

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ALCON RESEARCH LTD.,	:	CIVIL ACTION
	:	
Plaintiff,	:	
	:	
v.	:	
	:	
BARR LABORATORIES INC. et al.,	:	NO. 09-CV-0318-LDD
	:	
Defendants.	:	

OPINION

Legrome D. Davis, J.

December 13, 2011

I. Introduction

Plaintiff Alcon Research, Ltd. (“Alcon”) brought this patent infringement action in response to Defendants’ Par Pharmaceutical, Inc. (“Par”) and Barr Laboratories Inc. (“Barr”) filing of Abbreviated New Drug Applications (ANDAs)¹ for FDA approval to market generic versions of Alcon’s Travatan® and Travatan Z® products. Travatan® and Travatan Z® are topical prescription eye drops used to treat glaucoma and ocular hypertension, a condition associated with glaucoma. Although both Travatan® and Travatan Z® contain the same active ingredient, i.e., the prostaglandin Travoprost in a concentration of 0.004% w/v, Travatan® contains benzalkonium chloride (“BAC” or “BAK”), a conventional antimicrobial agent, while Travatan Z® does not.

¹Par submitted ANDA Nos. 91-340 and 91-341 seeking FDA approval to market generic versions of Alcon’s Travatan® and Travatan Z® products, respectively. Barr submitted ANDA No. 91-411 seeking FDA approval to market a generic version of Alcon’s Travatan Z® product. Barr also submitted, but subsequently withdrew, an ANDA for Travatan®.

Leading up to trial, Alcon asserted four (4) patents against the Defendants. Two (2) of the patents-in-suit – U.S. Patent Nos. 5,631,287 (“the ‘287 patent”) and 6,011,062 (“the ‘062 patent”), collectively the “Schneider patents” or the “castor oil patents” – relate to methods of enhancing the chemical stability of prostaglandin-containing compositions by adding polyethoxylated castor oil (“PECO”) to the compositions. The other two (2) patents – U.S. Patent Nos. 6,503,497 (“the ‘497 patent”) and 6,849,253 (“the ‘253 patent”), collectively the “Chowhan patents” or the “borate-polyol patents” – describe aqueous ophthalmic compositions containing a water soluble borate-polyol complex to enhance the antimicrobial activity of the compositions. Following a Markman hearing, we issued an Order on September 6, 2011, construing several disputed claim terms of the four (4) aforementioned patents-in-suit. (Doc. Nos. 213, 214).

We conducted a bench trial on the issues of infringement and validity from November 2, 2011, through November 8, 2011. As indicated above, trial began with four (4) patents and two (2) Defendants. However, following the first day of testimony, which focused on the Chowhan patents, Alcon and Par, the first ANDA filer, agreed to settle their dispute, leaving Barr as the only remaining Defendant. (Doc. No. 242). Barr then stipulated that it infringed the two (2) Chowhan patents and that those patents are not invalid (Doc. No. 243), leaving only the two (2) castor oil patents in contention. We then heard testimony from Alcon and Barr on the castor oil patents, and both Alcon and Barr fully briefed the salient issues post-trial. Having considered the documentary evidence and testimony, we make the following findings of fact and conclusions of law pursuant to Federal Rule of Civil Procedure 52(a).

II. Findings of Fact

A. The Castor Oil Patents (U.S. Patent Nos. 5,631,287 and 6,011,062)

1. Alcon contends that the manufacture of Barr's ANDA product, i.e., Barr's generic version of Travatan Z®, infringes Claim 12 of the '287 patent and Claim 19 of the '062 patent. (Tr. 471:3-21).
2. Claim 12 of the '287 patent depends from Claim 1 of the '287 patent ('287 patent, 10:53-54).
3. As such, Claim 12 of the '287 patent covers a method of enhancing the chemical stability of an aqueous composition comprising a therapeutically-effective amount of a prostaglandin, wherein the method comprises adding a chemically-stabilizing amount of a polyethoxylated castor oil to the composition, and wherein the composition is a topically administrable ophthalmic composition. ('287 patent, 8:57-61; 10:53-54).
4. Claim 19 of the '062 patent depends from Claim 12 of the '062 patent ('062 patent, 14:15-16).
5. As such, Claim 19 of the '062 patent covers a method of enhancing the chemical stability of an aqueous composition comprising a therapeutically-effective amount of a prostaglandin, wherein the method comprises adding a chemically-stabilizing amount of a polyethoxylated castor oil selected from the group of PEG-5 to PEG-200 hydrogenated castor oils to the composition, and wherein the composition is a topically administrable ophthalmic composition. ('062 patent, 11:65-12:3; 14:15-

16).

6. As should be readily apparent, the two (2) claims-in-suit are identical except that Claim 12 of the '287 patent is open to any PECO, while Claim 19 of the '062 patent limits the PECO to one selected from the group of PEG-5 to PEG-200 hydrogenated castor oils.

B. A Person of Ordinary Skill in the Art ("PHOSITA")

1. We agree with Dr. Kent, Barr's expert, that the hypothetical PHOSITA with respect to the technical field of the castor oil patents would have a Ph.D. in chemistry or a related field with limited experience (0 to 3 years), or a B.S. or M.S. with more practical experience (5 or more years) in the fields of pharmacy, analytical chemistry, organic chemistry, or chemical engineering. (Tr. 684:8-21).
2. Specifically, we believe that a PHOSITA would have a background in *chemistry* because the claimed invention is drawn to *chemically*-stabilizing a prostaglandin-containing composition using PECO. Therefore, the PHOSITA here should have significant chemistry-related knowledge and/or experience to understand and practice the claimed methods. (Tr. 685:3-20).
3. However, all of our factual findings and legal conclusions would remain the same if we were to adopt the PHOSITA definition espoused by Alcon in its pretrial proposed findings of fact and conclusions of law, i.e., that a PHOSITA in the art of pharmaceutical formulations and compositions

would have at least a master's degree in pharmacy, pharmaceuticals, or a related field, and have at least two (2) years experience working on the development of pharmaceutical formulations and/or compositions involving varying dosage forms. (Doc. No. 220, at 14). In other words, the relatively minor differences in the PHOSITA definitions propounded by Plaintiff Alcon and Defendant Barr have no material effect on our analysis and ultimate conclusions in this matter.

C. Infringement

1. The only disputed issue regarding infringement of Claim 12 of the '287 patent and Claim 19 of the '062 patent, i.e., the asserted castor oil patent claims, is whether or not the amount of PECO in the composition of Barr's ANDA product is a "chemically-stabilizing amount" such that Barr's method of manufacturing its ANDA product enhances the chemical stability of the composition. (Tr. 843:8-12).
2. As set forth in our claim construction Order, the phrase "enhance / enhancing the chemical stability" in the castor oil patent claims means "to increase or increasing the ability of the prostaglandin to resist chemical change (as distinguished from merely increasing the physical stability of the prostaglandin or composition.)" (Doc. No. 214). Travoprost is the prostaglandin in Barr's ANDA product. (Tr. 412:21-25).
3. One enhances the chemical stability of an ophthalmic composition such as Barr's ANDA product by reducing or decreasing the degradation of the

active ingredient, here, the prostaglandin Travoprost. (Tr. 412:1-25). As distinguished from chemical stability, physical stability refers to physical phenomena such as absorption, adsorption, and precipitation. (Tr. 320:20-322:23). If the PECO in Barr's ANDA product merely enhances the physical stability of Travoprost, as opposed to enhancing its chemical stability, at least in part, then Barr does not infringe Claim 12 of the '287 patent and Claim 19 of the '062 patent, i.e., the asserted castor oil patent claims.

4. Alcon failed to prove by a preponderance of the evidence that Barr manufactures its ANDA product, i.e., its generic version of Travatan Z®, by a method that comprises adding a chemically-stabilizing amount of PECO to its composition to enhance the chemical stability of the composition.
5. Given Barr's stipulation of infringement, Alcon proved by a preponderance of the evidence that Barr's ANDA product falls within the scope of Claims 7, 21, 41, and 43 of the '497 patent and Claim 18 of the '253 patent, i.e., the borate-polyol patents. (Doc. No. 243).

D. Enablement and Written Description Under 35 U.S.C. § 112, First Paragraph

1. The asserted castor oil patent claims are extremely broad. (Tr. 800-11).
2. The castor oil patent disclosures provide relatively limited information and guidance to a person skilled in the art regarding how to practice the claimed invention (Tr. 795-800).

3. The art of chemically stabilizing prostaglandins is quite unpredictable.
(Tr. 417:3-20; 420:13-25; 417:21-23; 418:22-419:4; 419:13-25; 692:11-693:9; 698-704; 708; 809-11; ‘287 patent, 6:23-26).
4. Given the breadth of the asserted claims, the relatively limited disclosure, and the unpredictability of the art, Barr proved by clear and convincing evidence that one skilled in the art could not carry out the full scope of the asserted castor oil patent claims without undue experimentation, and a person skilled in the art would not recognize that the inventors of the castor oil patents were in possession of the claimed invention at the time the castor oil patent applications were filed.

E. Indefiniteness Under 35 U.S.C. § 112, Second Paragraph

1. Barr failed to prove by clear and convincing evidence that the claim term “enhancing the chemical stability” is insolubly ambiguous, despite the lack of an explicit comparator in the patent disclosure or claims (“enhanced with respect to what?”). Specifically, one skilled in the art would understand the “enhancing the chemical stability” limitation in the asserted castor oil patent claims to mean that using PECO in the formulation must provide increased chemical stability as compared to not using PECO. Stated differently, using the claimed invention (adding a chemically stabilizing amount of PECO) must increase the chemical stability of the prostaglandin as compared to not using the invention.
2. The claim term “therapeutically effective amount” is not insolubly

ambiguous. As we suggested in our claim construction memorandum, a “therapeutically effective amount” is an amount necessary to achieve an intended, expected, or desired result. Relatedly, a specific amount of a drug can produce a therapeutic effect without being therapeutically effective. (Doc. No. 213, at 30). Here, Barr has not proven by clear and convincing evidence that one of ordinary skill in the art would have to engage in undue experimentation to determine a “therapeutically effective amount” of prostaglandin in the context of the asserted castor oil patent claims, which are limited to topically administrable ophthalmic compositions.

F. Anticipation Under 35 U.S.C. § 102

1. Barr’s expert Dr. Kent identified only one (1) potentially anticipatory reference, namely U.S. Patent No. 5,721,273, which was filed on Dec. 15, 1993 and issued on Feb. 24, 1998. (Tr. 825:6-828:18; 923:5-924:2; DTX 806). The ‘273 patent names Alcon as the assignee but does not have any overlapping inventorship with the castor oil patents-in-suit. (DTX 806).
2. L. Wayne Schneider, an inventor named on the castor oil patents, conceived and reduced to practice enough of his claimed invention prior to Dec. 15, 1993, the filing date of the ‘273 patent, such that the ‘273 patent does not constitute prior art with respect to the castor oil patent claims in suit. (Tr. 340-62).

G. Obviousness under 35 U.S.C. § 103

1. Other than the '273 patent, Barr's expert Dr. Kent relied on six (6) prior art references to conclude that Claim 12 of the '287 patent and Claim 19 of the '062 patent, i.e., the castor oil patent claims-in-suit, are obvious under 35 U.S.C. § 103: (1) U.S. Patent No. 4,684,633; (2) Japanese Patent Application S53-148518; (3) U.S. Patent No. 4,430,340; (4) U.S. Patent No. 5,296,504; (5) U.S. Patent No. 5,091,417; and (6) U.S. Patent No. 5,185,372. (Tr. 820-36).
2. Dr. Kent's testimony boils down to simply identifying the individual elements of the claimed invention in various prior art references. (Tr. 818-36). A PHOSITA would have had no reason or motivation to combine the teachings of the six (6) aforementioned prior art references absent impermissible hindsight. Therefore, Barr failed to prove by clear and convincing evidence that the prior art rendered the asserted castor oil patent claims obvious to a PHOSITA at the time the invention was made.

H. Alcon's Un-Litigated U.S. Patent Nos. 5,510,383 and 5,889,052

1. Alcon's original complaint initially asserted U.S. Patent Nos. 5,510,383 and 5,889,052 against Barr. (Doc. No. 1 ¶¶ 9-22, 50-63). However, Alcon did not assert these two patents in its pretrial filings or at trial, and Alcon did not present any evidence whatsoever on these patents at trial, although Alcon never formally withdrew its claims based on the patents.
2. At the close of Alcon's case-in-chief, Barr moved for judgment as a matter of law of non-infringement of the '383 and '052 patents, noting that Alcon

presented no evidence on these two patents and therefore cannot meet its burden of proving infringement by a preponderance of the evidence. (Tr. 563:2-15).

3. We recognize that the pleadings in this matter are not in complete harmony with the issues that were actually litigated and adjudicated. In situations such as this, we conform the pleadings to the judgment, not vice versa. As such, Barr is not entitled to a judgment of non-infringement with respect to the '383 and '052 patents, which were not actually litigated.

III. Conclusions of Law

A. Choice of Law

1. In this patent infringement action, we are bound by, and seek guidance from, the body of law developed by the United States Court of Appeals for the Federal Circuit, as well as its predecessor, the Court of Customs and Patent Appeals. See South Corp. v. United States, 690 F.2d 1368, 1370-71 (Fed. Cir. 1982) (adopting the body of law represented by the holdings of the Court of Claims and the Court of Customs and Patent Appeals).
2. Additionally, we apply Federal Circuit law to resolve issues pertaining to or unique to patent law, while we apply Third Circuit law to resolve all other issues. See Molins PLC v. Quigg, 837 F.2d 1064, 1066 (Fed. Cir. 1988) (noting that “we apply the law of that circuit to which district court

appeals normally lie, unless the issue pertains to or is unique to patent law.”) (citation omitted).

3. Here, all the issues we address in this Opinion either pertain to, or are unique to, patent law, so we look to Federal Circuit law to shape the resolution of this matter.
4. Of course, the Supreme Court’s patent-related jurisprudence also binds us, to the extent the Court has spoken on topics relevant to the issues facing us here.

B. Infringement

1. “To show literal infringement of a patent, a patentee must supply sufficient evidence to prove that the accused product or process meets every element or limitation of a claim.” Rohm & Haas Co. v. Brotech Corp., 127 F.3d 1089, 1092 (Fed. Cir. 1997). Regarding the burden of proof, “[i]nfringement requires proof by a preponderance of the evidence.” Id.
2. “An infringement analysis requires two separate steps. First, the court must construe the claims asserted to be infringed as a matter of law in order to establish their meaning and scope. Second, the claims as construed are compared to the allegedly infringing device or process.” Texas Instruments Inc. v. Cypress Semiconductor Corp., 90 F.3d 1558, 1563 (Fed. Cir. 1996) (internal citation omitted).
3. In ANDA litigation such as this, our infringement inquiry is the same as in

any other patent suit. Glaxo, Inc. v. Novopharm, Ltd., 110 F.3d 1562, 1569 (Fed. Cir. 1997). Specifically, we must evaluate “whether the patent in question is invalid or will not be infringed by the manufacture, use, or sale of the drug for which the [ANDA] is submitted. 21 U.S.C. § 355(j)(2)(A)(vii)(IV). The only difference in actions brought under § 271(e)(2) is that the allegedly infringing drug has not yet been marketed and therefore the question of infringement must focus on what the ANDA applicant will likely market if its application is approved, an act that has not yet occurred.” Id. As such, “the patentee’s burden of proving ultimate infringement is not met by the filing of the ANDA. The relevant inquiry is whether the patentee has proven by a preponderance of the evidence that the alleged infringer will likely market an infringing product.” Id. at 1570.

4. Before turning to the castor oil patents, the heart of the parties’ dispute, we first briefly address the borate-polyol patents. As mentioned *supra*, Alcon and Par settled after the first day of testimony, which focused on the borate-polyol patents. Barr, the lone remaining Defendant, then stipulated that it infringed the two (2) borate-polyol patents-in-suit and that those patents are not invalid (Doc. No. 243).
5. Notwithstanding Barr’s concessions, insofar as Alcon bears the burden of proof on infringement, we will briefly recite Alcon’s infringement evidence adduced at trial. Alcon’s expert Dr. George Zhanel testified that

the borate-polyol complex in Barr's BAC-free ANDA composition, i.e., its proposed generic version of Travatan Z®, enhances the antimicrobial activity of the composition, as required by the asserted borate-polyol claims, i.e., Claims 7, 21, 41, and 43 of the '497 patent and Claim 18 of the '253 patent. (Tr. 166-95). Additionally, another Alcon expert, Dr. Soumyajit Majumdar, testified that Barr's BAC-free ANDA product meets all the other limitations of the asserted claims, e.g., the specifically-claimed polyols, the ratios and weight percentages of various components, and the fact that Barr's ANDA product is "unpreserved." (Tr. 256-89).

6. The testimony of Alcon's two experts, viewed in light of Barr's concession of infringement, convinces us that Alcon proved by a preponderance of the evidence that Barr's BAC-free ANDA product infringes the asserted borate-polyol claims, i.e., Claims 7, 21, 41, and 43 of the '497 patent and Claim 18 of the '253 patent.
7. As such, the effective date of any FDA approval of Barr's BAC-free ANDA product shall be a date which is not earlier than the date of the expiration of the last to expire of the '497 and '253 patents.
8. We now come to the castor oil patents. At the outset, we note that determining infringement (or lack thereof) of the asserted castor oil patent claims in this matter is needlessly complex. As mentioned *supra*, the only contested issue with respect to infringement of the castor oil patent claims is whether or not the amount of PECO in Barr's ANDA product is a

“chemically-stabilizing amount.” (Tr. 843:8-12). If the PECO in Barr’s ANDA product chemically stabilizes the Travoprost, i.e., the active prostaglandin ingredient, then Barr infringes. If the PECO does not chemically stabilize the Travoprost, then Barr does not infringe.

9. Alcon could have determined, rather definitively, whether the PECO in Barr’s ANDA product (or the PECO in Travatan Z®, its own product, which is extremely similar, if not functionally identical, to Barr’s ANDA product) enhances the chemical stability of the Travoprost in the composition by running the appropriate chemical stability tests. (Tr. 680:4-18; 726-37). For whatever reason, Alcon did not perform this testing.² Therefore, instead of having a relatively clear answer to the infringement question, we are left drawing inferences and making educated guesses.
10. Of course, Alcon is free to prove its case as it sees fit. See *Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1272 (Fed. Cir. 1986) (patentee can prove infringement through direct or circumstantial evidence). Unfortunately for Alcon, the method of proof it chose merely invites us to speculate that the PECO in Barr’s ANDA product chemically stabilizes the Travoprost, and Alcon did not prove infringement by a preponderance of the evidence. See *Lucent Tech., Inc. v. Gateway, Inc.*,

²As far as we know, Barr did not perform this testing either. Of course, as the accused infringer, Barr does not bear the burden of proof on infringement.

543 F.3d 710, 722-24 (Fed. Cir. 2008) (recognizing that overly speculative circumstantial evidence will not suffice to prove infringement).

11. Speaking broadly, Alcon rests its infringement contentions on the testimony of (1) its expert Dr. Levinson and (2) L. Wayne Schneider, an inventor of the castor oil patents. We address each in turn.
12. Dr. Levinson relied primarily on a single document – an Alcon technical report entitled “Solubility of Travoprost in HCO-40 and Soaking Study of Polypropylene Material in Prototype Formulations” (the “Solubility Study”) – to reach his conclusion that Barr’s ANDA product infringes the castor oil patents. (Tr. 549:3-550:7; PTX 45; DTX 1012). In particular, Levinson relies on the data in Table 7 of the Solubility Study to conclude that the PECO in Barr’s ANDA product chemically stabilizes the Travoprost. (Tr. 492-504). To draw this conclusion, Levinson compares sample 92941, which contains no HCO-40 (a particular PECO), with sample 92957, an identical solution that contains 0.50% HCO-40. After eight (8) weeks at an elevated temperature, the sample without HCO-40 lost 12% of its Travoprost, while the sample with 0.50% of HCO-40 lost 8% of its Travoprost³. (PTX 45, Table 7).
13. Dr. Levinson’s infringement analysis fails to persuade us for a number of reasons. First, the Solubility Study on which Levinson relies mentions

³Table 7 shows an 8% decrease at eight (8) weeks for both samples, but as Dr. Levinson correctly points out, the authors of the Solubility Study did not normalize the data in Table 7 before reporting it. (Tr. 499:17-502:25).

nothing at all about chemical stability, and the study was designed to test something entirely different, i.e., the solubility of Travoprost and its compatibility with polypropylene packaging material in varying HCO-40 concentrations. (PTX 45, Summary). In other words, the authors of the study drew no conclusions about the effect of HCO-40 on the chemical stability of Travoprost; rather, Levinson drew that conclusion on his own based on the control sample data provided by the authors in Table 7.

While it is certainly possible to analyze another's data in a new light and draw valid conclusions, we believe such conclusions must withstand careful scrutiny. Levinson's do not.

14. As mentioned *supra*, in his analysis, Levinson relied on two discrete data points in Table 7: sample 92941 (0% HCO-40) at eight (8) weeks and sample 92957 (0.50% HCO-40) at eight (8) weeks. We think it more analytically sound to evaluate the data in its entirety. In doing so, several things become clear to us. First, the Travoprost in the tested composition has good stability even without any PECO / HCO-40. In sample 92941, which contains absolutely no PECO, 88% of the Travoprost remains after eight (8) weeks at an elevated temperature. (PTX 45, Table 7).
15. Second, the data in Table 7 is subject to at least some experimental error or uncertainty. For example, according to Table 7, the Travoprost concentration actually *increases* slightly over some period of time in some of the samples. (PTX 45, Table 7, sample 92956 between weeks 2 and 4;

sample 92954 between weeks 0 and 1). No one has suggested to us that the PECO actually generates Travoprost over time, so experimental error or uncertainty most likely explains the anomalous data.

16. Third, even small variations in the composition of a Travoprost-containing solution can, and do, have a noticeable effect on the stability of the Travoprost (chemical or physical stability, we do not know). For example, consider samples 92940 and 92941 in Table 7. Neither sample contains PECO, and the samples are identical in all respects except that 92940 contains 0.02% of BAC, while 92941 contains 0.01% of BAC. This minuscule change in BAC concentration apparently alters the stability of the composition such that the 0.02% BAC sample loses 15% of its Travoprost at eight (8) weeks while the 0.01% BAC sample loses only 12%.⁴ Relatively speaking, this is on the same order of magnitude as the 4% difference that Dr. Levinson finds so compelling in comparing the “no PECO” sample to the “0.50% PECO” sample. Additionally, the fact that BAC concentration appears to affect Travoprost stability to about the same extent as PECO concentration does is particularly instructive in evaluating the probative value of the Table 7 data because all of the samples in Table 7 *contain BAC*, while Barr’s ANDA product *does not*.
17. This observation comports with Alcon’s and Mr. Schneider’s own

⁴Like Dr. Levinson, we normalized this data for effective comparison. For example, in sample 92940, $[(76-64.5) / (76)] \times 100 = 15\%$.

recognition that various parameters including pH, buffer, buffer concentration, preservatives, chelating agents, and other excipients may affect the chemical stability of prostaglandins in ophthalmic formulations (Tr. 383:9-384:4; 417:3-20; 420:13-25; 790-92).

18. Fourth, with respect to Figures 1-3 of the castor oil patents, Dr. Levinson opined that the data in the aforementioned Figures shows chemical stability, not physical stability, because the data plotted linearly on a log scale, which indicates a first-order chemical reaction. (Tr. 479:2-481:20). Of course, the prostaglandin Mr. Schneider tested in the castor oil patents was *not* Travoprost, so it does little to inform our analysis of whether PECO chemically stabilizes Travoprost in Barr's ANDA product. Additionally, the data in Table 7 of the Solubility Study on which Dr. Levinson so heavily relies, and which does test Travoprost, is decidedly un-linear. In all the samples, very little Travoprost disappears in the first four (4) weeks, and then the Travoprost concentration drops off between four (4) and eight (8) weeks. (PTX 45, Table 7). If we believe Dr. Levinson's testimony on this topic, then the Table 7 data is not indicative of a first-order chemical reaction, unlike the data in the castor oil patents. This highlights the point we have already made: different prostaglandin-containing ophthalmic formulations have different stability profiles, which depend on a variety of factors.
19. Dr. Levinson also surmises that the decrease in Travoprost concentration

must result from chemical instability as opposed to physical loss (absorption, adsorption, precipitation) because (1) the loss occurs over time, while adsorption is rapid (Tr. 480:18-23), and (2) absorption does not occur in glass, and the tests resulting in the Table 7 data were carried out in glass ampules (Tr. 482:1-3; PTX 45, Table 7). However, Levinson does admit that some adsorption onto glass could occur. (Tr. 492:10-17). Notably, Levinson provides no authority or documentary evidence to support his assertion that adsorption would occur rapidly. (Tr. 539:11-540:2).

20. Additionally, one of Alcon's own patents, U.S. Patent No. 6,235,781 ("the '781 patent"), undercuts Dr. Levinson's conclusions regarding physical loss of prostaglandins. (DTX 183). The '781 patent discloses that PECO, including HCO-40, inhibits the adsorption of prostaglandin onto container walls. ('781 patent, 4:39-63). The '781 patent says nothing about chemical stability, but rather deals with prostaglandin loss to different packaging materials, i.e., physical loss. The graphs depicted in Figures 1-4 of the '781 patent show that, in fact, a substantial amount of prostaglandin physical loss may occur, *even in glass containers*. Second, the '781 patent inventors waited four (4) weeks before measuring prostaglandin loss. ('781 patent, Figures 1-4). If physical loss occurs so rapidly (mere hours or days, as Dr. Levinson opined), why wait four (4) weeks to test for it? Finally, the '781 patent inventors apparently believed

that physical loss occurs rather steadily over time ('781 patent, Figures 1-4, which depict a linear decrease in prostaglandin concentration over a four (4) week period). This is in tension with Dr. Levinson's opinion that adsorption occurs rapidly and then stops, or at least equilibrates.

21. In the end, the difference in missing Travoprost between the "no PECO" sample and the "0.50% PECO" sample is 4% – after eight (8) weeks, 92% of the Travoprost remains in the PECO-containing sample, while 88% of the Travoprost remains in the sample without PECO. We do not know for sure where the missing Travoprost went in either sample. However, this is an extremely small difference which could be attributed to a number of factors other than PECO enhancing the chemical stability of the Travoprost, e.g., experimental error or uncertainty, adsorption, precipitation, or other physical loss. These factors take on particular importance here because the Travoprost concentration is so low – 0.005% w/v in the Table 7 samples and 0.004% in Travatan Z® and Barr's generic version of the same. (PTX 45, Table 2). Therefore, even a small absolute amount of experimental error or physical instability (adsorption, etc.) would lead to a relatively large variation, percentage-wise, in Travoprost concentration.
22. Further, even assuming the data in Table 7 shows that PECO enhances the chemical stability of Travoprost in the tested formulations, which we have concluded it does not, the tested formulations differ significantly from

Barr's ANDA product. In particular, the Travoprost concentrations and pH's are slightly different; the Solubility Study formulations contain tromethamine, mannitol, EDTA, and BAC, and Barr's ANDA product does not; and Barr's ANDA product contains propylene glycol, sorbitol, and zinc chloride, while the Solubility Study formulations do not. (PTX 45, Table 2; Barr's ANDA 91-411; Tr. 740:2-742:4). Since variables such as pH, buffer, buffer concentration, preservatives, chelating agents, and other excipients can affect the chemical stability of prostaglandins in ophthalmic formulations (see ¶¶ 16-17 *supra*), the compositional differences between the Solubility Study formulations and Barr's ANDA product preclude us from relying on the Solubility Study data to draw any reliable inferences with respect to the stability of Barr's ANDA product. In other words, even if Table 7 of the Solubility Study shows that HCO-40 chemically stabilizes Travoprost in the tested samples, which is unclear, we have little reason to believe that HCO-40 would act similarly in Barr's ANDA product.

23. Finally, we note that Dr. Levinson admitted numerous times that he is not an expert in prostaglandin chemistry or chemical changes in prostaglandins. (Tr. 527:22-528:12; 529:9-14; 534:7-15; 532:11-18; 536:4-19; 542:24-543:2). To some extent, this undermines our faith in his ability to reliably assess whether or not the PECO in Barr's ANDA product chemically stabilizes Travoprost, the prostaglandin at issue.

24. We now turn to Mr. Schneider’s testimony. Mr. Schneider is the sole inventor named on the ‘287 patent and one of three joint inventors named on the ‘062 patent, i.e., the castor oil patents in suit. We begin by noting that Mr. Schneider was not held out as an expert in this matter and did not submit any expert reports. (Tr. 330:5-15; 406:8-10). At trial, Alcon’s counsel stated that Schneider would testify about the work he did to develop his invention and not draw any expert conclusions. (Tr. 330:5-15). With that stipulation, and over Defense counsel’s objection, we gave Schneider wide latitude to tell his invention story. (Tr. 329:22-330:15).
25. Nonetheless, in its post-trial brief, Alcon relies on Schneider’s testimony to support its infringement contentions. (Doc. No. 247, at 8-10). Therefore, we feel obliged to briefly discuss our reasons for finding Schneider’s testimony unpersuasive as far as infringement is concerned.
26. First, Schneider never tested Barr’s ANDA product, and he candidly admitted that he has no idea whether Barr’s ANDA product has any chemical degradation products under any conditions. (Tr. 440:23-25).
27. Second, we find that Mr. Schneider lacks credibility on the critical “chemical stability / loss v. physical stability / loss” issue in this case. For one thing, Schneider flip-flopped on whether or not he believes that anything other than pH would have an appreciable influence on the chemical stability of prostaglandin compositions. (Tr. 436-37). Specifically, he said “No” to the USPTO during the prosecution of his

castor oil patent application; “Yes” in his deposition; and “No” in an errata to his deposition. (Tr. 436-37).

28. In addition, Mr. Schneider, the inventor of the patents-in-suit, appears confused about whether PECO enhances the chemical stability of prostaglandins or merely enhances their physical stability. In his deposition, Schneider was asked whether the data in his patents might indicate that the PECO enhances the physical stability of the prostaglandin compositions. He answered: “Might. Yes, it might. I can’t deny that. But my feeling is that it indicates the chemical stability because the polyethoxylated castor oil affords solubility and prevents loss of physical absorption or physical -- the polyethoxylated castor oil prevents the physical loss of the prostaglandin from the solution.” (Tr. 416:3-17). This suggests to us that, at least at the time of Schneider’s deposition, he did not have a clear understanding of how PECO works to stabilize prostaglandins.
29. Third, many of the experiments and associated data about which Mr. Schneider testified, including all the castor oil patent data, involved prostaglandins other than Travoprost, the active ingredient in Travatan Z® and Barr’s ANDA product. (Tr. 340-62). This data has limited probative value with respect to the chemical stability of Travoprost in Barr’s ANDA product because even small differences in a prostaglandin’s chemical structure can significantly influence its stability. (Tr. 417:21-23; 418:22-

419:4 (isopropyl ester considerably more stable than butyl ester); 419:13-25).

30. Fourth, much of Schneider's current testimony regarding chemical stability, including his interpretation of HPLC graphs, finds very little support from the contemporaneous observations Schneider made during his invention process, e.g., in his lab notebooks and patent applications. For example, in the evidence we saw, Schneider only explicitly labeled prostaglandin degradation products ("Deg 1" and "Deg 2") on an HPLC graph on *one* single occasion, i.e., in a 1993 experiment involving AL-6045, a prostaglandin that is *not* Travoprost, and the surfactant Polysorbate 80, *not* PECO. (Tr. 340:5-343:22; 344:2-13). Additionally, Schneider did not include any HPLC graphs in the castor oil patents, much less explain the significance of any of the HPLC data he collected. (See '287 and '062 patents).
31. Despite the absence of contemporaneously-recorded observations, and despite the fact that Alcon never sought to qualify Schneider as an HPLC expert (Tr. 330:5-15; 406:15-16), at trial Schneider saw fit to offer relatively detailed and complex explanations of how he knew that certain HPLC data showed prostaglandin chemical stability or degradation as opposed to physical loss, or surfactant degradation, or impurities, or some other explanation for the HPLC results. (Tr. 361:14-362:11; 396-400; 441:17-445:18; 456-57; 459). This *post hoc* analysis of undoubtedly

cherry-picked data fails to convince us that PECO chemically stabilizes prostaglandins in ophthalmic compositions. Further, even if select HPLC data presented by Mr. Schneider supports the proposition that PECO chemically stabilizes prostaglandins in some instances, we could not reliably infer that the PECO would exhibit a similar chemically-stabilizing effect in Barr's ANDA formulation, which differs from all the formulations that Schneider tested. (See ¶¶ 16, 17, 29 *supra*, discussing how prostaglandin composition stability depends on a host of variables).

32. Fifth, similar to Dr. Levinson, Schneider opines that the prostaglandin concentration he measured, recorded, and submitted to the USPTO in Figures 1-3 of the '287 patent decreased linearly over a period of time, which indicates chemical loss as opposed to physical loss because physical loss occurs rapidly. (Tr. 375:24-376:17; 428:15-429:22). Relatedly, the '287 patent specification suggests that the patent data shows degradation occurring via a first-order chemical reaction. ('287 patent, 8:19-26). However, Schneider did not produce any documentary support for his hypothesis (Tr. 429:22 ("It's intuitively obvious to one skilled in the art"))).
33. In addition, we reiterate that the prostaglandin Schneider tested in the castor oil patents is not Travoprost, and the prostaglandin composition Schneider tested differs markedly from Barr's ANDA product ('287 patent, 7:25-47). Therefore, the patent data says little about whether

PECO would enhance the chemical stability of Travoprost in Barr's Travatan Z® generic. For example, while the prostaglandin concentration decreases linearly in Figures 1-3 of the castor oil patents, the Travoprost concentration in Table 7 of the Solubility Study *does not*. With this kind of variability, we cannot simply take data collected on one prostaglandin formulation and assume that it would translate to another.

34. Finally, we agree with Dr. Kent, Barr's expert, that Alcon's own internal documents demonstrate Alcon's belief that PECO works by physically stabilizing Travoprost, not by chemically stabilizing it. (Tr. 780:1-15).
35. For example, an Alcon memo from 1997, three (3) years after Schneider filed the '287 patent application, states that "[l]ess than 7% change of the stability profile of AL06221 [Travoprost] and no change of the stability profile of AL12419 (~1.5%) [a Travoprost degradation product] was discovered after 8 weeks at 55° C. No or trace amount of AL09584 and AL05848 [other degradation products] can be detected." (DTX 1283, at 8786:11). In other words, 7% of the Travoprost went missing, but it was *not* due to chemical degradation.
36. In its post-trial brief, Alcon attempts to explain this data by noting that the referenced study tested a formulation comprising PECO, so the study merely confirms that PECO prevents the chemical degradation of Travoprost. (Doc. No. 247, at 7). In other words, Alcon apparently argues that PECO works so well to chemically stabilize Travoprost that

absolutely no chemical degradation occurs. This position contradicts Alcon's own expert's testimony regarding the data in Table 7 of the Solubility Study. Specifically, the formulations tested to generate the data in Table 7 also included PECO, yet 8% of the Travoprost went missing in the "0.50% PECO" sample. (PTX 45, Table 7). And according to Dr. Levinson, Table 7 shows "immutable data that there's chemical degradation going on." (Tr. 499:10-11). In other words, Travoprost chemical degradation occurs even in PECO-containing compositions, contrary to what Alcon's post-trial brief would have us believe.

37. A second Alcon document from 1996, two (2) years after Schneider filed his castor oil patent application, also supports the proposition that Travoprost loss occurs through physical means, not chemical degradation (DTX 104). In particular, the 1996 document states that Travoprost loss "is now known to be related to the packaging interaction. Chemistry data shows no concurrent increase in degradation products which supports this conclusion." (DTX 104; Tr. 773:17-774:14). Again, no mention that PECO chemically stabilizes Travoprost, or even that the chemical stability of Travoprost is a concern.
38. Finally, Alcon's '781 patent, filed a mere two weeks after the second castor oil patent issued and containing much of the same disclosure, discloses that PECO, including HCO-40, inhibits the adsorption of prostaglandin onto container walls. (DTX 183; '781 patent, 4:39-63).

Other than briefly mentioning the ‘287 castor oil patent in the “Background of the Invention” section, the ‘781 patent says nothing about chemical stability, but rather deals with prostaglandin loss to different packaging materials, i.e., physical loss. Although the ‘781 patent does not negate the possibility that PECO might chemically stabilize prostaglandins such as Travoprost, the patent’s exclusive focus on physical stability weakens that inference.

39. For the aforementioned reasons, we hold that Alcon failed to prove by a preponderance of the evidence that the PECO in Barr’s ANDA product chemically stabilizes the composition. Stated differently, Alcon has not shown that Barr manufactures its Travatan Z® generic by “adding a chemically stabilizing amount of polyethoxylated castor oil” to the composition to “enhance the chemical stability” of the composition, as required by the asserted castor oil patent claims. Therefore, Barr does not infringe any of the asserted castor oil patent claims, i.e., Claim 12 of the ‘287 patent and Claim 19 of the ‘062 patent.

C. Enablement Under 35 U.S.C. § 112, First Paragraph

1. The first paragraph of 35 U.S.C. § 112 sets out the enablement requirement: “[t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms *as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make*

and use the same...” (emphasis added).

2. “The full scope of the claimed invention must be enabled. The rationale for this statutory requirement is straightforward. Enabling the full scope of each claim is part of the *quid pro quo* of the patent bargain. A patentee who chooses broad claim language must make sure the broad claims are fully enabled. The scope of the claims must be less than or equal to the scope of the enablement to ensure that the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims.” Sitrick v. Dreamworks, LLC, 516 F.3d 993, 999 (Fed. Cir. 2008) (internal citations and quotations omitted). In layman’s terms, a patentee must give a lot to get a lot. With that in mind, the Federal Circuit has emphasized that “[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.” Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366 (Fed. Cir. 1997).
3. In In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988), the Federal Circuit laid out eight (8) factors to consider in evaluating enablement: “(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

4. In accordance with these Wands factors, in unpredictable technologies, the Federal Circuit “has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim.” PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564 (Fed. Cir. 1996). For example, the court recently held that a particular patent (1) having extraordinarily broad claims but (2) providing only minimal guidance (three working examples) in (3) a highly unpredictable art failed the enablement requirement as a matter of law. Pharm. Res., Inc. v. Roxane Labs., Inc., 253 Fed. App’x 26, 27-31 (Fed. Cir. 2007).
5. Of course, as with all invalidity defenses, the accused infringer must prove lack of enablement by clear and convincing evidence. See Sitrick, 516 F.3d at 1000 (“[w]e are mindful that Defendants have the evidentiary burden to show facts supporting a conclusion of invalidity by clear and convincing evidence.”).
6. Here, we find that the asserted castor oil patent claims are extremely broad; the technology of stabilizing prostaglandins is highly unpredictable; and the castor oil patent disclosures, which provide experimental data on only one (1) prostaglandin compound and two (2) PECO compounds, provide minimal guidance to one skilled in the art regarding how to practice the full scope of the claimed invention.

Additionally, the chemical stability v. physical stability conundrum (see “Infringement” section, *supra*) adds another layer of complexity to the task facing one skilled in the art who wishes to carry-out the claimed method. Therefore, one skilled in the art would have to perform undue experimentation to practice the full scope of the asserted castor oil patent claims, and Barr has proven lack of enablement by clear and convincing evidence.

7. Beginning with Wands factors (2) and (3) (the amount of direction or guidance presented, and the presence or absence of working examples), the castor oil patents provide very little guidance to one skilled in the art. The working examples are limited to *a single prostaglandin compound* (“Compound No. 2”) (‘287 patent, Figures 1-3). Additionally, Schneider tested *only two (2) PECO compounds*, i.e., Cremophor® EL and Alkamuls® EL-620 (‘287 patent, Figures 1-3), and the two (2) PECO compounds he tested have similar chemical structures (Tr. 364:10-19 (“Alkamuls is a polyoxyl 30 castor oil, the Cremophor is a polyoxyl 35 castor oil”)). Additionally, while the castor oil patents baldly assert that PECOs chemically stabilize prostaglandins, the patents *do not disclose how*. For example, the patents do not discuss how PECOs might inhibit or prevent prostaglandins from chemically degrading. This is particularly problematic in light of the apparent difficulty in distinguishing between the chemical stability / loss and physical stability / loss of prostaglandins

in ophthalmic compositions. (See “Infringement” section, *supra*).

8. Turning next to Wands factors (4) and (7) (the nature of the invention and the predictability or unpredictability of the art), the technology at issue here is highly unpredictable. As discussed *supra*, even small variations in the composition of a prostaglandin-containing solution can, and do, have a noticeable effect on the stability of the prostaglandin. (See “Infringement” section ¶ 16). Various parameters including pH, buffer, buffer concentration, preservatives, chelating agents, and other excipients may affect the chemical stability of prostaglandins in ophthalmic formulations (Tr. 383:9-384:4; 417:3-20; 420:13-25; 790-92; 809-11). Minor differences in a prostaglandin’s chemical structure can significantly influence its stability. (Tr. 417:21-23; 418:22-419:4 (isopropyl ester considerably more stable than butyl ester); 419:13-25; 698-704). The ‘287 patent mentions that too much PECO may adversely affect a prostaglandin’s pharmacologic activity. (‘287 patent, 6:23-26). All of this convinces us of the unpredictability of prostaglandin stability in ophthalmic formulations.
9. Regarding Wands factor (5) (the state of the prior art), as discussed in detail below, the prior art teaches very little about chemically stabilizing prostaglandins, much less by using PECO in ophthalmic formulations. This gives us all the more reason to insist on an adequate disclosure in the castor oil patents.

10. Regarding Wands factor (6) (the relative skill of those in the art), we expect a PHOSITA in this technology to possess a relatively high level of skill. However, even a highly-skilled PHOSITA would have to undertake undue experimentation to practice the claimed invention, given the unpredictable technology, limited disclosure, and broad claims of the castor oil patents.
11. Finally, with respect to Wands factor (8) (the breadth of the claims), the asserted castor oil patent claims are extremely broad. Although our claim construction Order narrowed the galaxy of prostaglandin compounds covered by the claims somewhat⁵, we agree with Dr. Kent that the claims encompass a “rather inordinately large number of potential compounds.” (Tr. 677:23-678:7). Additionally, the asserted claims are open to a myriad of other components typically present in ophthalmic compositions (any buffer, any preservative, any excipient, etc.), in any concentration or ratio, and at any pH. (See Claim 12 of the ‘287 patent and Claim 19 of the ‘062 patent). Additionally, Claim 12 of the ‘287 patent is open to any PECO, and Claim 19 of the ‘062 patent is open to a wide variety of PECOs. In the context of the castor oil patent claims, this compositional breadth

⁵Per our claim construction Order, the claim term “prostaglandin” means “the natural compounds PGE₁, PGE₂, PGE₃, PGF_{1 α} , PGF_{2 α} , PGF_{3 α} , PGD₂, and PGI₂ (prostacyclin), as well as analogues and derivatives of such natural compounds (including the pharmaceutically acceptable esters and salts of such natural compounds and their analogues and derivatives), which have similar biological activities of either greater or lesser potencies.” (Doc. No. 214).

poses a huge challenge to one skilled in the art because, as previously discussed numerous times, these variables may affect the stability of a prostaglandin-containing composition. As Dr. Kent correctly observed, when “you have a lot of variables on top of one another, the experimentation gets out of control quickly.” (Tr. 812:1-5).

12. To conclude, we find the enablement issue here to be analogous to that in Pharmaceutical Resources, Inc. v. Roxane Laboratories, Inc., 253 Fed. App’x 26 (Fed. Cir. 2007). In a highly unpredictable art, Schneider claimed his invention broadly but disclosed relatively little. He claimed that PECO chemically stabilizes prostaglandins, but did not disclose how. He apparently failed to recognize, or at least did not disclose, that his data may reflect enhanced physical stability instead of, or in addition to, enhanced chemical stability. In other words, Schneider did not hold up his end of the patent bargain. After conducting the appropriate analysis under Wands, we conclude that one skilled in the art could not practice the invention claimed in the castor oil patents without undue experimentation. Barr has proven lack of enablement by clear and convincing evidence.

D. Written Description Under 35 U.S.C. § 112, First Paragraph

1. As with enablement, 35 U.S.C. § 112, first paragraph, provides the basis for the written description requirement: “[t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...” (emphasis added).

2. The “test for written description is whether the disclosure of the application reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.” Eli Lilly & Co. v. Teva Pharms. USA, Inc., 619 F.3d 1329, 1345 (Fed. Cir. 2010) (quoting Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc)).
3. As the en banc Federal Circuit recently reaffirmed, Section 112 “contains a written description requirement separate from enablement.” Ariad, 598 F.3d at 1351. However, the purpose of the written description requirement, or at least one of its purposes, mirrors that of the enablement requirement: “[a]s this court has repeatedly stated, the purpose of the written description requirement is to ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor’s contribution to the field of art as described in the patent specification. It is part of the *quid pro quo* of the patent grant and ensures that the public receives a meaningful disclosure in exchange for being excluded from practicing an invention for a period of time.” Id. at 1353-54 (internal citations and quotations omitted).
4. Additionally, the factors relevant to the written description inquiry are similar to the Wands factors we use to analyze enablement: “the nature

and scope of the invention at issue,” “the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.” Boston Scientific Corp. v. Johnson & Johnson, 647 F.3d 1353, 1363 (Fed. Cir. 2011).

5. Here, we have already set forth in detail our reasons for concluding that the asserted castor oil patent claims do not meet Section 112's enablement requirement. (See “Enablement” section, *supra*). Indeed, we believe that the Section 112, first paragraph, analysis in this case proceeds more cleanly through the enablement framework than through a written description-type inquiry.⁶ Nonetheless, given the current state of written description jurisprudence, we find that the castor oil patent claims also fail the written description requirement for essentially the same reasons that they fail the enablement requirement: the art in question is highly unpredictable and the claims are extremely broad, but the written description is relatively limited. (See “Enablement” section, *supra*). Barr has proven that Alcon’s castor oil patents lack an adequate written

⁶In this respect, we agree with Judge Gajarsa that “[t]he enablement requirement of 35 U.S.C. § 112 ¶ 1 is the appropriate tool for invalidating claims that are broader than their disclosure,” and in cases such as this, “the enablement analysis is simpler and more appropriate.” Boston Scientific, 647 F.3d at 1369-70 (Gajarsa, J., concurring-in-part). We certainly see the value in maintaining a separate written description requirement, e.g., “in curtailing claims that do not require undue experimentation to make and use, and thus satisfy enablement, but that have not been invented, and thus cannot be described.” Ariad, 598 F.3d at 1352. However, when a patentee discloses a little but claims a lot, it seems to us that lack of enablement, not lack of an adequate written description, is the primary concern.

description by clear and convincing evidence.

E. Indefiniteness Under 35 U.S.C. § 112, Second Paragraph

1. 35 U.S.C. § 112, second paragraph, requires a patent specification to “conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.” “The purpose of the definiteness requirement is to ensure that the claims delineate the scope of the invention using language that adequately notifies the public of the patentee’s right to exclude.” Young v. Lumenis, Inc., 492 F.3d 1336, 1346 (Fed. Cir. 2007) (citation omitted). In other words, members of the public should be able to read the claims and understand whether or not they infringe the patent. As with any invalidity defense, an accused infringer must prove indefiniteness by clear and convincing evidence. Spanson, Inc. v. Int’l Trade Comm’n, 629 F.3d 1331, 1344 (Fed. Cir. 2010) (“Because a patent is presumed to be valid, the evidentiary burden to show facts supporting a conclusion of invalidity is one of clear and convincing evidence.”) (citation omitted).
2. The Defendant bears a heavy burden in challenging claims as indefinite. “Claims are considered indefinite when they are not amenable to construction or are insolubly ambiguous.... Thus, the definiteness of claim terms depends on whether those terms can be given any reasonable meaning.” Young v. Lumenis, 492 F.3d at 1346 (internal citation and quotation omitted). Relatedly, “close questions of indefiniteness in

litigation involving issued patents are properly resolved in favor of the patentee.” Exxon Research & Eng’g Co. v. United States, 265 F.3d 1371, 1380 (Fed. Cir. 2001).

3. Additionally, “the fact that some experimentation may be necessary to determine the scope of the claims does not render the claims indefinite.” Id. at 1379 (citation omitted). More specifically, the term “‘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.” Geneva Pharms., Inc. v. GlaxoSmithKline PLC, 349 F.3d 1373, 1383-84 (Fed. Cir. 2003).
4. Barr submits that two (2) terms in the castor oil patent claims render the claims indefinite: “therapeutically-effective amount” and “enhancing the chemical stability.” We disagree. The aforementioned phrases are amenable to construction, so Barr failed to prove indefiniteness by clear and convincing evidence.
5. Regarding the “therapeutically-effective amount” limitation, Barr’s experts Dr. Stern and Dr. Kent essentially opine that the term is indefinite because it covers a broad range of prostaglandin concentrations. (Tr. 618:22-619:6; 628:10-629:24; 682). Perhaps it does, but that is not the appropriate test. A functional limitation like “therapeutically-effective amount” is not indefinite as long as a PHOSITA could determine the

claimed amounts without undue experimentation. Geneva, 349 F.3d at 1383-84.

6. Here, the castor oil patent claims are limited to topically administrable ophthalmic compositions. Barr's expert Dr. Stern identified only two (2) potential uses for prostaglandins in such compositions: (1) treating glaucoma / ocular hypertension, and (2) growing longer eyelashes. (Tr. 626:4-628:9). This cabins the amount of experimentation necessary to determine a "therapeutically-effective amount" of prostaglandin in the castor oil patent claims. Additionally, the prior art disclosed prostaglandin dosages effective to treat glaucoma. (Tr. 886-88; 893:7-10; 895:16-19). This makes it even easier for one skilled in the art to determine the metes-and-bounds of the asserted claims.
7. Moreover, Dr. Stern seeks to hold patentees to an overly stringent definiteness standard. According to Dr. Stern's testimony, for a claim to be definite, the patentee must disclose enough information to design a drug "as close to ideal as possible." (Tr. 636:14-23). Section 112 does not mandate such precision. For the aforementioned reasons, we are persuaded that the limitation "therapeutically-effective amount" adequately puts the public on notice of the scope of the asserted claims. Given that the claims are confined to topically administrable ophthalmic compositions, one skilled in the art could determine through routine experimentation what amounts of prostaglandin are "therapeutically-

effective,” especially in light of the prior art disclosures on the topic.

8. Turning now to the phrase “enhancing the chemical stability,” Dr. Kent believes this limitation is indefinite because neither the castor oil patent specification nor the claims disclose an appropriate comparator. (Tr. 682; 814:17-23). He asks, “enhanced [chemical stability] over what?” (Tr. 682:11). We agree that the castor oil patents do not explicitly answer the question, “enhanced over what?”. However, we do not believe this disposes of the indefiniteness question.
9. First, we have already construed the aforementioned limitation to mean “to increase or increasing the ability of the prostaglandin to resist chemical change (as distinguished from merely increasing the physical stability of the prostaglandin or composition.)” (Doc. No. 214). Of course, this still does not answer the “enhanced over what?” question. However, the castor oil patents do not manifest any intent to either (1) give the term “enhancing” any particular art-specific meaning, or (2) limit the claims to those methods in which PECO enhances the chemical stability over a particular alternative surfactant, e.g., Polysorbate 80. As such, we interpret “enhancing” to have its ordinary, customary meaning in the context of the claims. See Abbott Labs. v. Baxter Pharm. Prods., Inc., 334 F.3d 1274, 1278 (Fed. Cir. 2003) (noting that claim term is given its ordinary and customary meaning as long as patentee does not “deviate from the accustomed meaning of the disputed claim term.”).

10. Given the above, one of ordinary skill in the art would understand that the asserted castor oil patent claims require that using PECO in the formulation must provide increased chemical stability as compared to not using PECO. In other words, using the invention must increase the chemical stability of the prostaglandin as compared to not using the invention. Although somewhat shakily, Schneider confirmed this interpretation during his testimony. (Tr. 448:16-449:16 (Answering “[e]nhanced chemical stability in the presence of polyethoxylated castor oil compared to the same vehicles without polyethoxylated castor oils” to the question “[e]nhanced compared to what?”).
11. For these reasons, the claim term “enhancing the chemical stability” can be construed and is not insolubly ambiguous. In fact, if we could not construe the term, then we would not have performed the infringement analysis in this matter, *supra*. See Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1342 (Fed. Cir. 2003) (recognizing that “[o]ne cannot logically determine whether an accused product comes within the bounds of a claim of unascertainable scope.”).
12. For the aforementioned reasons, neither “therapeutically-effective amount” nor “enhancing the chemical stability” render the asserted claims insolubly ambiguous, and Barr failed to prove by clear and convincing evidence that the claims lack definiteness under 35 U.S.C. § 112, second paragraph.

F. Anticipation Under 35 U.S.C. § 102

1. Anticipation requires proof that all of the elements in a patent claim are described within the four corners of a single prior art reference. See Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1335 (Fed. Cir. 2002). Additionally, to establish that a patent is prior art under Section 102(e), it must be filed before the invention by the applicant for patent. Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc., 585 F. Supp. 2d 568, 574-75 (D. Del. 2008).
2. Here, Alcon and Barr dispute whether a particular reference qualifies as prior art. In this regard, Alcon has the initial burden of offering evidence that Mr. Schneider invented the subject matter of his patent prior to the critical date of the reference. Mahurkar v. C.R. Bard, Inc., 79 F.3d 1572, 1576-77 (Fed. Cir. 1996). However, once Alcon adduces such evidence, Barr must prove by clear and convincing evidence that the critical date of the reference precedes Schneider's invention date. Id. at 1578. Otherwise, the reference does not constitute prior art.
3. But what constitutes "invention"? "Conception is the touchstone of inventorship...It is the formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice. The test for conception is whether the inventor had an idea that was definite and permanent enough that one skilled in the art could understand the invention; the inventor must prove

his conception by corroborating evidence, preferably by showing contemporaneous disclosures.” Univ. of Pittsburgh of Commonwealth Sys. of Higher Educ. v. Hedrick, 573 F.3d 1290, 1297-98 (Fed. Cir. 2009) (internal citations and quotations omitted).

4. However, reduction of the invention to practice also matters, in that “priority of invention goes to the first party to reduce an invention to practice unless the other party can show that it was the first to conceive the invention and that it exercised reasonable diligence in later reducing that invention to practice.” Mahurkar, 79 F.3d at 1577 (citation omitted). “To show actual reduction to practice, an inventor must demonstrate that the invention is suitable for its intended purpose.” Id. at 1578.
5. Importantly, a patentee need not show prior inventorship of the entire scope of the claimed invention if the allegedly anticipatory reference discloses only a little. In In re Stempel, 241 F.2d 755, 759 (C.C.P.A. 1957), the court held that in a priority contest, “all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show. When he has done that he has disposed of the reference.” See also Eli Lilly & Co. v. Sicor Pharms., Inc., 705 F. Supp. 2d 971, 994-95 (S.D. Ind. 2010) (applying Stempel to a Section 102 analysis).
6. Here, Barr’s expert Dr. Kent identified only one (1) potentially anticipatory reference, namely U.S. Patent No. 5,721,273, which was filed

on Dec. 15, 1993 and issued on Feb. 24, 1998. (Tr. 825:6-828:18; 923:5-924:2; DTX 806). However, as discussed below, this reference is not prior art because Schneider conceived and reduced to practice enough of his claimed invention prior to Dec. 15, 1993, the filing date of the '273 patent, such that the '273 patent does not constitute prior art with respect to the castor oil patent claims in suit. (Tr. 340-62).

7. Specifically, Schneider testified, and his lab notebooks confirm, that prior to December 15, 1993, Schneider performed experiments to study the stability of AL-6534, a particular prostaglandin, in various vehicles employing different surfactants. (Tr. 350:6-21; 358:22-24). Two (2) of the surfactants Schneider studied were Cremophor® EL and Alkamuls® EL 620, both of which are PECO. (Tr. 355:22-356:8). In fact, these are the same two PECO. (Tr. 355:22-356:8). In fact, these are the same two PECO. ('273 patent, Figures 2-3). Using HPLC, Schneider analyzed samples of the various formulations to determine and compare prostaglandin loss over time. (Tr. 357-61). Schneider found that the tested PECO. (Tr. 357-61). Schneider found that the tested PECO prevented prostaglandin loss much more effectively than Polysorbate 80, a widely-used surfactant in ophthalmic formulations, and Schneider attributed these results to PECO chemically stabilizing the prostaglandin. (Tr. 358-62).
8. The allegedly-anticipatory '273 patent (DTX 806) focuses not on chemical stability, but rather on the efficacy of certain prostaglandin compounds in treating glaucoma. ('273 patent, 1:30-37). One of the disclosed

prostaglandin compositions includes Cremophor® EL ('273 patent, 15:9-36), but the reference does not mention that Cremophor® EL might have a chemically stabilizing effect on the prostaglandin.

9. For the aforementioned reasons, we hold that Schneider conceived and reduced to practice enough of his claimed invention prior to December 15, 1993, the filing date of the '273 patent reference, such that this reference is not prior art with respect to the asserted castor oil patent claims. Stated another way, prior to the '273 patent's filing date, Schneider demonstrated conception and reduction to practice of at least as much of his invention as the '273 patent showed. See Stempel, 241 F.2d at 759. Since the reference is not prior art, it cannot anticipate the claims.
10. Some might perceive a tension between this conclusion, in which we found that Schneider did invent a method of chemically stabilizing prostaglandins using PECO, and our finding of non-infringement that rested largely on the lack of evidence showing that PECO chemically stabilizes prostaglandins. There is no such tension. The different (1) burdens of proof and (2) relevant formulations dictate the different results. To prevail on infringement, *Alcon* had to prove that the PECO in *Barr's ANDA product formulation* chemically stabilizes the prostaglandin Travoprost. Alcon failed to clear this hurdle. On the other hand, in the Section 102 analysis, *Barr* had to prove by clear and convincing evidence that the PECO does not chemically stabilize the prostaglandin in the

formulations in the patent, i.e., that Schneider did not invent the claimed method prior to the critical reference date. Barr failed to meet this burden.

G. Obviousness Under 35 U.S.C. § 103

1. Under 35 U.S.C. § 103(a), “[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 at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.”
2. The Supreme Court’s seminal decision in Graham v. John Deere Co. of Kan. City, 383 U.S. 1, 17-19 (1966) sets forth the basic obviousness framework: in analyzing obviousness, “the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy.”
3. The Court most recently revisited the subject of obviousness in KSR International Co. v. Teleflex Inc., 550 U.S. 398 (2007). In KSR, the Court

endorsed “an expansive and flexible approach” to the obviousness inquiry, rejecting the purportedly “rigid approach” of the Federal Circuit. *Id.* at 415. More specifically, the Court declined to hold that a claim is invalid under Section 103 only if the prior art itself contained a “teaching, suggestion, or motivation” (TSM) to combine the elements of various references in a way that rendered the claimed invention obvious. Instead, the obviousness “analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *Id.* at 418. According to *KSR*, “[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *Id.* at 416.

4. However, post-*KSR*, “a flexible TSM test remains the primary guarantor against a non-statutory hindsight analysis.” *Ortho-McNeil Pharma., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008). Of course, “those teachings, suggestions, or motivations need not always be written references but may be found within the knowledge and creativity of ordinarily skilled artisans.” *Id.* at 1365. The mere fact that it may be “obvious to try” a certain combination does not necessarily render a combination claim obvious. *See Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1352 (Fed. Cir. 2008) (“The Court in *KSR* did not create a

presumption that all experimentation in fields where there is already a background of useful knowledge is ‘obvious to try,’ without considering the nature of the science or technology....Each case must be decided in its particular context...”).

5. Additionally, unexpected results support a finding of non-obviousness. KSR, 550 U.S. at 416 (“The fact that the elements worked together in an unexpected and fruitful manner supported the conclusion that Adams’ design was not obvious to those skilled in the art.”). See also Ortho-McNeil, 520 F.3d at 1365 (declaring that “powerful unexpected results” have “particular importance” to the obviousness inquiry).
6. Here, other than the ‘273 patent, which is not prior art (see “Anticipation” section, *supra*), Barr’s expert Dr. Kent relied on six (6) prior art references to conclude that the castor oil patent claims-in-suit are obvious under Section 103: (1) U.S. Patent No. 4,684,633; (2) Japanese Patent Application S53-148518; (3) U.S. Patent No. 4,430,340; (4) U.S. Patent No. 5,296,504; (5) U.S. Patent No. 5,091,417; and (6) U.S. Patent No. 5,185,372. (Tr. 820-36). However, Dr. Kent’s testimony boils down to simply identifying the individual elements of the claimed invention in various prior art references. (Tr. 818-36). A PHOSITA would have had no reason or motivation to combine the teachings of the six (6) aforementioned prior art references absent impermissible hindsight. Therefore, Barr failed to prove by clear and convincing evidence that the

prior art rendered the asserted castor oil patent claims obvious to a PHOSITA at the time the invention was made.

7. Although a detailed description of each and every prior art reference Barr cited is unwarranted, we will briefly discuss each reference and how it differs from the claimed invention. The '633 patent (DTX 801) is drawn to a prostaglandin emulsion suitable for IV administration. (Abstract). The patent does not concern topical ophthalmic compositions; merely discloses that any of a long list of surfactants, including PECO, may optionally be added to the emulsion as a "high molecular weight compound;" gives no indication that PECO is a preferred surfactant; and does not discuss chemical stabilization of the prostaglandin by PECO.
8. The '518 Japanese patent application (DTX 797) discusses chemically stabilizing PGE prostaglandins (p. 68) with non-ionic surfactants, including "POE castor oil or cured castor oil derivatives," but gives no reason for one skilled in the art to choose PECO from the long list of disclosed surfactants. (p. 68). Although the compositions in '518 may be liquid or solid, i.e., freeze-dried, the only example given containing PECO is freeze-dried. (p. 70).
9. The '340 patent (DTX 796) discloses stabilizing aqueous solutions of PGI₂ compounds with surfactants. (Abstract). However, the patent discloses both cationic and neutral surfactants, and does not even name PECO or castor oil as a potential surfactant. Rather, the surfactant may include

“polyoxyethylated vegetable oils,” (6:40-49), a broad genus that at least arguably includes PECO. Additionally, the ‘340 patent does not mention topically administrable ophthalmic compositions; on the contrary, the disclosed solution is administered via injection. (Tr. 906:10-16).

10. The ‘504 patent (DTX 804) discloses prostaglandin-containing ophthalmic compositions for topically treating glaucoma (Abstract). However, the ‘504 patent does not mention PECO at all. Instead, it discloses that the composition may contain surfactants such as “polysorbate 80, liposomes or polymers, for example methyl cellulose, polyvinyl alcohol, polyvinyl pyrrolidone and hyaluronic acid.” (5:30-42). Additionally, the ‘504 patent does not disclose that the surfactant chemically stabilizes the prostaglandin; rather, the surfactant is added “for increasing the viscosity.” (5:42).
11. The ‘417 patent (DTX 807) concerns a PGE emulsion used to treat hepatitis. (Abstract). The emulsion may contain a nonionic surfactant selected from a list including, among other things, PECO. (3:10-24). Like other previously discussed references, the ‘417 patent does not mention chemical stabilization at all, much less using PECO to chemically stabilize the PGE; provides no reason to choose PECO over the other disclosed nonionic surfactants; and has nothing to do with topically administrable ophthalmic compositions.
12. Finally, the ‘372 patent (DTX 803) is drawn to a “stable aqueous

preparation for ophthalmic topical administration containing vitamin A.” (Abstract). The reference discloses stabilizing vitamin A by emulsifying it in water with a nonionic surfactant. (2:65-3:1). Specifically, “[i]n the aqueous preparation of the present invention, a non-ionic surfactant is used in order to form an emulsion by dispersing vitamin A in the aqueous medium. For a non-ionic surfactant, any of the non-ionic surfactants which are conventionally used as constituents of eye drops may be conveniently used. For example, *either of polysorbate 80 and polyoxyethylenehydrogenated castor oil may advantageously be used.*” (3:32-40) (emphasis added). However, as previously mentioned, the ‘372 patent deals with vitamin A, not prostaglandins.

13. The combination of references that comes the closest to rendering the castor oil patent claims obvious is (1) the ‘504 patent, and (2) the just-discussed ‘372 patent. However, at best, these patents together suggest substituting PECO for polysorbate 80 in the ‘504 patent’s prostaglandin-containing formulations with the expectation of obtaining similar results. After all, the ‘372 patent expresses no preference for either “conventionally-used” surfactant and certainly does not mention that PECO may enhance the chemical stability of prostaglandins (or vitamin A, for that matter). This is not enough to prove obviousness in this case because the castor oil patents show that PECO and Polysorbate 80 are *not* equivalently effective in stabilizing prostaglandins. Instead, PECO

unexpectedly prevents prostaglandin loss much more effectively than Polysorbate 80 does, at least in the tested formulations. ('287 patent, Figures 2-3). These results, unexpected by the prior art, support a finding of non-obviousness. See KSR, 550 U.S. at 416; Ortho-McNeil, 520 F.3d at 1365.

14. At bottom, Barr failed to prove obviousness by clear and convincing evidence. It seems to us that Dr. Kent utilized the castor oil patents as a template and recreated the claimed invention by picking-and-choosing select portions of various references through impermissible hindsight. Even post-KSR, this kind of hindsight reasoning does not suffice to prove obviousness. See Ortho-McNeil, 520 F.3d at 1364 (“a flexible TSM test remains the primary guarantor against a non-statutory hindsight analysis.”). In Dr. Kent’s opinion, combining bits and pieces of the references here is not “an impossible reach.” (Tr. 891:12-17).
Respectfully, the obviousness standard has not gotten so lax, even after KSR. If it ever does, then virtually nothing could be patented.

H. Alcon’s Un-Litigated U.S. Patent Nos. 5,510,383 and 5,889,052

1. “Pleadings do not suffice to support a judgment when the subject matter was not litigated, or fairly placed in issue, during the trial....There must be sufficient and explicit notice of the claims at risk. When the pleadings are not in complete harmony with the issues that were litigated and adjudicated, it is the pleadings that may be conformed to the judgment, not

vice versa.” Tol-O-Matic, Inc. v. Proma Produkt-Und Marketing Gesellschaft m.b.H., 945 F.2d 1546, 1554-55 (Fed. Cir. 1991), *abrogated on other grounds*, Markman v. Westview Instruments, Inc., 52 F.3d 967 (Fed. Cir. 1995).

2. Relatedly, a reference to particular claims in a complaint is not enough to support a judgment with respect to claims not at issue during trial and not actually litigated by the parties. 800 Adept, Inc. v. Murex Sec., Ltd., 539 F.3d 1354, 1367-68 (Fed. Cir. 2008). In fact, passing judgment on patent claims that were never litigated or placed at issue during trial constitutes reversible error. See id. at 1368 (reversing trial court’s judgment of invalidity with respect to unasserted claims).
3. Here, Alcon initially asserted U.S. Patent Nos. 5,510,383 and 5,889,052 against Barr. (Doc. No. 1 ¶¶ 9-22, 50-63). However, Alcon did not assert these two patents in its pretrial filings or at trial, and Alcon did not present any evidence whatsoever on these patents at trial, although Alcon never formally withdrew its claims based on the patents. At the close of Alcon’s case-in-chief, Barr moved for judgment as a matter of law of non-infringement of the ‘383 and ‘052 patents, noting that Alcon presented no evidence on these two patents and therefore cannot meet its burden of proving infringement by a preponderance of the evidence. (Tr. 563:2-15).
4. Since these patents were not at issue during trial and not actually litigated by the parties, Barr is not entitled to a judgment of non-infringement of

these patents. 800 Adept, 539 F.3d at 1367-68. As neither party presented any evidence on the '383 and '052 patents at trial, we decline to make any findings or draw any conclusions about the infringement or validity of the patents.

IV. Conclusion

A. For the aforementioned reasons, we find and declare that (1) Barr's ANDA product, i.e., its generic version of Travatan Z®, does not infringe the asserted castor oil patent claims; (2) the asserted castor oil patent claims are not enabled and lack an adequate written description under 35 U.S.C. § 112, first paragraph; (3) the asserted castor oil patent claims are sufficiently definite under 35 U.S.C. § 112, second paragraph; (4) the prior art does not either anticipate under Section 102 or render obvious under Section 103 the asserted castor oil patent claims; and (5) given Barr's stipulation of infringement, Barr's ANDA product infringes Claims 7, 21, 41, and 43 of the '497 patent and Claim 18 of the '253 patent (the borate-polyol patents). As such, it is hereby ORDERED that the effective date of any FDA approval of Barr's BAC-free ANDA product shall be a date which is not earlier than the date of the expiration of the last to expire of the '497 and '253 patents.

BY THE COURT:

/s/ Legrome D. Davis
Legrome D. Davis, J.

