IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ABBVIE INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. 11-cv-648 (GMS)
	)	
HOSPIRA, INC.,	)	
	)	
Defendant.	)	
	)	

MEMORANDUM

I. INTRODUCTION

In this patent infringement action, plaintiff AbbVie Inc.[1] ("AbbVie") alleges that a pharmaceutical product proposed by defendant Hospira, Inc. ("Hospira") infringes the asserted claims of the patent-in-suit.[2] (D.I. 1.) The court held a two-day bench trial in this matter on November 12 through November 13, 2013. (D.I. 195-196.) Presently before the court are the parties' post-trial proposed findings of fact and conclusions of law concerning the validity of the patent-in-suit, specifically whether Hospira's proposed product infringes the patent-in-suit and whether the asserted claims are invalid as obvious under 35 U.S.C. § 103. (D.I. 190-191.)

Pursuant to Federal Rule of Civil Procedure 52(a), and after having considered the entire record in this case and the applicable law, the court concludes that: (1) the asserted claims of the patent-in-suit are not invalid due to obviousness; (2) Hospira's proposed product does not infringe U.S. Patent Number 6,136,799 ("the '799 Patent"); and (3) the parties' Rule 52(c) motions (D.I.

[1] The Parties stipulated to removal of Wisconsin Alumni Research Foundation from the caption on December 18, 2013. (D.I. 189.)

[2] In addition, AbbVie is no longer asserting U.S. Patent Nos. 6,361,758; 5,587,497; and 5,597,815 patents as the result of two stipulations of dismissal. (D.I. 112; D.I. 183.)

190-191) are granted in part and denied in part. These findings of fact and conclusions of law are set forth in further detail below.

II. FINDINGS OF FACT[3]

A. The Parties

1. Plaintiff AbbVie Inc. ("AbbVie") is a corporation organized and existing under the laws of the state of Delaware, having its headquarters and principal place of business at 1 North Waukegan Road, North Chicago, Illinois 60064. AbbVie was substituted for Abbott Laboratories ("Abbott") as a plaintiff in this action pursuant to the court's order of April 10, 2013. (D.I. 163.)

2. Defendant Hospira Inc. ("Hospira") is a corporation organized and existing under the laws of the state of Delaware, having its principal place of business at 275 North Field Drive, Lake Forest, Illinois 60045.

3. The court has subject matter jurisdiction, as well as personal jurisdiction over all parties.

B. Background

4. AbbVie is the current holder of approved New Drug Application ("NDA") No. 20-819 for injectable paricalcitol products.

5. Under the trade name Zemplar®, AbbVie sells paricalcitol injectable products in 2 mcg/mL, 5 μg/mL, and 10 μg/2 mL (5 μg/mL) formulations.

6. Zemplar® injection is indicated for the prevention and treatment of secondary hyperparathyroidism associated with Chronic Kidney Disease ("CKD") Stage 5.

7. Zemplar® injection was approved by the United States Food and Drug Administration ("FDA") on April 17, 1998.

8. The active pharmaceutical ingredient of Zemplar® injection is paricalcitol, a synthetically manufactured vitamin D analog. Paricalcitol is known as 1α,25-dihydroxy-19-nor-vitamin D2 or 19-nor-1α,3β,25-trihydroxy-9,10-secoergosta-5(Z),7(E),22(E)-triene.

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[3] Prior to trial, the parties submitted an exhibit of uncontested facts in conjunction with their Pretrial Order. (D.I. 175, Ex. A.) The court takes most of its findings of fact from the parties' uncontested facts. Where necessary, the court has overruled objections to the inclusion of these facts. The court has also reordered and renumbered some paragraphs, corrected some spelling and formatting errors, and made minor edits for the purpose of concision and clarity that it does not believe alters the meaning of the paragraphs from the Pretrial Order. Otherwise, any differences between this section and the parties' statement of uncontested facts are unintentional.

The court's findings of fact with respect to matters that were the subject of dispute between the parties are included in the Discussion and Conclusions of Law section of this opinion, preceded by the phrase "the court finds" or "the court concludes."

9. The inactive ingredients in Zemplar® injection are 20% (v/v) ethanol, 30% (v/v) propylene glycol, and 50% (v/v) water.

10. The '799 patent is currently listed in the FDA publication entitled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book") with respect to Zemplar® injection.

11. On January 22, 2010, AbbVie submitted a supplement to NDA 20-819 seeking approval to change the use and labeling of the Zemplar® injection 10 µg/2 mL presentation from a single-dose to a multi-dose vial.

C. The Patents-in-Suit

12. United States Patent Number 6,136,799 ("the '799 Patent"), entitled "Cosolvent Formulations," naming Lukchiu Li, Edward Anthony Pec, Daniel H. Robinson, Dennis A. Stephens, Kathee Jantzi, Thomas Barton May, and John Paul Oberdier as inventors, was issued on October 24, 2000.

13. AbbVie is the owner by assignment of the '799 Patent and has standing to bring suit on the '799 patent.

14. U.S. Application No. 09/057,143, which issued as the '799 patent, was filed with the PTO on April 8, 1998.

1. The Asserted Claims

15. AbbVie asserts claims 7-9 of the '799 patent.

i. *'799 Patent, Claim 7*

16. Claim 7 of the '799 patent depends on claim 6, which depends on claim 1. Read together, claim 7 states:

> A sterilized, self-preserved, aqueous pharmaceutical composition for parenteral administration consisting essentially of a therapeutically effective amount of par[i]calcitol or calcitriol, about 50% (v/v) of an organic solvent selected from the group consisting of ethanol in the range of about 15% to about 30% (v/v) and propylene glycol in the range of about 20% to about 35% (v/v), and about 50% (v/v) water.

ii. *'799 Patent, Claim 8*

17. Claim 8 of the '799 patent reads: The composition of claim 7 wherein the vitamin D compound is present between about 2 µg/ml and about 10 µg/ml.

iii. *'799 Patent, Claim 9*

18. Claim 9 of the '799 patent reads: The composition of claim 8, wherein the vitamin D compound is present at about 5 μg/ml.

2. The Accused Products

i. *NDA No. 201-657 Filed by Hospira*

19. On April 7, 2011, Hospira filed NDA No. 201-657 under § 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (31 U.S.C. § 355(b)(2)) seeking approval to market and sell paricalcitol injection products in 2 μg/mL, 5 μg/mL, and 10 μg/2 mL (5 μg/mL) formulations.

20. Hospira is seeking approval to manufacture, use, market, and sell its proposed NDA products in the United States prior to the expiration of the '799 patent (as well as other patents since dismissed from this suit).

21. Hospira is seeking approval for its proposed NDA products to be indicated for the treatment of secondary hyperparathyroidism associated with CKD Stage 5.

22. Hospira is seeking approval to market and sell its proposed NDA products as multi-dose products.

23. The inactive ingredients in Hospira's proposed NDA products are 40% (v/v) ethanol, 10% (v/v) propylene glycol, and 50% (v/v) water.

24. The active pharmaceutical ingredient in Hospira's proposed NDA products is paricalcitol.

25. Hospira's NDA No. 201-657 contains a certification, pursuant to 21 U.S.C. § 355(b)(2)(A)(iv) (a "Paragraph IV certification"), alleging that the '799 patent is invalid, unenforceable, and/or not infringed.

26. By letter dated June 7, 2011, Hospira sent notice to AbbVie of its NDA No. 201-657 for paricalcitol injection products in 2 μg/mL, 5 μg/mL, and 10 μg/2 mL (5 μg/mL) formulations.

III. DISCUSSION AND CONCLUSIONS OF LAW

The court has subject matter jurisdiction over this matter pursuant to 28 U.S.C. §§ 1331, 1338, and 2201. Venue is proper in this court under 28 U.S.C. §§ 1391 and 1400(b). The only issues remaining are whether the asserted claims are invalid due to obviousness and whether Hospira infringed the asserted claims of the patent-in-suit. After having considered the entire record

in this case, the substantial evidence in the record, the parties' post-trial submissions, and the applicable law, the court concludes that: (1) the asserted claims of the '799 patent are not invalid due to obviousness; and (2) AbbVie has failed to prove, by a preponderance of the evidence, that Hospira's proposed product infringes the asserted claims of the '799 patent. The court's reasoning follows.

A. Obviousness

Hospira challenges the validity of each of the asserted claims as obvious in light of the prior art. The court finds, for the reasons that follow, that Hospira has not established by clear and convincing evidence that the asserted claims of the '799 patent are, in fact, obvious.

1. The Legal Standard

35 U.S.C. § 103(a) provides that a patent may not be obtained "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious to a person having ordinary skill in the art." 35 U.S.C. § 103(a). Obviousness is a question of law that is predicated on several factual inquires. *See Richardson-Vicks v. Upjohn Co.*, 122 F.3d 1476, 1479 (Fed. Cir. 1997). Specifically, the trier of fact is directed to assess four considerations: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior art; and (4) secondary considerations of non-obviousness, such as commercial success, long felt but unsolved need, failure of others, acquiescence of others in the industry that the patent is valid, and unexpected results. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

"A patent shall be presumed valid." 35 U.S.C. § 282. A party seeking to challenge the validity of a patent based on obviousness must demonstrate by "clear and convincing evidence"[4] that the invention described in the patent would have been obvious to a person of ordinary skill in the art at the time the invention was made. Importantly, in determining what would have been obvious to one of ordinary skill in the art, the use of hindsight is not permitted. *See KSR Intern. Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007) (cautioning the trier of fact against "the distortion caused by hindsight bias" and "arguments reliant upon ex post reasoning" in determining obviousness). In *KSR*, the Supreme Court rejected the rigid application of the principle that there should be an explicit "teaching, suggestion, or motivation" in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art, in order to find obviousness. *See KSR*, 550 U.S. at 415. The *KSR* Court acknowledged, however, the importance of identifying "'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination." *Takeda Chem. Indus. v. Alphapharm Pty. Ltd.*, 492 F.3d 1350, 1356-57 (Fed. Cir. 2007) (quoting *KRS*, 550 U.S. at 418).

"Obviousness does not require absolute predictability of success," but rather, requires "a reasonable expectation of success." *See Medichem, S.A. v. Rolado, S.L.*, 437 F.3d 1157, 1165 (Fed. Cir. 2006) (quoting *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988)). To this end, obviousness "cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success." *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007). Moreover, while the Federal Circuit has noted that pharmaceuticals

[4] "Clear and convincing evidence is evidence that places in the fact finder 'an abiding conviction that the truth of [the] factual contentions are 'highly probable.'" *Alza Corp v. Andrx Pharms., LLC*, 607 F. Supp. 2d 614, 631 (D. Del. 2009) (quoting *Colorado v. New Mexico*, 467 U.S. 310, 316 (1984)).

can be an "unpredictable art" to the extent that results may be unexpected, it also recognizes that, per *KSR*, evidence of a "finite number of identified, predictable solutions" or alternatives "might support an inference of obviousness." *See Eisai Co. Ltd. v. Dr. Reddy's Labs. Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008).

2. The Level of Ordinary Skill in the Art

A person of ordinary skill in the art to whom the '799 patent is directed would have a Ph.D. degree in chemistry, biochemistry, pharmaceutics, pharmacology, or the biological sciences and at least two years of experience in developing pharmaceutical compositions for parenteral administration.[5] The court concludes, and the parties agree, that the parties' definitions of a person of ordinary skill in the art do not differ in a meaningful way.

3. The Scope and Content of the Prior Art and Differences Between the Claimed Subject Matter and the Prior Art

Hospira argues that the asserted claims are obvious for two reasons: (1) U.S. Patent No. 5,246,925 ("the '925 patent") in view of the Calcijex® label and the level of skill in the art; and (2) U.S. Patent No. 5,472,957 ("the '957 patent") in view of the '925 patent prosecution history or the Malluche reference. The court addresses each of these arguments in turn.

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[5] AbbVie's description of a person of ordinary skill in the art is derived from Dr. Moreton's testimony. (D.I. 190 at 10 (citing Tr. at 123:15-24).)

Hospira's identification of a person of ordinary skill in the art is derived from Dr. Pinal's testimony, and in its entirety, would require:

> [A] researcher, such as a pharmaceutical scientist, physical chemist, or medicinal chemist, involved in the research and development of pharmaceutical formulations and dosage forms, including small volume parenterals. The person of ordinary skill in the art has (1) a Ph.D. in a field related to pharmaceutical formulation and processing (such as pharmaceutical science, pharmacy, physical chemistry, medicinal chemistry, or pharmaceutics) and at least one year of experience in pharmaceutical formulation, (2) a similar master's degree and at least two to three years of experience in pharmaceutical formulation, or (3) a similar undergraduate degree and at least five years of experience in pharmaceutical formulation. A skilled formulator would also have some knowledge of formulations utilizing vitamin D and its analogs.

(D.I. 191 at 3-4 (quoting Tr. 324:2-15).)

a. The '925 Patent in View of the Calcijex® label and the Level of Skill in the Art

Hospira argues that the asserted claims are obvious because (1) the '925 patent provides for parenteral solutions with vitamin D analogs (D.I. 191 ¶ 60); (2) propylene glycol and ethanol were obvious solvents to make such a solution and routine testing would have arrived at the claimed range (*id.* at 62); and (3) Calcijex offered a suggestive formulation for the concentrations found in claims 8 and 9 (*id.* at 65). These discrete prior art references are taken in combination by Hospira to argue that the asserted claims would have been obvious to a person having ordinary skill in the art.

The '925 patent discloses sterilized vitamin D formulations. The '925 patent is directed towards a method of treatment with a therapeutically effective amount of paricalcitol. Tr. 370:8-13 (Pinal). The '925 patent expressly discloses the "sterilized, aqueous, pharmaceutical composition for parenteral administration," and "therapeutically effective amount" limitations of claim 7. Tr. at 370:17-21 (Pinal). The '925 patent does not disclose a pharmaceutical composition containing the claimed formulations at the claimed ranges. Further, the '925 patent provides no examples of formulations made with the disclosed compounds.

The prior art Calcijex® formulation used the surfactant Polysorbate 20 (also called Tween® 20) to solubilize calcitriol. Tr. at 99:22-24, 261:23-262:5 (Moreton); Tr. at 404:22-405:2, 406:10-17 (Pinal). Other excipients in Calcijex® included an antioxidant to prevent oxidation of the active ingredient, buffering agents to regulate the pH of the formulation, and a chelating agent to remove metal ions. Tr. at 97:6-98:5 (Moreton).

Hospira's expert, Dr. Pinal, testified that ethanol and propylene glycol were, at the time of the claimed invention, the two most commonly used cosolvents and the first two choices that a skilled formulator would test. Tr. at 371:9-13. In addition, Dr. Pinal asserted that a skilled

formulator would arrive at the claimed ranges of about 15% to about 30% ethanol and about 20% to about 35% propylene glycol through routine experimentation. Tr. at 370:23-371:8. Hospira also points to the deposition testimony of the named inventors in support of their argument that the process in arriving at the claimed invention was a common approach that would be employed by skilled formulators. (D.I. 191 at 25.)

The court notes, however, that the '799 patent did not follow the teachings of the prior art. Indeed, the '799 patent specifically criticizes the use of surfactants, antioxidants, buffering agents, and a chelating agent—the ingredients disclosed in the Calcijex® label. In reviewing the prior art, the court finds that one skilled in the art would not have found it obvious to use cosolvents rather than a surfactant to solubilize the active ingredient Vitamin D. The court concludes that the Calcijex® label and the '925 patent do not provide clear and convincing evidence of Hospira's obviousness contention.

b. The '957 Patent in View of the '925 Patent Prosecution History or the Malluche Reference

Hospira avers that the asserted claims would have been obvious over the '957 patent in combination with the prosecution history of the '925 patent or the Malluche reference and the knowledge of a skilled formulator at the time of the invention because (1) the '957 patent discloses a cosolvent system containing therapeutically effective amounts of vitamin D compounds (D.I. 191 ¶ 69); (2) the '957 patent discloses ethanol and propylene glycol as possible solvents (*id.* at ¶ 71); and (3) the Malluche reference and the '925 patent history teach that specific paracalcitol is soluble in ethanol and propylene glycol for non-oral, parenteral use (*id.* at ¶ 74).

Hospira argues that the '957 patent would have been understood to teach a ternary mixture because vitamin D compounds are not soluble in water. While the '957 patent discusses injectable products it does not describe a three-part mixture of water, ethanol, and propylene glycol. The

court finds that other excipients such as surfactants could be added to solubilize the drug, just as had conventionally been done with Calcijex® and other commercial formulations. *See* Tr. at 433:7-22 (Pinal).

The court finds that the claimed cosolvent ratios would not have been obvious to a skilled formulator. Rather, Hospira's arguments appears largely the result of hindsight and suggest that by using a patchwork of available information a skilled formulator would have been able to easily piece together the invention. The court finds this argument unpersuasive. Further, the court finds that Hospira has not identified a reason that would have prompted a person of ordinary skill to combine the cosolvents in the way the claims do. The court concludes that the asserted claims formulation was not the result of obvious selections made by the inventors informed by the '957 patent. Similarly, the Malluche reference and the '925 history do not support Hospira's obviousness assertions. Both the Malluche reference and the '925 history disclose formulations intended for use in animals. The court finds that neither would have suggested to the person of ordinary skill in the art a method or formulation for achieving the asserted claims.

Thus, the language of the '957 patent in view of the '925 patent or Malluche does not provide clear and convincing evidence of Hospira's obviousness contention.

4. <u>Secondary Considerations</u>

AbbVie contends that Hospira has failed to make a *prima facie* showing of obviousness under § 103, or, in the alternative, that the secondary considerations of non-obviousness rebut Hospira's *prima facie* showing. *See Graham*, 383 U.S. at 17-18. The court has found that Hospira failed to establish a *prima facie* case of obviousness. Assuming Hospira had satisfied its initial burden, however, the court finds that AbbVie's secondary considerations—unexpected results, commercial success, and copying—support a determination of non-obviousness.

a. Unexpected Results

Evidence that a combination of known components results in an effect greater than that predicted has been dispositive in holding that an invention is nonobvious. *See Crocs, Inc. v. Int'l Trade Comm'n*, 598 F.3d 1294, 1309 (Fed. Cir. 2010) ("Even if the [patent at issue] were a combination of known elements according to their established functions . . . it yields more than predictable results; thus, it is non-obvious.").

AbbVie asserts that the inventions of claims 7-9 of the '799 patent demonstrate unexpected antimicrobial properties. (D.I. 190 at ¶ 144.) The inventors discovered a "synergistic preservative effect," in which the cosolvents produced an antimicrobial effect greater than the sum of the effects of each agent alone. *See, e.g.*, JTX2; Tr. at 164:1-15. The prior art defines synergy as when the preservative effect of two cosolvents is greater than the sum of the individual effects. Tr. at 163:16-164:15 (Moreton); Tr. at 438:6-12 (Pinal). While Hospira argues that a prior art reference shows that the synergy tests are flawed, it does not provide clear and convincing evidence nor any credible, relevant experimentation to substantiate its argument.

The court agrees that the claimed invention possessed unexpected antimicrobial properties thus weighing in favor of a finding of non-obviousness.

b. Commercial Success

When commercial success has been demonstrated and "the successful product is the invention disclosed and claimed in the patent, it is presumed that the commercial success is due to the patented invention." *J.T. Eaton & Co. v. Atl. Paste & Glue Co*, 106 F.3d 1563, 1571 (Fed. Cir. 1997); *see also Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1394 (Fed. Cir. 1988) ("It is sufficient to show that the commercial success was of the patented invention itself.").

AbbVie asserts that the inventions of claims 7-9 of the '799 patent have demonstrated commercial success. (D.I. 190, ¶ 145.) Hospira attempts to discredit Ms. Coulombe's testimony related to AbbVie's market success by pointing to a decrease in sales since the multi-dose vial was launched. (D.I. 191 at 33.) However, the court finds credible Ms. Coulombe's assertion that the multi-dose vial has been successful and the decrease in sales is a result of the loss of a significant client for reasons unrelated to the Zemplar® multi-dose product. *See* Tr. at 65:7-12 (Coulombe).

The court agrees with AbbVie that the claimed invention has been commercially successful and weighs this consideration in favor of non-obviousness.

c. Copying

AbbVie asserts that Hospira's proposed product is a copy of the patented invention. (D.I. 190, ¶ 146.) Specifically, AbbVie contends that, "[t]he evidence of copying in this case is unusually probative for a Hatch-Waxman case, because Hospira deliberately copied the patented invention after attempting, but failing, to design a non-infringing formulation." (*Id.*) The issue of copying, in part, relates to the determination by the court, *infra*, that Hospira does not infringe the claims of the '799 patent. As such, this consideration does not support a finding of non-obviousness.

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In sum, Hospira has failed to present a *prima facie* case that the asserted claims of the patents-in-suit are invalid as obvious. Moreover, even assuming a *prima facie* case had been made, the court finds that the secondary, objective indicia point towards a finding of non-obviousness. The asserted claims are not invalid as obvious.

B. Infringement

AbbVie asserts that Hospira infringes the asserted claims of the '799 patent. The court finds, for the reasons that follow, AbbVie has failed to establish by a preponderance of the evidence that Hospira infringes the asserted claims.

1. The Legal Standard

The application of a patent claim to an accused product is a fact-specific inquiry. *See Kustom Signals, Inc. v. Applied Concepts, Inc.*, 264 F.3d 1326, 1332 (Fed. Cir. 2001). Literal infringement is present only when each and every element set forth in the patent claims is found in the accused patent. *See Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1575-76 (Fed. Cir. 1995). The patent owner has the burden of proving infringement by a preponderance of the evidence. *See Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 758 (Fed. Cir. 1984) (citing *Hughes Aircraft Co. v. United States*, 717 F.2d 1351, 1361 (Fed. Cir. 1983)). To this end, a patent owner does not have to produce "definite" proof of infringement, but must instead demonstrate that "infringement was more likely than not to have occurred." *See Warner-Lambert Co. v. Teva Pharms., USA, Inc.*, 418 F.3d 1326, 1341 n.15 (Fed. Cir. 2005) (citing *Advanced Cardiovascular Sys., Inc. v. Scimed Life Sys., Inc.*, 261 F.3d 1329, 1336 (Fed. Cir. 2001)). "Under [35 U.S.C.] § 271(e)(2)(a), a court must determine whether, if the drug were approved based upon the ANDA, the manufacture, use, or sale of that drug would infringe the patent in the conventional sense." *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1569 (Fed. Cir. 1997).

An infringement analysis entails two steps: (1) determining the meaning and scope of the asserted patent claims, a question of law; and (2) comparing the properly construed claims to the accused product or process, a question of fact. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en bank), *aff'd*, 517 U.S. 370 (1996).

For the reasons that follow the court concludes that Hospira's proposed product does not infringe the asserted claims of the patents-in-suit.

2. The "About" Element of the Asserted Claims

The parties' infringement arguments hinge on the range encompassed by the term "about" found in the asserted claims. There is no dispute as to the other elements of the asserted claims being met by Hospira's proposed product. As such, the court focuses on two arguments offered by Hospira to show non-infringement: (1) "about" does not widen the range claimed by the patent to encompass Hospira's 10/40 formulation and; (2) AbbVie disclaimed the 10/40 formulation during the course of the prosecution history. The court addresses these arguments in turn.

a. Formulations Encompassed by the Patents "About" Ranges

AbbVie contends that Hospira directly infringes the asserted claims of the '799 patent, which is directed to pharmaceutical compositions. (Exhibit A, ¶ 47.) Hospira asserts that it specifically developed a strategy to use an alternative formulation that would not infringe the patent in direct reliance on the final scope of the issued claims. Hospira focuses its non-infringement position on the assertion that the formulation of Hospira's NDA product is different from the asserted claims. (D.I. 191, ¶ 7.) Conversely, AbbVie maintains that they established evidence sufficient to prove infringement by a preponderance of the evidence. The issue of infringement hinges principally on whether the claimed ranges of ethanol and propylene glycol encompass the values of Hospira's NDA product, specifically 40% (v/v) ethanol and 10% (v/v) propylene glycol.

As described elsewhere the claims at issue, read together, state:

> A sterilized, self-preserved, aqueous pharmaceutical composition for parenteral administration consisting essentially of a therapeutically effective amount of par[i]calcitol or calcitriol, about 50% (v/v) of an organic solvent selected from the group consisting of ethanol in the range of about 15% to about 30% (v/v) and propylene glycol in the range of about 20% to about 35% (v/v), and about 50% (v/v) water.

The terms "about 15% to about 30%" ethanol and "about 20% to about 35%" propylene glycol were construed by the court to have their plain and ordinary meaning to skilled formulators. (D.I. 168.) Both experts—Dr. Pinal for Hospira and Dr. Moreton for AbbVie—provided testimony regarding what a person of ordinary skill in the art would have understood "about" to mean in the claim language. *See* Tr. at 343:20-346:16 (Pinal), Tr. 190:7-22 (Moreton).

AbbVie asserts that the '799 patent expressly discloses Hospira's proposed 40/10 formulation as a preferred embodiment (Figure 6). (D.I. 190 at ¶ 56.) AbbVie also highlights that the '799 patent cites to Figure 6 to conclude that "the ratio of ethanol and PG is not critical to the self-preserving properties" of the claim cosolvent formulations.[6] (*Id.*) Hospira contends that the 40/10 formulation was excluded from the claimed ranges during prosecution, when AbbVie amended the claims in response to rejections from the Patent Office. Tr. at 339:4-340:6 (Pinal).[7]

Dr. Pinal offered testimony asserting that under the plain and ordinary meaning of the term "about," Hospira's 40/10 formulation is not within the claimed ranges. Tr. at 326:13-19. Dr. Pinal testified that the use of the word "about" to a skilled formulator "would not stretch" to cover the 10-percentage point difference between Hospira's product and the outer limits of the ranges specified in the claims. Tr. at 342:24-343:3. Conversely, Dr. Moreton provided very little explanation for what a skilled formulator would understand "about" to encompass, testifying that "about is about." Tr. at 190:13.

The plain and ordinary meaning of "about" is context-dependent, and a skilled formulator utilizes the term so as to avoid rigid numerical boundaries. *Ortho-McNeil Pharm., Inc, v. Caraco Pharm. Labs., Ltd.*, 476 F.3d 1321, 1326 (Fed. Cir. 2007). Like all claim terms, "about" should be

[6] AbbVie attempts to supplement its infringement argument on the basis of statements made by Hospira to the FDA and a potential customer. (*See* D.I. 190, ¶ 57-58, 60.) These statements do not persuade the court that AbbVie has met its burden to prove literal infringement.

[7] The court fully discusses the parties' arguments regarding disclaimer *infra* at 2.b.

read in light of its proper stylistic and scientific context. *Id.* Courts should also consider how the term is used within the patent and prosecution history, the possible effects of varying its parameters, and extrinsic evidence of meaning and usage. *Id.*

As explained in detail by Dr. Pinal, the term "about" modifies the range of cosolvents employed in the formulations described in the '799 patent. A person of ordinary skill in the art would have understood that the term "about" facilitates communications among formulators when they are comparing multiple copies of different target formulations. While the term "about" provides some flexibility to account for the fact that no two copies of a target formulation are likely to be the same, it cannot extend to encompass other discrete target formulations. Hospira offered Table 1 from the '799 patent specification as supportive of its argument that "about" lends itself to minor variations. (D.I. 191 at 14.) Hospira posits that the experiments represented in Table 1 demonstrate that "about 30%" ethanol can encompass minor deviations on either side of 30%, but that 35%, for example, could not be considered "about 30%" in the plain and ordinary meaning of the term because both 35% and 30% are target values for the concentration of ethanol. (*Id.*)

Dr. Moreton offered no opinion on the plain and ordinary meaning of "about" to a skilled formulator aside from the need to "put it into context." Tr. at 190:22.

AbbVie argues that the '799 patent makes clear that "about" covers the disclosed embodiments, including the 40% (v/v) ethanol, 10% (v/v) PG formulation, because, in describing those embodiments, "the written description explicitly provides that 'the ratio of ethanol and [propylene glycol] is not critical to the self-preserving properties of [the] cosolvent formulation.'" (D.I. 190 at ¶ 67.)

The evidence presented at trial, however, does not support this conclusion. In consideration of the expert testimony presented at trial, the court finds Dr. Pinal's testimony credible and adopts

his interpretation of "about." The court is unconvinced that the term "about" would be understood by a person of ordinary skill in the art to extend far enough to cover the 10-percentage point difference between Hospira's product and the outer limits of the ranges specified in the asserted claim. The court concludes that a person of ordinary skill in the art would have understood that the term "about" facilitates communications among formulators when they are comparing multiple copies of different targets. While the term about provides some flexibility to account for the fact that no two copies of a target formulation are likely to be the same, it cannot extend so far as to meet AbbVie's burden of proving literal infringement.

b. Prosecution History of the '799 Patent

Prosecution history disclaimer limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution. *See ACCO Brands, Inc. v. Micro Sec. Devices, Inc.*, 346 F.3d 1075, 1078 (Fed. Cir. 2003). Even disclosed embodiments can be lost if they are not claimed. *See TIP Sys., LLC v. Phillips & Brooks/Gladwin, Inc.*, 529 F.3d 1364, 1373 (Fed. Cir. 2008); *see also N. Am. Container, Inc. v. Plastipak Packaging, Inc.*, 415 F.3d 1335, 1345-46 (Fed. Cir. 2005). Subject matter can be disavowed during prosecution based on amendments or arguments to the Patent Office, and it is irrelevant whether the applicant had to relinquish a particular interpretation to overcome the prior art. *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 979 (Fed. Cir. 1999). Prosecution history disclaimer "promotes the public notice function of the intrinsic evidence and protects the public's reliance on definitive statements made during prosecution." *Biogen Idec, Inc. v. GlaxoSmithKline, LLC*, 713 F.3d 1090, 1095 (Fed. Cir. 2013). Members of the public, including competitors, are entitled to rely on the prosecution history. *Hockerson-Halberstadt, Inc. v. Avia Grp. Int'l, Inc.*, 222 F.3d 951, 957 (Fed. Cir. 2000); *see also Biogen*, 713 F.3d at 1095 ("Competitors are entitled to rely on those representations when

determining a course of lawful conduct, such as launching a new product or designing-around a patented invention.") Allowing a patentee to assert infringement against subject matter it disavowed during prosecution "would undercut the public's reliance on a statement that was in the public record and upon which reasonable competitors formed their business strategies." *Hockerson-Halberstadt*, 222 F.3d at 957. Where a reasonable competitor would understand that subject matter was disclaimed, a patent holder's later infringement allegation against that subject matter "reduces to a request for a mulligan that would erase from the prosecution history the inventor's disavowal of a particular aspect of a claim term's meaning." *Id.*; *see also Springs Window Fashions LP v. Novo Indus., L.P.*, 323 F.3d 989, 996 (Fed. Cir. 2003).

When AbbVie's patent application was first filed it included broad claims, subsequently rejected by the patent examiner. As originally filed, claim 1 did not contain any limit on the amount of cosolvents. *See* JTX005 at 17. It covered any therapeutic agent and any concentration of organic solvent from 0 to 100%. *See* Tr. 333:13-335:5 (Pinal). The patent examiner rejected all the original claims and, in response, the applicants amended the claims. As evidence of unexpected synergistic antimicrobial results the applicants cited to all six of the Figures in Example 3.

In Amendment A, the applicants amended claim 1 to require a sterilized, self-preserved, aqueous pharmaceutical composition and parenteral administration. *See* JTX005 at 241. The applicants required "about 50 percent volume by volume of an organic" and "about 50 percent of water." Tr. at 177:5-178:6 (Moreton). The examiner again rejected all of the claims and, in response, the applicants narrowed the claims in Amendment B. Amendment B narrowed the range of concentrations for the organic solvent. The level of ethanol was change to "about 15% to about 30%" and the level of propylene glycol was changed to "about 20% to about 35%." Tr. at 339:9-

24 (Pinal). The applicants again submitted evidence of unexpected synergistic results, citing Figures 1 to 5 of Example 3 as support.

AbbVie asserts that the '799 patent expressly sets forth Hospira's proposed formulation as a preferred embodiment—Figure 6—and cites to that embodiment to support the concept that the ratio of ethanol and propylene glycol is not critical. (D.I. 190 at 29.) In support of its argument, AbbVie cites to *Invitrogen Corp. v. Biocrest Manufacturing., L.P.*, for the proposition that "construing a claim to exclude a preferred embodiment 'is rarely, if ever, correct and would require highly persuasive evidentiary support.'" 327 F.3d 1631, 1369 (Fed. Cir. 2003) (citation omitted). The Federal Circuit in *Invitrogen* addressed a very different set of facts relating to disclaimer in reversing the district court's claim construction order. The claim at issue involved a temperature range for growing E. coli cells. *Id.* at 1368. During the prosecution history, the patentee replaced a claim requiring the temperature be "less than 37° C" with "18° C to 32° C." *Id.* at 1369. In determining that the patentees had not disclaimed utilization of temperatures above 32° C, the court looked to statements made to the PTO during prosecution that emphasized the advantages of growth within the range without disclaiming the use of temperatures above the range. *Id.* at 1369. Specifically, the court looked to the patent's disclosure of preparative steps in finding that, "[the] specification thus supplies context about the understanding of skilled artisans and the field of invention that confirms that claim 1 does not preclude growth before the first step in the inventive process." *Id.*

Conversely, here, AbbVie excluded Figure 6 from Amendment B and narrowed the claimed range. Now, AbbVie seeks to expand the claimed range of the cosolvent formulation to include Hospira's proposed product. The court will not countenance AbbVie's attempt, and concludes that the Hospira's formulation cannot be said to be part of the specification supporting a broadening of

the claimed range after it was surrendered during prosecution. Because a reasonable competitor, such as Hospira, would have understood that the subject matter was disclaimed, AbbVie cannot now succeed in an infringement action that would effectively "erase from the prosecution history the inventor's disavowal of a particular aspect of a claim term's meaning." *See Hockerson-Halberstadt, Inc. v. Avia Grp. Int'l, Inc.*, 222 F.3d 951, 957 (Fed. Cir. 2001). As such, the court finds that there has been a clear disavowal of the previously claimed range.

IV. CONCLUSION

For the reasons stated above, the court concludes that: (1) the asserted claims of the '799 are not invalid due to obviousness; and (2) AbbVie has failed to prove, by a preponderance of the evidence, that Hospira's product infringes the asserted claims of the '799 patent.[8] An appropriate order will follow.

Dated: October 24, 2014

UNITED STATES DISTRICT JUDGE

[8] As noted, both parties submitted Proposed Findings of Fact and Conclusions of Law, requesting that the court find in its favor on issues of obviousness and infringement. For the reasons stated above and based on the court's findings, Hospira's Rule 52(c) motion is granted in part and denied in part.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ABBVIE INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. 11-cv-648 (GMS)
	)	
HOSPIRA, INC.	)	
	)	
Defendant.	)	
	)	

ORDER

At Wilmington this 24th day of October, 2014, IT IS HEREBY ORDERED THAT:

1. The asserted claims of the patents-in-suit are not invalid due to obviousness;

2. Hospira's proposed product does not infringe the asserted claims of the patents-in-suit; and

3. The parties' Rule 52(c) motions (D.I. 190-191) are GRANTED IN PART AND DENIED IN PART.

UNITED STATES DISTRICT JUDGE