

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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COALITION FOR AFFORDABLE DRUGS VII LLC,  
Petitioner,

v.

POZEN INC.,  
Patent Owner.

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Case IPR2015-01344  
Patent 8,858,996 B2

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

BONILLA, *Administrative Patent Judge*.

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

## I. INTRODUCTION

The Coalition for Affordable Drugs VII LLC (“Petitioner”) filed a Petition (Paper 1, “Pet.”) requesting an *inter partes* review of claims 1–19 of U.S. Patent No. 8,858,996 B2 (Ex. 1001, “the ’996 patent”). Pozen Inc. (“Patent Owner”) filed a Preliminary Response. Paper 14 (“Prelim. Resp.”).<sup>1</sup> 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 not established a reasonable likelihood that it would prevail in showing the unpatentability of any claim challenged in the Petition. Accordingly, we decline to institute an *inter partes* review.

### A. *Related Proceedings*

The parties identify a number of judicial matters involving the ’996 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 ’996 patent (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*

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<sup>1</sup> Patent Owner filed a Motion to File Under Seal its Preliminary Response and an associated exhibit, Ex. 2012. Paper 16. Along with the Motion to Seal, Patent Owner filed a redacted version of the Preliminary Response to be available to the public. Paper 13.

*v. Pozen Inc.*, IPR2015-01241 (PTAB)). Pet. 2–3; Paper 7, 8. In addition to Case No. IPR2015-01241, Petitioner filed two other Petitions for *inter partes* review involving patents related to the '996 patent or directed to similar subject matter in Case Nos. IPR2015-01680 and IPR2015-01718.

**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
Goldman, <sup>2</sup> Remington, <sup>3</sup> and Lindberg <sup>4</sup>	§ 103(a)	1–19
Gimet, <sup>5</sup> Goldman, and Lindberg	§ 103(a)	1–19
The '255 Publication <sup>6</sup>	§ 102(b)	1–19

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<sup>2</sup> U.S. Patent No. 5,204,118, issued April 20, 1993, to Goldman et al. (“Goldman”) (Ex. 1004).

<sup>3</sup> Robert E. King & Joseph D. Schwartz, *Oral Solid Dosage Forms*, in REMINGTON’S PHARMACEUTICAL SCIENCES 1603–32 (Alfonso R. Gennaro et al., eds.) (17th ed. 1985) (“Remington”) (Ex. 1005).

<sup>4</sup> U.S. Patent No. 5,714,504, issued Feb. 3, 1998, to Lindberg et al. (“Lindberg”) (Ex. 1007).

<sup>5</sup> U.S. Patent No. 5,698,225, issued December 16, 1997, to Gimet et al. (“Gimet”) (Ex. 1006).

<sup>6</sup> U.S. Patent App. Pub. No. US 2003/0069255 A1, published Apr. 10, 2003, filed by Plachetka (“the '255 Publication”) (Ex. 1008).

Petitioner supports its challenges in the Petition with the Declaration of Leon Shargel, Ph.D., R.Ph., executed on June 5, 2015 (“Shargel Declaration”) (Ex. 1003).

*C. The ’996 Patent (Ex. 1001)*

The ’996 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 ’996 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), 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 ’996 patent, preferred acid inhibitors are H<sub>2</sub>-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 ’996 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 1–19 of the ’996 patent. Independent claims 1 and 12, reproduced below, are illustrative.

1. A pharmaceutical composition in unit dosage form in the form of a tablet, said composition comprising:

naproxen in an amount of 200–600 mg per unit dosage form;  
and

esomeprazole in an amount of from 5 to 100 mg per unit dosage form,

wherein 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.

12. A pharmaceutical composition in unit dosage form in the form of a tablet, said composition comprising:

a core layer comprising naproxen, wherein said core layer has a coating that inhibits release of said naproxen from said core layer unless said dosage form is in a medium with a pH of 3.5 or higher; and

a layer comprising esomeprazole, wherein said layer has a non-enteric film coating that, upon ingestion by a patient, releases said esomeprazole into the stomach of said patient.

Ex. 1001, 21:23–35, 22:17–26.

## 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). 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 terms requiring interpretation for purposes of this Decision are “inhibit” and “acid inhibitor.”

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 “inhibit” is “to slow down, hinder, or prevent.” Pet. 10 (citing Ex. 1034, 51, Exs. 1036–38). Patent Owner contends that the ordinary meaning of “inhibits” refers to a coating that “prevents, hinders, or restrains the release of NSAID.” Prelim. Resp. 7 (citing Ex. 2006, 3; Ex. 2007, 3).

The specification of the ’996 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. Ex. 1035, 2; Ex. 1036, 49; Ex. 2006, 3; Ex. 2007, 3.

For example, claim 1 of the ’996 patent recites that “*release of at least a portion*” of naproxin “*is inhibited unless* the pH” is 3.5 or higher (emphasis added). Claim 12 recites a “coating that *inhibits release* of said naproxen from said core layer *unless* said dosage form is in a medium with a pH of 3.5 or higher” (emphasis added). Thus, “inhibits” 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 12 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 12) of the drug “unless” the dosage form is at a pH of 3.5 or higher.

Although Petitioner does not offer a construction of the term “acid inhibitor,” Patent Owner contends Petitioner mistakenly characterizes the term to include prostaglandins, such as misoprostol. Prelim. Resp. 8 (citing Pet. 28). Patent Owner argues that “the broadest reasonable interpretation of ‘acid inhibitor’ . . . excludes prostaglandins” because the “’996 specification plainly distinguishes PPIs, describing them as ‘acid inhibitors,’ from synthetic prostaglandins, describing them as ‘cytoprotective agents.’” *Id.* (citing Ex. 1001, 1:53–57). Patent Owner cites and compares passages of the specification in support of this proposition as follows:

(*Compare* Ex. 1001 at 1:53-57 (“In general, more potent and longer lasting acid inhibitors, such as proton pump inhibitors, are thought to be more protective during chronic administration of NSAIDs than shorter acting agents, e.g., histamine H<sub>2</sub> receptor antagonists . . . .”) *with id.* at 2:57-63 (“Other attempts to produce an NSAID therapy with less gastrointestinal toxicity have involved the concomitant administration of a cytoprotective agent” including Arthrotec<sup>TM</sup> which “contains misoprostol (a cytoprotective prostaglandin) and the NSAID diclofenac.”).)

Prelim. Resp. 8–9.



Nevertheless, the specification states that “[t]he term ‘acid inhibitor’ refers to agents that inhibit gastric acid secretion and increase gastric pH” (Ex. 1001, 3:38–40), that preferred acid inhibitors are H<sub>2</sub>-blockers, such as famotidine (*id.* at 3:40–47), and “[o]ther preferred agents that may be effectively used as acid inhibitors are the proton pump inhibitors” (*id.* at 3:48–51). Thus, the specification describes H<sub>2</sub>-blockers and PPIs as illustrative, rather than exclusive, acid inhibitors.

Moreover, even if we assume *arguendo* that the specification distinguishes the claimed invention from Arthrotec<sup>TM</sup> (a composition comprising a combination of misoprostol and the NSAID diclofenac) (Prelim. Resp. 8–9), the distinction is not unambiguously based on the presence of misoprostol in the composition—it could just as well be that the amount of misoprostol in the composition is insufficient to raise gastric pH to 3.5 or more, as required by all the challenged claims.

Accordingly, we are not persuaded that the broadest reasonable interpretation of “acid inhibitor” excludes prostaglandins in general, or misoprostol in particular.

*B. Asserted Obviousness over Goldman, Remington, and Lindberg*

*1. Goldman (Ex. 1004)*

Goldman teaches that “[t]he symptoms of overindulgence due to excessive or inappropriate intake of food and/or alcoholic beverage are well known and include headache as well as indigestion, upper abdominal discomfort, bloating, heartburn or pyrosis.” Ex. 1004, 1:28–32. “The

treatment of the symptoms of overindulgence often requires the co-administration of an analgesic to relieve the headache along with an agent to reduce gastric acidity which is generally believed to cause the indigestion and heartburn.” *Id.* at 2:52–56.

In order to “more effectively treat all the symptoms concurrently” (*id.* at 2:67–68), Goldman 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” (*id.* at 1:10–16). Goldman teaches that acceptable histamine receptor (e.g., H<sub>2</sub>) 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).

According to Goldman, “statistical methods are used to show that on the average, acetaminophen or non-steroidal inflammatory agents with H<sub>1</sub> histamine and/or H<sub>2</sub> histamine receptor blocking drugs are more efficacious” in treating the symptoms of overindulgence. *Id.* at 5:51–65. Finally, Goldman discloses “chewable and liquid dosage forms” (*id.* at 6:4–5), and further teaches that “[v]arious conventional techniques for preparing medicament tablets or caplets can be employed as would be known to those skilled in the art as is disclosed for example by Remington’s Pharmaceutical Sciences.”<sup>7</sup> *Id.* at 6:26–30.

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<sup>7</sup> This is the same Remington publication submitted as Exhibit 1005.

2. *Remington (Ex. 1005)*

Remington discusses generally the production of oral solid dosage forms, such as tablets and capsules, and the many considerations that influence the choice of a particular dosage form. Ex. 1005, 1603–33. Among the many dosage forms mentioned, Remington discusses various coated tablets, including enteric-coated tablets—“compressed tablets coated with substances that resist solution in gastric fluid but disintegrate in the intestine.” *Id.* at 1604.

Remington teaches that “[e]nteric coatings can be used for tablets containing drug substances which are inactivated or destroyed in the stomach, for those which irritate the mucosa, or as a means of delayed release of the medication.” *Id.* Remington further teaches that tablets may be coated in order to “[r]educ[e] the risk of interaction between incompatible components . . . by using coated forms of one or more of the offending ingredients (particularly active compounds).” *Id.* at 1633. The reference states that enteric coatings “can be used to give a simple repeat-action effect where unprotected drug coated *over* the enteric coat is released in the stomach, while the remainder, being protected by the coating, is released further down the gastrointestinal tract.” *Id.* at 1637.

3. *Lindberg (Ex. 1007)*

Lindberg 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. 1007, 1:17–63, 5:25–27; Ex. 1040, 2:14–

18. Lindberg further discloses that “oral and parenteral dosages will be in the range of 5 to 500 mg per day of active substance.” Ex. 1007, 6:21–25. Lindberg teaches that “[o]meprazole and its alkaline salts are effective gastric acid secretion inhibitors, and are useful as antiulcer agents.” *Id.* at 1:22–24. Lindberg states that its “novel salts of single enantiomers of omeprazole” provide “improved pharmacokinetic and metabolic properties.” *Id.* at 1:50–55.

#### 4. *Analysis*

Petitioner contends that Goldman discloses the combined use of acid inhibitors with NSAIDs, such as naproxen, to prevent the incidence of gastric ulcers and bleeding resulting from the use of the NSAIDs. Pet. 11–12. Petitioner also argues that an ordinary artisan would have known that “acid inhibitors are a well-known class of drugs that provide gastric acid inhibiting efficacy.” *Id.* at 12. Thus, according to Petitioner, an ordinary artisan would have had a reason, with a reasonable expectation of success, for “substituting different acid inhibitor compounds into a given combination therapy formulation,” including with “more effective compounds, such as PPIs, over previously known, less therapeutically effective compounds, such as prostaglandins and H<sub>2</sub> blockers.” *Id.* (citing Ex. 1003 ¶¶ 66–67). In addition, according to Petitioner, it would have been obvious to substitute Goldman’s PPI omeprazole with Lindberg’s PPI esomeprazole because it was known that the “enantiomeric magnesium salt of omeprazole” would have provided “improved pharmacokinetic and

metabolic properties.” *Id.* at 12–13 (citing Ex. 1007, 1:50–63; Ex. 1003 ¶¶ 68–69), 24.

Petitioner also contends that Goldman would have provided an ordinary artisan with a reason “to look to conventional techniques for preparing medicament tablets as set forth in Remington,” which Goldman incorporates by reference. *Id.* at 11, 15, 22–23. Petitioner points to where Remington teaches that an enteric coating can be used to give an effect “where unprotected drug . . . coated *over* the enteric coat is released in the stomach, while the remainder . . . , being protected by the coating, is released further down the gastrointestinal tract.” *Id.* at 15 (citing Ex. 1005, 1637), 25. Petitioner also contends that Remington teaches using enteric coatings to delay the release of drugs, such as those that “may cause nausea or bleeding by irritating the gastric mucosa (eg, aspirin . . . ),” and that many enteric coatings “remain undissociated in the low pH environment of the stomach, but readily ionize when the pH rises to about 4 or 5.” *Id.* at 16 (citing Ex. 1005, 1637), 22–23.

Patent Owner responds that Goldman “does not disclose formulations with an immediate release acid inhibitor and a delayed release NSAID that would provide coordinated release,” or that “coordinated release of an acid inhibitor with an NSAID is in any way desirable.” Prelim. Resp. 17. Patent Owner also contends that Petitioner “fails to identify any specific passage in Remington supporting a motivation to combine the Goldman and Lindberg references.” *Id.*

In addition, Patent Owner contends that “Lindberg teaches that esomeprazole must be enteric coated to protect it from the acidic environment of the stomach,” because it states that granules and tablets of esomeprazole “may be coated with an enteric coating which protects the active compound from acid catalyzed degradation as long as the dosage form remains in the stomach.” *Id.* at 18; Ex. 1007, 5:35–39. Patent Owner also contends that because “PPIs were well known in the art to be acid labile,” an ordinary artisan would have coated a PPI with an enteric coating, as taught in Remington, rather than use a non-enteric coated PPI, such as esomeprazole. Prelim. Resp. 18–19 (citing Ex. 1005, 1604).

We agree that Petitioner has not established that the teachings of Goldman, Remington, and Lindberg would have given an ordinary artisan a reason to formulate a tablet with the structural and functional features required by the challenged claims. Although Goldman discloses a combination dosage form comprising a PPI and NSAID (discussed above), Petitioner does not point to anything in Goldman that describes or suggests adequately why one would have prepared, for any reason, a composition as claimed, where at least some PPI (i.e., esomeprazole) is released regardless of pH and the release of at least some NSAID (i.e., naproxen) is inhibited unless the pH is 3.5 or higher (e.g., via a coating).

Moreover, although Goldman incorporates Remington’s discussion of oral solid dosage forms by reference (Ex. 1004, 6:26–33), Petitioner does not identify anything in Goldman that points to any particular dosage form

among the many disclosed by Remington. Goldman’s citation to Remington generally in relation to “[v]arious conventional techniques for preparing medicament tablets or caplets” does not persuade us that an ordinary artisan would have made the connection that Petitioner contends. *Id.*; Pet 11, 14–16, 22–25. Nor does Petitioner explain adequately how Lindberg remedies the deficiencies discussed above in relation to Goldman and Remington.

Having considered the evidence and arguments presented in the Petition, we are not persuaded that Petitioner has established a reasonable likelihood of prevailing in its challenge of claims 1 and 12, or their dependent claims, on the basis of obviousness over Goldman, Remington, and Lindberg.

*C. Asserted Obviousness over Gimet, Goldman, and Remington*

*1. Gimet (Ex. 1006)*

Gimet 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. 1006, 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 Gimet, “[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.

Gimet 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—diclofenac or piroxicam—and the outer mantle consists of a prostaglandin—e.g., misoprostol. *Id.* at 1:11–17, 39–47.

Figure 2 of Gimet, reproduced below, depicts tablet 16 in cross-section.

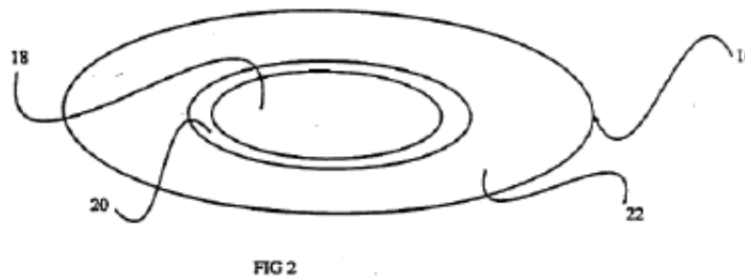


Figure 2 of Gimet depicts tablet 16. Tablet 16 includes an NSAID—diclofenac or piroxicam—in inner core 18. Enteric coating 20 surrounds core 18, and mantle 22—consisting of a prostaglandin, e.g., misoprostol—surrounds the coated inner core. *Id.* at 6:24–44.

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.



“When the prostaglandin is misoprostol . . . [it] is present in an amount from about 50 to about 500 mcg and preferably from about 100 to about 200 mcg.” *Id.* at 6:20–23.

2. *Analysis*

Petitioner contends that an ordinary artisan would have known that both Gimet and Goldman disclose a combination therapy oral unit dosage form comprising an acid inhibitor (e.g., misoprostol, a prostaglandin, in Gimet) in combination with an NSAID (e.g., naproxen in Goldman). Pet. 28 (citing Ex. 1003 ¶¶ 236, 237). In relation to naproxen, Petitioner also argues that an ordinary artisan would have had a reason, as well as a reasonable expectation of success, to substitute different NSAID compounds—i.e., replace diclofenac or piroxicam in Gimet’s composition, as shown in Figure 2, with naproxen disclosed in Goldman—“because doing so would be a simple substitution of one known element for another to obtain predictable results.” *Id.* at 28–29 (citing Ex. 1003 ¶¶ 238, 239), 31–32.

The only evidence that Petitioner cites for its assertion regarding “predictable results” in relation to NSAIDs is Dr. Shargel’s Declaration at paragraphs 238 and 239, which repeat the statements presented in the Petition on this point, without citing any evidence themselves. *Id.* Conclusory assertions by Petitioner, merely repeated in conclusory and unsupported statements by an expert witness in support, are not persuasive here. *See* 37 C.F.R. § 42.65(a) (“Expert testimony that does not disclose the

underlying facts or data on which the opinion is based is entitled to little or no weight.”).

In relation to esomeprazole, Petitioner also argues an ordinary artisan would have had a reason, with a reasonable expectation of success, to substitute different acid inhibitors—i.e., replace misoprostol in Gimet’s composition with esomeprazole disclosed in Lindberg—“where the acid inhibitor compound contributes its individual therapeutic attributes (e.g., acid inhibition and gastric pH raising) to the combination.” Pet. 29–30 (citing Ex. 1003 ¶ 241). Petitioner further contends that an ordinary artisan would have had a reason, with a reasonable expectation of success, “in employing more recently obtained and therapeutically more effective compounds, such as PPIs, over previously known, less therapeutically effective compounds, such as prostaglandins and H2 blockers.” *Id.* at 30 (citing Ex. 1003 ¶ 242).<sup>8</sup>

Petitioner also argues that it would have been obvious to select “Lindberg’s disclosed PPI esomeprazole and substitute it for Gimet’s disclosed acid inhibitor (prostaglandin) because Goldman specifically teaches that ‘[p]roton pump inhibitors have been recently introduced as effective gastric acid inhibitors.’” *Id.* at 30 (citing Ex. 1004, 1:25–27; Ex. 1003 ¶ 243). Petitioner also points to teachings in Lindberg indicating that

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<sup>8</sup> In support of these contentions, Petitioner once again cites paragraphs in Dr. Shargel’s Declaration that simply repeat statements presented in the Petition on these points, without citing supporting evidence themselves. Pet. 29–30 (citing Ex. 1003 ¶¶ 241, 242).

its “novel salts of single enantiomers of omeprazole” provide “improved pharmacokinetic and metabolic properties” and “high stability against racemization.” *Id.* at 30–31 (quoting Ex. 1007, 1:50–63, 3:48–55) (citing Ex. 1003 ¶¶ 244, 245), 33 (citing Ex. 1007, 1:50–63; Ex. 1003 ¶ 262), 43 (citing Ex. 1003 ¶¶ 351, 352).

In response, Patent Owner points to a number of references indicating that an ordinary artisan would have understood that PPIs were acid labile and should be protected from degradation in acidic environments, such as the stomach. Prelim. Resp. 23–25 (citing Ex. 2003, 15, 17; Ex. 2009, 3; Ex. 2010, 2; Ex. 2011, 5; Ex. 1048, 2, 3, 5). For example, a review article by Stedman et al., published in 2000, comparing the “pharmacokinetics, acid suppression and efficacy of proton pump inhibitors,” indicates that PPIs “are all acid-labile, so when administered orally they must be formulated in an enteric coating to protect them from rapid degradation in the stomach. They are rapidly absorbed in the duodenum.” Ex. 2009, 1 (Title), 3. Similarly, in an article published in 1992, Bell et al. state in relation to the related parent compound of esomeprazole: “As omeprazole is acid-labile, it is formulated as enteric-coated granules dispensed in a gelatine capsule.” Ex. 2010, 2.

In addition, in an article published in 1985, Pilbrant et al. teach that “[o]meprazole degrades very rapidly in water solutions at low pH-values.” Ex. 1048, 1. In this context, Pilbrant et al. teaches 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 2.

As an initial matter, we are not persuaded that Petitioner establishes adequately that esomeprazole administered in an non-enteric-coated form (thereby allowing it to be released regardless of pH) would have obtained “improved pharmacokinetic, metabolic, and therapeutic properties” as compared to misoprostol in any formulation. Pet. 32–33 (citing Ex. 1007, 1:50–63; Ex. 1003 ¶ 262). For example, we are not persuaded that Lindberg indicates such an improvement. Rather, Lindberg suggests that esomeprazole may have improved properties over omeprazole (a related PPI). Ex. 1007, 1:17–63.

Moreover, even if we assume that one would have understood that prostaglandins and H<sub>2</sub> blockers were “less therapeutically effective compounds” than PPIs (Pet. 30), Petitioner has not explained adequately why one would have had reason to make the composition taught in Gimet, e.g., in Figure 2, with a PPI rather than a prostaglandin in “mantle 22” located on the outside of “enteric coating 20” surrounding “inner core 18” of an NSAID. Ex. 1006, 6:15–44, Fig. 2. Petitioner does not address teachings in the art indicating that PPIs were acid liable, nor explain adequately why one would have used any PPI (much less esomeprazole) in place of a prostaglandin in an uncoated form (as taught in Gimet), when other relevant references taught the use of PPIs with an enteric coating to avoid degradation of the drug. *See, e.g.*, Ex. 2009, 3; Ex. 2010, 2; Ex. 1048, 2

(discussed above); *see also* Prelim. Resp. 23–28 (discussing other references).

Petitioner’s contention that Lindberg discloses “uncoated dosage units of esomeprazole in the form of tablets” and “esomeprazole pellets ‘coated with a solution of hydroxypropyl methylcellulose’” does not persuade us otherwise. Pet. 34 (citing Ex. 1007, 5:25–36; Ex. 1003 ¶ 267 (citing same)), 44 (citing Ex. 1007, 13:3–5; Ex. 1003 ¶¶ 358–360). For example, immediately after the first quoted passage in Lindberg (Ex. 1007, 5:25–36), Lindberg teaches that “[g]ranules and tablets may be coated with an enteric coating which protects the active compound from acid catalyzed degradation as long as the dosage form remains in the stomach.” Ex. 1007, 5:36–39. Likewise, in relation to the second quoted passage (*id.* at 13:3–5) included in Example 13 in Lindberg, Example 13 also teaches preparing an enteric coated tablet and a capsule comprising pellets with a second coating (*id.* at 12:13–13:15). Thus, even Lindberg suggests using an enteric or some type of protective coating when administering esomeprazole. Petitioner does not persuade us that Lindberg adequately suggests a composition where at least a portion of esomeprazole “is released regardless of the pH” (e.g, in the stomach where pH is low), much less such a composition that also includes other elements recited in the challenged claims.

Accordingly, we agree with Patent Owner that Petitioner has not established that the teachings of Gimet, Goldman, and Lindberg would have given an ordinary artisan a reason to formulate a composition with the

structural and functional features required by the challenged claims. Prelim. Resp. 22–29.

Having considered the evidence and arguments presented in the Petition, we are not persuaded that Petitioner has established a reasonable likelihood of prevailing in its challenge of claims 1 and 12, or their dependent claims, on the basis of obviousness over Gimet, Goldman, and Lindberg.

*D. Asserted Anticipation by the '255 Publication*

As noted by both parties, the '996 patent is a fifth generation descendent of an application (the '216 application) that published as the '255 Publication (Ex. 1008), and the '996 patent claims priority to the '216 application and its parent provisional application. Pet. 48–49; Prelim. Resp. 31–32; Ex. 1001, 1:7–21. Nonetheless, Petitioner asserts that the '255 Publication is prior art to the '996 patent under 35 U.S.C. § 102(b). Pet. 48–49.

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.* 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 '996 patent, which creates a “break in the priority.” *Id.* at 50. Petitioner supports this contention with its arguments that the claims of the '996 patent are broad enough to encompasses compositions that “release at least a

portion of the naproxen immediately at any pH,” “‘inhibit’ or slow down the release of all of the naproxen at a pH below 3.5 until the pH reaches 3.5 or higher,” and “do not have a ‘coordinated release’ or sequential release of the esomeprazole and the naproxen.” *Id.* By contrast, according to Petitioner, the pre-2003 applications only support compositions that “release none of the NSAID immediately,” “‘prevent’ or stop the release of all of the NSAID until reaching a pH of 3.5 or higher,” and “have a ‘coordinated release’ or sequential release of the acid inhibitor and the NSAID.” *Id.*

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 the claims in the ’996 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 50–51. 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 ’996 patent. *Id.* at 51–60.

As an initial matter, we note that Petitioner’s arguments logically apply to claim 1 and dependent claims 3–11, but not dependent claim 2 or claim 12 or its dependent claims. Claim 1 of the ’996 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. By contrast, dependent claim 2 and claim 12 and its dependent claims recite “a coating that *inhibits* [] *release* [of naproxen] from [the dosage form or core layer] *unless* said dosage form is in a medium with a pH of 3.5 or higher,” without reciting “at least a portion.” As noted above, the term “inhibits” in the claims means to prevent (stop), hinder, or restrain.

Petitioner does not explain adequately how claims 2 and 12–19 encompass 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. 50–51.

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.*

Here, Petitioner cites nothing in the record to support its assertions regarding a lack of written description in the pre-2003 applications, other than to refer to those pre-2003 applications generally. Pet. 47–51. When asserting a “break in priority,” Petitioner does not identify, specifically, the features or claims that allegedly lack written description support. Instead, Petitioner discusses in very general terms what “the ’996 Patent claims are broad enough to encompass” and what the “pre-2003 applications disclose” (*id.* at 50–51) without referring to any specific challenged claim or providing specific citations to any specification at issue.

Even if we assume Petitioner adequately raises the issue, however, we are persuaded that Patent Owner provides a sufficient showing of entitlement to the filing date of at least the ’216 application (the ’255 Publication), in a manner that is commensurate in scope with the points and contentions raised by Petitioner. For example, Patent Owner points to paragraphs 10, 13, and 82 in the ’255 Publication. Prelim. Resp. 35–38 (citing Ex. 1008 ¶¶ 10, 13, 82). Paragraph 10 describes a release of NSAID that “*minimizes* the adverse effects of the NSAID on the gastroduodenal mucosa.” Ex. 1008 ¶ 10 (emphasis added). Similarly, paragraph 13 describes “*preferably* provid[ing] for coordinated drug release” that

“*reduces* the deleterious effects of the NSAID on the gastroduodenal mucosa.” *Id.* ¶ 13 (emphasis added). Paragraph 13 also describes a “most preferred form” where an inner core is “surrounded by a polymeric barrier coating that *does not dissolve unless* the surrounding medium is at a pH of at least 3.5.” *Id.* (emphasis added). Paragraph 82 in Example 7 also refers to a coordinated delivery dosage that provides “the *delayed* release” of naproxen. *Id.* ¶ 82 (emphasis added).

Although we recognize that the ’255 Publication (and indeed the ’996 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 ’996 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).

Here, words such as “minimizes,” “reduces,” and “delayed” in paragraphs 10, 13, and 82 in the ’255 Publication, as well as disclosure of

different preferred forms in paragraph 13, indicate that the inventors possessed a dosage form and/or coordinated drug release where a portion (e.g., a small portion) of the NSAID (e.g., “most preferred NSAID” naproxen (Ex. 1008 ¶ 12)) 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. *See, e.g., id.* ¶ 13 (also stating in one sentence that 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” without referring to when or under what conditions NSAID is released).

Moreover, every species in a genus need not 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, as opposed 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 that the inventors of the ’996 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.

The paragraphs in the '255 Publication cited by Patent Owner show an entitlement to the filing date of the '216 application (the '255 Publication) in a manner that is commensurate in scope with the general points and contentions raised by Petitioner (Pet. 47–52). Because Patent Owner establishes sufficiently that the challenged claims of the '996 patent properly claim priority to the '216 application, the '255 Publication is not prior art to the challenged claims under 35 U.S.C. § 102.

Having considered the evidence and arguments presented in the Petition, we are not persuaded that Petitioner has established a reasonable likelihood of prevailing in its challenge to claims 1–19 on the basis that the '255 Publication anticipates those claim under 35 U.S.C. § 102(b).

*E. Motion to Seal*

Patent Owner's Preliminary Response (Paper 14) was accompanied by a Motion to File Under Seal its Preliminary Response and Exhibit 2012, an associated exhibit (Paper 16, "Motion to Seal"), as well as a redacted version of the Preliminary Response (Paper 13).

Because we do not rely on the material Patent Owner seeks to seal, we decline to address the merits of the Motion to Seal. Patent Owner is authorized to file a motion to expunge any material that it seeks to keep

confidential within thirty (30) days of the date of this Decision, or within thirty (30) days of a decision on rehearing, if rehearing is requested.

### III. CONCLUSION

For the foregoing reasons, we are not persuaded that the Petition establishes a reasonable likelihood that Petitioner would prevail in showing that claims 1–19 of the '996 patent are unpatentable under 35 U.S.C. § 103(a) or § 102(b).

### IV. ORDER

Accordingly, it is  
ORDERED that the Petition is denied and no *inter partes* review is instituted.

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Patent 8,858,996 B2

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