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Paper 28
Entered: October 9, 2015

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. REDDY'S LABORATORIES, INC.,
Petitioner,

v.

POZEN INC.,
Patent Owner.

Case IPR2015-00802
Patent No. 8,557,285 B2

Before SHERIDAN K. SNEDDEN, SUSAN L. C. MITCHELL, ROBERT A. POLLOCK, *Administrative Patent Judges.*

MITCHELL, *Administrative Patent Judge*.

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

I. INTRODUCTION

A. Background

Petitioner Dr. Reddy's Laboratories, Inc. ("Petitioner") filed a petition (Paper 2, "Pet.") to institute an *inter partes* review of claims 1–4 (the "challenged claims") of U.S. Patent No. 8,557,285 B2 (Exhibit 1001, "the '285 patent"). *See* 35 U.S.C. §§ 311-319. Patent Owner Pozen Inc. ("Patent Owner") filed a Preliminary Response. Paper 23 ("Prelim. Resp.").

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." 35 U.S.C. § 314(a). Upon considering the Petition and Preliminary Response, we conclude that Petitioner has not established a reasonable likelihood that it would prevail in showing the unpatentability of any challenged claim of the '285 patent. Therefore, we do not authorize an *inter partes* review for any claim of the '285 patent.

B. Related Proceedings

Petitioner identifies five related district court proceedings in the United States District Court of New Jersey. Pet. 2.

C. The '285 Patent (Ex. 1001)

The '285 patent is directed to drug dosage forms that have a coordinated release of an agent that raises the pH of a patient's gastrointestinal tract to a safe level, followed by a non-steroidal anti-inflammatory drug ("NSAID")), to reduce unwanted gastrointestinal side effects. Ex. 1001, Abs., 1:20–26. Although NSAIDs are effective agents for controlling pain, their use can cause gastroduodenal lesions, such as ulcers and erosions, and a major factor for developing these lesions

appears to be a low pH environment (acid) in the upper small intestine. *Id.* at 1:30–36.

D. Illustrative Claim

Claim 1, the sole independent claim of the '285 patent, is illustrative of the claimed subject matter. Claim 1 is reproduced below.

> 1. A pharmaceutical composition in unit dosage form comprising therapeutically effective amounts of:
>
> (a) esomeprazole, wherein at least a portion of said esomeprazole is not surrounded by an enteric coating; and
>
> (b) naproxen 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;
>
> 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.

Id. at 22:8–18.

E. Prior Art Relies Upon

Petitioner challenges the patentability of claims 1–4 on the basis of the following prior art references:

Plachetka	US 2003/0069255	Apr. 10, 2003	(Ex. 1021)
Stephen P. Clissold and Deborah M. Campoli-Richards, "*Omeprazole: A Preliminary Review of its Pharmacodynamic and Pharmacokinetic Properties, and Therapeutic Potential in Peptic Ulcer Disease and Zollinger-Ellison Syndrome*, 32 DRUGS 15–47 (1986)			(Ex. 1029)
Depui	WO 97/125064	July 17, 1997	(Ex. 1030)
Lundberg	WO 00/78293	Dec. 28, 2000	(Ex. 1031)
Phillips	WO 00.26185	May 11, 2000	(Ex. 1032)

F. The Asserted Grounds of Unpatentability

Petitioner contends that the challenged claims are unpatentable based on the following grounds (Pet. 4–11):

References	Basis	Claims challenged
Plachetka Publication	§ 102(b)	1–4
Depui, Lundberg, Phillips and/or Clissold	§ 103(a)	1–4

II. ANALYSIS

A. Claim Construction

In an *inter partes* review, claim terms in an unexpired patent are given their broadest reasonable construction in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b); *see also In re Cuozzo Speed Techs., LLC*, 793 F.3d 1268, 1279 (Fed. Cir. 2015) ("Congress implicitly approved the broadest reasonable interpretation standard in enacting the AIA,"[1] and "the standard was properly adopted by PTO regulation."). Significantly, claims are not interpreted in a vacuum but are part of, and read in light of, the specification. *United States v. Adams*, 383 U.S. 39, 49 (1966) ("[I]t is fundamental that claims are to be construed in the light of the specifications and both are to be read with a view to ascertaining the invention . . . ."). 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). An inventor may rebut that presumption

[1] The Leahy-Smith America Invents Act, Pub. L. No. 112–29, 125 Stat. 284 (2011) ("AIA").

by providing a definition of the term in the specification with reasonable clarity, deliberateness, and precision. *In re Paulsen*, 30 F.3d 1475, 1480 (Fed. Cir. 1994). In the absence of such a definition, limitations are not to be read from the specification into the claims. *In re Van Geuns*, 988 F.2d 1181, 1184 (Fed. Cir. 1993).

Petitioner proposes constructions for the terms "comprising . . . naproxen surrounded by a coating," "inhibit," and "at least a portion of said esomeprazole." Pet. 24–30. Patent Owner proposes a construction for the three terms defined by Petitioner, as well as the claim terms "enteric coating" and "unit dosage form." We address the construction of "enteric coating" in this section. Because the arguments concerning why the Plachetka Publication is prior art under 35 U.S.C. 102(b) is so intertwined with Petitioner's proposed constructions and Patent Owner's proposed construction of "unit dosage form," we construe the remaining terms as we address the ground asserting the Plachetka Publication.

"enteric coating"

Petitioner adopted the definition of "enteric coating" from a district court construction of the term for U.S. Patent No. 6,926,907 ("the '907 patent) that shares the same specification as the '285. Pet. 11, n.1, 13 (quoting Patent Owner's statement that the '907 patent shares the same specification of the '285 patent). The district court interpreted "enteric coating" to mean "a delayed release coating" and noted that although such coating is "commonly and perhaps frequently pH-dependent, the evidence shows that other types of enteric coating are utilized in the field." Ex. 1019, 12.

Patent Owner similarly contends that the proper construction of "enteric coating" means "a delayed release coating," but agrees with the district court that the broadest reasonable interpretation of the term "should not be construed as 'strictly a pH-dependent form.'" Prelim. Resp. 11. Petitioner does not appear to disagree with this construction. *See* Pet. 11, n.1. On the present record, we conclude that the broadest reasonable interpretation of "enteric coating" is a delayed release coating that is not limited to a strictly pH-dependent form. *See* Ex. 1001, 4:59–64 ("Alternatively, a barrier coating may be employed which controls the release of NSAID by time, as opposed to pH, with the rate adjusted so that NSAID is not released until after the pH of the gastrointestinal tract has risen to at least 3.5, preferably at least 4, and more preferably at least 5.").

B. Principles of Law

A claim is unpatentable under 35 U.S.C. § 102 if a single prior art reference expressly or inherently describes each and every limitation set forth in the claim. *See Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1375 (Fed. Cir. 2005); *Verdegaal Bros., Inc. v. Union Oil Co.*, 814 F.2d 628, 631 (Fed. Cir. 1987).

A claim is unpatentable under 35 U.S.C. § 103 if the differences between the claimed subject matter 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).
The question of obviousness is resolved on the basis of underlying factual determinations including: (1) the scope and content of the prior art; (2) any differences between the claimed subject matter and the prior art; (3) the level

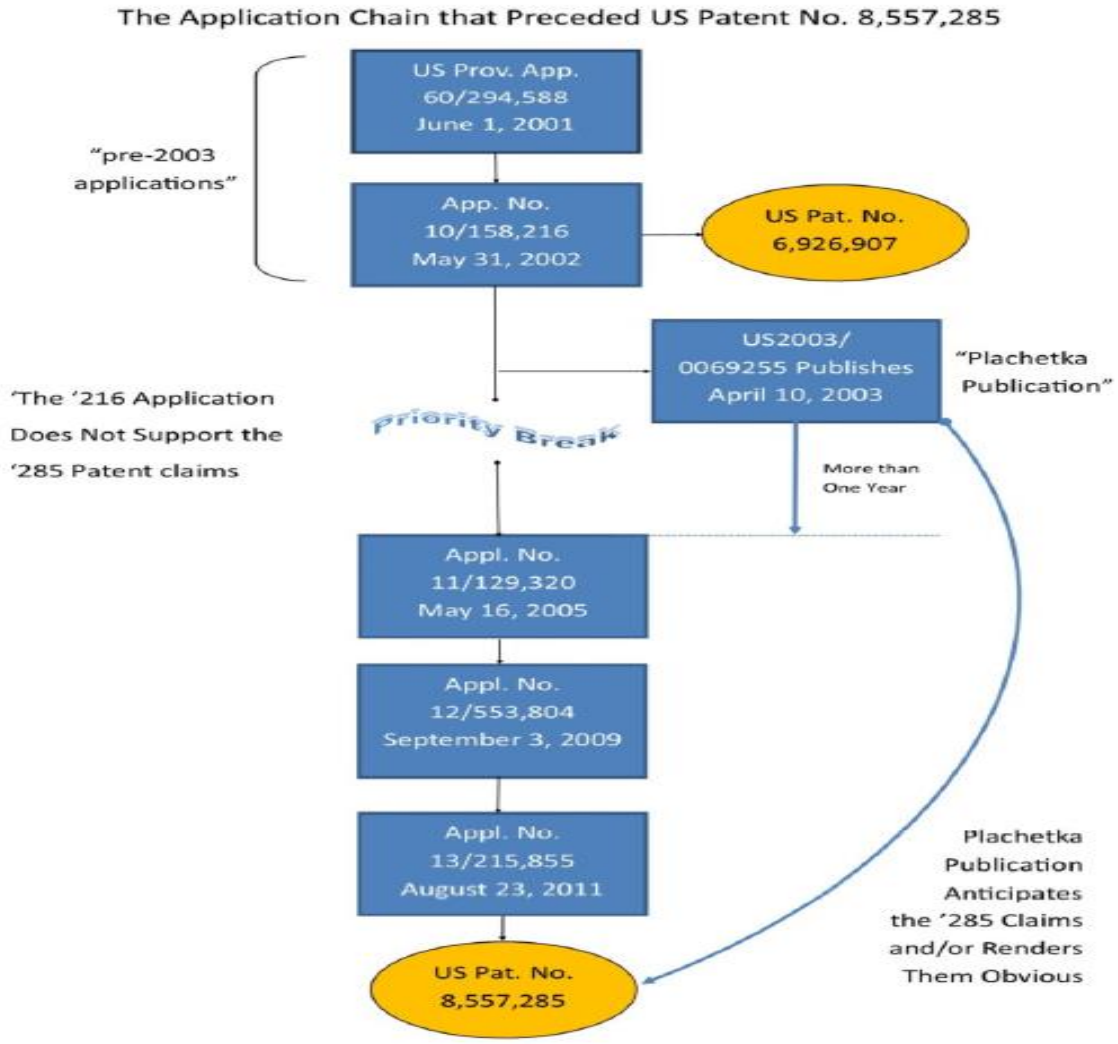
of ordinary skill in the art; and (4) objective evidence of nonobviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966).

A prima facie case of obviousness is established when the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. *In re Rinehart*, 531 F.2d 1048, 1051 (CCPA 1976). The level of ordinary skill in the art is reflected by the prior art of record. *See Okajima v. Bourdeau*, 261 F.3d 1350, 1355 (Fed. Cir. 2001); *In re GPAC Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995); *In re Oelrich*, 579 F.2d 86, 91 (CCPA 1978).

We analyze the asserted grounds of unpatentability in accordance with the above-stated principles.

C. Anticipation by or Obviousness Over the Plachetka Publication

Petitioner asserts that the claims of the ’285 patent are not entitled to an effective filing date earlier than May 16, 2005, because the two applications filed before this date in the listed chain of priority on the face of the ’285 patent do not provide written description support for five features of the claims of the ’285 patent. Pet. 4. This alleged break in the chain of priority for the claims of the ’285 patent is illustrated in the following figure provided by Petitioner.



Id. at 7.

As the above figure shows, the '285 patent issued from a series of five applications all of which Petitioner characterizes as addressing "compositions combining an acid inhibitor and an NSAID and related methods," all naming John R. Plachetka as the sole inventor. *Id*. at 12; Ex. 1001. Petitioner admits that the specifications of these five applications are similar. *Id*. As shown in the figure above, US Provisional Application 60/294,588 ("the '588 application") and US Application No. 10/158,216 ("the '216 application") are two pre-2003 applications in the priority chain that Petitioner asserts do not provide written description support for five of

the features of the claims of the ’285 patent. Because the Plachetka Publication was published more than two years before the earliest effective filing date, Petitioner asserts, the Plachetka Publication is prior art under 35 U.S.C. 102(b). *Id*. at 5–6.

Petitioner asserts that under the broadest reasonable construction standard, the claims of the ’285 patent are broad enough to encompass formulations that have the following features:

- releases most of its naproxen immediately at any pH;
- release all of its naproxen slowly at any pH;
- delays release of most of its esomeprazole until reaching a particular pH;
- does not have “coordinated release,” or
- may be administered orally or in any other manner.

Id. at 8.

In contrast, despite admitting that the specifications of the applications in the priority chain for the ’285 are similar (*see id*. at 12–13), Petitioner asserts that the ’588 and ’216 applications disclose naproxen/esomeprazole formulations that:

- release no naproxen immediately, and delay[] naproxen release until reaching a pH of 3.5 or 4;
- prevents the release [of] all of their naproxen until reaching a pH of 3.5 or 4 (as opposed to merely slowing it down, *i.e.*, “inhibiting” it);
- releases all their esomeprazole immediately regardless of pH;
- have “coordinated release,” and
- are orally administered.

Id.

Patent Owner notes that Petitioner has identified no new matter in the specification of the ’285 patent relevant to priority that is not identical to the disclosure in the ’216 application. Prelim. Resp. 14; *see* Ex. 2009 (comparison between the ’216 application and the ’285 patent). Patent Owner states that despite that lack of substantial differences in the specifications, Petitioner argues that the ’285 patent claims are *not* supported by its priority application. Prelim. Resp. 15.

Petitioner’s arguments are rooted in its overbroad claim interpretations, and specifically, as to the application of the transitional term “comprising,” and the claim terms “inhibits” and “portion.” We will address Petitioner’s proposed constructions in turn as they relate to the five features that Petitioner asserts are encompassed by the claims of the ’285 patent, but not supported by the ’588 or the ’216 applications.

1. *“comprising therapeutically effective amounts of . . . naproxen surrounded by a coating . . .” allegedly encompasses formulations that release most of its naproxen at any pH*

Petitioner asserts that the broadest reasonable interpretation of “‘comprising . . . naproxen surrounded by a coating’ allows additional naproxen that is *not* surrounded by a release inhibiting coating in the “unit dosage.” Pet. 26. Petitioner concludes that because the transitional phrase “comprising” allows for additional unrecited elements, “[a]s long as a minimal ‘therapeutically effective’ amount of naproxen in a unit dosage is surrounded by the claimed inhibition coating, any amount of additional uncoated naproxen could be incorporated into the unit dosage.” *Id.* at 27 (citing Ex. 1010, 49–51, in which Patent Owner makes a similar argument in District Court). Petitioner posits that under this interpretation, a unit dosage

could have more than 96.5% of its naproxen released immediately at any pH and not be subject to coordinated release.[2] Pet. 27–28.

Patent Owner relies on the claim phrase "therapeutically effective" to frame its interpretation. Prelim. Resp. 7. The claim language requires that a therapeutically effective amount of naproxen be "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. 1001, 22:12–14. Patent Owner asserts that the specification of the '285 patent explicitly defines "therapeutically effective amount" of NSAID to be "an amount effective to reduce or eliminate pain or inflammation." Prelim. Resp. 7 (citing Ex. 1001, 3:66–4:1). The specification of the '285 patent further defines the therapeutically effective ranges for naproxen, preferably 50 mg to 1500 mg, and most preferably, 200 mg to 600 mg. *Id.* (citing Ex. 1001, 4:11–14).

Because a *therapeutically effective amount* of naproxen must be surrounded by a coating, Patent Owner asserts that Petitioner's position that the transitional phrase "comprising" may be read to include the bulk amount of naproxen to be uncoated is unreasonable. Patent Owner concludes that

> [a]ccordingly, while other components may be present in a unit dosage form that includes but is not limited to the recited therapeutically effective amount of coated naproxen, Petitioner cannot expand this claim term to include *uncoated* naproxen—or any other hypothetical additional components that do not satisfy the expressly recited *coated* naproxen requirement—within this claim limitation.

[2] Petitioner bases this statement on the 50 mg to 1500 mg range for naproxen provided in the specification of the '285 patent (*see* Ex. 1001, 4:11–14), wherein Petitioner asserts that a formulation within the scope of the claims of the '285 patent includes a 50 mg minimum amount of naproxen surrounded by the coating, but 1450 mg outside of the coating.

Prelim. Resp. 8. Patent Owner concludes that "comprising . . . naproxen surrounded by a coating" should be interpreted as "a therapeutically effective amount of naproxen is surrounded by a coating." *Id.* at 9.

Both parties acknowledge that the claim requires a therapeutically effective amount of naproxen must be surrounded by a coating. Pet. 27; Prelim. Resp. 7. Petitioner's interpretation, however, turns this requirement on its head. As Patent Owner notes, using the transitional term "comprising" means that additional components may be present, but does not change the elements that are stated in the claim. Prelim. Resp. 8 (citing *Outside the Box Innovations, LLC v. Travel Caddy, Inc.*, 695 F.3d 1285, 1305 (Fed. Cir. 2012)). Petitioner's interpretation, however, would encompass a composition where the vast majority of the naproxen, i.e., a therapeutically effective amount, would be *outside* of the coating. This is not a reasonable interpretation of the claim.

We agree with Patent Owner that the broadest reasonable interpretation of the term "comprising . . . naproxen surrounded by a coating" means "a therapeutically effective amount of naproxen is surrounded by a coating," but do not agree with Patent Owner's arguments that this claim term excludes *any* uncoated naproxen from the claim.

As Petitioner notes, the Patent Owner has previously addressed the meaning of this limitation in response to invalidity contentions asserting lack of written description support and enablement, stating that the specification of the '285 patent supports the interpretation "that, in addition to naproxen surrounded by a coating that inhibits its release unless the surrounding medium of the unit dosage form is at least 3.5, the disclosed dosage forms may include additional naproxen outside the coating." Ex. 1010, 49 (Patent

Owner's responses to invalidity contentions for the '285 patent) (relying on statements in the specification of the '285 patent where the combination of an acid inhibitor and an NSAID may be in *multi*-layer tablet form and where the drug combinations may typically be prepared in admixture with conventional excipients). Patent Owner also has previously stated that the transitional term "comprising" does not exclude the presence of additional naproxen outside of the coating. *Id.* at 51. We agree. Although the claim term requires that a therapeutically effective amount of naproxen in a unit dosage form is surrounded by a coating, it does not exclude a unit dosage form that has an amount of naproxen outside of the coating that is not therapeutically effective.

Therefore, we do not agree that the claims of the '285 patent encompass a formulation that releases most of its naproxen immediately at any pH as asserted by Petitioner.

2. *"naproxen surrounded by a coating that <u>inhibits</u> its release from said unit dosage form unless said dosage form is in a medium with a pH of 3.5 or higher" allegedly encompasses formulations that release all of its naproxen slowly at any pH*

Petitioner asserts that the claim term "inhibits," which characterizes the action of the naproxen-release coating, be assigned its ordinary meaning. Pet. 28–29. Petitioner uses a dictionary definition to define "inhibits" as "to slow down or stop." *Id.* at 29 (citing Ex. 1038 (Merriam Webster's online dictionary)).

Although Patent Owner agrees that the term, "inhibits" should be afforded its ordinary meaning, Patent Owner states that "inhibits" is better interpreted in light of the specification of the '285 patent and the claims as "prevents, hinders, or restrains." Prelim. Resp. 10.

We do not discern a significant difference between the definitions offered by the parties and are not convinced that we need to provide an explicit definition encompassing the ordinary meaning of the claim term.

Petitioner, however, utilizes its interpretation of the term "inhibits" to support its assertion that the claims of the '285 patent encompass formulations that releases all of its naproxen slowly at any pH, instead of preventing release until the formulations are in a medium with a pH of 3.5 or higher. Pet. 8–9. Petitioner admits that the '216 application discloses eight composition examples where "[h]alf of them describe a release coating whose function is to 'prevent' the release of naproxen or naproxen sodium from the unit dosage until it reaches the desired pH.. The other half describes a release coating that 'delays' the release of naproxen or naproxen sodium from the unit dosage until it reaches a pH [of] 3.5 or 4." Pet. 32 (citations omitted). Petitioner concludes that

> The pre-2003 applications teach that *all* NSAID release must be "delayed" or "prevented"—period. Nowhere in the originally filed pre-2003 applications is there any discussion or even a suggestion that any of the NSAID in the unit dosage may be released below a pH of 3.5.

Id. at 37.

We disagree with Petitioner's interpretation of the difference in breadth between "inhibit," "prevent," and "delay" would lead to the conclusion that the claims of the '285 patent encompass a formulation that releases all of its naproxen slowly at any pH. The distinction between the ordinary meanings of these terms is not so vast to be able to reach such a conclusion. Accordingly, we do not accept Petitioner's argument that the

claims of the ’285 patent encompass a formulation that releases all of its naproxen slowly at any pH.

3. *“at least a portion of said esomeprazole” allegedly encompasses formulations that delay release of most of its esomeprazole until reaching a particular pH*

Petitioner proposes an ordinary meaning construction of “portion” as “a part of any whole.” Pet. 30. Patent Owner agrees that “portion” should be assigned its ordinary meaning, but offers that “portion” is “a part of a larger amount.” Again, we do not discern a significant difference between the definitions offered by the parties and find that we do not need to provide an explicit definition for the ordinary meaning of this claim term.

Petitioner asserts, however, that the pre-2003 applications disclose only acid inhibitor or esomeprazole layers that are entirely uncoated and subject to immediate release. Pet. 9, 36. Patent Owner, however, points to Example 4 in the ’216 application where the controlled-release core tablet of naproxen also contains the acid inhibitor famotidine. Prelim. Resp. 18–19; Ex. 1012, 17–18. This example is also in the specification of the ’285 patent. Ex. 1001, 13:1–14:20.

Both the ’216 application and the specification of the ’285 patent describe Example 4 as follows:

> The controlled-release core tablet of naproxen and famotidine [acid inhibitor] is film coated with a pharmaceutically acceptable enteric coating. The function of the enteric coat is to delay the release of naproxen until the dosage form reaches an environment where the pH is above about 4.
>
> . . . .
>
> The outermost [layer] contains an “acid inhibitor” which is released from the dosage form immediately after

> administration to the patient. The acid inhibitor in the present example is a proton pump inhibitor or, preferably, the H2 blocker famotidine which consistently raises the pH of the stomach to above 4.

Ex. 1012, 17:12–14, 18–21; Ex. 1001, 13:18–22, 29–34. In addition to famotidine, both documents disclose the use of the proton pump inhibitor esomeprazole as an acid inhibitor to raise gastric pH. *See, e.g.*, Ex. 1012, 4:17–18, 10:5–9; Ex. 1001, 3:44–47; 8:5–15. Therefore, we disagree with Petitioner that the pre-2003 applications only disclose formulations that release all their esomeprazole immediately regardless of pH, while the '285 patent claims encompass formulations that delay release of most of its esomeprazole until reaching a particular pH.

4. "unit dosage form" does not encompass non-oral administration

Although Petitioner asserts that the claims of the '285 patent encompass formulations that may be administered in ways other than orally (*see* Pet. 8; Ex. 1036 ¶ 81), only Patent Owner offers an explicit definition of "unit dosage form" and asserts it means "a unit dosage form suitable for oral administration to a patient." Prelim. Resp. 11. To support its interpretation, Patent Owner relies on the claim language and a statement in the specification of the '285 patent that "[a]ll dosage forms are designed for oral delivery and provide for the coordinated release of therapeutic agents, i.e., for the sequential release of acid inhibitor followed by analgesic." *Id.* at 11–12 (citing Ex. 1001, 6:20–23); *see also* Pet. 14–15 (recognizing that the specification of the '285 patent describes a first aspect of the invention directed to a unit dosage form suitable for oral administration and

acknowledging the statement that all the dosage forms were designed for oral delivery).

We agree with Patent Owner that the specification of the '285 patent describes only oral dosage forms for administering the claimed formulations. For instance, in addition to the statement identified by Patent Owner above, in defining and describing "unit dosage form," the specification of the '285 patent states:

> The term "unit dosage form" as used herein 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. 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 of the GI tract has risen.

Ex. 1001, 4:42–51. Moreover, the specification of the '285 patent describes a solution to prevent damage caused to the gastrointestinal tract of patients using NSAIDS, which focuses on the production of tablets and capsules. *See*, *e.g.*, Ex. 1001, 1:20–3:7; *see also id*. at 8:17–21 ("The pharmaceutical compositions of the invention include tablets, dragees, liquids and capsules."). It is hard to imagine how the administration of these dosage forms could be accomplished in a way other than oral administration.

As Patent Owner notes, Petitioner gives no examples of any administration of the claimed pharmaceutical composition that could be used in non-oral administration. Patent Owner also points out that Petitioner does not explain how any other potential non-oral route of administration "would expose the unit dosage to the anticipated pH variations described by the claims and the specification other than the stomach and intestinal tract."

Prelim. Resp. 12. We agree with Patent Owner that "[a]ny administration route other than oral simply makes no sense in the context of the '285 patent." *See id.*

The only explanation offered by Petitioner for its position is that the '285 patent claims do not require the unit dosage form to be "suitable for oral administration" is that this limitation is expressly set forth in the composition claims of the '907 patent. Pet. 25 (comparing '907 and '285 claims), 27. In addition, Petitioner's declarant, Dr. Kibbe, opined that even though "[t]he person of ordinary skill in the art would . . . understand that all of the dosage forms disclosed in the '285 patent are formulated for oral administration," claim 1 of the '285 patent allows for formulations that are suitable for any other type of administration because "there are several other types of administration for which a dosage may be formulated" including "rectal, intravenous, intramuscular, topical, nasal, inhaled, ophthalmic, transdermal, and subcutaneous." Ex. 1036 ¶ 81. Neither of these explanations convinces us that the claimed unit dosage form may be suitable for non-oral administration. Therefore, we construe "unit dosage form" to mean "a single entity for drug administration that is suitable for oral administration."

Because we construe "unit dosage form" to require suitability for oral administration, we disagree with Petitioner that the pre-2003 applications require formulations that are orally administered while the claims of the '285 patent do not.

5. "coordinated release" is required

Finally, Petitioner asserts that the claims of the '285 patent do not require coordinated release of naproxen and esomeprazole. Pet.9, 26 (stating

"'285 patent claims do not require a 'coordinated release' of all of naproxen in the formulation" based on Petitioner's claim construction for "comprising . . . naproxen surrounded by a coating").

Both the '216 application and the specification of the '285 patent state that

> The present invention is directed to drug dosage forms that release an agent that raises the pH of a patient's gastrointestinal tract, followed by a non-steroidal anti-inflammatory drug. The dosage form is designed so that the NSAID is not released until the intragastric pH has been raised to a safe level. The invention also encompasses methods of treating patients by administering *this coordinated release*, gastroprotective, antiarthritic/analgesic combination unit dosage form to achieve pain and symptom relief with a reduced risk of developing gastrointestinal damage such as ulcers, erosions and hemorrhages.

Ex. 1012, 36 (Abs.) (emphasis added); Ex. 1001, Abs. (emphasis added).

Petitioner bases its assertion that the claims of the '285 patent do not require "coordinated release" on its incorrect construction of the claim language to encompass a unit dosage form "that releases most of its naproxen immediately or begins to release all of its naproxen immediately, but at a slow rate." Pet. 35, *see id.* at 35–38. As we have found, neither is a requirement of the claims of the '285 patent. *See supra* Section II.C.1.–3. The claims of the '285 patent do require coordinated release of naproxen and esomeprazole.

For the reasons set forth above, Petitioner fails to convince us that the claims of the '285 patent are not supported by at least the '216 application. Therefore, the Plachetka Publication does not qualify as prior art under 35 U.S.C. § 102(b). Consequently, Petitioner has failed to establish a

reasonable likelihood that it would prevail in showing that claims 1–4 are unpatentable as anticipated by the Plachetka Publication.

D. Obviousness over Depui, Phillips, Lundberg, and Clissold

Petitioner contends that each of claims 1–4 is unpatentable under 35 U.S.C. § 103 as obvious over the combination of Depui, Phillips,[3] Lundberg, and Clissold. Pet. 43–56. We begin our discussion with a brief summary of the references before addressing the parties' contentions.

1. *Depui*

Depui teaches oral pharmaceutical preparations that comprise an acid susceptible proton pump inhibitor in combination with one or more NSAID(s) in a fixed unit dosage form such as a tablet. Ex. 1030, 3:7–9. Depui observes that

> [s]ome anti-ulcer drugs such as proton pump inhibitors are susceptible to degradation/transformation in acid reacting and neutral media as mentioned above. In respect of the stability properties, it is obvious that the one of the active substances being a proton pump inhibitor must be protected from contact with acidic gastric juice by an enteric coating layer.

Id. at 5:24–28. Depui teaches that the proton pump inhibitor is protected by an enteric coating layer. Therefore, Depui teaches that its fixed unit dosage

[3] Although Petitioner lists Daneshmend in the heading for this obviousness ground, Petitioner does not discuss the reference except in the claim chart relating to the "naproxen surrounded by a coating" limitation, where Petitioner states that Daneshmend discloses "the pKa [disassociation constant] of aspirin of 3.5 and explains why stomach acidity is a contributing factor to NSAID damage." Pet. 53; Daneshmend et al., *Abolition by Omeprazole of Aspirin Induced Gastric Mucosal Injury in Man*," 31 GUT 514–517 (1990) (Ex. 1046). We observe that its inclusion in the ground is a clerical error when the Phillips reference that was discussed and relied upon in supporting the ground was intended.

form is an enteric coating layered tablet, capsule, or multiple unit tableted dosage form. *Id.* at Abs.

2. *Lundberg*

Lundberg describes a dosage form with a core material coated with a semipermeable membrane, which changes its permeability after a pre-determined time, where the core material contains an active ingredient that may be omeprazole[4] with one or more alkaline additives, and one or more swelling agents. Ex. 1031, 3:15–19. Lundberg specifically states that the dosage form is without an enteric coating layer. *Id.* at 3:12–13, 3:25–27 ("Surprisingly, the formulation according to the present invention is prepared without an enteric coating, which previously have been almost an axiom for dosage forms containing omeprazole or any other proton pump inhibitor compounds.").

Lundberg describes how the dosage form works as follows.

> When the coated pellets pass the stomach small amounts of gastric fluid will be absorbed through the semipermeable membrane. The alkalizing agent in the core material will neutralize the absorbed acidic fluid and protect the active ingredient against degradation. At the same time the swelling agent, will be exposed to the penetrating fluid or moisture, and it will start to expand. After a predetermined time interval this expansion leads to disruption of the superimposed semipermeable membrane by the built-up pressure or to a swelling that will increase the permeability of the membrane. The time interval is to be determined so that the pellets have had time to pass the stomach at the very moment, and have reached the small intestines. The entire dose of the active ingredient will then start to be released into the small intestine where absorption can occur.

[4] Omeprazole is a racemic compound where esomeprazole is its S-enantiomer. Ex. 1036 ¶ 43.

Ex. 1031, 4:12–22.

3. *Phillips*

Phillips describes a pharmaceutical composition, in an aqueous solution/suspension or dry formulations, of a proton pump inhibitor, such as omeprazole, in a pharmaceutically acceptable carrier including a bicarbonate salt. Ex. 1032, 18:2–9. In Phillips' preferred embodiment, the enteric coating of omeprazole particles is dissolved by mixing them with a sodium bicarbonate solution. *Id.* at 19:19–23.

Phillips describes the following advantages of the omeprazole solution/suspension over enteric–coated time-release capsules: (1) a decreased drug absorbance time; (2) the sodium bicarbonate solution protects the omeprazole from acid degradation prior to absorption; (3) the sodium bicarbonate acts as an antacid during absorption of the omeprazole; and (4) the solution suspension can be administered through an existing indwelling tube without clogging. *Id.* at 19:23–20:8.

4. Clissold

Clissold describes *in vitro* and *in vivo* animal studies demonstrating that omeprazole produces long lasting inhibition of gastric acid secretion. Ex. 1029, 17. Clissold describes a single-dose study where "omeprazole has been administered as an alkaline (sodium bicarbonate) suspension as uncoated granules in capsules containing sodium bicarbonate or as capsules of enteric-coated granules." *Id.* at 24. Clissold notes that "omeprazole, a highly acid-labile compound, may increase its own relative bioavailability by virtue of its antisecretory activity which reduces the acid degradation of the parent molecule, consequently enhancing the extent of its absorption." *Id.* at 32.

5. Analysis

When the claims are construed properly, it is clear that the prior art does not teach the combination of the limitations set forth in the challenged claims of the '285 patent. Petitioner focuses on whether the references teach the first limitation of the challenged claims: "esomeprazole, wherein at least a portion of said esomeprazole is not surrounded by an enteric coating"—and ignores the coordinated release of esomeprazole and naproxen 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." *See* Pet. 43–53; Ex. 1001, 22:8–19 (describing a single dosage form that combines non-enteric coated esomeprazole with naproxen surrounded by a pH sensitive coating that inhibits its release for coordinated or sequential release of esomeprazole and naproxen).

In particular, Petitioner's discussion of the limitation, "naproxen 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," is limited to a single entry in a claim chart listing Naprosyn Physicians' Desk Reference and Daneshmend to support a teaching of this limitation. Pet. 53 (citing Daneshmend (Ex. 1046, 3) as disclosing the pKa of aspirin of 3.5 and explaining why stomach acidity is a contributing factor to NSAID damage, and Naprosyn Physicians' Desk Reference (Ex. 1063) as disclosing that "Naprocyn" are "enteric-coated tablets"). Petitioner, however, does not discuss these references or explain how one of skill in the art would combine the teachings from these references with the other cited references to arrive at the claimed invention.

We also agree with Patent Owner that Petitioner has not shown from the cited references a rationale to combine or expectation of success for the claimed combination of coordinated release of esomeprazole and naproxen. *Id.* at 30. Petitioner relies on Pilbrant and testimony of its declarant, Dr. Kibbe, to show why one of skill in the art would combine the teachings of the cited references to arrive at the claimed invention. Pet. 47–53. Petitioner states:

> The person of ordinary skill in the art would have had a reasonable expectation of success because the claimed unit dosages incorporate commonly prescribed compounds . . . . To the extent that a correction needed to be made to the PPI dosage due to a lack of enteric coat, the person of ordinary skill in the art would have understood from Pilbrant's estimation that about half of omeprazole gets degraded, that doubling the dose would compensate for any degradative loss of esomeprazole. The person of ordinary skill in the art would have known about the self-amplification of the omeprazole . . . .

Pet. 47–48 (citing Ex. 1036 ¶¶ 56–60 (Kibbe Declaration)).

Petitioner's reliance on Pilbrant's statement that "more than half of the dose was lost due to degradation in the acidic stomach" to support its motivation to combine is not supported. For instance, Dr. Kibbe states:

> Even though increasing the dosage [of esomeprazole] would be approaching the maximal FDA-approved daily amount (of the enteric-coated form), the person of ordinary skill in the art would have known that PPI's are safe and have minimal side effects and that such dosing carried little risk.

Ex. 1036 ¶ 114 (relying on references stating side effects from the administration of omeprazole were not observed). Pilbrant does state that without buffer protection for omeprazole, "more than half of the dose was lost due to degradation in the acidic stomach." Ex. 1064, 117. Instead of

indicating a doubling of the dose of omeprazole is the answer, Pilbrant concluded that the results "clearly show that a conventional, non-buffered, oral dosage form [non-enteric coated] of omeprazole will have a low systemic bioavailability owing to preabsorption degradation of omeprazole in the stomach." *Id.*

In summarizing the studies' results, Pilbrant observed

> There are two principle options for the formulation of an oral, solid dosage form of omeprazole:
>
> - A conventional oral dosage form from which omeprazole is released and absorbed rapidly enough to avoid degradation in the stomach.
>
> - An enteric-coated dosage form, which releases omeprazole for absorption in the small intestine.
>
> The first option was ruled out in a pilot bioavailability study . . . where it was shown that more than half of the omeprazole in a rapidly dissolving dosage form degrades in the stomach.
>
> An enteric-coated dosage form, which does not release the active ingredient for dissolution and absorption until it has been transported down to the neutral reacting part of the small intestine, offers the best possibilities. . . .
>
> An enteric-coated dosage form of omeprazole must be perfectly coated and acid resistant, since, if any drug leaks out of the dosage form in the stomach, it is almost immediately degraded. The same is the case if an acidic medium can diffuse into the dosage form through pin-holes or damage in the enteric-coating.

We agree with the Patent Owner that Pilbrant teaches away from the claimed combination. Prelim. Resp. 36 ("Petitioner's failure to acknowledge the complete disclosure of Pilbrant, which negates any

motivation to use the non-enterically coated form of esomeprazole, despite the testimony of Petitioner's own expert, is an incurable flaw in the Petition"). When a prior art reference teaches away from combining known elements, discovery of a successful means of combining them is more likely to be nonobvious. *See KSR Internat'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). A reference teaches 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), *cited in In re Mouttet*, 686 F.3d 1322, 1333-34 (Fed. Cir. 2012).

We disagree with Petitioner's conclusion that although one of skill in the art "might have believed" that enteric coated esomeprazole was generally the better option, "that does not exclude the use of non-enteric coated esomeprazole as still 'good enough' to be obvious, at least in a combination product where all the esomeprazole needs to do is raise the stomach pH to 3.5." Pet. 51. Here, the very statement that Petitioner relies upon from Pilbrant to support its rationale to combine concerning preabsorption degradation of omeprazole caused Pilbrant to rule out the use of conventional oral dosage forms without an enteric coating. We agree with the Patent Owner that Petitioner's "[m]otivation to combine in the face of an express teaching away must be found in the prior art itself and reliance on the teachings of the '285 patent is impermissible hindsight." Prelim. Resp. 37.

III. CONCLUSION

For the foregoing reasons, we are not persuaded that the Petition establishes a reasonable likelihood that Petitioner would prevail in showing

any of claims 1–4 of the ’285 patent are unpatentable. Because we are not instituting an *inter partes* review for any challenged claim, we need not reach the real party-in-interest issue raised by Patent Owner. Prelim. Resp. 43–49.

IV. ORDER

Accordingly, it is

ORDERED that the Petition is *denied* at to all challenged claims of the ’285 patent.

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