The '285 Patent as § 102(e)[9] Prior Art

Before turning to the merits of Petitioner's obviousness challenge, we address whether the '285 patent is prior art to the '208 patent. Petitioner has the

[9] Because the application for the '208 patent was filed before the March 16, 2013, effective date of the Leahy-Smith America Invents Act ("AIA"), we refer to the pre-AIA version of the statute.

initial burden of production to show that the ’285 patent is prior art to the challenged claims under § 102(e). *See Dynamic Drinkware*, 800 F.3d at 1378–79 (burden of production regarding availability of a reference as prior art placed initially on a petitioner). If Petitioner meets its burden of production, then the burden of production shifts to Patent Owners to come forward with evidence that the ’285 patent is not prior art. *See id.* at 1379.

Petitioner contends that the ’285 patent is prior art to the ’208 patent under 35 U.S.C. § 102(e) because it is a “patent granted on an application for patent *by another* filed in the United States before the invention by the applicant for patent.” Pet. 20; Pet. Reply 3 (quoting 35 U.S.C. § 102(e) (emphasis added)). Petitioner points to the ’285 patent’s identification of John R. Plachetka as the sole inventor, and the ’208 patent’s identification of Brian Ault, Everardus Orlemans, John R. Plachetka, and Mark Sostek as inventors as evidence that the two patents have different inventive entities. Pet. Reply. 3–4; *see also* Ex. 1001, [72] (’208 patent); Ex. 1005, [72] (’285 patent). Petitioner also supports its argument with citations to the trial and deposition transcripts of Drs. Orlemans and Sostek. Pet. Reply 4 (citing Ex. 2018, 21:6–14, 22:7–7 (Dr. Orlemans’ testimony describing his contributions to the ’208 patent); Ex. 2019, 130:14–24 (Dr. Sostek’s testimony describing his contributions to the ’208 patent)).

Patent Owners argue that Petitioner has not met its burden to establish by a preponderance of the evidence that the ’285 patent qualifies as § 102(e) prior art. PO Resp. 21–22; PO Sur-reply 5–8. Specifically, Patent Owners counter that what is significant in comparing inventive entities “is not merely the differences in the listed inventors, but whether the portions of the references relied on as prior art, and the subject matter of the claims in question represent the work of a common

inventive entity." PO Resp. 23 (citing *Riverwood Int'l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1356 (Fed. Cir. 2003)).

Patent Owners also rely on *Duncan Parking Technology, Inc. v. IPS Group*, 914 F.3d 1347 (Fed. Cir. 2019), to suggest that Petitioner failed to establish that the '285 patent is work "by another." PO Sur-reply 6.

In *Duncan Parking* the Federal Circuit explained, in deciding whether a reference patent is "by another" for the purposes of § 102(e):

> [T]he Board must (1) determine what portions of the reference patent were relied on as prior art to anticipate the claim limitations at issue, (2) evaluate the degree to which those portions were conceived "by another," and (3) decide whether that other person's contribution is significant enough, when measured against the full anticipating disclosure, to render him a joint inventor of the applied portions of the reference patent.

Duncan Parking, 914 F.3d at 1358. The facts before us here, however, differ from those in *Duncan Parking*. In *Duncan Parking*, the Federal Circuit determined whether a certain person (Schwarz), who was a named inventor on the asserted prior art but not on the challenged patent, had made significant contributions to the relied-upon disclosures of the asserted prior art, thereby making him an inventor of the relied-upon disclosures of that patent, and, in turn, making the relied-upon disclosures work "by another" and hence prior art to the challenged patent. *Id.* at 1357–59.

Here, in contrast, there is no dispute that the work in the '285 patent asserted as prior art is Dr. Plachetka's alone. *See, e.g.*, PO Sur-reply 6; Ex. 2082, 46:21–24. We need to determine instead whether Drs. Ault, Sostek, and Orlemans made significant contributions to the challenged claims of the '208 patent. If so, then the '285 patent is work "by another" and prior art under § 102(e).

As we note above, Petitioner points to the different inventors listed on the '285 patent and the '208 patent and cites to certain testimony regarding Drs. Orlemans', Sostek's, and Ault's contributions to the '208 patent. Patent Owners do not disagree that all four named inventors contributed to the '208 patent. Indeed, Patent Owners cite to the testimony of Dr. Plachetka in the related district court litigation as evidence that he was responsible for the design and dosage form that exhibits coordinated release of the two active ingredients. PO Resp. 24 (citing Ex. 2015 (Plachetka trial testimony) at 25:5–15). Patent Owners further acknowledge that Dr. Plachetka collaborated with "AstraZeneca" to further refine the dosage form and relied on Dr. Orlemans and AstraZeneca scientists, Drs. Ault and Sostek, to design and implement a series of clinical trials, including PN400–104, the clinical trial that provided the PK/PD data included in the claims of the '208 patent. *Id.*

Comparing "not merely the differences in the listed inventors, but whether the portions of the references relied on as prior art, and the subject matter of the claims in question represent the work of a common inventive entity," *Riverwood*, 324 F.3d at 1356, we find that the evidence demonstrates that Dr. Plachetka did not invent the subject matter of the '208 patent challenged claims alone. Rather, the evidence supports that Drs. Plachetka, Orlemans, Ault, and Sostek are co-inventors of the subject matter of the challenged claims of the '208 patent and, thus, a different inventive entity than solely Dr. Plachetka, invented the relied-upon subject matter of the '285 patent.

Patent Owners urge that Petitioner's argument that the '285 patent and the '208 patent "describe the work of different inventive entities is incompatible with [Petitioner's] position that the '285 and '208 patents claim the same invention,"

and that Petitioner states that the '208 patent claims the precise formulation and precise method of administration disclosed in the '285 patent. PO Resp. 24, 25.

However, Patent Owners misstate Petitioner's position. Specifically, Petitioner contends:

> Drs. Orlemans, Ault, and Sostek—named inventors of the '208 patent—designed and implemented the trials that led to recognizing the PK properties of the formulation claimed in the '208 patent. Dr. Orlemans testified that he "helped with the design of the study," which was "one of the first studies that was done actually to find out what the effect is of the tablet on intragastric pH . . . ." Ex. 2018, 21:6-14, 22:7-8. Dr. Sostek testified that several people, including he and Dr. Orlemans, "contributed . . . as a team in designing the study." Ex. 2019, 130:14-24. Dr. Sostek further testified that Drs. Orlemans and Ault contributed to "the clinical trials and the data generated from their end . . . ." *Id.* at 132:19-133:6. Drs. Orlemans, Ault, and Sostek identified the '208 patent's PK/PD limitations.

Pet. Reply 4. Petitioner argues that the '285 patent discloses the *formulation* claimed in the '208 patent. *Id.* at 6. Petitioner further argues that the PK/PD values in the '208 patent's claims are inherent to the formulation, but are still limitations of the claims entitled to patentable weight. *See, e.g.*, Tr. 10:10–16. Patent Owners agree that the PK/PD values are claim limitations. PO Resp. 8. Thus, we do not find Petitioner's position on the prior art status of the '285 patent inconsistent with its obviousness arguments.

Applying the general reasoning of *Duncan Parking* to the facts before us, we find: (1) Petitioner relies on, as invalidating prior art, the combined naproxen and omeprazole formulation and twice daily dosing that Petitioner asserts the '285 patent discloses; (2) Dr. Plachetka solely invented the formulation and dosing disclosed in this relied-upon art; and (3) Dr. Plachetka was not solely responsible for the data resulting from the PN400–104 clinical trial study, which forms the

basis of the challenged claims of the ’208 patent. In other words, Petitioner has met its burden of production to show the ’285 patent was granted on an application for patent by another, i.e., solely by Dr. Plachetka, filed in the United States before the invention by the applicant for patent of the ’208 patent, thereby shifting the burden of production to Patent Owners to come forward with evidence that the ’285 and ’208 patents have the same inventive entity. *See Dynamic Drinkware*, 800 F.3d at 1379. As explained above, however, Patent Owners acknowledge that Dr. Plachetka alone invented the subject matter relied upon in the ’285 patent and that Drs. Orlemans, Sostek, and Ault contributed to the subject matter claimed in the ’208 patent. Thus, Patent Owners do not present evidence that the ’285 and ’208 patents have the same inventive entity. Accordingly, we determine that the ’285 patent qualifies as §102(e) prior art.

3. Does 35 U.S.C. § 103(c) Preclude Use of the ’285 Patent as Prior Art?

Patent Owners also argue that 35 U.S.C. § 103(c)(2) precludes Petitioner’s use of the ’285 patent as prior art. PO Resp. 34–37. Section 103(c) states:

> (1) Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person.
>
> (2) For the purposes of this subsection, subject matter developed by another person and a claimed invention shall be deemed to have been owned by the same person or subject to an obligation of assignment to the same person if –
>
> > (A) the claimed invention was made by or on behalf of parties to a joint research agreement that was in effect on or before the date the claimed invention was made;

> (B) the claimed invention was made as a result of activities undertaken within the scope of the joint research agreement; and
>
> (C) the application for patent for the claimed invention discloses or is amended to disclose the names of the parties to the joint research agreement.
>
> (3) For purposes of paragraph (2), the term "joint research agreement" means a written contract, grant, or cooperative agreement entered into by two or more persons or entities for the performance of experimental, developmental, or research work in the field of the claimed invention.

35 U.S.C. § 103(c). Patent Owners bear the burden of production "that the safe haven of § 103(c) applies." Pet. Reply 12 (quoting *MaxLinear, Inc. v. Cresta Tech. Corp.*, IPR2015-00594, Paper 90 at 24 (PTAB Aug. 15, 2016)); *see In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1376 (Fed. Cir. 2016) (explaining that "shifting of the burden of production is warranted" where a patent owner "affirmatively seeks to establish a proposition not relied on by the patent challenger and not a necessary predicate for the unpatentability claim asserted—effectively an affirmative defense").

Patent Owners argue that Pozen and AstraZeneca entered into a collaboration and license agreement on August 1, 2006.[10] PO Resp. 36 (citing Ex. 2015, 70:21–25, 71:11–12; Ex. 2067). According to Patent Owners, the inventions claimed in the '208 patent resulted from activities undertaken within the scope of the collaboration and license agreement, and "[t]he '584 application[11]

[10] The parties do not dispute that Patent Owner Nuvo purchased Pozen's assets on September 18, 2018. *See* Ex. 1051 (bankruptcy court order authorizing sale of certain of debtors' assets); Ex. 1052 (Asset Purchase Agreement).

[11] The '208 patent issued from U.S. application No. 14/980,639 ("the '639 application") and is a continuation of U.S. application No. 12/553,107, now U.S. Pat. No. 9,220,698. Ex. 1001, [63]. The '208 patent claims priority to Provisional

that resulted in the '208 patent was filed in 2008 with Pozen and AstraZeneca as co-owners." PO Resp. 36–37. Patent Owners point to the following language in the agreement as support:

> POZEN controls certain patents and other intellectual property pertaining to pharmaceutical products having gastroprotective agents in single fixed combination oral solid dosage form with non-steroidal anti-inflammatory drugs.
>
> AstraZeneca desires to obtain a license to POZEN's intellectual property and to enter into a collaboration with Pozen for the purpose of developing and commercializing certain pharmaceutical products.

Id. at 36 (quoting Ex. 2067, 8).

Assuming that the collaboration and license agreement qualifies as a joint research agreement under § 103(c)(3), Patent Owners do not direct us to any record evidence that the '639 application, which issued as the '208 patent, discloses or has been amended to disclose the names of the parties to the joint research agreement, as § 103(c)(2)(C) requires. As Petitioner points out, the '208 patent lists Pozen and Horizon, not Pozen and AstraZeneca, as assignees. Pet. Reply 12; *see* Ex. 1001, [73]. And Patent Owners do not identify any language in the '639 application (or the '208 patent specification) disclosing the collaboration agreement between Pozen and AstraZeneca, or naming AstraZeneca as an interested or involved party. *See generally* PO Resp.; PO Sur-Reply.[12] Further, although Patent Owners

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application No. 61/095,584 ("the '584 application"), filed on September 9, 2008. *Id.* [60].

[12] Patent Owners note that "Astra Zeneca Pharmaceuticals LP" filed the provisional application from which the '208 patent claims priority, i.e., the '584 application. *See* PO Sur-Reply 13; *see also* Ex. 1080, 1 (listing Astra Zeneca Pharmaceuticals LP, of Wilmington, DE as the filer). However, the collaboration and license agreement is between Pozen Inc. and AstraZeneca AB, "a Swedish corporation having an office at . . . Mölndal, Sweden." Ex. 2067, 2, 3.

contend that Horizon acquired AstraZeneca's rights to the '584 application in November 2013, PO Resp. 37, n.8, Patent Owners' cite no evidence to support this contention. Patent Owners' bare attorney argument is not entitled to weight. *Estee Lauder Inc. v. L'Oreal, S.A.*, 129 F.3d 588, 595 (Fed. Cir. 1997) ("Counsel's argument cannot take the place of evidence lacking in the record."). Given the foregoing, we determine that Patent Owners do not provide sufficient evidence that § 103(c)(2) applies to preclude Petitioner from asserting the '285 patent as prior art to the '208 patent.

4. Analysis for Claim 1

Having addressed the preliminary issues, we turn to Petitioner's assertion that claim 1 of the '208 patent would have been obvious over the '285 patent. The parties' dispute centers on three issues: (1) whether the '285 patent discloses the formulation and dose of esomeprazole and naproxen recited in claim 1; (2) whether the '285 patent discloses or would have rendered obvious twice daily dosing; and (3) whether the recited PK/PD parameters are inherent in administering the formulation disclosed in the '285 patent. We address each of these issues below.

a. Whether the '285 Patent Discloses the Formulation and Dosage Recited in Claim 1

Petitioner argues that the '285 patent expressly discloses the drug formulation and twice daily dosing that claim 1 recites. Pet. 32–35; Pet. Reply 6–9. Petitioner identifies Figure 2 of the '285 patent and its associated description as disclosing enteric-coated naproxen covered in a PPI that is "released

"AstraZeneca" is not further defined in the agreement to include Astra Zeneca Pharmaceuticals LP. In any event, this does not change the fact that the '639 application (and '208 patent specification) fails to include any reference to any AstraZeneca entity or the collaboration and license agreement.

. . . immediately." Pet. Reply 6–7 (citing Ex. 1005, 10:49–11:2; Ex. 1074 ¶ 14). Petitioner notes that the '285 patent identifies naproxen as "[t]he most preferred NSAID," and esomeprazole as a "preferred" PPI. *Id.* at 7 (citing Ex. 1005, 44–46, 4:11–12; Ex. 1074 ¶ 13). Petitioner asserts that the naproxen-esomeprazole formulation is the only formulation claimed in the '285 patent, and that claims 2–4 of the '285 patent disclose dosage ranges for naproxen (200–600mg) and esomeprazole (5–100mg) that encompass the claimed 500 mg of naproxen and 20 mg of esomeprazole. *Id*. Petitioner supports its arguments with citations to the '285 patent that correspond to the limitations it contends are expressly disclosed, as well as with the testimony of Drs. Metz and Mayersohn. Pet. 32–39 (citing portions of Exs. 1002, 1003, and 1005); Reply 6–10 (citing portions of Exs. 1002, 1003, 1005, 1074).

According to Petitioner, one of ordinary skill in the art reading the '285 patent would have known of the commercially available dosage forms of naproxen (500mg), and esomeprazole (20mg and 40mg), and would have understood and envisioned a combined esomeprazole-naproxen tablet containing 20 mg esomeprazole and 500mg naproxen. *Id.* (citing Ex. 1002 ¶ 68; Ex. 1003 ¶¶ 128, 158; Ex. 1059 ¶ 31). Relying on Dr. Mayersohn's testimony, Petitioner asserts that, to the extent that the '285 patent does not expressly disclose the 20 mg esomeprazole dose, such a dose would have been obvious to the ordinarily skilled artisan. Pet. 43 (citing Ex. 1003 ¶ 154). Dr. Mayersohn testifies that the '285 patent discloses an esomeprazole dose range of 5 mg to 100 mg, and identifies the 40 mg dose as "preferred." Ex. 1003 ¶ 154. Dr. Mayersohn testifies that 20 mg and 40 mg esomeprazole doses were approved and available on the market as of the September 9, 2008, priority date of the '208 patent, and that 20 mg

omeprazole[13] (used in combination with 500 mg naproxen in Example 9 of the '285 patent) was known to be effective when dosed in a tablet having the structure the '285 patent teaches, even though it was known to be somewhat less effective than esomeprazole. *Id.* Petitioner thus argues that one of ordinary skill in the art would have found it obvious to use 20 mg of esomeprazole in combination with 500 mg of naproxen. Pet. 43.

Patent Owners assert that the '285 patent fails to disclose which of all possible formulations target the claimed pharmacokinetic parameters when administered as an AM and PM dose. PO Resp. 30–33. In that regard, Drs. Taft and Johnson both opine that "the '285 patent discloses 1,000 possible combinations of a composition consisting of an acid inhibitor and an NSAID." Ex. 2025 ¶ 53; Ex. 2026 ¶ 65.

Patent Owners' arguments and expert opinions, however, do not account for the '285 patent's explicit teaching of "a pharmaceutical composition in unit dosage form" comprising "esomeprazole in an amount of from 5 to 100 mg" "wherein at least a portion of said esomeprazole is not surrounded by an enteric coating" and naproxen "in an amount between 200–600 mg" "surrounded by a coating that inhibits its release from said unit dosage form unless said dosage form is in a medium with a pH of 3.5 or higher." Ex. 1005, 22:8–28 (claims 1–5). The '285 patent also discloses that "[t]he most preferred NSAID is naproxen," "more preferably in an amount of between 200 and 600 mg," and that "[o]ther preferred agents that may be effectively used as acid inhibitors are the proton pump

[13] Omeprazole is a PPI that contains a racemic mixture of R- and S-enantiomer, which are mirror images of the compound. Ex. 1002 ¶ 57 n. 2. Esomeprazole is the S-enantiomer of omeprazole, and was known, as of at least 1999, to be more effective than omeprazole. *Id.* (citing Ex. 1007, abstract).

inhibitors such as omeprazole, esomeprazole, ..." *Id.* at 3:44–46, 4:11–14. Dr. Metz testifies credibly that the dosages claimed in the '208 patent fall within the narrow ranges disclosed and claimed in the '285 patent, and the doses used in commercially available formulations of naproxen and esomeprazole in 2008 fell within those ranges. Ex. 1002 ¶ 68.

"Where a claimed range overlaps a range disclosed in the prior art, there is a presumption of obviousness." *Ormco Corp. v. Align Tech., Inc.*, 463 F.3d 1299, 1311 (Fed. Cir. 2006) (citing *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004)); *see also E.I. DuPont de Nemours & Co. v. Synvina C.V.*, 904 F.3d 996, 1008 (Fed. Cir. 2018) ("[I]n the absence of evidence indicating that there is something special or critical about the claimed range, an overlap suffices to show that the claimed range was disclosed in—and therefore obvious in light of—the prior art."). "A *prima facie* case of obviousness typically exists when the ranges of the claimed composition overlap the ranges disclosed in the prior art." *In re Peterson*, 315 F.3d 1325, 1329 (Fed. Cir. 2003); *see also In re Malagari*, 499 F.2d 1297, 1303 (CCPA 1974) (concluding that a claimed invention was rendered prima facie obvious by a prior art reference whose disclosed range (0.020–0.035% carbon) overlapped the claimed range (0.030–0.070% carbon)). The presumption of obviousness can be rebutted if it can be shown that the prior art teaches away from the claimed range, or the clamed range produces new and unexpected results. *Ormco Corp.*, 463 F.3d at 1311 (citing *Iron Grip*, 392 F.3d at 1323). Patent Owners also argue that the '208 patent teaches away from the use of 20 mg dosage strength of immediate-release esomeprazole, relying on Dr. Taft's testimony. PO. Resp. 39–40 (citing Ex. 2025 ¶ 63). Dr. Taft testifies that "the '285 patent actually taught away from the 20 mg of immediate-release esomeprazole by disclosing that a 40 mg dose was preferred." Ex. 2025 ¶ 63.

Teaching away, however, requires that a reference "criticize, discredit, or otherwise discourage the solution claimed" by Patent Owners. *In re Fulton*, 391 F.3d 1195, 1201 (Fed. Cir. 2004) ("The prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed in the '198 application."). "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994). However, the existence of better alternatives in the prior art does not mean that an inferior combination is inapt for obviousness purposes. *In re Mouttet*, 686 F.3d 1322, 1333 (Fed. Cir. 2012) (citing *In re Gurley*, 27 F.3d at 553). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d at 553. At most, the '285 patent discloses a preference for 40 mg of immediate-release esomeprazole, but such teaching is insufficient to teach away. *See Galderma Labs., L.P., v. Tolmar, Inc.*, 737 F.3d 731, 738 (Fed. Cir. 2013) (explaining that teaching away requires more than the mere expression of a general preference).

In addition, although Patent Owners argue that the claimed pharmacokinetic parameters are surprising and unexpected, Patent Owners produce no evidence of any criticality in the amounts of esomeprazole and naproxen claimed in comparison to the dosages disclosed in the '285 patent. *See DuPont*, 904 F.3d at 1006–07 (explaining, in the context of an *inter partes* review that "[t]here are several ways by which the patentee may rebut" the presumption of obviousness due to an overlapping range, including showing that the claimed invention

"[p]roduces a new and unexpected result"); *cf In re Geisler*, 116 F.3d 1465, 1470–71 (Fed. Cir. 1997) ("When an applicant seeks to overcome a prima facie case of obviousness by showing improved performance in a range that is within or overlaps with a range disclosed in the prior art, the applicant must 'show that the [claimed] range is *critical,* generally by showing that the claimed range achieves unexpected results relative to the prior art range.'") (quoting *In re Woodruff*, 919 F.2d. 1575, 1578 (Fed. Cir. 1990)). Moreover, as discussed *infra*, Patent Owners' arguments regarding the existence of unexpected results are not supported with sufficient evidence.

After having considered the parties' arguments, we find that a preponderance of the evidence demonstrates that the '285 patent at least would have rendered obvious the dosage formulation claimed in the '208 patent, i.e. 20 mg of esomeprazole and 500 mg of naproxen.

b. Whether the '285 Patent Discloses Twice Daily Dosing

The claims of the '208 patent require administering an AM unit dose form and a PM unit dose form 10 hours (±20%) later. Ex. 1001, 46:35–36.

Petitioner argues that the '285 patent discloses twice daily oral administration of a unit dose form. Pet. 33 (citing Ex. 1005, 20:40–22:6 and Ex. 1003 ¶ 127). Citing Dr. Metz's testimony for support, Petitioner contends that a skilled artisan would have understood that twice daily administration means giving AM and PM doses, and that the PM dose would be administered 8 to 12 hours later than the AM dose. *Id.* (citing Ex. 1002 ¶ 67).

Patent Owners argue that Petitioner fails to demonstrate that the '285 patent discloses the twice daily dosing. PO Resp. 31. Patent Owners point out that only two examples in the '285 patent mention twice daily dosing, these are descriptions of clinical studies of patients who received naproxen and either famotidine or

omeprazole, and the studies did not involve the claimed coordinated release solid oral dosage form comprised of immediate release esomeprazole and enteric coated naproxen. *Id.* at 31–32.

Although the '285 patent does not explicitly teach twice daily dosing of a unit dosage of immediate release esomeprazole and enteric coated naproxen, it does claim the coordinated release solid oral dosage form of naproxen and esomeprazole and teaches twice daily dosing of naproxen. Ex. 1005, 6:31–33, 20:42–46, 21–12–15, 22:8–14. Here, we credit Dr. Metz's testimony that a person of ordinary skill in the art would have understood that twice daily means administration of an AM and a PM unit dose, where the PM unit dose is given within the window of 8 to 12 hours after the AM dose. Ex. 1002 ¶ 67.[14]

A combination of familiar elements (twice daily dosing of naproxen and a unit dosage form of naproxen combined with esomeprazole) according to known methods is likely to be obvious when it does no more than yield predictable results. *KSR*, 550 U.S. at 416. "If a person of ordinary skill in the art can implement a predictable variation, and would see the benefit of doing so, § 103 likely bars its patentability." *Id.* at 417. One of ordinary skill can use his or her ordinary skill, creativity, and common sense to make the necessary adjustments and further modifications to result in a properly functioning product or method. *See id.* at 418 ("a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ").

Administration of a unit dosage form of naproxen and esomeprazole twice daily, in the AM and PM, is a predictable variation on the '285 patent's teaching of

[14] Patent Owners adduce no evidence to counter Dr. Metz's testimony. *See generally* PO Resp.

twice daily dosing of naproxen. *See* Ex. 1002 ¶¶ 59, 63, 68; Ex. 1003 ¶¶ 84, 127; Ex. 1059 ¶¶ 30–32, 34; Ex. 1074 ¶¶ 25–26, 31. A skilled artisan would have seen a benefit in twice daily dosing of the unit dosage form in terms of patient compliance with a medication schedule, ease of use, lack of confusion, and minimizing different medications to be taken. On the facts before us, a preponderance of the evidence supports the obviousness of twice daily dosing of a unit dosage form of esomeprazole and naproxen.

c. Whether the Claimed PK/PD Parameters are Inherent

Next, we consider whether the claimed pharmacokinetic parameters would have been obvious. Petitioner asserts that the PK/PD elements are inherent in the formulation and method disclosed in the '285 patent, and are the result of routine testing that one of ordinary skill in the art could have performed on the disclosed formulation. Pet. 35–39.

With respect to inherency, Petitioner relies on Dr. Mayersohn's testimony in arguing that, given a certain formulation and method of administration, a drug will produce a certain PK/PD profile as a natural result of basic biological processes. Pet. 37 (citing Ex. 1003 ¶¶ 133–36). According to Petitioner, the only parameters that determine the drug's PK/PD profile are biological, not technological, in nature. *Id.* Thus, Petitioner argues that the PK/PD profile is a characteristic of the formulation, and not a result of any kind of manipulation of the formulation. *Id.*

Patent Owners caution that inherency "must be carefully circumscribed in the context of obviousness." PO Resp. 37 (quoting *Par Pharm., Inc. v. TWI Pharm., Inc.*, 773 F.3d 1186, 1195–96 (Fed. Cir. 2014). In particular, Patent Owners argue that the pharmacokinetic parameters claimed in the '208 patent were surprising and unexpected. *Id.* at 39. The only evidence of these surprising and unexpected pharmacokinetic parameters Patent Owners present, however, is the

attorney argument in the Response to Final Office Action submitted during prosecution of the '639 application leading to the '208 patent and that in the briefing in this case. *See id.* at 6–7, 39 (citing Ex. 2024, 7).[15]

"Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art." *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002). "[M]ere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not distinguish a claim drawn to those things from the prior art." *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981). Inherency is more limited in an obviousness analysis than in anticipation. As the predecessor court to the Federal Circuit held:

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.

Oelrich, 666 F.2d at 581.

Many Federal Circuit decisions hold that the natural results of an obvious formulation—including PK/PD results like those recited in claim 1—are inherent in that formulation. Pet. Reply 14 (citing *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1354 (Fed. Cir. 2012) ("The initial blood serum concentration resulting from administering a PPI dosage is an inherent property of the formulation, and an obvious formulation cannot become nonobvious simply by administering it to a

[15] We address Patent Owners' argument that one of ordinary skill in the art would not have expected to be able to use unprotected PPIs in section II.D.4.c., *infra*.

patient and claiming the resulting serum concentrations."); *In re Huai-Hung Kao*, 639 F.3d 1057, 1070 (Fed. Cir. 2011) (claimed "food-effect" related serum concentration level is inherent property of drug); *King Pharm., Inc. v. Eon Labs, Inc.*, 616 F.3d 1267, 1275 (Fed. Cir. 2010) (drug's bioavailability is natural result of prior art explicated limitations)). Here, we credit Dr. Mayersohn's testimony that the natural result of the basic biologic processes of adsorption, distribution, metabolization, and excretion of the obvious unit dose form of naproxen and esomeprazole is the PK/PD profile as claimed in the '208 patent. *See* Ex. 1003 ¶¶ 133–36. The preponderance of the evidence shows that the PK/PD profile is a characteristic of the formulation and the natural result of its administration.

Further, in relation to obviousness of the pharmacokinetic parameters, as discussed above, Petitioner contends that the PK/PD elements are the product of routine testing. Pet. Reply. 16 n.8 (citing Pet., 47–48). Petitioner supports its position with testimony from Dr. Mayersohn. Pet. 47–48 (citing Ex. 1003 ¶¶ 155–158). For instance, Dr. Mayersohn testifies that it was well within the skill of an ordinary artisan to quantitatively test a drug or dosage form's behavior in the body and analyze "the relevant biological data to determine the 'desired pharmacodynamic response and pharmacokinetic values.'" Ex. 1003 ¶ 156. Patent Owners fail to dispute Petitioner's contention.

"A person of ordinary skill is also a person of ordinary creativity, not an automaton." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007). Patent Owners' arguments ignore the disclosure in the '285 patent that the invention provides a method for increasing compliance in a patient requiring frequent daily dosing of NSAIDS by providing both an acid inhibitor and NSAID in a single convenient, preferably coordinated unit dosage form, thereby reducing the number of individual doses to be administered during any given period. Ex. 1005, 5:57–

62. The arguments also fail to take into account the '285 patent's disclosure that naproxen and naproxen sodium are long-acting NSAIDs having half-lives of about 12 to 15 hours (Ex. 1005, 6:29–33) and the evidence that one of ordinary skill in the art would have known that enteric coated naproxen was dosed twice daily (Ex. 1003 ¶ 127). *See also* Reply 9 (citing Ex. 1059 ¶ 34 and Ex. 1074 ¶ 25).

After having reviewed the evidence and arguments, we find that the PK/PD limitations are inherent in administering the unit dose form of naproxen and esomeprazole. Dr. Mayersohn testified that the PK/PD elements are characteristic of the administration of the dosage form of naproxen and esomeprazole disclosed in the '285 patent, and a skilled artisan need only have administered the dosage form to achieve the PK/PD limitations. Ex. 1003 ¶ 133. This does not end our inquiry, however, because Patent Owners present arguments and evidence regarding objective indicia of nonobviousness that we must consider before reaching our conclusion on obviousness. *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1328 (Fed. Cir. 2016). We consider those arguments and evidence below.

d. Objective Indicia of Nonobviousness

Factual inquiries for an obviousness determination include secondary considerations (objective indicia) based on evaluation and crediting of objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966). When secondary considerations are present, they must be considered. *In re Huai-Hung Kao*, 639 F.3d at 1067–68. Notwithstanding what the teachings of the prior art would have suggested to one of ordinary skill in the art at the time of the invention, the totality of the evidence submitted, including objective evidence of nonobviousness, may lead to a conclusion that the challenged claims would not have been obvious to one of ordinary skill in the art. *In re Piasecki*, 745 F.2d 1468, 1471–72 (Fed. Cir. 1984). "Although secondary considerations must be

taken into account, they do not necessarily control the obviousness conclusion." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1372 (Fed. Cir. 2007).

Secondary considerations may include any of the following: long-felt but unsolved needs, failure of others, unexpected results, commercial success, copying, licensing, and praise. *See Graham*, 383 U.S. at 17; *Leapfrog Enters., Inc. v. Fisher-Price, Inc.*, 485 F.3d 1157, 1162 (Fed. Cir. 2007).

Patent Owners assert that the submitted evidence of secondary considerations lead to a conclusion that the claims of the '208 patent would not have been obvious over the '285 patent. PO Resp. 47–48. Patent Owners specifically argue (1) there was a long-felt, but unmet need for reducing NSAID-induced gastropathology, (2) the use of unprotected PPIs produced surprising and unexpected results, and (3) persons of skill in the art at the time of the invention were skeptical of administering PPIs without protection from gastric acid. PO Resp. 48–52.

Petitioner argues that Patent Owners' evidence regarding secondary considerations lacks the required nexus to the unique features of the claims of the '208 patent, which are the PK/PD values for an already-known formulation. Pet. Reply 22–23.

To be accorded substantial weight, there must be a nexus between the merits of the claimed invention and the evidence of secondary considerations. *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995); *In re Huai-Hung Kao*, 639 F.3d 1057, 1068 (Fed. Cir. 2011) ("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.*") (quoting *Wyers v. Master Lock Co.*, 616 F.3d 1231, 1246 (Fed. Cir. 2010)). "Nexus" is a legally and factually sufficient connection between the objective evidence and the claimed invention,

such that the objective evidence should be considered in determining nonobviousness. *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988).

For nexus to be presumed present, the product must be or contain "the invention disclosed and claimed in the patent." *WBIP*, 829 F.3d at 1329. That is, a nexus is presumed when the commercial product "both 'embodies the claimed features' and is 'coextensive' with the claims at issue." *Sight Sound Techs., LLC v. Apple Inc.*, 809 F.3d 1307, 1319 (Fed. Cir. 2015). But if the secondary consideration is the result of a feature that was known in the prior art, the secondary consideration is not pertinent. *Ormco Corp.*, 463 F.3d at 1312 (commercial success was due to either features not claimed or features that were not new). The burden of producing evidence showing that there is a nexus lies with the patent owner. *Id.*; *Prometheus Labs., Inc. v. Roxane Labs., Inc.*, 805 F.3d 1092, 1101–02 (Fed. Cir. 2015).

Evidence of nonobviousness must be commensurate in scope with the claimed invention to be relevant. *In re Huai-Hung Kao*, 639 F.3d at 1068 (citing *In re Tiffin*, 448 F.2d 791, 792 (CCPA 1971)); *In re Hiniker Co.*, 150 F.3d 1362, 1369 (Fed. Cir. 1998).

As explained further below, we are not persuaded that Patent Owners' arguments and evidence support the nonobviousness of the challenged claims.

(1) Long-Felt Need

Relying on the testimony of Dr. Johnson, Patent Owners contend there was a long-felt need for a convenient single pill to provide upper gastrointestinal protection by esomeprazole while allowing unimpeded bioavailability of EC naproxen for patients requiring long-term use of EC naproxen. PO Resp. 48 (citing Ex. 2026 ¶¶ 28–30, 37–52, 84–87). Specifically, Patent Owners argue that as of

2007, numerous pharmaceutical companies were actively trying to develop an effective way to ameliorate gastrointestinal damage associated with NSAID use. *Id.* (citing Ex. 2026 ¶ 85). Patent Owners contend that none of these companies thought to combine a non-enteric-coated PPI with an NSAID in a single dosage form, despite the magnitude of the NSAID market and huge population suffering from NSAID-induced gastric pathology. *Id.* at 48–49 (citing Ex. 2026 ¶ 85). Patent Owners argue that co-therapy with separate administration of NSAIDs and gastroprotective agents has compliance issues and requires physicians to prescribe and patients to take multiple pills on a schedule. *Id.* at 49 (citing Ex. 2026 ¶¶ 88–90).

We are not persuaded that Patent Owners demonstrate that the claimed method satisfied a long-felt but unmet need for concomitant NSAID and gastroprotective agent treatment. For example, although Patent Owners present evidence that at some time there may have existed a need for concomitant therapy and improved patient compliance (i.e., twice daily dosing of a unit dosage form of naproxen and esomeprazole), the prior art '285 patent discloses the unit dosage form and twice daily dosing. *See* Ex. 1005, 22:8–28. Patent Owners fail to tie their evidence of long-felt need to the limitations recited in the claims, rather than the disclosure in the '285 patent. Accordingly, we are not persuaded that Patent Owners' evidence of long-felt need supports the nonobviousness of the challenged claims.

(2) Unexpected Results

Patent Owners argue that, prior to the release of Vimovo,[16] one of ordinary skill in the art would not have expected PPIs that did not have enteric coating or

[16] Vimovo is Patent Owners' commercial product comprising a unit dosage form of

were not administered with a buffer to be effective in reducing NSAID-associated gastric ulcers. PO Resp. 50–51. Patent Owners contend that scientists continue to teach that PPIs must be protected from gastric acid. *Id.* Patent Owners argue that Drs. Metz and Mayersohn have each stated publicly that PPIs must be protected from gastric acid. *Id.* at 51.

In arguing unexpected results, however, Patent Owners do not compare the claimed method to the closest prior art (the '285 patent). *Kao Corp. v. Unilever United States, Inc.*, 441 F.3d 963, 970 (Fed. Cir. 2006) ("when unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art" (internal quotations and citation omitted)); *see generally* PO Resp. 50–51. Rather, Patent Owner simply reiterates its teaching away arguments.

Petitioner argues that the '285 patent discloses combined therapies (naproxen in a unit dose form with esomeprazole) and formulations with uncoated PPIs and NSAID. Pet. Reply 24.

Patent Owners have not demonstrated how the claimed method produces results that would have been unexpected upon consideration of the '285 patent, which discloses the claimed formulation (with at least a portion of esomeprazole not surrounded by an enteric coating) and twice daily administration. *See* Ex. 1005, 22:8–28. Accordingly, we reject Patent Owners' arguments in the context of unexpected results.

(3) Skepticism

Patent Owners argue that experts in the field of PPIs never suggested that a PPI could be administered without protection from gastric acid. PO Resp. 52

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naproxen and esomeprazole. *See, e.g.*, Ex. 1003 ¶¶ 74, 184.

(citing Ex. 2026 ¶ 97). Patent Owners rely on a series of emails allegedly from AstraZeneca scientists that state in part "the current formulation is NOT optimal from an acid suppression standpoint (because of PPI is degradation [sic] in the stomach) . . . . It could be difficult to explain to physicians why PPI 'protection' is not necessary for this product unlike all other PPIs." *Id.* (quoting Ex. 2032, 3). Patent Owners also cite to Dr. Johnson's testimony that, as a physician practicing in the field at the time Vimovo was released, he was skeptical that the drug would be an effective therapy, and did not understand how it worked. *Id.* (citing Ex. 2032, 100).

Petitioner argues that Vimovo's features are not unique to the '208 patent, which adds only PK/PD values for an already-known formulation. Pet. 23.

Patent Owners' arguments and evidence are unpersuasive. Exhibit 2032 does not identify any particular drug formulation as the subject of the emails and thus lacks a nexus between the merits of the claimed invention and the evidence of skepticism. *See In re Huai-Hung Kao*, 639 F.3d at 1068 (proponent of secondary consideration of nonobviousness must establish nexus between the evidence and the merits of the claimed invention). Patent Owners also fail to address the inconsistency between the argument that "PPIs never suggested that a PPI could be administered without protection from gastric acid" (PO Resp. 52) and the '285 patent's disclosure of "esomeprazole, at least a portion of which is not surrounded by an enteric coating" (Ex. 1005, 22:10–11). The secondary consideration argued is the result of a feature that was known in the prior art '285 patent and, thus, is "not pertinent." *Ormco Corp.*, 463 F.3d at 1312.

e. Conclusion as to obviousness of Claim 1

Having considered the parties' arguments and evidence, we evaluate all of the evidence together to make a final determination of obviousness. *In re*

Cyclobenzaprine Hydrochloride Extended–Release Capsule Patent Litig., 676 F.3d 1063, 1075 (Fed. Cir. 2012) (stating that a fact finder must consider all evidence relating to obviousness before finding patent claims invalid). In so doing, we conclude that Petitioner has satisfied its burden of demonstrating, by a preponderance of the evidence, that the subject matter of claim 1 of the '208 patent would have been obvious over the '285 patent.

f. Claims 2–7

Petitioner further asserts that the additional limitations in independent claims 2–7 would have been obvious over the '285 patent because they "recite routine elements" that are either disclosed in the '285 patent or "well within the skilled artisan's knowledge." Pet. 39–42 (explaining how the '285 patent discloses the limitations of claims 2–7 and citing Ex. 1002 ¶¶ 73–80; Ex. 1003 ¶¶ 139–146, 150–152, 166; Ex. 1005, 1:50, 3:2–3, 3:11–14, 16:1–17:47, claim 1, Figs. 1–2), 43 (referring back to earlier analysis for claims 2–7). Patent Owners do not address separately the merits of Petitioner's assertions as to claims 2–7. *See generally* PO Resp.; PO Sur-reply. Accordingly, such arguments are waived. *See* Paper 10, 3 (Scheduling Order cautioning Patent Owners that "any arguments for patentability not raised in the response will be deemed waived"); *cf. In re Nuvasive*, 842 F.3d 1376, 1381 (Fed. Cir. 2016) (explaining that a patent owner waives an argument presented in the preliminary response if it fails to renew that argument in the patent owner response after the Board institutes trial).

Because a preponderance of the evidence (as demonstrated in the citations to supporting evidence above) supports Petitioner's arguments regarding the teachings of the '285 patent, we adopt Petitioner's arguments as our own and determine that Petitioner has satisfied its burden of demonstrating that the subject matter of claims 2–7 of the '208 patent would have been obvious over the '285

patent. *See* Pet. 39–42, 43; *see also In re Nuvasive*, 841 F.3d 966, 974 (Fed. Cir. 2016) (explaining that the Board need not make specific findings as to claim limitations that a patent owner does not dispute are disclosed in the prior art). Our determination that Petitioner has demonstrated, by a preponderance of the evidence, that claims 1–7 would have been obvious over the '285 patent involves all challenged claims of the '208 patent. Therefore, we need not address Petitioner's grounds asserting based on anticipation by the '285 patent and obviousness over the '285 patent in view of the EC Naprosyn label and Howden 2005. *See, e.g.*, *Nippon Suisan Kaisha Ltd. v. Pronova Biopharma Norge AS*, PGR2017-00033, Paper 37 at 27 (PTAB Jan. 16, 2019).

III. EVIDENTIARY MOTIONS

Patent Owners and Petitioner each filed motions to exclude certain evidence. We first address Petitioner's motion, and then turn to Patent Owners' motion.

A. Petitioner's Motion to Exclude

Petitioner filed a motion to exclude various exhibits as improper direct testimony without an affidavit under 37 C.F.R. § 42.53, hearsay under FRE 801–803, and lacking adequate authentication under FRE 901. Paper 56. Even if we consider the objected-to evidence, however, we determine the challenged claims of the '208 patent are unpatentable as obvious. Thus, rather than exclude the objected-to evidence, we find the better course of action is to maintain a complete record of the evidence to facilitate public access and appellate review.

Accordingly, we *dismiss* Petitioner's Motion to Exclude *as moot*.

B. Patent Owners' Motion to Exclude

Patent Owners move to exclude in their entirety Exhibits 1008–1010, 1020, 1030, 1064–66, 1074, 1076, 1083, and 1088, and to exclude portions of Exhibits 1059, 1074, and 2083. Paper 55.

1. Exhibits 1008–1010, 1020, 1030, and 1083

Petitioner describes Exhibit 1009 as "EC-Naprosyn prescribing information (2007)," Exhibit 1010 as "Zegerid approval letter and prescribing information (2004)," Exhibit 1020 as "Naprosyn/EC-Naprosyn/Anaprox DS Prescribing Information (2017)," and Exhibit 1030 as "Vimovo prescribing information (2014.)" Paper 59, 2–4. Petitioner describes Exhibit 1008 as "Products on NDA 020067 (EC-Naprosyn)," citing an FDA website where the document was visited in 2017, and Exhibit 1083 as "FDA Website, Orange Book, Vimovo," citing another FDA website visited in 2019. Paper 59, 2, 8.

We do not rely on Exhibits 1008–1010, 1020, 1030, or 1083 in making our ultimate determination on the patentability of the challenged claims. Accordingly, we need not decide Patent Owners' motion as to those exhibits, and we dismiss that portion of Patent Owners' motion as moot.

2. Exhibits 1064–1066, 1074, 1076, and 1088

Patent Owners move to exclude Exhibits 1064, 1065, 1066, 1076, and 1088, which Petitioner submitted for the first time with the reply, as untimely new evidence, in violation of 37 C.F.R. § 42.23(b). Paper 55, 5. Patent Owners also move to exclude paragraphs 25 and 35 of Dr. Mayersohn's Reply Declaration (Exhibit 1074), which rely on these allegedly untimely exhibits. *Id.*

Petitioner argues that Patent Owners do not identify any objections in the record, as required by 37 C.F.R. § 42.64(c), and do not seek to exclude the exhibits on any evidentiary basis. Paper 58, 11–12.

"The Board acts as both the gatekeeper of evidence and as the weigher of evidence." *South-Tek Sys., LLC v. Engineered Corrosion Sols., LLC*, IPR2016-00136, Paper 52 at 8 (PTAB May 10, 2017). We do not exclude evidence that is allegedly untimely, but rather give it little weight or do not rely on it at all, as appropriate. *Id.* Sitting as a non-jury tribunal with administrative expertise, we are well positioned to determine and assign appropriate weight to evidence presented, including giving it no weight. *See, e.g.*, *Donnelly Garment Co. v. NLRB*, 123 F.2d 215, 224 (8th Cir. 1941) ("One who is capable of ruling accurately upon the admissibility of evidence is equally capable of sifting it accurately after it has been received . . . .").

We deny Patent Owners' motion to exclude Exhibits 1064–1066, 1076, and 1088, as well as paragraphs 25 and 35 of Exhibit 1074.

3. Exhibits 1059 and 2083

Patent Owners move to exclude portions of Dr. Metz's Reply Declaration (Exhibit 1059) and his deposition testimony taken after Petitioner filed its Reply (Exhibit 2083) as untimely new opinions. Paper 55, 7–8.

As discussed in III.B.2 immediately above, we do not exclude evidence that is allegedly untimely. We give the evidence the weight it deserves.

We, therefore, deny Patent Owners' motion to exclude portions of Exhibits 1059 and 2083.

IV. CONCLUSION

Petitioner establishes by a preponderance of the evidence that claims 1–7 of the '208 patent would have been obvious over the '285 patent.

V. ORDER

In consideration of the foregoing, it is hereby:

ORDERED that Petitioner has shown by a preponderance of the evidence that claims 1–7 of U.S. Patent No. 9,383,208 are unpatentable as obvious under 35 U.S.C. § 103 over the '285 patent;

FURTHER ORDERED that Petitioner's Motion to Exclude is denied as moot;

FURTHER ORDERED that Patent Owners' Motion to Exclude is dismissed-in-part as moot and denied-in-part;

FURTHER ORDERED that, because this is a Final Written Decision, parties to the proceeding seeking judicial review of the decision must comply with the notice and service requirements of 37 C.F.R. § 90.2.

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