

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

LUPIN LTD. and LUPIN PHARMACEUTICALS INC.,
Petitioner,

v.

POZEN INC.,
Patent Owner.

Case IPR2015-01775
Patent 8,865,190 B2

Before TONI R. SCHEINER, LORA M. GREEN, and
JACQUELINE WRIGHT BONILLA, *Administrative Patent Judges*.

BONILLA, *Administrative Patent Judge*.

DECISION
Institution of *Inter Partes* Review
37 C.F.R. § 42.108

Therabody EX2021
Hyper Ice v. Therabody
PGR2026-00051

I. INTRODUCTION

Lupin Ltd. and Lupin Pharmaceuticals, Inc. (“Petitioner”) filed a Corrected Petition (Paper 4, “Pet.”) requesting an *inter partes* review of claims 1–8 of U.S. Patent No. 8,865,190 B2 (Ex. 1001, “the ’190 patent”). Pozen Inc. (“Patent Owner”) filed a Preliminary Response. Paper 14 (“Prelim. Resp.”). Under 35 U.S.C. § 314, we may not institute an *inter partes* review “unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition.”

Upon consideration of information presented in the Petition and the Preliminary Response, we determine that Petitioner has established a reasonable likelihood that it would prevail in showing the unpatentability of challenged claims 1, 2, and 4–8, but not claim 3, of the ’190 patent. We institute *inter partes* review of claims 1, 2, and 4–8 of the ’190 patent.

A. *Related Proceedings*

The parties identify a number of judicial matters involving the ’190 patent (e.g., *Horizon Pharma, Inc. v. Actavis Labs. FL, Inc.*, 3:15-cv-03322 (D.N.J.)), as well as a number of judicial and administrative matters involving patents related to the ’190 patent or directed to similar subject matter (e.g., *AstraZeneca AB v. Dr. Reddy’s Labs. Inc.*, 3:11-cv-02317 (D.N.J.); *Dr. Reddy’s Labs., Inc. v. Pozen Inc.*, Case IPR2015-00802 (PTAB); *Coalition for Affordable Drugs VII LLC v. Pozen Inc.*, IPR2015-01241 (PTAB); *Coalition for Affordable Drugs VII LLC v. Pozen Inc.*,

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Coalition for Affordable Drugs VII LLC v. Pozen Inc., IPR2015-01344 (PTAB); IPR2015-01680 (PTAB); *Coalition for Affordable Drugs VII LLC v. Pozen Inc.*, IPR2015-01718 (PTAB)). Pet. 3–4; Paper 8, 8–9. Petitioner also filed two other Petitions for *inter partes* review involving patents related to the '190 patent in Case Nos. IPR2015-01773 and IPR2015-01774. Paper 8, 9.

B. Asserted Grounds of Unpatentability

Petitioner asserts the challenged claims are unpatentable on the following grounds. Pet. 4–5, 11–60.

Reference(s)	Basis	Claims Challenged
The '255 publication ¹	§ 102(b)	1–8
The '556 patent ² and Chandramouli ³ or the '225 patent ⁴	§ 103(a)	1–8

¹ U.S. Patent App. Pub. No. US 2003/0069255, published Apr. 10, 2003, filed by Plachetka (“the '255 publication”) (Ex. 1006).

² U.S. Patent No. 6,544,556, issued Apr. 8, 2003, to Chen et al. (“the '556 patent”) (Ex. 1007)

³ Chandramouli et al., *Prevention and management of NSAID-Induced Gastropathy*, J. PHARM. PAIN AND SYMPTOM CONTROL, 8(4):27–40 (2000) (“Chandramouli”) (Ex. 1009).

⁴ U.S. Patent No. 5,698,225, issued Dec. 16, 1997, to Gimet et al. (“the '225 patent”) (Ex. 1013).

Reference(s)	Basis	Claims Challenged
The '118 patent, ⁵ the '225 patent, and the '192 patent ⁶	§ 103(a)	1–8
The '225 patent, Chandramouli and WO '185 ⁷	§ 103(a)	1–8

Petitioner supports its challenges in the Petition with the Declaration of Umesh V. Banakar, Ph.D. (Ex. 1002).

C. The '190 Patent (Ex. 1001)

The '190 patent discloses pharmaceutical compositions “that provide for the coordinated release of an acid inhibitor and a non-steroidal anti-inflammatory drug (NSAID)” (Ex. 1001, 1:25–28), such that there is “a reduced likelihood of causing unwanted side effects, especially gastrointestinal side effects, when administered as a treatment for pain” (*id.* at 1:28–31).

Specifically, the '190 patent discloses “a pharmaceutical composition in unit dosage form . . . contain[ing] an acid inhibitor present in an amount effective to raise the gastric pH of a patient to at least 3.5” (*id.* at 3:31–37),

⁵ U.S. Patent No. 5,204,118, issued Apr. 20, 1993, to Goldman et al. (“the '118 patent”) (Ex. 1014).

⁶ U.S. Patent No. 5,877,192, issued Mar. 2, 1999, to Lindberg et al. (“the '192 patent”) (Ex. 1008).

⁷ PCT Int'l Patent Appl. WO 00/26185, published May 11, 2000, by Phillips (“WO'185”) (Ex. 1015).

and an NSAID “in an amount effective to reduce or eliminate pain or inflammation” (*id.* at 4:3–5). “The term ‘unit dosage form’ . . . refers to a single entity for drug administration. For example, a single tablet or capsule combining both an acid inhibitor and an NSAID would be a unit dosage form.” *Id.* at 4:46–49.

A unit dosage form of the present invention preferably provides for coordinated drug release in a way that elevates gastric pH and reduces the deleterious effects of the NSAID on the gastroduodenal mucosa, i.e., the acid inhibitor is released first and the release of NSAID is delayed until after the pH in the GI tract has risen.

In a preferred embodiment, the unit dosage form is a multilayer tablet, having an outer layer comprising the acid inhibitor and an inner core which comprises the NSAID. In the most preferred form, coordinated delivery is accomplished by having the inner core surrounded by a polymeric barrier coating that does not dissolve unless the surrounding medium is at a pH of at least 3.5, preferably at least 4 and more preferably, at least 5.

Id. at 4:49–63.

“The term ‘acid inhibitor’ refers to agents that inhibit gastric acid secretion and increase gastric pH.” *Id.* at 3:38–40. According to the ’190 patent, preferred acid inhibitors are H₂-blockers, such as famotidine (*id.* at 3:40–47), but “[o]ther preferred agents that may be effectively used as acid inhibitors are the proton pump inhibitors such as . . . esomeprazole,” for example, in a typical amount of 5–100 mg (*id.* at 3:48–51, 8:17–18).

The ’190 patent also discloses that the NSAID may be a number of different options, such as aspirin, acetaminophen, etc., where the “most

preferred NSAID is naproxen in an amount of between 50 mg and 1500 mg, and more preferably, in an amount of between 200 mg and 600 mg.” *Id.* at 4:5–18.

D. Illustrative Claims

Petitioner challenges claims 1–8 of the ’190 patent. Claim 1, the only independent claim, reproduced below, is illustrative.

1. A process for preparing a pharmaceutical composition in unit dosage form comprising therapeutically effective amounts of esomeprazole and naproxen, said process comprising the steps of:

- a) providing a first layer comprising said naproxen; and
- b) applying a second layer to said first layer, wherein said second layer comprises said esomeprazole; wherein said unit dosage form provides for release of said esomeprazole such that upon introduction of said unit dosage form into a medium, at least a portion of said esomeprazole is released regardless of the pH of the medium and release of at least a portion of said naproxen is inhibited unless the pH of said medium is 3.5 or higher.

Ex. 1001, 21:24–22:6. In relation to the layer comprising naproxen, dependent claim 3 further requires that the “first layer comprises 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.” *Id.* at 22:11–14. Dependent claims 4–6 require an “enteric film coat” that surrounds, in some capacity, the layer comprising naproxen. *Id.* at 22:15–23.

II. ANALYSIS

A. *Claim Construction*

In an *inter partes* review, claim terms in an unexpired patent are interpreted according to their broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1275–79 (Fed. Cir. 2015); *cert. granted sub nom., Cuozzo Speed Techs., LLC v. Lee*, No. 15-446, 2016 WL 205946 (U.S. Jan. 15, 2016). Under that standard, claim terms are given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art in the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007).

We determine that the only claim term requiring interpretation for purposes of this Decision is “inhibit.” The challenged claims recite the terms “inhibited” or “inhibits” in relation to the release of naproxen from a unit dosage form when introduced into a medium with a pH of 3.5 or higher. Petitioner asserts that the broadest reasonable interpretation of the term “inhibits” is “‘slows down,’ which allows for immediate release of some naproxen.” Pet. 11. Patent Owner contends that the ordinary meaning of “inhibits” refers to “prevents, hinders, or restrains” release of the NSAID. Prelim. Resp. 6–8 (citing Ex. 2014, Ex. 2015).

The specification of the ’190 patent does not define expressly the term “inhibit.” Considering the ordinary and customary meaning of the term in view of the specification and the claims themselves, however, we construe

“inhibit” to mean prevent (stop), hinder, or restrain, as Patent Owner proposes. *Id.* (citing Ex. 2014, Ex. 2015).

For example, claim 1 of the ’190 patent recites “*release of at least a portion*” of naproxen “*is inhibited unless* the pH of said medium is 3.5 or higher” (emphasis added). Dependent claim 3 recites a “coating that *inhibits its release*” from the unit dosage form “*unless* said dosage form is in a medium with a pH of 3.5 or higher” (emphasis added). Thus, “inhibit” refers to preventing, hindering, or restraining the release of naproxen “unless” the dosage form is exposed to a pH of 3.5 or higher. The use of “unless” in claim 1 and 3 and “at least a portion” in claim 1 indicates that the terms “inhibited” and “inhibits” in the claims do not encompass a “slowing down” of a release when the pH is below 3.5 (which would make “at least a portion” superfluous in claim 1), but rather refers to no release of “at least a portion” (claim 1) or all (claim 3) of the drug “unless” the dosage form is in a medium with a pH of 3.5 or higher.

B. Asserted Anticipation by the ’255 publication

As noted by both parties, the ’190 patent is a fifth generation descendent of an application (the ’216 application) that published as the ’255 publication (Ex. 1006), and the ’190 patent claims priority to the ’216 application and its parent provisional application. Pet. 9–10; Prelim. Resp. 9–10; Ex. 1001, 1:7–21. Nonetheless, Petitioner asserts that the ’255 publication is prior art to the ’190 patent under 35 U.S.C. § 102(b). Pet. 9–11.

In this regard, Petitioner first notes that the '255 publication published more than one year before the filing of its child continuation-in-part application (the '320 application) in the chain. *Id.* at 9. Petitioner then contends that the '216 application and its parent provisional ("the pre-2003 applications") do not provide written description support of the claims of the '190 patent, which creates a "priority break." *Id.* at 9–10. Petitioner supports this contention with its arguments that the claims of the '190 patent are broad enough to encompasses compositions "wherein some, or even most, of the naproxen is released before the medium is raised to 3.5 or higher." *Id.* at 10–11. According to Petitioner, the "broadest reasonable construction of 'inhibits' in the context of the '190 patent is 'slows down,' which allows for immediate release of some naproxen," and the "'255 publication does not teach this immediate release." *Id.* at 11. Rather, according to Petitioner, the pre-2003 applications only support compositions where "the NSAID is not released until the pH has been raised to 3.5 or higher." *Id.* at 10.

To put it another way, Petitioner essentially argues that the pre-2003 applications provide written description support of only a species (release of all naproxen only when pH is 3.5 or higher) of a broader genus recited in claim 1 in the '190 patent (encompassing release of at least some NSAID when pH is below 3.5 *and* when pH is 3.5 or higher), but not written description support of that genus. *Id.* at 10–11. Moreover, Petitioner suggests that because a species anticipates a genus, the species disclosed in

the '255 publication anticipates the genus recited in the challenged claims in the '190 patent. *Id.* at 11–14.

Patent Owner responds that the specifications of the '255 publication (i.e., the '216 application) and the '190 patent “are extremely similar,” referring us to an exhibit that provides a “redline” comparison between the texts of the two documents. Prelim. Resp. 10–11 (citing Ex. 2016). Patent Owner also points us to certain paragraphs in the '255 publication, stating that disclosures “in the '216 application demonstrate its broad applicability to any type of pH sensitive coatings.” Prelim. Resp. 12–13 (citing Ex. 1008 ¶¶ 4, 8, 44). Patent Owner further argues that “depending on the amount of drug released, one of skill in the art would recognize that delayed-release enteric coatings have differing levels of permeability that prevent, hinder, and/or restrain (i.e., inhibit) the release of the drug at low pH.” *Id.* at 14. Patent Owner points to paragraph 44 in the '216 application as expressly disclosing “how to control these dissolution characteristics of a pH-sensitive coating.” *Id.* Patent Owner additionally contends that “[s]atisfying the written description requirement does not require express examples ‘explicitly covering the full scope of the claim language.’” *Id.* at 15 (citing *LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005)).

In an *inter partes* review, the burden is on the petitioner to show a reasonable likelihood that it would prevail on a ground of unpatentability. 35 U.S.C. § 314(a). With respect to entitlement to any earlier effective filing

date, however, a patent owner is not presumed to be entitled to the earlier filing dates of ancestral applications that do not share the same disclosure, such as in a continuation-in-part situation. *Focal Therapeutics, Inc. v. SenoRx, Inc.*, Case IPR2014-00116, slip op. at 9 (Paper 8) (PTAB Apr. 22, 2014); *see also PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1305–06 (Fed. Cir. 2008) (stating that once a defendant establishes that a reference is § 102(b) prior art, burden is on patent owner to come forward with evidence proving priority to an earlier filing date). Nonetheless, a petitioner first must raise the issue by identifying, specifically, the features, claims, and ancestral applications allegedly lacking written description support for the claims based on the identified features. *Focal Therapeutics*, Case IPR2014-00116, slip op. at 10 (Paper 8). Then, the patent owner must make a sufficient showing of entitlement to earlier filing date(s), in a manner that is commensurate in scope with the specific points and contentions raised by the petitioner. *Id.*

We are persuaded that Patent Owner provides a sufficient showing of entitlement to the filing date of the '216 application (the '255 publication) in a manner that is commensurate in scope with the specific points and contentions raised by Petitioner. Although we recognize that the '255 publication (and similarly the '190 patent specification itself) does not use the exact words “at least a portion” in relation to a release of naproxen, the '255 publication “does not have to describe exactly the subject matter claimed.” *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir.

1991) (citing *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989). Rather, the description must “‘reasonably convey[] to the artisan that the inventor had possession at that time of the later claimed subject matter.’” *Id.* at 1563 (quoting *Ralston Purina Co. v. Far–Mar–Co, Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985)). Thus, we consider whether the ’255 publication as a whole conveys to one of ordinary skill in the art, either explicitly or inherently, that the inventors of the ’190 patent invented the subject matter claimed in the challenged claims. *Reiffin v. Microsoft*, 214 F.3d 1342, 1346 (Fed. Cir. 2000) (citing *Vas–Cath*, 935 F.2d at 1563).

As an initial matter, we note that Petitioner’s arguments regarding the effective filing date of the ’190 patent logically apply to certain challenged claims, but not dependent 3, in view of our claim construction of “inhibit.” Pet. 9–11. Claim 1 of the ’190 patent recites that the “release of *at least a portion of* said naproxen is inhibited unless the pH of said medium is 3.5 or higher” (emphasis added), which Petitioner suggests encompasses the release of at least some naproxen when the pH is below 3.5. Pet. 9 (asserting that the challenged claims “allow for release of some amount of naproxen immediately at any pH”). Dependent claim 3 recites, however, “a coating that *inhibits* [naproxen] *release* from [the dosage form] *unless* said dosage form is in a medium with a pH of 3.5 or higher,” without reciting “at least a portion.” As discussed above, the term “inhibit” in the claims means to prevent (stop), hinder, or restrain. Petitioner does not explain adequately how claim 3 encompasses the release of at least some naproxen when the pH

is below 3.5 when those claims require inhibiting the release of naproxen (and not a portion of naproxen) at that lower pH. Pet. 9–11.

In addition, as part of Petitioner’s argument, when stating that “[i]n each description of the invention of the ’255 publication, the NSAID is released only after stomach pH is raised above at least 3.5,” Petitioner contends that paragraphs 3, 5, and 20 in the ’255 publication describe “[a]ll of the dosage forms” as pertaining to “sequential release of acid inhibitor followed by analgesic,” or “criticize[] prior art formulations that allow for the immediate release of NSAIDs.” Pet. 10 (citing Ex. 1006 ¶¶ 3, 5, 20). Those paragraphs are present in both the ’255 publication and the ’190 patent. Ex. 2016, 2–3, 20. We do not agree that those paragraphs indicate that the ’216 application (or the ’190 patent specification) merely describes formulations that only provide release of naproxen when the pH is 3.5 or higher.

Patent Owner points us to paragraph 44 in the ’255 publication (the ’216 application), for example. Prelim. Resp. 12–14 (citing Ex. 1006 ¶ 44; Ex. 1001, 8:40–53). Paragraph 44 states that “[e]nteric coating layer(s) may be applied onto the core or onto the barrier layer of the core using standard coating techniques,” and that the “pH at which the enteric coat will dissolve can be controlled” and “dissolution characteristics of the polymer film can be altered” by using different components in the enteric coating. Ex. 1006 ¶ 44. That description alone reasonably conveys that the inventors had possession of relevant formulations having different types of enteric

coatings, including those providing different dissolution profiles. We further see that paragraph 10 in the '255 publication describes a release of NSAID that “*minimizes* the adverse effects of the NSAID on the gastroduodenal mucosa.” Ex. 1006 ¶ 10 (emphasis added). In addition, paragraph 82 in Example 7 refers to a coordinated delivery dosage that provides “the *delayed* release” of naproxen (emphasis added). *Id.* at ¶ 82. Considering such descriptions, we are persuaded that the inventors possessed a relevant composition where a portion (e.g., a small portion) of NSAID was released when the pH of the medium was below 3.5, even if most or nearly all of the drug was not released until the pH was 3.5 or higher.

Additionally, not every species in a genus need be described in order for the genus to meet the written description requirement. *Regents of U. California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) (citing *Utter v. Hiraga*, 845 F.2d 993, 998–99 (Fed. Cir. 1988)). In this case, the genus at issue has two easily identified species, i.e., inhibiting the release of all or a portion of a drug unless a pH is reached, in contrast to a complex chemical genus, for example, encompassing a large number of possible species. *Id.*; see also *Hynix Semiconductor Inc. v. Rambus Inc.*, 645 F.3d 1336, 1352 (Fed. Cir. 2011) (stating that whether disclosure of a species supports a genus “depends upon the state of the art and the nature and breadth of the genus,” finding sufficient support where the genus consisted of only two species). We are persuaded that the '255 publication as a whole conveys to one of ordinary skill in the art that the inventors of the '190

patent invented the subject matter claimed in the challenged claims, i.e., a composition where release of all or at least a portion of naproxen is inhibited unless the pH is 3.5 or higher.

In view of the information before us, Patent Owner establishes sufficiently that the challenged claims of the '190 patent properly claim priority to the '216 application. Thus, the '255 publication is not prior art to the challenged claims under 35 U.S.C. § 102. Consequently, we are not persuaded that Petitioner has established a reasonable likelihood of prevailing in its challenge to claims 1–8 on the basis that the '255 publication anticipates those claim under 35 U.S.C. § 102(b).

C. Asserted Obviousness over the '556 patent alone, or in view of Chandramouli or the '225 patent

Petitioner asserts that claims 1–8 of the '190 patent would have been obvious over the '556 patent alone, or in view of Chandramouli or the '225 patent. Pet. 15–32.

1. The '556 patent (Ex. 1007)

The '556 patent discloses dosage forms, such as oral tablets, comprising a non-steroidal antiinflammatory drug (“NSAID”) and a proton pump inhibit (“PPI”). Ex. 1007, 1:8–13; 4:30–33. The '556 patent lists a number of “well known examples of NSAIDs,” including naproxen. *Id.* at 5:58–6:5. It states that “NSAIDs have been widely used in arthritis therapy for several years,” and incorporates by reference a list of patents that “describe various NSAIDs suitable for use in the invention described herein, and processes for their manufacture.” *Id.* at 6:6–31.

The '556 patent also discloses that PPIs “typically include benzimidazole compounds,” and incorporates by reference a list of patents disclosing “benzimidazole compounds suitable for use in the invention.” *Id.* at 6:32–50. The '556 patent states that in “certain preferred embodiments, the proton pump inhibitor is omeprazole, either in racemic mixture or only the (-)-enantiomer of omeprazole (i.e. esomeprazole), as set forth in U.S. Pat. No. 5,877,192, hereby incorporated by reference.” *Id.* at 6:50–58 (citing the '192 patent, Ex. 1008).

The '556 patent teaches that “[a]s is well known in the art, proton pump inhibitors are susceptible to degradation and/or transformation in acidic and neutral media,” and that the half-life of “omeprazole in water solutions at pH-values less than three is shorter than ten minutes.” *Id.* at 8:9–17. Thus, according to the '556 patent, “it is preferable that in an oral solid dosage form they be protected from contact with the acidic gastric juice and the active substance must be transferred in intact form to that part of the gastrointestinal tract where pH is near neutral and where rapid absorption of the medication can occur.” *Id.* at 8:18–29.

Along these lines, the '556 patent discloses embodiments where “the tablet contains the NSAID within a sustained release matrix and the proton pump inhibitor coated into the tablet in an enteric coated layer.” *Id.* at 12:4–7. It discloses embodiments where “coatings are provided to permit either pH-dependent or pH-independent release, e.g., when exposed to gastrointestinal fluid.” *Id.* at 12:17–19. The '556 patent further states that

“[a] pH-dependent coating serves to release the proton pump inhibitor in desired areas of the gastro-intestinal (GI) tract, e.g., the small intestine, such that an absorption profile is provided which is capable of providing at least about twelve hour and preferably up to twenty-four hour relief to a patient.” *Id.* at 12:19–24. It states it is “preferable to formulate compositions which release a portion of the dose, preferably the NSAID, in one desired area of the GI tract, e.g., the stomach, and release the remainder of the dose, preferably the proton pump inhibitor, in another area of the GI tract, e.g., the small intestine.” *Id.* at 12:27–32.

2. *Analysis of Asserted Obviousness over the '556 patent*

Petitioner asserts that the '556 patent alone renders claims 1–8 of the '190 patent obvious. Pet. 15–22, 24–32. In relation to the drug release limitations of claims 1 and 3, Petitioner points us to column 12 in the '556 patent as teaching “a combination tablet that releases the NSAID and PPI at different times using pH-dependent and pH-independent coatings,” and the “use of these coatings to ‘release a portion of the dose [. . .] in one desired area of the GI tract, e.g., the stomach, and release the remainder of the dose [. . .] in another area of the GI tract, e.g., the small intestine.’” Pet. 16, 18, 26–27 (citing Ex. 1007, 12:17–18, 27–40).

Although Petitioner acknowledges that “the '556 patent discloses a preferred formulation that would release the NSAID in the stomach and omeprazole in the small intestine,” essentially the opposite of what is recited in the challenged claims, Petitioner asserts that the '556 patent “is not

limited to such formulations.” *Id.* at 17. Citing Dr. Banakar’s Declaration in support, Petitioner contends that a person of ordinary skill in the art (“POSA”) “would have understood that PPIs are preferably released in the gastrointestinal tract prior to reaching the small intestine” because PPIs act “by inhibiting H₂ receptors on the surface of parietal cells,” which “are primarily concentrated in the duodenum, the portion of the GI tract directly following the stomach.” *Id.* at 17 (citing Ex. 1002 ¶¶ 35, 49). Petitioner also argues that it was known that NSAIDs “caused significant topical injury to the GI tract when exposed to acidic environments,” and the risk of this injury “is reduced if the NSAID is released in a more neutral environment, such as the small intestine,” and a POSA would have “been motivated to release the NSAID later in the GI tract.” *Id.* at 17–18 (citing 1002 ¶¶ 32, 35, 49, 55).

In the specific portions of the reference cited by Petitioner, the ’556 patent teaches an “NSAID within a sustained release matrix and the proton pump inhibitor coated into the tablet in an enteric coated layer,” where the “pH-dependent coating serves to release the proton pump inhibitor in desired areas of the gastro-intestinal (GI) tract, e.g., the small intestine” (where the pH is higher than 3.5), and that it is “preferable” to release the NSAID in the stomach (i.e., at a pH at 3.5 or lower). *Id.* at 16; Ex. 1007, 12:4–7, 27–32; Prelim. Resp. 19–21. Thus, Petitioner does not rely on teachings in the ’556 patent itself as disclosing or suggesting the particular release profiles of esomeprazole (PPI) and naproxen (NSAID) based on pH as recited in

challenged claim 1.⁸ Instead, the Petition cites to Dr. Banakar's testimony in support of its contention that an ordinary artisan would have done the opposite of what the '556 patent itself teaches and suggests.

Dr. Banakar's testimony cites other references (not cited in the Petition) in support of the contention that it was known PPIs act on parietal cells in the GI tract. Ex. 1002 ¶¶ 32, 35, 48, 49. Dr. Banakar thereafter summarily concludes that a "POSA would have understood that esomeprazole should be released early in the GI tract to reduce the acidity

⁸ In its analysis and claim chart pertaining to claim 1 and its "release" limitation, Petitioner quotes the '556 patent in a manner that fails to include relevant portions of the cited passage. Pet. 16, 26–27 (citing Ex. 1007, 12:33–40). The passage at column 12, lines 33–40, actually states: "Formulations according to the invention that utilize pH-dependent coatings to obtain formulations may also impart a repeat-action effect whereby **unprotected drug, preferably the NSAID**, is coated over the enteric coat and **is released in the stomach, while the remainder, preferably containing the proton pump inhibitor, being protected by the enteric coating, is released further down the gastrointestinal tract.**" Ex. 1007, 12:33–40 (emphasis added, including to indicate portions omitted in Petitioner's claim chart). Elsewhere in columns 8 and 12 of the '556 patent, the '556 patent repeatedly refers to using a pH dependent coating (e.g., enteric coating) to facilitate release of PPI in the small intestines, while not coating NSAID so that it is released the stomach. *Id.* at 12:4–40, *see also id.* at 8:17–40 (disclosing protecting PPIs so they are released "where the pH is near neutral"). Petitioner has not pointed adequately to where the '556 patent discloses or suggests doing the reverse, e.g., enterically coating NSAID so that it is released further down the GI tract (where the pH is higher), and releasing "unprotected" PPI at any pH, such as in the stomach (where the pH is 3.5 or lower).

(inhibit proton pumps) while naproxen may be released simultaneously, or preferably later than the release of esomeprazole, in order to reduce the risk of NSAID-associated gastroduodenal injury,” without citing additional information in support. *Id.* at ¶¶ 35, 32, 48, 55.

Such conclusory statements by Petitioner and its declarant do not explain sufficiently, nor provide adequate support as to, why an ordinary artisan would have prepared the composition of claim 1 (requiring release of at least some esomeprazole regardless of the pH, e.g., in the stomach, not just the small intestine), or done the opposite of what the '556 patent taught to address the issue of PPI stability at lower pHs. Ex. 1007, 8:17–40, 12:4–40. Petitioner’s conclusory assertions that the subject matter of claim 1 would have been “obvious to try” are likewise inadequate to address these points. Pet. 18.

Regarding a reasonable expectation of success, Petitioner also argues, essentially, that the '556 patent fails to teach away from the challenged claims. Pet. 18–22 (stating, for example, that the '556 patent “does not suggest formulas with non-enteric coated PPIs would result in no bioavailability of the PPI,” *id.* at 18–19). A lack of teaching away regarding the bioavailability of non-enteric coated esomeprazole in the '556 patent, by itself, does not indicate a reasonable expectation of success in making the compositions recited in the challenged claims.

Petitioner also relies on the Pilbrant reference (Ex. 1010)⁹ to support the argument that “it would have been obvious to a POSA that a viable, therapeutically effective formulation could be developed using non-enteric coated esomeprazole.” *Id.* at 19–22. Petitioner refers to a decision by the Federal Circuit, alleging that the court previously “acknowledged that Pilbrant teaches non-enteric solid dosage forms of PPIs as a ‘viable alternative to enteric coating.’” Ex. 21–22 (citing *Santarus, Inc. v. Par Pharm.*, 694 F.3d 1344, 1355–56 (Fed. Cir. 2012)).

Consistent with the ’556 patent, Pilbrant teaches that “[o]meprazole degrades very rapidly in water solutions at low pH-values.” Ex. 1010, 113. In this context, Pilbrant describes the use of an “enteric-coated dosage form, which releases omeprazole for absorption in the small intestine,” while stating that a conventional oral dosage “was ruled out” because “more than half of the omeprazole in a rapidly dissolving dosage form degrades in the stomach.” *Id.* at 114. In addition, Pilbrant states that a “rapidly dissolving *suspension* of micronised omeprazole is the second best choice” to the enteric-coated dosage form. *Id.* at 116 (emphasis added). Pilbrant describes combining that suspension “together with sodium bicarbonate buffer,” and states that “results clearly show that a conventional, non-buffered, oral dosage form of omeprazole will have a low systemic bioavailability owing to preabsorption degradation of omeprazole in the stomach.” *Id.* at 117.

⁹ Pilbrant et al., *Development of an Oral Formulation of Omeprazole*, 20 (108) SCAND. J. GASTROENTEROL. 113–120 (1985) (“Pilbrant”).

Petitioner's arguments regarding Pilbrant and statements by the Federal Circuit ignore a distinction between a solid oral formulation (such as a tablet having layers) and a solution/suspension comprising omeprazole. As stated by the Federal Circuit, "Pilbrant discusses four options: 1) solutions; 2) suspensions of buffered non-enteric coated omeprazole; 3) conventional oral dosage forms—tablets, capsules or granules—with nonenteric coated PPIs; and 4) conventional oral dosage forms with enteric-coated PPIs." *Santarus*, 694 F.3d at 1355. As further stated by the court, "Pilbrant explicitly 'ruled out' the third option—non-enteric coated conventional oral dosage forms such as tablets, capsules, or granules—because they degrade too quickly in the stomach to be absorbed in sufficient amounts to be effective." *Id.* By contrast, regarding the second option, Pilbrant "teaches that, although suspensions of buffered non-enteric coated omeprazole may be the 'second best choice,' they are a viable alternative to enteric coating." *Id.* at 1355–56.

In other words, Pilbrant teaches preparing buffered suspensions of non-enteric coated omeprazole, but teaches away from preparing non-enteric coated tablets of the drug, e.g., a composition with layers where the PPI is released regardless of pH, e.g., in the stomach. Ex. 1010, 114, 116–117. Petitioner's arguments regarding Pilbrant do not explain sufficiently why an ordinary artisan would have had a reasonable expectation of success in making a relevant composition comprising a first and second layer where "at least a portion of said esomeprazole is released regardless of the pH of the

medium and release of at least a portion of said naproxen is inhibited unless the pH of said medium is 3.5 or higher,” as recited in independent claim 1, especially in view of teachings in the ’556 patent, as discussed above.

3. *Chandramouli (Ex. 1009)*

Chandramouli is entitled “Prevention and Management of NSAID-Induced Gastropathy.” Ex. 1009, 27. Chandramouli teaches that because “NSAID-associated GI injury is dependent on the presence of acid, the prophylactic use of an H2 blocker seems reasonable.” *Id.* at 36.

Chandramouli also states that PPIs “suppress acid secretion to a greater degree than H2-receptor antagonists,” and “[n]evertheless, omeprazole is more effective against duodenal than gastric ulceration.” *Id.* Chandramouli further states that a study called the “OMNIUM study (Omeprazole versus Misoprostol for NSAID-Induced Ulcer Management) concluded however that omeprazole may be as effective or more effective than misoprostol for the prevention of NSAID-induced gastropathy.” *Id.*

In addition, Chandramouli discloses that although misoprostol “is the only agent labeled for co-therapy with NSAIDs,” and “prevents both gastric and duodenal ulceration,” “[s]ignificant dose-related diarrhea and abdominal pain limits its tolerability,” and “its use in women of childbearing potential is contraindicated.” *Id.* at 37. The reference also teaches that “[i]n an attempt to be more cost-effective, [misoprostol] was combined with diclofenac (Arthrotec®),” and the “combination is as effective for arthritis

pain and symptoms as diclofenac alone with a decreased incidence of ulcers.” *Id.*

4. *Analysis of Asserted Obviousness over the ’556 patent and Chandramouli*

Petitioner contends that challenged claims 1–8 would have been obvious over the ’556 patent in view of Chandramouli. Pet. 22–23. Petitioner states that Chandramouli teaches that “use of NSAIDs results in significant deleterious effects on the upper gastrointestinal tract,” including the small intestines, and that PPIs, such as omeprazole, can reduce that risk. *Id.* at 22 (citing Ex. 1009, 31–32, 36). Petitioner further contends “[g]iven the structure and function of the dosage form taught in the ’556 patent, a POSA would have been strongly motivated by Chandramouli to make a combination tablet described in the ’556 patent with esomeprazole released first in the stomach followed by naproxen in the small intestine. *Id.* at 23.

Petitioner’s contentions here, once again, do not explain sufficiently, nor provide adequate support as to why an ordinary artisan would have done the opposite of what the ’556 patent taught to address the issue of PPI stability at lower pHs, especially in view of teachings in Pilbrant regarding compositions comprising omeprazole, as discussed above. Ex. 1007, 8:17–40, 12:4–40; Ex. 1010, 114, 116–117.

5. *The ’225 patent (Ex. 1013)*

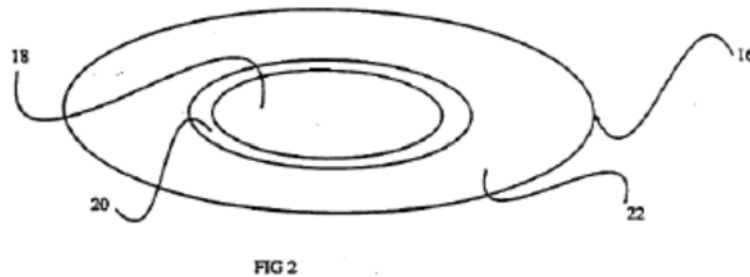
The ’225 patent teaches that NSAIDs have “high therapeutic value especially for the treatment of inflammatory conditions such as . . . osteoarthritis (OA) and rheumatoid arthritis,” but “also exhibit undesirable

side effects.” Ex. 1013, 1:20–24. “An especially undesirable side effect of the administration of NSAIDs is the ulcerogenic effects generally associated with chronic use.” *Id.* at 1:24–27. “NSAID induced ulcers in the stomach . . . generally exhibit few or no symptoms and may cause dangerous bleeding when undetected . . . [and] [i]n some instances . . . can prove fatal.” *Id.* at 1:29–33.

According to the ’225 patent, “[c]ertain prostaglandins have been shown to prevent NSAID induced ulcers.” *Id.* at 1:39–40. Misoprostol, for example, “is a pharmaceutically acceptable prostaglandin which has been accepted for use in the treatment of NSAID induced ulcers.” *Id.* at 1:43–49.

The ’225 patent discloses a pharmaceutical composition comprising a tablet having an inner core and an outer mantle coating surrounding the inner core, designed to “counter (by inhibiting, reducing or preventing) the ulcerogenic side effects attendant to NSAID administration.” *Id.* at 1:61–63. The inner core consists of an NSAID—disclufenac or piroxicam—and the outer mantel consists of a prostaglandin—e.g., misoprostol. *Id.* at 1:11–17, 39–47.

Figure 2 of the '225 patent, reproduced below, depicts tablet 16 in cross-section.



In Figure 2, tablet 16 includes an NSAID—diclofenac or piroxicam—in inner core 18. Enteric coating 20 surrounds core 18, and mantle 22—consisting of a prostaglandin, e.g., misoprostol—surrounds the coated inner core. *Id.* at 6:24–44.

The enteric coating “can be formulated from any suitable enteric coating material,” and “aids in segregating the NSAID from the prostaglandin and in directing the dissolution of the NSAID core in the lower G.I. tract as opposed to the stomach.” *Id.* at 6:29–30, 33–36.

6. *Analysis of Asserted Obviousness over the '556 patent and the '225 patent*

Petitioner contends that claims 1–8 of the '190 patent would have been obvious over the '556 patent in view of the '225 patent. Pet. 23–24. Petitioner acknowledges that the acid inhibitor disclosed in the '225 patent is a prostaglandin, but argues that “[a] POSA would have known that like misoprostol, esomeprazole is an acid inhibitor that reduces the risk of NSAID-associated gastrointestinal injury by increasing gastrointestinal pH to at least 3.5.” *Id.* at 24 (citing Ex. 1002 ¶ 65). Otherwise, Petitioner relies

on arguments discussed above as to why an ordinary artisan would have had reason “to develop an immediate-release esomeprazole composition and would have reasonably expected non-enteric coated esomeprazole to be therapeutically effective.” *Id.* at 24.

Petitioner’s contentions here, once again, do not explain sufficiently, nor provide adequate support as to why an ordinary artisan would have done the opposite of what the ’556 patent taught to address the issue of PPI stability at lower pHs, especially in view of teachings in Pilbrant regarding compositions comprising omeprazole, as discussed above. Ex. 1007, 8:17–40, 12:4–40; Ex. 1010, 114, 116–117.

7. *Conclusions Regarding Asserted Obviousness over the ’556 patent alone or in view of Chandramouli or the ’225 patent*

Having considered information and arguments presented in the Petition, we are not persuaded that Petitioner has established a reasonable likelihood of prevailing in its challenge of claim 1, or its dependent claims, on the basis of obviousness over the ’556 patent, either alone or in view of Chandramouli or the ’225 patent.

D. *Asserted Obviousness over the ’118 patent, the ’225 patent, and the ’192 patent*

Petitioner asserts that claims 1–8 of the ’190 patent would have been obvious over the ’118 patent, the ’225 patent, and the ’192 patent. Pet. 32–38.

1. *The '118 patent (Ex. 1014)*

The '118 patent discloses “a pharmaceutical composition for treating the symptoms of overindulgence . . . [comprising] a combination of non-steroidal anti-inflammatory drug or acetaminophen and a histamine receptor blocker and/or a proton pump inhibitor composition.” Ex. 1014, 1:10–16. The '118 patent teaches that acceptable histamine receptor (e.g., H₂) blockers include famotidine (*id.* at 3:27), acceptable proton pump inhibitors (PPIs) include omeprazole (*id.*), and acceptable NSAIDs include naproxen and piroxicam (*id.* at 3:17–22). The '118 patent discloses using “naproxen from 200 to 500 mg per doses” (*id.* at 5:18–19), and “omeprazole from 60 to 500 mg per dose” (*id.* at 9:25–27). Examples 11 and 12 in the '118 patent disclose tablets consisting of 500 mg of acetaminophen or 200 mg ibuprofen, 60 mg of omeprazole, “and other auxiliary agents and coloring agents.” *Id.* at 7:24–42.

2. *The '192 patent (Ex. 1008)*

The '192 patent discloses omeprazole and pure crystalline enantiomeric salts of the same, including a magnesium salt of *S*-omeprazole, esomeprazole, in the form of a “dosage unit.” Ex. 1008, 1:17–63; 5:25–27. The '192 patent states that a previous “in vitro study on inhibition of acid secretion in isolated gastric glands showed no significant difference in effect between the two single enantiomers of omeprazole and the racemic mixture.” *Id.* at 2:4–13. The '192 patent further discloses giving daily doses

of 60 mg or 15 mg of such compounds to patients “to measure the effect on gastric acid secretion.” *Id.* at 5:6–13.

3. *Analysis*

Petitioner contends that the ’118 patent “describes combination tablets comprising therapeutic amounts of an NSAID and a PPI, where the PPI is not enteric coated,” as well as 200–500 mg dosages of naproxen and 60–500 mg dosages of omeprazole, which “was known to be substantially equivalent to esomeprazole,” as taught in the ’192 patent. Pet. 32 (citing Ex. 1014, 5:18–19, 9:26–27). Petitioner further contends that although an ordinary artisan would have known that omeprazole and esomeprazole are acid labile, the ’118 patent “makes no indication the PPI must be enteric coated in order to be effective,” nor does it “use the term coating at all,” referring to Examples 11 and 12, for example. *Id.* at 32–33 (citing Ex. 1014, 7:34–42, 6:1–9).

Citing two paragraphs in Dr. Banakar’s Declaration that Petitioner previously cites in prior grounds making the same assertion, Petitioner summarily asserts that “a POSA would have been motivated to create a combination tablet that releases esomeprazole prior to naproxen in the GI tract, as discussed above.” Pet. 33 (citing Ex. 1002 ¶¶ 35, 48). Petitioner then argues that “[t]he ’225 patent discloses a structure that would allow for precisely this goal.” *Id.* (citing Ex. 1013, 6:33–36).

In this ground, Petitioner does not explain adequately why one would have had a reason to substitute, with a reasonable expectation of success, the

prostaglandin in the composition disclosed in the '225 patent (Ex. 1013, Fig. 2, 6:24–44) with esomeprazole disclosed in the '192 patent. Pet. 32–38. Neither the Petition, nor the cited paragraphs in Dr. Banakar's Declaration (Ex. 1002 ¶¶ 35, 49), explain sufficiently why one would have engaged in such a substitution, or otherwise prepared a composition with two layers that releases PPI esomeprazole at any pH, especially when considering the teachings in Pilbrant and the '556 patent, as discussed above.

Petitioner's citation to Examples 11 and 12 in the '118 patent, for example, does not provide adequately such reasoning or reasonable expectation of success when the '118 patent does not acknowledge or address that omeprazole degrades rapidly in an acid environment or that the drug requires an enteric coating or suspension buffer to address degradation in the stomach, as disclosed in Pilbrant and the '556 patent. Prelim. Resp. 32; Ex. 1010, 113, 114, 116–17; Ex. 1007, 8:9–48, 12:4–7, 17–32.

Having considered the information and arguments presented in the Petition, we are not persuaded that Petitioner has established a reasonable likelihood of prevailing in its challenge of claim 1, or its dependent claims, on the basis of obviousness over the '118 patent in view of the '225 patent and the '192 patent.

E. Asserted Obviousness over the '225 patent in view of Chandramouli and WO '185

Petitioner asserts that claims 1–8 of the '190 patent would have been obvious over the '225 patent in view of Chandramouli and WO '185. Pet. 39–45.

1. WO '185 (*Ex. 1015*)

WO '185 discloses pharmaceutical preparations containing a PPI, such as omeprazole. *Ex. 1015*, 1:5–28, 4:8–15. WO '185 refers to Pilbrant, noting that it teaches a buffered omeprazole suspension that can be stored in the refrigerator or freezer. *Id.* at 15:3–6. WO '185 describes solutions and suspensions of proton pump inhibitors, such as omeprazole, that may be stored at room temperature or in a refrigerator for longer periods of time. *Id.* at 15:19–24.

In this capacity, WO '185 discloses “a pharmaceutical composition including a proton pump inhibitor in a pharmaceutically acceptable carrier including a bicarbonate salt of a Group IA metal.” *Id.* at 16:16–23. In this regard, in addition to a solution or suspension, WO '185 also discloses dry formulations, such as a powder, tablet, capsule, or granules, where the “dosage form is not enteric coated or time-released.” *Id.* at 57: 17–24 (claim 8), 16:24–17:7, 25:19–26:4, 26:26–27:9.

Those solid formulations “then create the present invention when acted upon by a suitable vehicle, for example water.” *Id.* at 27:2–4. As stated in WO '185, “[t]he water may be added either prior to ingestion or the dry formulation may be ingested first and then acted upon by the water utilized to swallow the solid formulation,” or a “third mechanism enables water in the stomach secretions to produce the present invention.” *Id.* at 27:4–9.

WO '185 teaches that in a preferred embodiment, “enterically-coated omeprazole particles are obtained from delayed release capsules,” and those “particles are mixed with a sodium bicarbonate (NaHCO_3) solution which dissolves the enteric coating and forms an omeprazole solution/suspension.” *Id.* at 19:16–23.

2. Analysis

Petitioner contends that “the '225 patent discloses a combination tablet comprising enteric-coated NSAID in the core and further surrounded by an uncoated acid inhibitor, misoprostol.” Pet. 39. Petitioner also argues that an ordinary artisan reading the '225 patent and Chandramouli would have known about stability issues and contraindications associated with misoprostol, and that omeprazole could be used in its place. *Id.* (citing Ex. 1013, 1:51–53; Ex. 1009, 36–37). Furthermore, according to Petitioner, upon reading WO '185, an ordinary artisan would have had additional reason to use, with a reasonable expectation of success, omeprazole (and therefore esomeprazole as an equivalent) that was not enterically coated, instead of misoprostol, in the system taught in the '225 patent. *Id.* at 39–40 (citing Ex. 1015, 57:23–24, 1:23–28; 2:4–9, 4:8–15, 17:25–27; Ex. 1002 ¶¶ 73–75, 79). Petitioner further asserts that an ordinary artisan would have understood that the “addition of even a small amount of buffer would substantially increase bioavailability” of a PPI such as esomeprazole. *Id.* at 40–41 (citing Ex. 1002 ¶¶ 70, 30).

For purposes of institution, based on the record before us, Petitioner reasonably contends that one would have had reason to use omeprazole (or the related PPI, esomeprazole) instead of misoprostol to prevent NSAID-associated GI injury, as a general matter, based on teachings in Chandramouli. Ex. 1009, 36–37. Petitioner also reasonably contends that the '225 patent discloses a tablet that is similar to the composition recited in claim 1, except that the '225 patent uses misoprostol in place of a PPI. A question, therefore, is whether Petitioner reasonably contends that one would have had reason to substitute a PPI, such as esomeprazole, for misoprostol in the tablet of the '225 patent, especially in light of the acid labile nature of PPIs and teachings in the '556 and Pilbrant, as discussed above.

Considering the information and the references before us, including Pilbrant and the '556 patent, WO '185 is the only reference cited by Petitioner that may teach or suggest a viable solid (non-suspension) form of a PPI that is not enterically coated. Petitioner persuades us that WO '185 teaches using a bicarbonate salt of a Group IA metal (such as sodium) in a tablet immediate release formulation of a PPI. Petitioner does not contend, however, WO '185 teaches or suggest a combination drug composition comprising a PPI and another drug, such as an NSAID, much less a composition comprising both a PPI released at any pH and an NSAID released only when the pH is 3.5 or higher, as required in the challenged claims. *See also* Prelim. Resp. 38 (noting that WO '185 does not mention

NSAIDs). Petitioner instead relies on the '225 patent as teaching a combination drug tablet composition having the recited release profiles.

Notably, WO '185 discloses that enterically-coated omeprazole particles, obtained from delayed release capsules, “are mixed with a sodium bicarbonate (NaHCO_3) solution which dissolves the enteric coating and forms an omeprazole solution/suspension.” Ex. 1015, 19:16–23. In other words, WO '185 suggests that a bicarbonate salt, i.e., the buffer salt used in WO '185 to prepare an immediate release solid form of a PPI, dissolves enteric coatings, thereby causing coated drugs to be released in solution or suspension.

Patent Owner responds that WO '185 indicates that “the PPI and bicarbonate solutions of WO '185 cannot be combined with the enteric coated NSAID of the '225 patent” because a bicarbonate salt solution would “quickly dissolve” the enteric coating in the tablet disclosed in the '225 patent, as well the NSAID core, thereby facilitating the immediate release (i.e., release regardless of pH) of both the NSAID and PPI. Prelim. Resp. 38–39 (citing Ex. 1015, 19:16–23). Patent Owner’s response has merit because Petitioner does not address the teaching on page 19 of WO '185 regarding the impact of a bicarbonate salt on an enteric coating, a coating that the '225 patent discloses as surrounding the NSAID, a coating that inhibits NSAID release until the pH is 3.5 or higher (i.e., in the lower G.I. tract), as recited in the challenge claims. Ex. 1015, 19:16–23; Ex. 1013, Fig. 2, 6:24–44.

Dr. Banakar, Petitioner's witness, refers to page 19 in WO '185 when asserting that "WO'185 would have motivated a POSA to try a combination tablet with uncoated esomeprazole." Ex. 1002 ¶ 79; *see also* Pet. 39 (citing Ex. 1002 ¶ 79). Like Petitioner, however, Dr. Banakar does not address the impact of a bicarbonate salt on an enteric coating, nor whether a bicarbonate salt in the "mantle" in the tablet of the '225 patent (Ex. 1013, Fig. 2, 6:24–44) might destroy the enteric coating surrounding the NSAID, causing immediate release of the NSAID in a medium at any pH.

Challenged claim 1 recites a composition comprising two layers where "*at least a portion of said esomeprazole is released regardless of the pH of the medium and release of at least a portion of said naproxen is inhibited unless the pH of said medium is 3.5 or higher.*" Ex. 1001, 21:24–22:6 (emphasis added). Neither party, thus far, has addressed adequately whether an ordinary artisan would have had reason to believe that making a tablet as disclosed in the '225 patent, where misoprostol is substituted with the bicarbonate salt buffered PPI disclosed in WO '185 and the NSAID is naproxen, would have resulted in a composition where release of at least some (even if not all) naproxen would have been "inhibited unless the pH of said medium is 3.5 or higher" (Ex. 1001, 21:34–35), even assuming the bicarbonate in the PPI "mantle" layer would have dissolved the enteric coating surrounding the NSAID eventually, for the reasons stated on page 19 of WO '185 (Ex.1015, 19:19–23).

Based on the record and information before us at this time, which indicates a close call on at least the above-mentioned issue, we are persuaded to go forward with a trial in relation to independent claim 1 and dependent claims 2 and 4–8.

Claim 3 recites a “first layer comprises a coating that inhibits [naproxen] release from said unit dosage form unless said dosage form is in a medium with a pH of 3.5 or higher.” Thus, this claim differs from claim 1 in that release of all, not just a portion, of naproxen is inhibited unless the pH of said medium is 3.5 or higher. In view of the above-mentioned teachings in the WO ’185 regarding the impact of a bicarbonate salt on an enteric coating, Petitioner does not persuade us adequately that one would have had a reason to make, with a reasonable expectation of success, a tablet of the ’225 patent, substituting misoprostol with a bicarbonate salt buffered PPI, such that the tablet would not release any NSAID at a pH lower than 3.5, i.e., in the stomach.

Having considered the information and arguments presented in the Petition, we are persuaded that Petitioner has established a reasonable likelihood of prevailing in its challenge of claims 1, 2, and 4–8 on the basis of obviousness over the ’225 patent in view of Chandramouli and WO ’185. We are not persuaded that Petitioner has established a reasonable likelihood of prevailing in its challenge of claim 3 on that basis.

III. CONCLUSION

For the foregoing reasons, based on the present record, we determine that Petitioner has demonstrated that there is a reasonable likelihood that it would prevail in showing that claims 1, 2, and 4–8, but not claim 3, of the '190 patent are unpatentable. At this stage of the proceeding, the Board has not made a final determination with respect to the patentability of those challenged claims or any underlying factual or legal issues.

IV. ORDER

Accordingly, it is

ORDERED that, pursuant to 35 U.S.C. § 314(a), *inter partes* review is instituted as to the ground of unpatentability that claims 1, 2, and 4–8 of the '190 patent would have been obvious over the '225 patent (Ex. 1013) in view of Chandramouli (Ex. 1009) and WO '185 (Ex. 1015);

FURTHER ORDERED that *inter partes* review commences on the entry date of this Order, and pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial; and

FURTHER ORDERED that the trial is limited to the ground of unpatentability listed above, and no other ground of unpatentability is authorized for *inter partes* review.

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Patent 8,865,190 B2

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