UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN JOSE DIVISION

TAKEDA PHARMACEUTICAL CO., LTD., TAKEDA PHARMACEUTICALS U.S.A., INC., AND TAKEDA PHARMACEUTICALS AMERICA, INC., Plaintiff, v. MYLAN INC. AND MYLAN PHARMACEUTICALS INC., Defendants.	Case No.: 13-CV-04001-LHK Consolidated and Related Cases: 13-CV-04002-LHK 14-CV-00314-LHK ORDER CONSTRUING DISPUTED CLAIM TERMS OF U.S. PATENT NOS. 6,939,971, 7,339,064, AND 8,173,158

These related cases involve patent infringement claims by Plaintiffs (collectively, "Takeda") against Defendants (collectively, "Mylan"), who filed an Abbreviated New Drug Application under the Hatch-Waxman Act for generic forms of the branded drug Dexilant®. The parties now seek construction of four disputed terms in the claims of three asserted patents: U.S. Patent Nos. 6,939,971 (the "'971 Patent"), 7,339,064 (the "'064 Patent"), and 8,173,158 (the "'158 Patent"). The Court held a technology tutorial and claim construction hearing on October 9, 2014. The Court has reviewed the claims, specifications, and other relevant evidence, and has considered the briefing and arguments of the parties. The Court now construes the terms at issue.

I. BACKGROUND

A. The Drug and Asserted Patents

Takeda manufactures and sells Dexilant®, a drug for treatment of gastroesophageal reflux disease ("GERD") or acid reflux disease. *See* Compl. (ECF No. 1[1]) ¶ 21. The active ingredient in Dexilant® is dexlansoprazole, which belongs to the class of compounds known as protein pump inhibitors, or "PPIs." Dexlansoprazole is an enantiomer of lansoprazole, the active ingredient in Prevacid®. Dexilant® is designed to release dexlansoprazole in two stages, based on different acidity levels in the human intestine, to provide overnight relief from acid reflux. *See id.* ¶ 22. Takeda owns patents relating to Dexilant® that are listed in the U.S. Food and Drug Administration's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"). *See id.* ¶¶ 17-20. Takeda asserts multiple Orange Book patents in this set of lawsuits,[2] and the parties dispute claim terms in three of those patents.

The '971 Patent is entitled "Benzimidazole Compound Crystal" and is directed to "a crystal of a benzimidazole compound showing antiulcer action," specifically dexlansoprazole. '971 Patent col.1 ll.13-14. The '971 Patent includes claims to methods of treating reflux esophagitis with crystalline forms of dexlansoprazole. *E.g.*, *id.* cl.5. The inventors state that they "succeeded in optically resolving and crystallizing" dexlansoprazole and "for the first time found that this crystal serves satisfactorily as a pharmaceutical." *Id.* col.1 ll.24-34. Accordingly, "[t]he crystal of the present invention is useful . . . because it shows excellent antiulcer action, gastric acid secretion-inhibiting action," and improved stability. *Id.* col.14 ll.35-39. The '971 Patent issued on September 6, 2005 and claims priority to a foreign application filed on June 17, 1999.

The '064 Patent is related to the '971 Patent (issuing from a continuation of the '971 Patent's application) and is also entitled "Benzimidazole Compound Crystal." The '064 Patent shares largely the same specification with the '971 Patent, but claims crystalline forms of benzimidazole derivatives in a pharmaceutical composition for treating or preventing digestive

[1] All ECF entries correspond to Case No. 13-CV-04001 unless otherwise stated.

[2] *See id.*; Compl. ¶¶ 17-26 (ECF No. 1), Case No. 13-CV-04002; Compl. ¶¶ 17-18 (ECF No. 1), Case No. 14-CV-00314.

ulcers. '064 Patent col.1 ll.38-59. The '064 Patent issued on March 4, 2008 and claims priority to a foreign application filed on June 17, 1999, the same application to which the '971 Patent claims priority. The '064 Patent is not currently listed in the Orange Book for Dexilant®.

The '158 Patent is entitled "Methods of Treating Gastrointestinal Disorders Independent of the Intake of Food" and is directed to methods of "treating heartburn, acid reflux or gastroesophageal reflux disease in a patient" by administering a "pharmaceutical composition" with two types of solid particles. '158 Patent cl.1. The '158 Patent notes the preexisting problem that giving patients PPIs (such as dexlansoprazole) together with food can reduce the drugs' effectiveness: "the administration of such PPIs in conjunction with the intake of food decreases the systemic exposure of the PPI." *Id.* col.10 ll.7-9. To address this problem, the inventors discuss use of a pharmaceutical composition that "comprises at least two solid particles each of which contain at least one proton pump inhibitor," which permits administration "independent of the intake of food." *Id.* col.1 ll.15-20. The '158 Patent issued on May 8, 2012 and claims priority to a provisional application filed on October 12, 2007.

B. Prior and Related Litigation

This patent litigation is the third set of cases in this district involving Takeda and Dexilant®. The first set of cases, assigned to Magistrate Judge Joseph Spero, involves other generic manufacturers and six disputed patents, five of which also appear in the above-captioned cases. In the first cases, Judge Spero construed several claim terms across multiple patents. *See* Claim Construction Order (ECF No. 106), *Takeda Pharm. Co. v. Handa Pharms., LLC*, No. 11-CV-00840-JCS (N.D. Cal. Apr. 11, 2012) ("Spero Order"); Claim Construction Order (ECF No. 81), *Takeda Pharm. Co. v. Sandoz, Inc.*, No. 12-CV-00446-JCS (N.D. Cal. May 16, 2013). Following a bench trial, Judge Spero entered judgment in those lawsuits, which have been appealed to the Federal Circuit.

In the second set of cases, consolidated before this Court, Takeda asserts two additional patents (including the '158 Patent) against generic manufacturers. This Court has already construed claim terms in both patents in those lawsuits. *See* Order Construing Disputed Claim

Terms (ECF No. 95), *Par Pharm., Inc. v. Takeda Pharm. Co.*, No. 13-CV-01927-LHK (N.D. Cal. June 6, 2014) ("1927 Order").

As noted above, this third set of cases involving Mylan includes several Takeda patents already asserted and construed in the first and second sets of cases. Takeda and Mylan stipulated to adopt the claim construction rulings and briefing in the first and second sets of cases for purposes of this litigation, while preserving their respective rights to appeal the prior claim constructions. *See* ECF No. 80 (order granting stipulation).

C. Procedural History

Mylan filed Abbreviated New Drug Application ("ANDA") No. 205-205 with the U.S. Food and Drug Administration ("FDA") to seek approval to market a generic version of Dexilant® in 30 mg and 60 mg dosage forms. *See* Compl. ¶ 24. Mylan has certified pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV Certification") that Takeda's asserted Orange Book patents are invalid, unenforceable, and/or not infringed. *See generally Caraco Pharm. Labs., Ltd. v. Forest Labs., Ltd.*, 527 F.3d 1278, 1282-86 (Fed. Cir. 2008) (explaining ANDA procedures and patent infringement claims under the Hatch-Waxman Act).

On August 28, 2013, Takeda filed two separate infringement cases against Mylan (Nos. 13-CV-04001, -04002), asserting a total of seven Orange Book patents. Mylan counterclaimed against an eighth Orange Book patent. *See* Counterclaims (ECF No. 15) ¶ 21. On January 21, 2014, Takeda filed a third suit against Mylan (Case No. 13-CV-00314), asserting the '064 Patent. On February 7, 2014, the Court consolidated these three cases for all purposes. ECF No. 53.

On June 20, 2014, the parties filed a Joint Claim Construction and Prehearing Statement, identifying disputed claim terms, proposed constructions, and citations to supporting evidence. ECF No. 78 ("Joint Statement"). On July 31, 2014, at a case management conference, the Court and parties discussed whether Mylan's indefiniteness defenses should be raised during claim construction, and the Court ordered that those issues be briefed concurrently. *See* ECF No. 83. On August 7, 2014, Takeda filed its opening claim construction brief and supporting expert declarations. *See* ECF No. 89 ("Takeda Br."). On September 8, 2014, Mylan filed its responsive

claim construction brief and expert evidence. *See* ECF No. 120 ("Mylan Br."). On September 19, 2014, Takeda filed its reply brief. *See* ECF No. 128 ("Takeda Reply"). The Court held a technology tutorial and claim construction hearing on October 9, 2014.

II. LEGAL STANDARDS

A. Claim Construction

The Court construes patent claims as a matter of law based on the relevant intrinsic and extrinsic evidence. *See Lighting Ballast Control LLC v. Philips Elecs. N. Am. Corp.*, 744 F.3d 1272 (Fed. Cir. 2014) (en banc); *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (en banc). "Ultimately, the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim." *Phillips*, 415 F.3d at 1316 (internal quotation marks and citation omitted). Accordingly, a claim should be construed in a manner that "stays true to the claim language and most naturally aligns with the patent's description of the invention." *Id.*

In construing disputed terms, a court looks first to the claims themselves, for "[i]t is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude.'" *Id*. at 1312 (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1115 (Fed. Cir. 2004)). Generally, the words of a claim should be given their "ordinary and customary meaning," which is "the meaning that the term[s] would have to a person of ordinary skill in the art in question at the time of the invention." *Id.* at 1312-13. In some instances, the ordinary meaning to a person of skill in the art is clear, and claim construction may involve "little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314.

In many cases, however, the meaning of a term to a person skilled in the art will not be readily apparent, and a court must look to other sources to determine the term's meaning. *See id*. Under these circumstances, a court should consider the context in which the term is used in an asserted claim or in related claims and bear in mind that "the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed

term appears, but in the context of the entire patent, including the specification." *Id.* at 1313. Indeed, the specification "'is always highly relevant'" and "'[u]sually . . . dispositive; it is the single best guide to the meaning of a disputed term.'" *Id.* at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). Where the specification reveals that the patentee has given a special definition to a claim term that differs from the meaning it would ordinarily possess, "the inventor's lexicography governs." *Id.* at 1316. Likewise, where the specification reveals an intentional disclaimer or disavowal of claim scope by the inventor, the inventor's intention as revealed through the specification is dispositive. *Id.* A court may also consider the patent's prosecution history, which consists of the complete record of proceedings before the United States Patent and Trademark Office ("PTO") and includes the cited prior art references. The prosecution history "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.* at 1317.

A court is also authorized to consider extrinsic evidence in construing claims, such as "expert and inventor testimony, dictionaries, and learned treatises." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). Expert testimony may be particularly useful in "[providing] background on the technology at issue, . . . explain[ing] how an invention works, . . . ensur[ing] that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or . . . establish[ing] that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Phillips*, 415 F.3d at 1318. Although a court may consider evidence extrinsic to the patent and prosecution history, such evidence is considered "less significant than the intrinsic record" and "less reliable than the patent and its prosecution history in determining how to read claim terms." *Id.* at 1317-18 (internal quotation marks and citations omitted). Thus, while extrinsic evidence may be useful in claim construction, ultimately "it is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1319. Any

expert testimony "that is clearly at odds with the claim construction mandated by the claims themselves, the written description, and the prosecution history" will be significantly discounted. *Id.* at 1318 (internal quotation marks and citation omitted). Finally, while the specification may describe a preferred embodiment, the claims are not necessarily limited only to that embodiment. *Id.* at 1323; *see also Prima Tek II, L.L.C. v. Polypap, S.A.R.L.*, 318 F.3d 1143, 1151 (Fed. Cir. 2003) ("The general rule, of course, is that claims of a patent are not limited to the preferred embodiment, unless by their own language.").

B. Indefiniteness

Under 35 U.S.C. § 112, ¶ 2 (2006 ed.),[3] a patent must "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as [the] invention." Section 112, ¶ 2 includes what is commonly called the "definiteness" requirement. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120, 2125 (2014). Prior to the Supreme Court's decision in *Nautilus*, the Federal Circuit applied an "insolubly ambiguous" standard to indefiniteness questions. *See, e.g., Datamize, LLC v. Plumtree Software*, Inc., 417 F.3d 1342, 1347 (Fed. Cir. 2005). Under the insolubly ambiguous standard, a claim failed to meet § 112, ¶ 2, and was indefinite only when it was "not amenable to construction" or "insolubly ambiguous." *Id.* In *Nautilus*, the Supreme Court rejected the insolubly ambiguous standard and replaced it with a "reasonable certainty" standard, holding that "a patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus*, 134 S. Ct. at 2124. In addition to the specification, "an ordinarily skilled artisan must consult the prosecution history to confirm the proper understanding of a claim term's meaning, especially if other aspects of the inquiry raise questions." *Ancora Techs., Inc. v. Apple, Inc.*, 744 F.3d 732, 738 (Fed. Cir. 2014).

[3] Paragraph 2 of 35 U.S.C. § 112 was replaced with newly designated § 112(b) when § 4(c) of the America Invents Act ("AIA"), Pub. L. No. 112-29, took effect on September 16, 2012. Because the applications resulting in the patents at issue in this case were filed before that date, the Court refers to the pre-AIA version of § 112.

The Federal Circuit applied the *Nautilus* standard in *Interval Licensing LLC v. AOL, Inc.*, 766 F.3d 1364 (Fed. Cir. 2014). The two patents covered an "attention manager for occupying the peripheral attention of a person in the vicinity of a display device." *Id.* at 1366. In one embodiment, the patents involved placing advertising on websites in areas surrounding the principal content of the webpage, for example in the margins of an article. Several of the asserted claims included a limitation that the advertisements ("content data") would be displayed "in an unobtrusive manner that does not distract a user of the display device." *Id.* at 1368. The district court found that the terms "in an unobtrusive manner" and "does not distract the user" were indefinite, and the Federal Circuit affirmed. *Id.* at 1368-69.

The Federal Circuit found that the "'unobtrusive manner' phrase is highly subjective and, on its face, provides little guidance to one of skill in the art" and "offers no objective indication of the manner in which content images are to be displayed to the user." *Id.* at 1371. Accordingly, the Court looked to the written description for guidance. The Court concluded that the specification lacked adequate guidance to give the phrase a "reasonably clear and exclusive definition, leaving the facially subjective claim language without an objective boundary." *Id.* at 1373. Accordingly, the claims containing the "unobtrusive manner" phrase were indefinite.

In another case decided while *Nautilus* was pending before the Supreme Court, the Federal Circuit affirmed a district court's determination that claim terms were not indefinite because "the claim language and the prosecution history leave no reasonable uncertainty about the boundaries of the terms at issue, even considering certain aspects of the specification that could engender confusion when read in isolation." *Ancora*, 744 F.3d at 737. In *Ancora*, the defendants argued that the terms "volatile memory" and "non-volatile memory" were indefinite. *Id.* Recognizing that those terms "have a meaning that is clear, settled, and objective in content" to one of ordinary skill, the Federal Circuit rejected the indefiniteness challenge. *Id.* Although the specification contained a few references to a computer hard disk as volatile memory, which is ordinarily considered non-volatile, the court nonetheless concluded that "we doubt that an ordinarily skilled artisan could

have a *reasonable* uncertainty about the governing scope of the claims . . . ." *Id.* at 738 (emphasis in original).

The Court therefore reviews the claims, specification, and prosecution history to determine whether the claims "inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus*, 134 S. Ct. at 2124. Indefiniteness renders a claim invalid, and must be shown by clear and convincing evidence. *See Halliburton Energy Servs. v. M-I LLC*, 514 F.3d 1244, 1249 (Fed. Cir. 2008); *cf. Nautilus*, 134 S. Ct. at 2130 n.10.

III. DISCUSSION

The parties request construction of one term of the '971 Patent, one term of the '064 Patent, and two terms of the '158 Patent. Additionally, the parties stipulate to the following construction of one term in the '971 Patent (Takeda Reply at App'x A; Mylan Br. at 1 n.2):

Patent	Term	Agreed Construction
6,939,971	"reflux esophagitis"	"inflammation or irritation of the esophagus caused by gastroesophageal reflux disease (GERD) of the erosive or non-erosive type"

A. The '971 Patent

As explained above, the '971 Patent is generally directed to methods of treating reflux esophagitis with crystalline forms of dexlansoprazole. Takeda asserts claims 6 and 8, which depend from independent claim 5. *See* Takeda Br. at 10 n.3. Claim 5 covers a method of "treating reflux esophagitis in a mammal in need thereof which comprises administering to said mammal an effective amount of" crystalline dexlansoprazole. The parties dispute one term, "effective amount," which appears in independent claim 5 and is incorporated by reference in asserted claims 6 and 8.

1. Level of Ordinary Skill in the Art

The Court first addresses the level of ordinary skill in the relevant art at the time of the claimed invention. *See Phillips*, 415 F.3d at 1312-13. Here, the parties have submitted expert declarations with opinions regarding the level of ordinary skill. For the '971 Patent, Takeda relies on opinions from Dr. Brian Fennerty (*see* ECF No. 103 ("Fennerty Decl.")), while Mylan cites the opinions of Dr. William Stagner (*see* ECF No. 122 ("Stagner Decl.")).

The parties disagree about the relevant fields and level of ordinary skill in the art. According to Takeda's expert Dr. Fennerty, "the art relevant to the claimed subject matter of the '971 patent is the art of gastroenterology and clinical treatment of gastrointestinal disorders," and "[a] person ordinarily skilled in the art of clinical treatment of gastrointestinal disorders would have an advanced degree (Master's degree, Ph.D., or M.D.) with an in-depth understanding of gastrointestinal physiology, pharmacology, and cell and organ biology, as well as experience in determining appropriate dosages for the treatment of gastrointestinal diseases." Fennerty Decl. ¶ 64. Thus, Takeda contends that the relevant art involves clinical treatment of gastrointestinal disorders (such as acid reflux), with knowledge about "appropriate dosages" of drugs.

On the other hand, Mylan's expert Dr. Stagner states that "[t]he relevant art of the '971 and '158 patents, in my opinion, is interdisciplinary, spanning aspects of the field of pharmacy such as pharmaceutics and medicinal chemistry, as well as all stages of pharmaceutical development and formulation of a drug candidate," and that the person of ordinary skill "would have had a Ph.D. in pharmaceutics or a similar discipline in the pharmaceutical sciences such as medicinal chemistry, and at least five years of experience in formulating chemical compounds to obtain safe and effective pharmaceutical formulations." Stagner Decl. ¶¶ 19, 22. In contrast to Takeda's proposal, Mylan characterizes the relevant field as pharmaceutical sciences and formulation of drugs, as opposed to clinical treatment and dosing. Mylan also contends that the '158 Patent (discussed below) and the '971 Patent share the same art, while Takeda disagrees.[4]

The parties' dispute has potential relevance to the sole disputed claim term, "effective amount," because Mylan contends that this term is indefinite in that a person of ordinary skill in the art would not know how much drug would be "effective" to treat a patient. Takeda's hypothetical

[4] Neither side proposes that the '064 and '971 Patents involve the same level of skill, even though those patents are related and share substantially the same specification. Also, in the first set of Dexilant® cases, those parties agreed that the'971 Patent "focus[es] on organic chemistry, crystallization, and crystal forms," and that the level of skill "is either a Ph.D. in chemical engineering or related disciplines or a bachelor's degree in chemistry, chemical engineering, or a related field and three to five years of experience in crystallization and characterization of crystals by routine methods such as x-ray diffraction analysis." Findings of Fact and Conclusions of Law ¶ 145, *Takeda Pharm. Co. v. Handa Pharms., LLC*, No. 11-CV-00840-JCS (N.D. Cal. Oct. 17, 2013). Here, neither side addresses this definition, and Takeda abandons its previous position.

person of ordinary skill has experience in "determining appropriate dosages," and therefore would more likely have knowledge relevant to understanding what "effective amount" means. By contrast, Mylan's ordinarily skilled person lacks clinical treatment experience. However, at the claim construction hearing, the parties agreed that their disputes regarding the level of ordinary skill for the '971 Patent are not dispositive of claim construction. *See* Oct. 9, 2014 Hearing Tr. ("Tr.") at 10:2-17 ("The Court: Let me ask, what does the difference in skill level matter to the claim constructions? . . . Ms. Laughton: . . . [S]peaking specifically right now about the '971 and the '158, we don't think that there is a particular difference in terms of the claim constructions. . . . Mr. Lorenzo: Your Honor, I think we join in that.").

The level of ordinary skill in the relevant art could affect discovery and other questions of validity and infringement going forward. *See id.* at 10:9-10 ("It may be the case that it would affect issues later in the case with respect to validity . . . ."). Furthermore, "[t]he inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation." *Phillips*, 415 F.3d at 1313. Therefore, the Court addresses the parties' dispute here.

The Federal Circuit addressed a similar question for a pharmaceutical patent in *Daiichi Sankyo Co. v. Apotex, Inc.*, 501 F.3d 1254 (Fed. Cir. 2007). The court first noted non-exhaustive factors that guide determination of the level of ordinary skill in the art: "(1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in the field." *Id.* at 1256 (quotation and citations omitted). The court then addressed the level of skill for the disputed invention, which involved "the creation of a compound to treat ear infections without damaging a patient's hearing." *Id.* at 1257. Looking to the problem the inventors tried to solve and the patent's specification, the Federal Circuit found that the district court erred in defining the ordinarily skilled artisan as "a pediatrician or general practitioner" because the patent involved both disease treatment and drug formulation: "while a general practitioner or pediatrician could (and would) prescribe the invention of the '741 patent to

treat ear infections, he would not have the training or knowledge to develop the claimed compound absent some specialty training such as that possessed by the '741 patent's inventors." *Id.* Accordingly, the court defined the level of ordinary skill as that of a person who developed "treatment methods for the ear" but "also has training in pharmaceutical formulations." *Id.*

In this case, the Court takes a similar approach and adopts portions of Mylan's and Takeda's positions. The Court agrees with Mylan that the '971 Patent primarily discusses synthesis and characterization of crystalline dexlansoprazole and formulation of dosage forms. "The present invention relates to a crystal of a benzimidazole compound showing antiulcer action." '971 Patent col.1 ll.13-14. The inventors sought to meet "a demand for a more stable and excellently absorbable antiulcer agent." *Id.* col.1 ll.20-21. To this end, the specification identifies methods of synthesizing and isolating dexlansoprazole. *See id.* col.2 ll.19-63 (defining methods for optical resolution). The patent includes three "Reference Examples" that discuss isolation of dexlansoprazole from racemic lansoprazole. *See id.* col.7 l.52-col.8 l.59. Next, the specification identifies methods for crystallizing dexlansoprazole and characterizing those crystals. *See id.* col.2 l.64-col.3 l.53 (defining "[m]ethods of crystallization"), col.8 l.61-col.10 l.60 (Reference Example 4, discussing X-ray powder diffraction). Additionally, the patent discusses formulation of drugs with crystalline dexlansoprazole, identifying numerous "[p]harmacologically acceptable carriers" for producing "the pharmaceutical composition of the present invention," such as "excipients" and "lubricants." *See id.* col.4 l.25-col.5 l.61. Thus, Mylan's emphasis on "medicinal chemistry" and "formulation" (Stagner Decl. ¶ 19) is appropriate because the majority of the patent's disclosure is dedicated to chemistry and drug formulation. *See Daiichi*, 501 F.3d at 1257 (referring to what "most of the written description details"). Moreover, as Dr. Stagner points out, "Dr. Fennerty's person of ordinary skill in the art would not have been able to prepare a product that would deliver an effective amount of dexlansoprazole in an appropriate drug delivery system to treat patients . . . ." Stagner Decl. ¶ 24.

At the same time, the '971 Patent also discusses aspects of clinical use. The specification states that "[t]he crystal of the present invention is useful in mammals" and refers to administration

to patients. '971 Patent col.3 l.54-col.4 l.24. The claims of the '971 Patent recite methods of "treating reflux esophagitis" and "administering" drugs. *E.g.*, *id.* cls. 5, 10. Dr. Stagner also stated at his deposition that the relevant art could include "design of clinical trials" and "assessments of safety and efficacy." ECF No. 129-2 ("Stagner Depo.") at 58:4-24; *see also* Mylan Br. at 8 ("The '971 patent relates to . . . treating a number [of] gastrointestinal conditions."). Accordingly, the intrinsic and extrinsic evidence supports Takeda's position that "clinical treatment" experience (Fennerty Decl. ¶ 64) is a necessary part of the level of ordinary skill.

In light of the foregoing, the Court determines that the relevant art of the '971 Patent is "interdisciplinary, spanning aspects of the field of pharmacy such as pharmaceutics and medicinal chemistry, as well as all stages of pharmaceutical development and formulation of a drug candidate" (Stagner Decl. ¶ 19), and "clinical treatment of gastrointestinal disorders" (Fennerty Decl. ¶ 64). A person of ordinary skill in this art "would have had a Ph.D. in pharmaceutics or a similar discipline in the pharmaceutical sciences such as medicinal chemistry, and at least five years of experience in formulating chemical compounds to obtain safe and effective pharmaceutical formulations" (Stagner Decl. ¶ 22), and experience in clinical treatment of gastrointestinal disorders (*see* Fennerty Decl. ¶ 64).

2. "effective amount" (claims 6 and 8)

Mylan's Proposed Construction	Takeda's Proposed Construction
Indefinite.	"an amount sufficient to help ameliorate or cure reflux esophagitis"

The first disputed phrase appears in claim 5 of the '971 Patent, from which asserted claims 6 and 8 depend. Independent claim 5 recites:

> 5. A method of treating reflux esophagitis in a mammal in need thereof which comprises administering to said mammal an **effective amount** of a crystalline compound of (R)-2-(((3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl)methyl) sulfinyl)-1 H-benzimidazole or a salt thereof and a pharmaceutically acceptable excipient, carrier or diluent.

'971 Patent cl.5 (emphasis added).

Mylan asserts that "effective amount" is indefinite under *Nautilus* because the patent fails to convey with reasonable certainty what quantities of dexlansoprazole are effective for treating

reflux esophagitis in all mammals. According to Mylan, "where a patent ascribes an impermissibly broad range and is directed to the treatment of every mammal, it cannot satisfy the Supreme Court's standard of conveying 'reasonable certainty.'" Mylan Br. at 17. In Mylan's view, the disputed term is boundless: "Because the term 'effective amount' broadly encompasses *any* amount of the claimed composition effective to treat reflux esophagitis through *any* diverse route of administration, in *any* mammal, the sheer breadth of the claim renders the amount essentially limitless." *Id.* at 22 (emphases in original). Mylan does not propose an alternative construction.

Takeda disagrees, arguing that the Federal Circuit and other courts have construed terms like "effective amount" without finding them indefinite. *See* Takeda Br. at 11. Takeda also contends that the specification provides sufficient dosage information to inform a person of ordinary skill as to what "effective amount" means. *See* Takeda Reply at 10-11. Furthermore, Takeda argues that a person of ordinary skill would have been able to conduct clinical studies without "undue experimentation": "Determining the 'effective amount' to administer to a desired nonhuman mammal would, again, be matter of routine experimentation for one of ordinary skill in the art." *Id.* at 13. Takeda also points out that Judge Spero already accepted Takeda's proposed construction for this term in the first set of Dexilant® cases. *See* Spero Order at 19-23.

The Court addresses Mylan's indefiniteness arguments and the propriety of Takeda's proposed construction. For the reasons below, the Court determines that "effective amount" as used in the '971 Patent is not indefinite and adopts Takeda's construction.

a. Intrinsic Evidence

Starting with the claim language itself, the claims contain little express guidance about the meaning of "effective amount." Claim 5 states that the "effective amount" is for "treating reflux esophagitis in a mammal in need thereof," without reciting numerical dosing limitations. Other independent claims of the '971 Patent also recite "effective amount," but no other claims provide specific dosing information. Thus, while the claims do not recite specific doses, their plain language indicates that the claimed "effective amount" refers to an amount effective to treat reflux

esophagitis, not necessarily a fixed quantity or quantities of drug, which is consistent with Takeda's proposed construction.

The prosecution history provides no assistance for this term. Neither party or expert cites any portions of the prosecution record to support their positions. Indeed, Dr. Stagner observes that "[t]he term is also not addressed in the prosecution history." Stagner Decl. ¶ 36.

As a result, Takeda and Mylan rely almost exclusively on the specification. The parties argue primarily about two portions. First, the patent contains three paragraphs that discuss how crystalline dexlansoprazole "is useful in mammals (e.g., humans, monkeys, sheep, bovines, horses, dogs, cats, rabbits, rats, mice, etc.) for the treatment and prevention of digestive ulcer (e.g., gastric ulcer, duodenal ulcer, stomal [sic] ulcer, Zollinger-Ellison syndrome, etc.), gastritis, reflux esophagitis," and other diseases. '971 Patent col.3 l.54-col.4 l.24. The specification further states:

> The content of the crystal of the present invention in the pharmaceutical composition of the present invention is about 0.01 to 100% by weight relative to the entire composition. Varying depending on subject of administration, route of administration, target disease etc., its dose is normally about 0.5 to 1,500 mg/day, preferably about 5 to 150 mg/day, based on the active ingredient, for example, when it is orally administered as an antiulcer agent to an adult human (60 kg). The crystal of the present invention may be administered once daily or in 2 to 3 divided portions per day.

Id. col.4 ll.15-24. Second, "Experimental Example 1" in the specification describes a study on "[s]uppressive action on gastric mucosal injury due to stress of water immersion restraint in rat," in which the inventors experimented with crystalline dexlansoprazole in rat stomachs. *Id.* col.13 ll.14-54. The parties disagree about whether these disclosures provide sufficient explanation about what an "effective amount" of dexlansoprazole would be.

As an initial matter, the parties dispute the law as to what degree of experimentation would render a claim term indefinite. Both parties cite *Geneva Pharmaceuticals, Inc. v. GlaxoSmithKline PLC*, where the Federal Circuit observed: "Our predecessor court has stated that 'effective amount' is a common and generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without *undue experimentation*." 349 F.3d 1373, 1383-84 (Fed. Cir. 2003) (emphasis added). Takeda claims that even if the specification does not identify effective amounts for treating reflux

esophagitis in all mammals, a person of ordinary skill could conduct routine clinical studies without "undue experimentation" to determine appropriate doses. *See* Takeda Br. at 14; Fennerty Decl. ¶¶ 47-50 (describing Phase I/II/III clinical trials). Mylan disagrees, saying that "separate clinical trials would need to be conducted for every type of mammal being treated" after first determining "the appropriate dosage form" based on multiple formulation variables. Mylan Br. at 21. According to Mylan, "one of ordinary skill could not have determined the meaning of the term 'effective amount' without undue experimentation, rendering such term indefinite under the clear mandate of *Geneva* . . . and *Nautilus*." *Id.* at 22.

The parties' arguments about whether clinical trials require "undue experimentation" are misplaced to the extent they invoke enablement under 35 U.S.C. § 112. Indefiniteness deals with whether a patent "fail[s] to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus*, 134 S. Ct. at 2124. By contrast, the "undue experimentation" test generally applies to enablement. *See Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014) ("To prove that a claim is invalid for lack of enablement, a challenger must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without 'undue experimentation.'" (quoting *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988))); *see also Augme Techs., Inc. v. Yahoo! Inc.*, 755 F.3d 1326, 1340 (Fed. Cir. 2014) ("Appellants' arguments appear to be based on the wrong legal standard, i.e., written description or enablement as opposed to indefiniteness."). The Federal Circuit has previously explained that "[m]erely claiming broadly" does not "prevent the public from understanding the scope of the patent," *Ultimax Cement Mfg. Corp. v. CTS Cement Mfg. Corp.*, 587 F.3d 1339, 1352 (Fed. Cir. 2009), and that "breadth is not indefiniteness," *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1341 (Fed. Cir. 2005) (quotation and citation omitted).

This Court does not read *Geneva*'s passing reference to "undue experimentation" as applying an enablement standard for deciding whether "effective amount" claims are indefinite. The Federal Circuit observed in *Geneva* that "*[o]ur predecessor court* has stated that 'effective

amount' is a common and generally acceptable term for pharmaceutical claims and is not ambiguous or indefinite, provided that a person of ordinary skill in the art could determine the specific amounts without *undue experimentation*." 349 F.3d 1383-84 (emphases added). For this proposition, *Geneva* cited a case from the Court of Customs and Patent Appeals ("CCPA"), *In re Halleck*, 422 F.2d 911 (C.C.P.A. 1970). In *Halleck*, the CCPA dealt with an appeal from the PTO where an Examiner rejected the phrase "an effective amount . . . for growth stimulation" as "too broad and . . . functional." *Id.* at 914. The *Halleck* court ruled that "it does not appear from the facts of record that determination of such amounts would be beyond the skill of the art nor that it would involve *undue experimentation* to ascertain them." *Id.* (emphasis added). However, *Halleck* noted expressly that the Examiner rejected the phrase on the "statutory basis [of] 35 U.S.C. § 112, second paragraph" (corresponding to indefiniteness at the time), but that "such rejections are more properly considered under the first paragraph of 35 U.S.C. § 112" (corresponding to enablement). *Id.* at 914 n.3.

Furthermore, the *Halleck* court referenced two concurrent cases to clarify the distinction between indefiniteness and enablement under § 112. *See id.* In one such case, *In re Borkowski*, the CCPA explained that "if the '*enabling*' disclosure of a specification is not commensurate in scope with the subject matter encompassed by a claim, that fact *does not render the claim imprecise or indefinite* or otherwise not in compliance with the second paragraph of § 112; rather, the claim is based on an insufficient disclosure." 422 F.2d 904, 909 (C.C.P.A. 1970) (emphasis added). Thus, the CCPA explicitly warned against confusing indefiniteness and enablement. Accordingly, *Halleck*'s recitation of "undue experimentation" did not actually address indefiniteness, but rather enablement. Thus, the instant Court does not interpret *Geneva*'s reliance on *Halleck* as importing an enablement standard into the indefiniteness inquiry for the claims at issue.

For this reason, the parties' reliance on legal standards for enablement has limited value. For example, Takeda cites *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.*, as an instance of a court upholding a claim to a broad dosage range of "30-2000 milligrams." 520 F.3d 1358, 1365 (Fed. Cir. 2008); *see* Takeda Br. at 13 (citing *id.*). However, that case resolved an

enablement defense—not indefiniteness—holding that the specification "adequately enables" the disputed claims. *Ortho-McNeil*, 520 F.3d at 1365. Similarly, Takeda relies on *Cephalon, Inc. v. Watson Pharmaceuticals, Inc.*, 707 F.3d 1330 (Fed. Cir. 2013), to argue that a "reasonable amount of routine experimentation is not 'undue,'" Takeda Br. at 12 (quoting *id.*). Again, *Cephalon* is an enablement case that does not mention indefiniteness, and thus has little relevance here. *See* 707 F.3d at 1336-40.

Returning to the specification of the '971 Patent, column 4 discloses dosing ranges that inform the meaning of "effective amount." The specification teaches: "Varying depending on subject of administration, route of administration, target disease etc., its dose is normally about 0.5 to 1,500 mg/day, preferably about 5 to 150 mg/day, based on the active ingredient, for example, when it is orally administered as an antiulcer agent to an adult human (60 kg)." '971 Patent col.4 ll.18-22. The patent further notes that "[t]he crystal of the present invention may be administered once daily or in 2 to 3 divided portions per day." *Id.* col.4 ll.23-24. Thus, the specification indicates that the proper dose may vary by patient and route of administration, but that such a dose is generally "about 0.5 to 1,500 mg/day." Mylan points out that in this range "the top end is 3,000 times that of the low end" and argues that this variability "does not provide one with reasonable certainty." Mylan Br. at 18. Mylan's argument is unpersuasive. Even if the dosage range is broad, "breadth is not indefiniteness." *SmithKline*, 403 F.3d at 1341. Mylan further argues that the specification refers to treating a variety of diseases in non-human mammals, not just treating acid reflux in people, and that "the purported invention may be used in the treatment and prevention of MALT lymphoma in a rabbit." Mylan Br. at 18 (citing '971 Patent col.3 l.54-col.4 l.4). This argument is also unpersuasive. The asserted claims are limited to treating "reflux esophagitis," not other diseases such as MALT lymphoma. Moreover, the question of whether a person of ordinary skill could practice all embodiments relates to enablement. *See Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1382 (Fed. Cir. 2001) (noting that "inoperable embodiments" raise "an issue of enablement, and not indefiniteness").

Next, the parties dispute the significance of Experimental Example 1. In that experiment, a solution of crystalline dexlansoprazole was administered to rats, the rats were "stressed" in restraint cages partially submerged in water, and the rats' stomachs were removed and examined for mucosal injuries. '971 Patent col.13 ll.14-54. The study concluded that the medicated rats suffered less extensive mucosal injuries than a control group. Mylan argues that this experiment is useless for construing "effective amount" because it addressed prevention of injury instead of treatment, it studied the stomach instead of the esophagus, and it used rats instead of humans (or other mammals). *See* Mylan Br. at 19; Stagner Decl. ¶¶ 43-45. Takeda responds by citing extrinsic evidence that Prevacid® (lansoprazole) was known to be effective for both treating and preventing acid reflux, and Dr. Stagner's testimony that animal testing provides information about humans. *See* Takeda Reply at 11-12; Fennerty Decl. ¶ 84. The Court finds that Experimental Example 1 does little to elucidate the meaning of "effective amount." Takeda fails to tie Experimental Example 1 to Prevacid® or any of the extrinsic evidence that discusses PPIs other than dexlansoprazole. The experiment provides some data about what amounts of dexlansoprazole might prevent injuries in rat stomachs, but does not discuss doses suitable for treating reflux esophagitis in other mammals (such as humans). Dr. Stagner testified generally that animal tests can give "a signal" that a drug "might be effective" in humans, but did not admit that Experimental Example 1 discloses "effective amounts." Stagner Depo. at 123:21-124:3.

Mylan also argues that the '971 Patent fails to explain how to create a proper dosage form (such as a pill or tablet) for treating reflux esophagitis in any mammal, which would be necessary for any clinical trials. "Determining the appropriate dosage form is an entirely separate inquiry which requires, among other things, testing for stability, solubility, bioavailability, and a host of other factors." Mylan Br. at 21; *see also* Stagner Decl. ¶ 48. These arguments are misplaced. Whether a person of ordinary skill could have formulated an appropriate dosage form is an issue of enablement. The asserted claims do not claim dosage forms, but rather methods of administering dexlansoprazole with "a pharmaceutically acceptable excipient, carrier or diluent." '971 Patent cl.5. Also, the specification teaches that the claimed drug "may be prepared as a preparation for

oral administration," such as an "orally disintegrating tablet," and lists numerous methods and excipients for making such dosage forms. *Id.* col.5 l.62-col.6 l.45. To the extent Mylan argues that the specification must disclose all variables for formulating a precise dosage form to avoid indefiniteness (*see* Mylan Br. at 21-22), that is not the law.

Overall, the specification explains appropriate dosage ranges for dexlansoprazole, variables that affect dosing in individual patients, and techniques for formulating dosage forms. As detailed above, the person of ordinary skill in the art of the '971 Patent is highly educated and has—even under Mylan's proposal—a Ph.D. and at least five years of experience. This evidence indicates that the term "effective amount" would not have been indefinite.

b. Extrinsic Evidence

The parties rely on their respective experts' opinions. The Court finds that these competing opinions provide limited help in construing the disputed term. First, both experts generally echo the parties' characterizations of the specification and extrinsic evidence. *See* Fennerty Decl. ¶¶ 81-91; Stagner Decl. ¶¶ 36-66. Second, each expert has notable qualifications but lacks certain relevant expertise. Takeda's expert Dr. Fennerty admitted that he lacks formulation experience, and is therefore not a person of ordinary skill in the art. *See* ECF No. 121-5 ("Fennerty Depo.") at 30:1-10 ("I'm not a formulator. I'm not a medicinal chemist. And I have really no expertise in that other than understanding some of the principles that are described to me about those compounds."). At the hearing, Takeda admitted that Dr. Fennerty is not a person of ordinary skill under either party's proposal. *See* Tr. at 5:6-6:11.[5] This concession diminishes the persuasiveness of Dr. Fennerty's opinions. However, it is undisputed that Dr. Fennerty has expertise in clinical treatment of reflux esophagitis. Mylan's expert Dr. Stagner opines that formulating an appropriate dosage form would require substantial experimentation, and that "determination of an effective amount in clinical studies would likely *not* be routine, easily performed or inexpensive." Stagner

[5] Takeda cites *Endress + Hauser, Inc. v. Hawk Measurement Systems Pty. Ltd.*, 122 F.3d 1040, 1042 (Fed. Cir. 1997), for the proposition that a testifying expert need not be a person of ordinary skill. *See* Takeda Reply at 4. However, *Endress + Hauser* rejected the argument that "a person of *exceptional* skill in the art would be disqualified from testifying," and did not address an expert who *lacked* requisite credentials. 122 F.3d at 1042.

Decl. ¶ 57. However, Dr. Stagner admitted that he has not worked with dexlansoprazole or any PPIs. *See* Stagner Depo. at 40:8-16. While Dr. Stagner is an accomplished formulator and chemist, he lacks experience in treating gastrointestinal disorders. *See* Stagner Decl. ¶¶ 3-10.

The Court notes that Dr. Stagner provided indications that "effective amount" would have been readily understood, which undercuts Mylan's indefiniteness arguments. Dr. Stagner opined that a person of ordinary skill would not be able to determine a particular effective amount as claimed in the patent, but testified that "[e]ffective amount would be in the case of patient treatment, that you would get an acceptable patient outcome for the disease that's being treated," and agreed that "effective amount" and "therapeutically effective amount" are "commonly used terms in pharmaceutical development and treatment of patients with pharmaceuticals." Stagner Depo. at 51:13-52:24. Also, Takeda notes that Dr. Stagner is a named inventor on published patent applications that use the same claim terms. *See, e.g.*, U.S. Patent Appl. No. 2008/0039433 (ECF No. 129-8) cl.1 (claiming "an effective amount of a tetracycline"). Dr. Stagner testified that "effective amount" in his own applications is not indefinite, even though those applications provide no clinical testing results. *See* Stagner Depo. at 84:9-23.

Turning to extrinsic references, Takeda relies on "published literature in gastroenterology regarding effective amounts of other PPIs." Takeda Br. at 12. Takeda cites seven scientific articles that pre-date the '971 Patent's priority date. *See* ECF Nos. 110-1, 110-2, 111, 111-1, 112, 112-1, 113. Each paper discusses the effectiveness of other PPIs (such as lansoprazole and omeprazole) in reducing gastric acid in humans. As an example, Takeda provides a February 1998 article from the American Journal of Gastroenterology, "A Placebo-Controlled Dose-Ranging Study of Lansoprazole in the Management of Reflux Esophagitis," by David Earnest *et al*. ECF No. 110-1. The Earnest article reports a study where human patients with reflux esophagitis received daily doses of 15, 30, or 60 mg of lansoprazole. *Id.* at 239. The investigators concluded that lansoprazole was "significantly superior to placebo" and that the optimum daily dose was 30 mg. *Id.* at 238. The other papers report experiments on similar doses of PPIs. *See, e.g.*, ECF No. 111 (evaluating "lansoprazole 30mg versus omeprazole 40mg"). Takeda asserts that these papers

"would inform a person of ordinary skill in the art about an effective amount of dexlansoprazole to treat reflux esophagitis," and that one "would be able to further determine the optimal effective amounts by conducting a routine clinical trial." Takeda Br. at 13-14; *see also* Fennerty Decl. ¶¶ 86-87 ("A person of ordinary skill in the art would further be guided by the dosage amounts for which other PPIs are prescribed.").

Takeda's cited articles provide partial support for Takeda's position that "effective amount" is not indefinite. Mylan correctly notes that none of Takeda's cited papers discuss dexlansoprazole or correlate effective amounts of one drug to another. *See* Mylan Br. at 20-21. However, a person of ordinary skill in the art who was trying to administer dexlansoprazole to treat reflux esophagitis would have known of other PPIs for treating the same disease, and would also have known of the dosing information in the scientific literature. Dr. Stagner claims that Takeda's articles have limited use because dexlansoprazole is a "unique compound" with "unique properties," but does not explain how dexlansoprazole differs from other PPIs with any specificity. Stagner Decl. ¶ 60. Furthermore, as noted above, Dr. Stagner has not worked with dexlansoprazole or other PPIs. By contrast, Dr. Fennerty states that lansoprazole, omeprazole, and dexlansoprazole are chemically related (all are benzimidazoles) and have similar drug characteristics. Fennerty Decl. ¶¶ 88-89. Overall, Takeda's literature indicates that a person of ordinary skill would have known proper dosing ranges for closely related PPIs. However, the literature is not dispositive of indefiniteness because it does not specifically address crystalline dexlansoprazole.

Takeda also relies on a May 1998 FDA Guidance for Industry that contains recommendations on conducting clinical trials and "the evidence to be provided to demonstrate effectiveness." ECF No. 113-1 at 1. Takeda claims that such guidances provided sufficient information to conduct clinical trials to determine effective amounts of dexlansoprazole. *See* Takeda Br. at 14; Fennerty Decl. ¶ 90. The Court disagrees. As explained above, the parties' arguments regarding clinical trials and "undue experimentation" are more appropriately addressed with enablement, which is not at issue here. The fact that procedures for performing FDA-approved clinical trials were well known at the time does not show that a person of ordinary skill

would have known with reasonable certainty what constituted an "effective amount" of dexlansoprazole.

Next, Takeda cites the prescribing information for Dexilant® to point out that Dexilant® is currently sold in 30 and 60 mg doses, which fall within the specification's dosage ranges. *See* Takeda Br. at 14 (citing ECF No. 109). Takeda also argues that the fact that companies have sought FDA approval for dexlansoprazole shows that they were able to determine effective amounts. *See id.* at 12. Takeda's arguments are flawed because they rely on information not available to the person of ordinary skill at the relevant time. *See Phillips*, 415 F.3d at 1312-13. The Dexilant® prescribing information is dated August 2013, fourteen years after the '971 Patent's priority date. ECF No. 109 at 1.

Finally, the Court reviews other cases where "effective amount" or similar terms have been construed. In particular, Judge Spero previously construed "effective amount" in the '971 Patent in the first set of Dexilant® cases. *See* Spero Order at 71. There, the defendants contended that "effective amount" was indefinite, raising essentially the same arguments that Mylan asserts here, but prior to the Supreme Court's decision in *Nautilus*. *See id.* at 20-21. Judge Spero adopted the construction that Takeda proposes here, but deferred resolution of indefiniteness for summary judgment. *See id.* at 23. The parties did not seek summary judgment regarding indefiniteness, and Judge Spero's construction was not appealed. *See* Tr. at 30:15-32:1, 33:12-22. While Judge Spero's ruling is not binding on this Court, that construction is persuasive, and consistency counsels in favor of adopting it here. Moreover, at the hearing Mylan conceded that if "effective amount" is not indefinite, "Judge Spero's construction would control." *Id.* at 36:7-17.

Other courts have construed "effective amount" terms similarly to Takeda's proposal. *See, e.g.*, *Abbott Labs. v. Baxter Pharm. Prods., Inc.*, 334 F.3d 1274, 1277 (Fed. Cir. 2003) ("[T]his court notes that the term 'effective amount' has a customary usage."); *Astra Aktiebolag v. Andrx Pharm., Inc.*, 222 F. Supp. 2d 423, 481 (S.D.N.Y. 2002) ("'Therapeutically effective amount' means an amount that is effective in therapy, or an amount sufficient to provide a therapeutic effect. An amount that is effective in therapy is an amount which produces a biological activity

and will depend, among other things, on the individual."); *King Pharms., Inc. v. Purdue Pharma, L.P.*, 718 F. Supp. 2d 703, 718 (W.D. Va. 2010) (holding "effect" not indefinite); *Biogen Idec Inc. v. GlaxoSmithKline LLC*, No. 10-CV-00608, 2011 WL 4949042, at *11 (S.D. Cal. Oct. 18, 2011) ("[T]he term 'effective to treat the chronic lymphocytic leukemia' shall be construed as 'providing a positive clinical benefit to the chronic lymphocytic leukemia patient.'"); *Medicis Pharm. Corp. v. Acella Pharms. Inc.*, No. CV 10-1780, 2011 WL 810044, at *7 (D. Ariz. Mar. 2, 2011) ("So, the 'effective amount' is the quantity of dermatologically active ingredients that is adequate to produce the intended result."); *Teva Pharms. USA, Inc. v. Amgen, Inc.*, No. 09-5675, 2010 WL 3620203, at *12-13 (E.D. Pa. Sept. 10, 2010); *Cytomedix, Inc. v. Little Rock Foot Clinic, P.A.*, No. 02 c 4782, 2004 WL 1921070, at *4 (N.D. Ill. Aug. 4, 2004). These cases pre-date *Nautilus*, construe different patents, and are not controlling. However, they suggest that "effective amount" is a commonly used and understood term.

Based on the intrinsic and extrinsic evidence analyzed above, the Court concludes that Mylan has not shown by clear and convincing evidence that the term "effective amount" is indefinite. Mylan does not propose an alternative construction, and Takeda's construction has support in the record and was adopted by Judge Spero in the first set of Dexilant® cases. Moreover, Mylan concedes that if the term is not indefinite, Judge Spero's construction controls. Accordingly, the Court construes "effective amount" to mean **"an amount sufficient to help ameliorate or cure reflux esophagitis."**

B. The '064 Patent

The '064 Patent is a continuation of the '971 Patent and is generally directed to a novel crystal of dexlansoprazole. Takeda asserts claims 1 through 3 of the '064 Patent. The asserted claims read:

> 1. A crystal of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl] sulfinyl]-1H-benzimidazole hydrate.
>
> 2. The crystal according to claim 1, which is (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole 1.5 hydrate.
>
> 3. A pharmaceutical composition comprising: a crystal of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole 1.5 hydrate

and a pharmaceutically acceptable excipient, carrier or diluent that is compatible with the crystalline nature of the hydrate product.

'064 Patent cls. 1-3.

The parties agree that (1) the term "(R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole" refers to the R-enantiomer of lansoprazole, or dexlansoprazole; (2) the term "hydrate" means "a crystalline compound in which water is part of the crystalline structure"; and (3) the term "1.5 hydrate" means "a crystalline compound in which 1.5 molecules of water are incorporated within the crystalline structure for each molecule of dexlansoprazole." Joint Statement at 4-5. The parties request construction of the term "compatible with the crystalline nature of the hydrate product" in claim 3.

1. Level of Ordinary Skill in the Art

As with the '971 Patent, the parties dispute the level of ordinary skill in the relevant art. The parties submitted expert declarations opining as to both the relevant art of the '064 Patent and the level of ordinary skill. For the '064 Patent, Takeda relies on the opinions of Dr. Allan Myerson (*see* ECF No. 90 ("Myerson Decl.")), while Mylan relies on the opinions of Dr. Michael Zaworotko (*see* ECF No. 123 ("Zaworotko Decl.")).

Takeda asserts that the art relevant to the claimed subject matter of the '064 Patent is "the art of crystallization, polymorphism, nucleation, pharmaceutical manufacturing, and the industrial use of crystallization." Takeda Br. at 5. Takeda's expert Dr. Myerson opined that the level of skill in the art is "a bachelor's degree in chemistry, chemical engineering, or related disciplines, with a minimum of three years' experience in the pharmaceutical industry related to organic synthesis, API (active pharmaceutical ingredient) manufacturing, crystallization or detection and/or evaluation of solid state forms, or an advanced degree in chemistry, chemical engineering, or related disciplines, with less or no experience." Myerson Decl. ¶ 50.

Mylan's expert Dr. Zaworotko opined that the "relevant art of the '064 patent, in my opinion, is interdisciplinary, spanning aspects of the field of chemistry such as medicinal chemistry, crystallography, analytical chemistry, materials science, including how they relate to pharmaceutical science and pre-clinical studies involving the development of dosage forms. A

person of ordinary skill in the relevant art of the '064 patent, as of the relevant date, would likely have been part of, or had access to, a team of individuals with various skills spanning the chemical arts listed above." Zaworotko Decl. ¶ 27. A person of ordinary skill "would have earned a Ph.D. in organic chemistry, analytical chemistry, materials science or medicinal chemistry and have at least one to two years of experience in crystallizing chemical compounds to obtain different crystal forms and characterizing the crystal forms by routine methods such as X-ray diffraction analysis. Such a person would have either personal knowledge or had [sic] access to a team with knowledge regarding design of dosage forms." *Id.* ¶ 29.

Dr. Zaworotko faulted Dr. Myerson's definition of the person of ordinary skill in the art because it did not address the design and evaluation of drug dosage forms and the selection of excipients. *Id.* ¶ 30. Dr. Zaworotko also opined that "a typical bachelor's degree holder with only three years of experience would not be able to elucidate the crystal structures of the claimed crystals of the '064 patent, especially where the purported crystals have different forms." *Id.*

As with the '971 Patent, the parties agree that the dispute over the person of ordinary skill is not dispositive of claim construction. Tr. at 61:5-9 ("The Court: Is the dispute over the level of education and experience for a person of ordinary skill in the art dispositive or impactful in any way in the construction? Mr. Lorenzo: For the '064 Patent, Your Honor, I don't think it makes a difference."). Nonetheless, because the issue of the level of ordinary skill in art is the starting point for claim construction, *Phillips*, 415 F.3d at 1313, the Court addresses the dispute here.

Applying the factors identified in *Daiichi*, 501 F.3d at 1256, the Court adopts a hybrid definition derived from Takeda's and Mylan's proposals.

As to the relevant art, the specification and claims of the '064 Patent are primarily directed to the synthesis and characterization of crystalline forms of dexlansoprazole, and to a lesser extent formulating a dosage form. Dr. Myerson agreed at his deposition that the '064 Patent "is dealing with the art of crystalline forms of a particular drug, and then their use in a pharmaceutical composition." ECF No. 121-4 ("Myerson Depo.") at 31:18-21. Nonetheless, the definition of the relevant art proposed by Takeda is limited to crystallization, *see* Takeda Br. at 5, and does not

address the fact that asserted claim 3 is directed to a pharmaceutical composition including a "pharmaceutically acceptable excipient, carrier or diluent." '064 Patent cl.3. Mylan's identification of the relevant art as including both crystallography and the development of dosage forms better addresses the entire subject matter of the claims. Mylan's definition also recognizes that the relevant art is likely to be covered by a team of individuals, rather than a single person.

As to the level of experience required, the parties dispute whether a person of ordinary skill must have a Ph.D. or if the person of ordinary skill could obtain sufficient crystallography or related experience in an industrial, rather than academic, setting. *See* Takeda Reply at 2. Takeda's expert testified that a bachelor's degree with three years of experience, a Master's degree with "some industrial experience," or a Ph.D. with no additional experience would qualify a person of ordinary skill in the art. Myerson Depo. at 34:2-8 (bachelor's degree plus three years of experience); *id*. at 37:22-23 (Master's degree plus "some industrial experience"); *id.* at 37:23-25 (Ph.D. with no additional experience). Mylan's expert required a Ph.D. plus "at least one to two years of experience in crystallizing chemical compounds to obtain different crystal forms and characterizing the crystal forms by routine methods such as X-ray diffraction analysis," Zaworotko Decl. ¶ 29, but testified that the "one to two years of experience" could come "as part of a Ph.D.," ECF No. 129-1 ("Zaworotko Depo.") at 77:12-78:5.

Mylan defends the Ph.D. requirement by pointing to the challenges involved in identifying the different crystalline forms of a compound. Zaworotko Decl. ¶¶ 30, 32, 50. However, Dr. Zaworotko recognized that "some" bachelor's degree holders and graduate students would be able to "elucidate crystal structures of various compounds." Zaworotko Depo. at 85:25-86:12. Dr. Zaworotko also recognized that the tests used to characterize crystalline compounds were well known in the art. Zaworotko Decl. ¶ 49. Finally, at the claim construction hearing, Mylan's counsel acknowledged that drawing a distinction between academic and industrial experience "straddled the line a bit." Tr. at 62:4-12.

In support of Dr. Myerson, Takeda argues that a person of ordinary skill only needs to be able to practice the invention, not recreate the inventive process. Takeda Reply at 2; *see also* 35

U.S.C. § 112, ¶ 1 (enablement requirement); *AK Steel Corp. v. Sollac & Ugine*, 344 F.3d 1234, 1244 (Fed. Cir. 2003) (discussing enablement requirement). Dr. Zaworotko testified that his definition was based on the level of skill necessary to "*discover* and characterize . . . a hydrated crystal form of a compound." Zaworotko Depo. at 77:18-19 (emphasis added). Accordingly, while Dr. Zaworotko makes many statements about the difficulty in identifying the 1.5 hydrate of dexlansoprazole in the first instance, he does not appear to take the position that it would require a Ph.D. to follow the teachings of the patent. *Id.* Indeed, his statements that the tests used to characterize crystalline compounds were well known in the art would suggest otherwise. Zaworotko Decl. ¶ 49; Zaworotko Depo. at 69:11-19.

In the end, both experts simply point to their own expertise and experience in support of their definitions of one of ordinary skill. *See* Myerson Depo. at 32:13-20; Zaworotko Depo. at 77:12-19. Because the experts do not appear to dispute that the techniques used to characterize a crystalline compound in the patent were routine, would be performed both in academia and industry, or that a Ph.D. would not be required to perform those techniques, the Court adopts Dr. Myerson's definition of a person of ordinary skill in the art, with the addition of Dr. Zaworotko's recognition that "[s]uch a person would have either personal knowledge or ha[ve] access to a team with knowledge regarding design of dosage forms." Zaworotko Decl. ¶ 29.

For the reasons discussed, the Court determines that the relevant art of the '064 Patent is "interdisciplinary, spanning aspects of the field of chemistry such as medicinal chemistry, crystallography, analytical chemistry, materials science, including how they relate to pharmaceutical science and pre-clinical studies involving the development of dosage forms. A person of ordinary skill in the relevant art of the '064 patent, as of the relevant date, would likely have been part of, or ha[ve] access to, a team of individuals with various skills spanning the chemical arts listed above." Zaworotko Decl. ¶ 27. A person of ordinary skill in this art would also have "a bachelor's degree in chemistry, chemical engineering, or related disciplines, with a minimum of three years' experience in the pharmaceutical industry related to organic synthesis, API (active pharmaceutical ingredient) manufacturing, crystallization or detection and/or

evaluation of solid state forms, or an advanced degree in chemistry, chemical engineering, or related disciplines, with less or no experience," Myerson Decl. ¶ 50, and "[s]uch a person would have either personal knowledge or ha[ve] access to a team with knowledge regarding design of dosage forms," Zaworotko Decl. ¶ 29.

2. "compatible with the crystalline nature of the hydrate product" (claim 3)

Mylan's Proposed Construction	Takeda's Proposed Construction
Indefinite.	Plain and ordinary meaning. Alternative: "a pharmaceutically acceptable excipient, carrier or diluent that is compatible with the crystalline nature of the hydrate product" is an excipient that will not alter the crystal structure or the degree of hydration of the hydrate.

The disputed phrase appears in claim 3 of the '064 Patent. Independent claim 3 recites:

> 3. A pharmaceutical composition comprising: a crystal of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole 1.5 hydrate and a pharmaceutically acceptable excipient, carrier or diluent that is ***compatible with the crystalline nature of the hydrate product***.

'064 Patent cl.3 (emphasis added).

Takeda claims that plain and ordinary meaning governs, but proposes in the alternative that "compatible" should mean "will not alter the crystal structure or the degree of hydration of the hydrate." Takeda Br. at 8. Mylan argues that the phrase "compatible with the crystalline nature of the hydrate product" is indefinite. Mylan also argues that Takeda's alternative construction is itself indefinite. Mylan does not argue that Takeda's alternative construction does not reflect the plain and ordinary meaning of the claim term, and does not propose any alternative construction.

Mylan raises two primary arguments in support of indefiniteness. First, Mylan argues that the phrase "crystalline nature" is indefinite, because it does not appear in the specification and does not have an accepted meaning in the art. Second, Mylan argues that "compatible" is an indefinite term of degree, and the claim does not specify what type of compatibility—physical, chemical, or other—is required.

For the reasons explained below, the Court finds that the claim term is not indefinite. The Court adopts Takeda's proposed alternative construction, but substitutes "excipient, carrier or diluent" for "excipient" in Takeda's proposal to match the actual claim language. Thus, the Court construes the phrase to mean: "an excipient, carrier or diluent that will not alter the crystal structure or the degree of hydration of the hydrate."

a. "crystalline nature of the hydrate product"

The phrase "crystalline nature of the hydrate product" is sufficiently definite when read in the context of the patent. First, there is nothing indefinite about "a crystal of (R)-2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole 1.5 hydrate," which is "the hydrate product" in question.[6] The bounds of "hydrate product" are as precise as the art allows, and the parties have agreed as much. Joint Statement at 4-5 (stipulating to various claim terms); *Nautilus*, 134 S. Ct. at 2128.

Takeda contends that "crystalline nature" would be understood by one of ordinary skill as both the degree of hydration and the specific crystal structure of the 1.5 dexlansoprazole hydrate, as shown by its proposed construction, which parses "crystalline nature" into both "crystal structure" and "the degree of hydration of the hydrate." The Court agrees that this interpretation is supported by the specification and would be reasonably clear to a person of ordinary skill.

The '064 Patent specification implies that "crystalline nature" refers to both the physical crystal structure and the degree of hydration of the hydrate by describing different crystal forms of dexlansoprazole by both their representative powder X-ray diffraction (PXRD) data and degree of hydration. The '064 Patent discloses four dexlansoprazole crystals, and gives PXRD data for each. *See* '064 Patent col.8 ll.61-63 ("Reference Example 4" crystal), col.10 ll.48-51 (PXRD data for "Reference Example 4"); col.10 ll.60-62 ("Example 1" crystal), col.11 l.15 (PXRD data for "Example 1" crystal); col.11 ll.48-50 ("Example 2" crystal), col.12 ll.16-17 & Tbl. 2 (PXRD data

[6] To the extent that Mylan argues that the specification "would not even convey to a person of ordinary skill that a crystal hydrate had even been formed," that argument goes to enablement or written description, and not indefiniteness. Mylan Br. at 11. As explained *infra*, because one of ordinary skill in the art would recognize that a 1.5 hydrate of dexlansoprazole has a specific crystal structure and a specific stoichiometric ratio, one of ordinary skill in the art would understand the phrase "crystalline nature of the hydrate product" with reasonable certainty.

for "Example 2" crystal); col.12 ll.48-50 ("Example 3" crystal), col.12 1.67 & Tbl. 3 (PXRD data for "Example 3" crystal), col.12 l.50 (identifying "Example 3" crystal as the 1.5 hydrate). In addition to describing the example crystals by their PXRD data, the '064 Patent describes different hydrates as separate embodiments of the invention. *See id.* col.2 ll.9-12. Thus, the specification supports Takeda's proposed construction by characterizing the hydrate product with both PXRD data and degree of hydration.

Both experts also confirmed that crystals can be described through their PXRD data and degree of hydration. Dr. Zaworotko opined that a PXRD graph "is a fingerprint of that compound" and also may show "whether a chemical compound is crystalline or not." Zaworotko Decl. ¶ 57. Dr. Myerson also referred to the PXRD data as a "signature or fingerprint" for a crystal. Myerson Decl. ¶ 30. That fingerprint "can be used to identify a compound and its crystalline phase." *Id.* ¶ 33. The experts also agreed that a specific crystal hydrate has a specific degree of hydration, or stoichiometric ratio. *Id.* ¶ 38 ("For any given solvate, there typically is a fixed ratio of the number of water molecules to the number of molecules of the chemical species."); Zaworotko Decl. ¶ 38 ("Solvates and hydrates are typically named based on the ratio of solvent (or water) molecules to molecules of the compound within the crystal."). Thus, one of ordinary skill in the art would understand that "crystalline nature" is shorthand for degree of hydration and crystal structure. Again, Mylan does not argue that Takeda's construction does not represent the plain and ordinary meaning of "crystalline nature."

Looking beyond the specification, both "degree of hydration" and "crystal structure" are terms that are reasonably clear in the art. The term "degree of hydration" is quite clear—it is a specific ratio of solvent to water. *See* Zaworotko Decl. ¶ 38 ("hydrates are typically named based on the ratio of solvent (or water) molecules to molecules of the compound within the crystal."); Zaworotko Depo. at 95:13-24 (explaining that the stoichiometric ratio refers to the "composition of the hydrate"); Myerson Decl. ¶ 38. The term "crystal structure" is also clear—it is the "unique and distinct three-dimensional structure [of the crystal] that is dictated by arrangement of the individual atoms and molecules." Zaworotko Decl. ¶ 35.

Having considered the entire specification and the extrinsic evidence, the Court finds that one of ordinary skill would be able to determine, with reasonable certainty, the meaning of the term "crystalline nature of the hydrate product." Takeda's proposed alternative construction further clarifies that the plain and ordinary meaning, which Mylan does not dispute, of "crystalline nature" includes both the degree of hydration and crystal structure.

b. "compatible with" or "will not alter"

As an initial matter, both parties agree that one of ordinary skill in the art would recognize that a drug formulator must select excipients, carriers and diluents[7] that are appropriate for use with a specific drug or active pharmaceutical ingredient. Myerson Decl. ¶ 60; Zaworotko Decl. ¶ 89. An inappropriate excipient would at least be one that causes the drug to degrade or change in a way that affects its efficacy.

Mylan argues that the phrases "compatible with," which appears in claim 3, and "will not alter," which appears in Takeda's proposed construction, are indefinite because both phrases are terms of degree. Mylan Br. at 12.[8] Mylan presumably focuses on the "term of degree" argument because post-*Nautilus* case law has also addressed terms of degree and other subjective claim language. *See, e.g.*, *Interval Licensing*, 766 F.3d at 1370-71; Mylan Br. at 14-15.

First, it is not clear that "compatible" and "alter" are terms of degree in the context of the '064 Patent, because the tests used to determine compatibility/alteration are binary. Takeda Reply at 7. Specifically, the ratio of water to solvate (the "degree of hydration") either changes from 1.5 to something else or it does not, and the PXRD data of the compound (which is unique to the "crystal structure") either matches Example 3 of the '064 Patent or it does not.

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[7] In discussing the intrinsic and extrinsic evidence, the Court (like the parties) refers to "excipients, carriers and diluents" collectively as "excipients" for convenience.

[8] To the extent Mylan argues that the specification does not include sufficient examples of compatible excipients, *see* Mylan Br. at 12-13, that argument goes to enablement or written description, and not indefiniteness. Mylan makes a more on-point argument that without a reference to a "compatible" excipient, one of ordinary skill will not know how to determine if a proposed excipient is compatible. *Id.* The '064 Patent specification includes numerous examples of potential excipients and other formulation additives. *See* col.4 l.28-col.5 l.63. An ordinary artisan would be capable of determining compatibility using known methods in the art of pharmaceutical formulation, as discussed *infra*.

To determine whether an excipient altered the crystal structure or degree of hydration of the 1.5 hydrate of dexlansoprazole, one of ordinary skill in the art would likely use a PXRD test to compare the hydrate before and after formulating with an excipient. Dr. Zaworotko recognized that a PXRD graph can determine whether two crystals are the same or not. *See* Zaworotko Decl. ¶ 55 ("Two crystal forms are considered to be distinct if even one of these [PXRD] peaks does not match, or if even one of these [PXRD] peaks is missing from one diffractogram relative to the other."); *id.* ¶ 57 (a PXRD graph "is a fingerprint of that compound" and also may show "whether a chemical compound is crystalline or not."). Dr. Myerson also viewed PXRD data in the same way. Myerson Decl. ¶ 33 ("The x-ray pattern (particularly the location of the peaks) acts as a 'fingerprint' for a given crystal form of a particular compound and a selection of peaks from an XRPD [PXRD] pattern can be used to identify a compound and its crystalline phase."). The '064 Patent specification also suggests that crystals can be analyzed using PXRD data or "by a mechanical method, an optical method, etc." '064 Patent col.3 ll.31-34.

As the '064 Patent provides the PXRD data for the purported 1.5 hydrate of dexlansoprazole, *see* Tbl. 3, col.13 ll.15-18, one of ordinary skill could compare PXRD graphs and determine whether or not they had the same compound disclosed in the '064 Patent, and therefore evaluate whether their treatment of the crystal (*i.e.*, by mixing it with an excipient) alters the crystal or not. Comparing two PXRD charts is within the skill of an ordinary artisan and provides an objective measure for identifying the 1.5 hydrate. Zaworotko Depo. at 69:11-19, 93:4-24, 96:17-24 (PXRD and other tests were common and routine); Myerson Depo. at 82:4-18, 85:14-18, 94:17-97:8, 52:20-53:19, 90:19-91:5 (same). *See also Interval Licensing*, 766 F.3d at 1371 ("The claims, when read in light of the specification and the prosecution history, must provide objective boundaries for those of skill in the art." (citing *Nautilus*, 134 S. Ct. at 2130 & n.8)); *Advanced Display Techs. of Tex., LLC v. AU Optronics Corp.*, No. 6:11-CV-0391-LED, 2012 WL 2872121, at *13 (E.D. Tex. July 12, 2012). The Court therefore disagrees with Dr. Zaworotko's statement that the '064 Patent "would not have provided a person of ordinary skill in the art any identifying information regarding the purported 1.5 dexlansoprazole hydrate which could have been used as [a]

reference standard for any subsequent measurements and/or characterizations." Zaworotko Decl. ¶ 86.

Even if "alter" and "compatible" are terms of degree, "terms of degree are [not] inherently indefinite" if the patent provides "enough certainty to one of skill in the art when read in the context of the invention." *Interval Licensing*, 766 F.3d at 1370. Here, the '064 Patent provides enough certainty to one of ordinary skill through its description of the 1.5 hydrate in Example 3, because it gives the PXRD "fingerprint" for the crystal. '064 Patent col.12 l.46-col.13 l.17.

Mylan also argues that the various types of compatibility studies known in the art make the claim indefinite because it is unclear whether physical or chemical compatibility, or both, are required. This is unpersuasive as the claim term reads "compatible with the *crystalline nature*" of the hydrate product. *Id.* cl.3 (emphasis added). By calling out "crystalline nature" the claim is clearly referring to physical compatibility. Mylan's expert, Dr. Zaworotko, even recognized that degree of hydration and crystalline nature "would be likely considered as physical testing." Zaworotko Decl. ¶ 104.[9]

This reading is also supported by the prosecution history, which the court must consider in evaluating indefiniteness. *Ancora*, 744 F.3d at 738 ("[A]n ordinarily skilled artisan must consult the prosecution history to confirm the proper understanding of a claim term's meaning, especially if other aspects of the inquiry raise questions."). The phrase "compatible with the crystalline nature of the hydrate product" was added to claim 3 in response to an enablement rejection. *See* ECF No. 129-5 ('064 Patent Pros. Hist., 11/24/06 Office Action) at 2-3. The Examiner rejected claim 3 because "it is not seen where the instant specification enables the [person of ordinary skill] to make a pharmaceutical composition of a crystal of 1.5 hydrate when the diluents [are] water or some other excipient, carrier or diluent[] that does not allow for a crystal to maintain its crystal[l]inity." *Id.* In other words, the specification allegedly did not enable a person of ordinary

[9] The Court does agree with Dr. Zaworotko's opinion that chemical stability studies are unlikely to allow one of ordinary skill in the art to draw conclusions about the "crystalline nature" or "degree of hydration" of a drug compound. Zaworotko Decl. ¶ 104.

skill to make a composition with an excipient "compatible with the crystalline nature of the hydrate product."[10]

In response, Takeda amended claim 3 to add the phrase at issue, and explained that

> [Issued Claim 3] has been amended editorially. While Applicants believe [Issued Claim 3] was acceptable in its former state, the revision obviates any issues based on an alleged inconsistency between the components of the composition and the crystalline nature of the active agent. Accordingly, Applicants respectfully submit that [Issued Claim 3 is] enabled.

See ECF No. 129-6 ('064 Patent, Pros. Hist., 4/24/07 Response) at 3. The Examiner then issued a Notice of Allowance. *See* Takeda Reply at 8.

This exchange in the prosecution history supports Takeda's construction that the phrase "compatible with" is directed to physical compatibility, or maintenance of the crystallinity, between the excipient and the 1.5 dexlansoprazole hydrate. '064 Patent Pros. Hist., 11/24/06 Office Action at 2-3. Physical compatibility, or compatibility with the crystal structure and degree of hydration, are easily evaluated through PXRD and other testing, as discussed above.

In addition to the disclosure in the specification, the prosecution history, and the experts' consistent statements about the knowledge of a skilled artisan, Takeda also points to extrinsic evidence that discusses drug-excipient compatibility studies. Dr. Myerson explained that one of ordinary skill in the art would have recognized that drugs and excipients must be compatible, and would look to various tests to confirm compatibility, including draft guidance issued by the FDA. Myerson Decl. ¶¶ 60, 70.

Mylan's complaints about the extrinsic evidence are unconvincing. Mylan emphasizes that the phrases "compatible with the crystalline nature," "alter the crystal structure," and "degree of hydration" do not appear in the extrinsic evidence Takeda cites. This is of little persuasive value as the substance of the extrinsic evidence relates to those concepts, even though it does not use the same words. Furthermore, although the extrinsic evidence focuses on chemical stability studies, the extrinsic evidence does include PXRD testing and physical stability testing. *See, e.g.*, Zaworotko Decl. ¶¶ 115 (discussing PXRD results), 120 (discussing physical stability tests in FDA

[10] Again, the Court is not addressing enablement issues at this stage.

guidance). As both experts agree, such tests are routine in the art. Zaworotko Depo. at 69:11-19, 93:4-24, 96:17-24 (PXRD and other tests were common and routine); Myerson Depo. at 82:4-18, 85:14-18, 94:17-97:8, 52:20-53:19, 90:19-91:5 (same). To the extent that running routine tests in a trial-and-error approach to select excipients would be unduly burdensome, Mylan has not presented sufficient evidence to that effect, and such an inquiry would go to enablement, not indefiniteness. *See AK Steel*, 344 F.3d at 1244 (discussing enablement requirement).

In sum, Mylan's arguments that one of ordinary skill in the art would not be reasonably certain as to what a "compatible" excipient would be are unpersuasive after reviewing the claim language, specification, prosecution history, and extrinsic evidence. Accordingly, the Court does not find the phrase "compatible with the crystalline nature of the hydrate product" indefinite, and gives the term Takeda's alternative construction, but modifies the proposal to specify "excipient, carrier or diluent" to match the claim language. Thus, the Court construes the disputed phrase to mean **"an excipient, carrier or diluent that will not alter the crystal structure or the degree of hydration of the hydrate."**

C. The '158 Patent

The '158 Patent is generally directed to methods of treating stomach problems with "pharmaceutical compositions" of dexlansoprazole. Takeda asserts claims 1, 2, and 4-8 against Mylan. *See* Fennerty Decl. ¶ 58. The parties dispute two terms.

1. Level of Ordinary Skill in the Art

The parties again contest the pertinent art and level of skill, citing the respective opinions of Drs. Fennerty and Stagner. Dr. Fennerty believes that the field is "the art of pharmacy, and in particular the fields of the formulation of oral drugs and biopharmaceutics, including clinical pharmacokinetics and clinical pharmacodynamics," and that "[a] person of ordinary skill in formulation and biopharmaceutics as of October 2007 would have had a graduate degree (M.S., Ph.D., or Pharm.D.) in pharmaceutical sciences, or a related field, and relevant experience in pharmaceutical formulations. This could mean a relatively recent Ph.D. graduate with at least a year of relevant experience, or an individual with a master's degree and many years relevant

experience." Fennerty Decl. ¶ 65. Dr. Stagner proposes the same art and level of skill that he proposed for the '971 Patent. *See* Stagner Decl. ¶¶ 19, 22.

The scope of the parties' disagreement is minimal. Mylan admits frankly that its proposal "is similar to Takeda's proposal." Mylan Br. at 9. Dr. Stagner testified that he does not disagree with Dr. Fennerty's definition. Stagner Depo. at 69:1-4. Moreover, as noted above, the parties conceded at the hearing that this does not affect claim construction. *See* Tr. at 10:2-17.

In the second set of Dexilant® cases, Takeda proposed the same definition of the person of ordinary skill in the art for the '158 Patent, which was largely undisputed. Based on the parties' agreements, the Court concluded that "the relevant art for both patents would be the related fields of pharmacy or pharmaceutical drug development, pharmacokinetics, and pharmacodynamics," and "the person of ordinary skill in the art would have had a doctorate degree (Ph.D. or Pharm.D.) in pharmaceutical sciences or a related field and one year of relevant experience, or a Master's Degree with many years of experience." 1927 Order at 6-7.

Mylan contends that the '158 and '971 Patents should have the same level of ordinary skill. Mylan Br. at 9. The Court adopts a separate and distinct definition of the level of ordinary skill for the '971 Patent, as detailed above. However, the '158 and '971 Patents are not related and have different disclosures and priority dates (October 12, 2007 and June 17, 1999, respectively), so there is no requirement that both patents share the same level of skill. Mylan provides no other convincing reason to depart from the Court's prior conclusion. For consistency, the Court adopts the same definition set forth in the 1927 Order.

2. "therapeutically effective amount" (claim 1)

Mylan's Proposed Construction	Takeda's Proposed Construction
Indefinite.	Plain and ordinary meaning. Alternative: "a nontoxic but sufficient amount of dexlansoprazole to help ameliorate or cure heartburn, acid reflux or gastroesophageal reflux disease."

The first disputed phrase appears in claim 1 of the '158 Patent, from which all asserted claims depend. Independent claim 1 recites:

> 1. A method of treating heartburn, acid reflux or gastroesophageal reflux disease in a patient in need of treatment thereof, the method comprising the steps of:
>
> a) obtaining a pharmaceutical composition comprising dexlansoprazole from a group of pharmaceutical compositions comprising proton pump inhibitors; and
>
> b) administering to a patient suffering from heartburn, acid reflux or gastroesophageal reflux, regardless of whether the patient is under fasted or fed conditions, a ***therapeutically effective amount*** of the pharmaceutical composition obtained in step a), wherein the pharmaceutical composition comprises:
>
> (i) a first solid particle, wherein said first solid particle comprises dexlansoprazole and a first enteric coating, wherein the first enteric coating releases the proton pump inhibitor from the solid particle at a pH of about 5.0 to about 5.5; and
>
> (ii) a second solid particle, wherein said second solid particle comprises dexlansoprazole and a second enteric coating, wherein the second enteric coating releases the proton pump inhibitor from the solid particle at a pH of about 6.2 to about 6.8; wherein the first solid particle comprises from about 15% to about 50% by weight of the pharmaceutical composition and the second solid particle comprises from about 50% to about 85% by weight of the pharmaceutical composition.

'158 Patent cl.1 (emphasis added). Claim 4 also recites "a therapeutically effective amount of the pharmaceutical composition." *Id.* cl.4.

For "therapeutically effective amount," the parties rely primarily on their arguments regarding "effective amount" for the '158 Patent. Mylan contends that the term is indefinite. *See* Mylan Br. at 22-23 ("'therapeutically effective amount' is equally indefinite for the exact reasons discussed with respect to the '971 patent"). Takeda does not propose the same construction it seeks for the '158 Patent. Instead, Takeda argues that "plain and ordinary meaning" applies because no construction is required. *See* Takeda Br. at 15-17. As an alternative to plain meaning, Takeda proposes: "a nontoxic but sufficient amount of dexlansoprazole to help ameliorate or cure heartburn, acid reflux or gastroesophageal reflux disease." *Id.* at 16 n.5.

As with the '971 Patent, the parties focus almost entirely on the specification. The '158 Patent's claim language provides minimal guidance about the meaning of "therapeutically effective amount." The preamble of claim 1 recites a method "of treating heartburn, acid reflux or gastroesophageal reflux disease," indicating that a "therapeutically effective" amount refers to treatment of those diseases. The claims provide no numerical doses, further suggesting that

"therapeutically effective amount" is not restricted to an enumerated range. As to prosecution history, neither side identifies any relevant portions. *See* Stagner Decl. ¶ 75 ("The term 'effective amount' is not addressed in the prosecution history.").

Turning to the specification, the Court first observes that the '158 Patent contains an express definition for "therapeutically effective amount":

> By an "effective amount" or a "therapeutically effective amount" of a dosage form ***is meant a nontoxic but sufficient amount of the active ingredient to provide the desired effect.*** The amount of active ingredient that is "effective" will vary from subject to subject, depending on the age and general condition of the individual, the particular active ingredient or active ingredient, and the like. Thus, it is not always possible to specify an exact "effective amount." However, an appropriate "effective amount" in any individual case may be determined by one of ordinary skill in the art using routine experimentation.

'158 Patent col.7 ll.34-44 (emphasis added). Despite this explicit language, neither side contends that this is the correct construction. Indeed, Dr. Stagner reproduces this passage in his declaration but opines that the term "is not specifically defined in the patent, but is addressed in general terms." Stagner Decl. ¶ 74.

The Court finds that the inventors acted as their own lexicographers by defining "therapeutically effective amount." "The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012). One exception to this rule occurs "when a patentee sets out a definition and acts as his own lexicographer." *Id.* Here, the specification contains an express definition. The inventors stated that it "*is meant*" that "effective amount" and "therapeutically effective amount" both refer to "a nontoxic but sufficient amount of the active ingredient to provide the desired effect." *E.g., 3M Innovative Props. Co. v. Avery Dennison Corp.*, 350 F.3d 1365, 1369-71 (Fed. Cir. 2003) (holding that patentee "clearly acted as its own lexicographer" where specification said "'Multiple embossed' *means* two or more embossing patterns are superimposed on the web to create a complex pattern of differing depths of embossing" (emphasis added)).

At the hearing, Takeda did not object to the definition in the patent, but also advocated its alternative construction, which resembles the inventors' definition but "specifies the active ingredient and then says the desired effect" (Tr. at 14:8-16:14):

> • **'158 Patent col.7 ll.34-44:** "a nontoxic but sufficient amount of the active ingredient to provide the desired effect"
>
> • **Takeda's Alternative Construction:** "a nontoxic but sufficient amount of dexlansoprazole to help ameliorate or cure heartburn, acid reflux or gastroesophageal reflux disease"

The Court finds no basis for altering the inventors' language as Takeda proposes. Claim 1 recites "dexlansoprazole" and "heartburn, acid reflux or gastroesophageal reflux disease," so Takeda's additional language would be redundant.

Setting aside the definition in the specification, Mylan insists that the term is indefinite. Mylan observes that the claims refer to treating a "patient," and the specification defines "patient" as "an animal, preferably a mammal, including a human or non-human." '158 Patent col.7 ll.61-63. Thus, according to Mylan, "the patent purports to cover the treatment of any animal." Mylan Br. at 22. These arguments target the breadth of the claims, which are more properly addressed under enablement. Mylan next argues that the '158 Patent "provides no [dosage] range at all" and further "fails to list critical factors that were known to cause variability and uncertainty in determining what would constitute an effective amount of a pharmaceutical composition." *Id.* at 22-23. However, the specification provides some guidance regarding both appropriate doses and formulations. Example 2 describes a Phase 1 study in which the inventors administered TAK-390MR (another name for Dexilant®) to human subjects under different food conditions and measured plasma concentrations of dexlansoprazole and intragastric pH levels. *Id.* col.24 ll.11-38. The subjects received daily 90 mg doses. *Id.* col.24 ll.1-4. Mylan claims this example has "no value" for determining proper treatments because the subjects were healthy. Mylan Br. at 23. However, Dr. Stagner conceded that intragastric pH levels are commonly used to evaluate the effectiveness of PPIs. *See* Stagner Depo. at 130:3-16; *see also* Fennerty Decl. ¶¶ 44, 96. Example 1 teaches methods for making TAK-390 capsules, listing specific quantities of excipients. '158

Patent col.20 l.42-col.23 l.35. Therefore, Mylan's indefiniteness arguments fare no better here than for the '971 Patent.

The parties have not identified any additional extrinsic evidence specific to the '158 Patent. In their declarations, Drs. Fennerty and Stagner refer to their arguments for the '971 Patent and the portions of the specification discussed above, but largely repeat the positions in the parties' briefs. At the hearing, Mylan suggested that if "therapeutically effective amount" is not indefinite, the term "would just revert to Judge Spero's construction" for the '971 Patent. Tr. at 14:21-15:5. Dr. Fennerty also testified that "therapeutically effective amount" in the '158 Patent is "not substantially different" from "effective amount" in the '971 Patent, Fennerty Depo. at 168:16-169:1, and Takeda agreed at the hearing that the terms are "reasonably equivalent," Tr. at 13:23-14:7. However, the '158 and '971 Patents are not related and have different specifications. "A particular term used in one patent need not have the same meaning when used in an entirely separate patent, particularly one involving different technology." *Medrad, Inc. v. MRI Devices Corp.*, 401 F.3d 1313, 1318 (Fed. Cir. 2005). Given the '158 inventors' express definition for "therapeutically effective amount," the Court does not conclude that this term must have precisely the same construction as "effective amount" in the '971 Patent.

Mylan has not met its burden to show that "therapeutically effective amount" is indefinite. Mylan stated at the hearing that if this term is not indefinite, Mylan did not object to the definition in the specification. Tr. at 18:6-12. The Court rejects Takeda's proposals to apply "plain and ordinary meaning" or its alternative construction. Following the inventors' express definition, the Court construes "therapeutically effective amount" to mean **"a nontoxic but sufficient amount of the active ingredient to provide the desired effect."**

3. "about ___% to about ___% by weight of the pharmaceutical composition" (claim 1)

Mylan's Proposed Construction	Takeda's Proposed Construction
Plain meaning.	"about ___% to about ___% by weight of the solid particles in the pharmaceutical composition, and excluding the weight of the capsule"

The second disputed phrase also appears in claim 1 of the '158 Patent, and therefore all asserted claims. Claim 1 recites a "pharmaceutical composition" that comprises first and second solid particles, "wherein the first solid particle comprises from about 15% to about 50% by weight of the pharmaceutical composition and the second solid particle comprises from about 50% to about 85% by weight of the pharmaceutical composition." '158 Patent cl.1. The parties dispute how this limitation applies to capsules, which may have a coating or shell that holds all the particles. Takeda claims that the recited weight percentages are relative to the total weight of the solid particles, not including the weight of the capsule coating. *See* Takeda Br. at 20-22. Mylan disagrees and advocates plain meaning for this phrase.

The claim language favors Mylan's position. It is presumed that "claim terms must be given their plain and ordinary meaning to one of skill in the art." *Thorner*, 669 F.3d at 1367. Claim 1 plainly states that each weight percentage is "of the pharmaceutical composition," not of the total solid particle weight. By contrast, Takeda seeks to add the words "of the solid particles in" the pharmaceutical composition. Claim 1 does not refer to a "capsule" or other specific dosage form, only a "pharmaceutical composition." Thus, the claim contains no antecedent basis for "*the* capsule" in Takeda's proposed construction. Furthermore, dependent claim 8 recites: "The method of claim 1, wherein the pharmaceutical composition comprising dexlansoprazole is in the form of a tablet or a capsule." '158 Patent cl.8. Claim 8 demonstrates that a "pharmaceutical composition" can take multiple forms including tablets and capsules, and that claim 1 does not distinguish between tablets or capsules for purposes of calculating the claimed weight percentages.

Takeda argues that in a capsule, the weight percentages cannot include the weight of the capsule coating because those percentages add up to 100%: "The minimum percentage of the first solid particle is 15%; the maximum percentage of the second solid particle is 85%. Together, these

equal 100%." Takeda Br. at 21. Takeda reasons that the weight of the capsule coating must be separate because the solid particles cannot constitute 100% of a capsule. This argument brushes aside the fact that claim 1 states approximate ranges of weight percentages—*e.g.*, "*about* 15% to *about* 50%." As noted above, claim 8 indicates that claim 1 encompasses both capsules and non-capsule forms such as tablets. Thus, in a claimed capsule, 15% of the weight could be the first solid particle, 50% the second solid particle, and 35% the coating and other excipients.

The specification does not support Takeda's effort to further limit the claim language. Takeda points to a "second embodiment," disclosed in column 3, which is an example of a capsule with a first and second granule, "wherein the first granule comprises about 25% of the capsule and the second granule comprises from about 75% of the capsule." '158 Patent col.3 ll.21-39. Takeda asserts that this example is "based solely on *the contents of* the capsule, and treats the capsule's own weight as of no moment." Takeda Br. at 21. This mischaracterizes the second embodiment. That example refers only to approximate percentages, does not mention "weight," and is silent about the weight of any capsule coating. Next, Takeda argues that Example 1 teaches an example of dexlansoprazole capsules where the first particle constitutes "15%-50% by weight," and the second particle "50-85% by weight %," as a "Proportion of TAK-390 Dose." '158 Patent col.20 ll.42-56, Tbl. 1. Takeda claims that this reference to "dose" means "the capsule contents, rather than those contents plus the capsule itself." Takeda Br. at 22. Takeda provides no basis for its interpretation of "dose" as only "the capsule contents," and Example 1 contains no such statement. Also, like claim 1, Example 1 refers to ranges of weight percentages that are consistent with possible additional components such as a capsule coating. Accordingly, these examples in the specification do not warrant importing a limitation into the claims. *See Phillips*, 415 F.3d at 1323.

The parties offer no expert opinions or extrinsic references to support their positions. Mylan claims that Takeda took an inconsistent position about the meaning of "pharmaceutical composition" in another case, *Takeda Pharmaceutical Co. v. Teva Pharmaceuticals USA Inc.*, 542 F. Supp. 2d 342 (D. Del. 2008). *See* Mylan Br. at 24. There, the district court construed "pharmaceutical composition" as "a medicinal drug product in a state suitable for administration to

a patient," rejecting the argument that the term "excludes any excipients used for coating the composition." *Teva*, 542 F. Supp. 2d at 348. The court reached that conclusion because the defendant engaged in "an impermissable attempt to read process limitations into a product claim," which is not an argument here. *Id.* *Teva* also involved a different patent and drug, so it has minimal relevance here.

Accordingly, the Court construes "about ___% to about ___% by weight of the pharmaceutical composition" to have its plain and ordinary meaning.

IV. CONCLUSION

In summary, and for the reasons stated herein, the Court construes the parties' disputed terms as follows:

Patent	Disputed Term	Court's Construction
6,939,971	"effective amount"	"an amount sufficient to help ameliorate or cure reflux esophagitis"
7,339,064	"compatible with the crystalline nature of the hydrate product"	"an excipient, carrier or diluent that will not alter the crystal structure or the degree of hydration of the hydrate"
8,173,158	"therapeutically effective amount"	"a nontoxic but sufficient amount of the active ingredient to provide the desired effect"
	"about ___% to about ___% by weight of the pharmaceutical composition"	Plain and ordinary meaning.

IT IS SO ORDERED.

Dated: November 11, 2014

LUCY H. KOH
United States District Judge