IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

SENJU PHARMACEUTICAL CO., LTD., KYORIN PHARMACEUTICAL CO., LTD., AND ALLERGAN, INC.,	)	
Plaintiffs,	)	
v.	)	Civ. No. 11-271-SLR (Consol.)
LUPIN LIMITED AND LUPIN PHARMACEUTICALS, INC.,	)	
Defendants.	)	

SENJU PHARMACEUTICAL CO., LTD., KYORIN PHARMACEUTICAL CO., LTD., AND ALLERGAN, INC.,	)	
Plaintiffs,	)	
v.	)	
HI-TECH PHARMACAL CO., INC.,	)	
Defendants.	)	

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OPINION

Dated: August 9, 2013
Wilmington, Delaware

ROBINSON, District Judge

I. INTRODUCTION

This patent infringement litigation is a consolidation of four separate actions by Senju Pharmaceutical Co., Ltd. ("Senju"), Kyorin Pharmaceutical Co., Ltd. ("Kyorin"), and Allergan Inc. ("Allergan") (collectively, "plaintiffs") asserting infringement of reexamined claims 6 and 12-16 of U.S. Patent No. 6,333,045 ("the '045 patent")[1] against Lupin Limited and Lupin Pharmaceuticals, Inc. ("LPI") (collectively, "Lupin"), and Hi-Tech Pharmacal Co. Inc. ("Hi-Tech") (all three collectively "defendants").[2] (D.I. 33, 35; 11-439 D.I. 8; 11-926 D.I. 11; 11-1059 D.I. 9) Defendants answered and Lupin counterclaimed seeking a declaratory judgment of non-infringement and invalidity. (D.I. 138, 139, 143, 144) Plaintiffs answered the counterclaims. (D.I. 146, 147)

On October 8, 2012, Lupin moved for judgment on the pleadings alleging that the narrower reexamined claims of the '045 patent were invalid for obviousness and plaintiffs should be collaterally estopped from relitigating these claims based on the court's finding in *Apotex II*.[3] (D.I. 105) The court found that, although Lupin might later

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[1]Plaintiffs also alleged infringement of original claim 7; however, the Federal Circuit upheld the court's finding that claim 7 was invalid for obviousness. *See Senju Pharmaceutical, Co., Ltd. v. Apotex, Inc.*, No. 2012-1179 (Fed. Cir. Oct. 5, 2012).

[2]The above caption case, filed March 31, 2011, was consolidated with Civ. Nos. 11-439, filed May 18, 2011, against Lupin, as well as 11-926, filed October 11, 2011 and 11-1059, filed October 31, 2011, against Hi-Tech. (D.I. 47) All D.I. # references are to Civ. No. 11-271, unless indicated by "Civ. No. D.I. #." Plaintiffs also alleged infringement by United States Patent No. 5,880,283; however, the parties stipulated to dismiss all claims and counterclaims related to this patent. (D.I. 84, 97)

[3]On June 21, 2010, the court entered judgment in *Apotex I* that original claims 1-3, 6, 7, and 9 of U.S. Patent No. 6,333,045 were infringed, but invalid. *See Senju Pharm Co. Ltd. v. Apotex Inc.*, 717 F. Supp. 2d 404 (D. Del. 2010) (*Apotex I*), aff'd,

succeed in showing that the reexamined claims were invalid, plaintiffs did not fully litigate a claim with a limitation of 0.01 w/v% disodium edetate ("EDTA") and, therefore, collateral estoppel could not apply.[4] (D.I. 135)

The '045 patent is directed to aqueous liquid pharmaceutical compositions comprising gatifloxacin and disodium edetate, as well as various methods utilizing these compositions. (D.I. 33 at ex. A) Plaintiffs allege infringement by Lupin's Abbreviated New Drug Application ("ANDA") Nos. 202-653, 0.5 w/v% gatifloxacin ("Lupin 0.5%") and 202-709, 0.3 w/v% gatifloxacin ("Lupin 0.3%"), as well as Hi-Tech's ANDA Nos. 203189, 0.5 w/v% gatifloxacin ("Hi-Tech 0.5%") and 203190, 0.3 w/v% gatifloxacin ("Hi-Tech 0.3%"),[5] which seek FDA approval to market and sell generic copies of plaintiffs' FDA approved 0.3 w/v % gatifloxacin ophthalmic solution (sold under the trademark "Zymar®") and/or 0.5 w/v % gatifloxacin ophthalmic solution (sold under the trademark "Zymaxid®"), which are the commercial embodiments of reexamined claims 6 and 12-16 of the '045 patent. (*See* JTX 4 (Lupin 0.5%); JTX 5 (Lupin 0.3%); JTX 6 (Hi-Tech 0.5%); JTX 7 (Hi-Tech 0.3%))

The court held a claim construction hearing on December 19, 2012. A bench trial was conducted from January 14-17, 2012, principally to resolve the issues of

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Senju Pharmaceutical, Co., Ltd. v. Apotex, Inc., No. 2012-1179 (Fed. Cir. Oct. 5, 2012) (as to claim 7). After the reexamination certificate issued, plaintiffs filed *Apotex II*, based on reexamined claims 6 and 12-16. *See Senju Pharm Co. Ltd. v. Apotex Inc.*, 891 F. Supp. 2d 656 (D. Del. 2012) (*Apotex II*). The court granted Apotex Inc.'s motion for judgment on the pleadings finding that claim preclusion applied. (*Id.* at 662)

[4]The court declines to entertain defendants' renewed collateral estoppel argument. (D.I. 188 at 49-21)

[5]Collectively "the 0.3% products" and "the 0.5% products."

infringement and invalidity, which have been fully briefed post-trial. (D.I. 163, 172, 178, 179, 182, 183) Having considered the documentary evidence and testimony, the court makes the following findings of fact and conclusions of law pursuant to Fed. R. Civ. P. 52(a).

II. FINDINGS OF FACT

A. The Parties

Senju and Kyorin are corporations organized under the laws of Japan with principal places of business in Osaka and Tokyo, Japan, respectively. (D.I. 33 at ¶ 2, 3) Senju develops pharmaceutical products that have applications regarding the eye, ear, nose, throat and skin. Kyorin engages in the development of pharmaceuticals directed to infectious, immunological, allergic and metabolic diseases. Allergan is a Delaware corporation, having its principal place of business in Irvine, California. (*Id.* at ¶ 4) The business of Allergan is directed to the development and sale of pharmaceuticals, biologies and medical devices.

Lupin Limited is an Indian corporation with a place of business in Mumbai, India. (D.I. 37 at ¶ 5) Lupin develops and manufactures pharmaceutical products, including generic drug products. LPI is a Virginia corporation, having a place of business in Baltimore, Maryland. (*Id.* at ¶ 7) LPI distributes and sells pharmaceutical products. Hi-Tech Pharmacal, Inc is a Delaware corporation with a place of business at 369 Bayview Avenue, Amityville, NY 11701. (11-926 D.I. 1 ¶ 5; 11-926 D.I. 14 ¶ 5) Hi-Tech manufactures, sells and/or offers to sell generic products in the United States.

B. The Patent

On December 25, 2001, the original '045 patent, entitled "Aqueous Liquid Pharmaceutical Composition Comprised of Gatifloxacin," was issued listing Shinichi Yasueda and Katsuhiro Inada as inventors and Senju and Kyorin as assignees. (D.I. 33, ex. A) On February 25, 2011, plaintiffs filed a request for reexamination of claims 1-3, 6, 8 and 9 of the '045 patent and on October 25, 2011, the examiner allowed the following reexamined claims, each of which is at issue:

> 6. A method for raising corneal permeability of an aqueous pharmaceutical Gatifloxacin eye drop solution comprising Gatifloxacin or its salt, having a pH of from above 5 to about 6 containing from about 0.3 to about 0.8 w/v% Gatifloxacin or its salt, which comprises incorporating about 0.01 w/v% disodium edetate into [eye drops containing Gatifloxacin or its salt] said Gatifloxacin eye drop solution.
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> 12. An aqueous liquid pharmaceutical eye drop composition which comprises from about 0.3 to about 0.8 w/v% Gatifloxacin or its salt, about 0.01 w/v% disodium edetate, and wherein the aqueous liquid pharmaceutical composition has a pH of from about 5 to about 6.
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> 13. The aqueous liquid pharmaceutical eye drop composition according to claim 12, comprising about 0.3 w/v% Gatifloxacin or its salt.
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> 14. The aqueous liquid pharmaceutical eye drop composition according to claim 12, comprising about 0.5 w/v% Gatifloxacin or its salt.
>
> 15. The aqueous liquid pharmaceutical eye drop composition according to claim 12, comprising at least one isotonic agent selected from the group consisting of sodium chloride, potassium chloride, glycerin, mannitol and glucose.
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> 16. The aqueous liquid pharmaceutical eye drop composition according to claim 14, wherein the at least one isotonic agent is sodium chloride.

'045 patent, 1:25-2:24.

C. The Asserted Prior Art

1. Gatifloxacin

Fluoroquinolones, otherwise known as quinolone carboxylic acids or simply "quinolones," are a class of broad spectrum antibacterial compounds[6] that share a common core chemical structure. (*See* U.S. Patent No. 4,980,470 ("the '470 patent"), abstract; D.1. 166 at 595:22-596:15) The '470 patent,[7] which was before the examiner during the prosecution of the '045 patent, claims gatifloxacin[8] and its acid derivatives. The properties of this fourth generation quinolone are revealed following a discussion of previously discovered quinolones, to wit, norfloxacin, ofloxacin and ciprofloxacin. ('470 patent, 1:32-61) The '470 patent teaches that gatifloxacin represents an improvement over the prior art quinolones in that it exhibits a broader antibacterial activity, higher selective toxicity and safe oral and parenteral administration. (1:62-2:7) In a passing reference to chemical structure, the '470 patent explains that each of the disclosed quinolones have "similar substituents." (1:41-43) Defendants' expert, Dr. Sherman, testified that the prior art quinolones and gatifloxacin are structurally similar. (D.I. 166 at 595:22-596:15) Dr. Sherman further testified that gatifloxacin is a polar compound due to its ability to readily ionize and because it contains several polar moieties. (*Id.* at 596:16-597:2)

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[6]Quinolones demonstrate high activity against both gram-negative and gram-positive bacteria. ('470 patent, 1:32-35)

[7]The '470 patent issued to Kyorin on December 25, 1990. (JTX 12)

[8]The IUPAC, or systematic, name for gatifloxacin is 1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7(3-methyl-1-piperazinyl)-4-oxo-3-quinoline carboxylic acid.

2. Disodium edetate

Disodium edetate is the disodium salt of ethylenediamine tetraacetic acid (commonly known as "EDTA").[9] (D.I. 166 at 600:25-601:4) EDTA, a multi-purpose excipient,[10] is widely known as a chelating agent.[11] (*Id.* at 589:10-590:12) In Griffith,[12] a September 1967 article, EDTA was found to prevent coloration in a variety of active pharmaceutical ingredients by "sequestering" metal ions through a chelating mechanism. (DTX-981; D.I. 166 at 610-612) Griffith teaches that disodium edetate, in concentrations of between 0.005 and 0.02 w/v%, prevented coloration of papaverine hydrochloride and that, in concentrations between 0.005 and 0.04 w/v%, it similarly prevented coloration in other pharmaceutical agents. (DTX-981)

EDTA is also known to increase corneal permeability of certain polar compounds. (*See* JTX 9) A layer of epithelial cells, bound tightly together by calcium ions, forms a protective barrier that prevents foreign molecules from entering the eye.

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[9]Because the principles of solution chemistry render EDTA and disodium edetate functionally equivalent, and insofar as the parties make no distinguishing arguments on these grounds, the court treats a prior art disclosure of a property of one compound as the disclosure of the property with respect to both, and refers to these compounds interchangeably.

[10]The 1986 Handbook of Pharmaceutical Excipients discloses that EDTA, in addition to its chelating function, may act as an antibacterial synergyst/preservative enhancer. (DTX 1097)

[11]A chelating agent can complex with certain undesirable ions (generally metals), thereby removing them from solution. (D.I. 166 at 589-90)

[12]"Griffith" is D.E. Griffith, *Improvement of the Color Stability of Parenteral Solutions of Papaverine Hydrochloride*, 56 Journal of Pharm. Sciences, 1197-98 (1967). (DTX-981)

(*Id.* at 111) In Grass (1985),[13] considered during the prosecution and reexamination of the '045 patent, the authors sought to determine the effect of EDTA on the permeability of organic and inorganic compounds with respect to the corneal epithelia.[14] (*Id.* at 110) Grass (1985) teaches that EDTA can reduce the number of calcium ions through chelation, thus creating small channels between corneal epithelial cells. (*See id.*) These channels allow polar molecules to penetrate through the cornea into the aqueous humor of the eye. (*See id.*) In reporting the results of this study, Grass (1985) describes how the addition of 0.5 w/v% disodium edetate to separate solutions of glycerol and cromolyn resulted in increased corneal permeability in both solutions. (*Id.* at 112) A lower unspecified concentration of EDTA was also shown to function in this manner, albeit to a lesser extent.[15] (*Id.*) The authors of Grass (1985) conclude that the propensity of EDTA to increase corneal permeability of polar compounds has a "direct bearing upon ophthalmic solutions currently in use."[16] (JTX 12 at 112-13)

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[13]"Grass (1985)" is Grass et al., *Effects of Calcium Chelating Agents on Corneal Permeability*, 26 Investigative Ophthalmology & Visual Science 110 (1985). (JTX 9)

[14]The authors note that "the effects of chelating agents such as EDTA on the permeability of inorganic and organic solutes have been well documented in other epithelia, as well as the corneal endothelium, [but] no definitive studies examining the effects of these compounds upon the corneal epithelia have been reported." (Id.)

[15]In one example, the authors inhibited corneal permeability of a solution of glycerol and 0.5 w/v% EDTA by adding calcium to the solution. This calcium complexes with the EDTA, leaving less EDTA to interact with the calcium ions in the corneal epithelia.

[16]Glycerol is a small polar compound, while cromolyn is a large pharmaceutically active polar compound. (JTX 12 at 112; see also D.I. 166 at 495-97)

After building on this work, Dr. Grass authored two additional papers in 1988.[17] These papers tested lower concentrations of 0.1, 0.05 and 0.01 w/v% EDTA, finding increased corneal permeability at these lower concentrations. (JTX 50; JTX 53) Rojanasakul[18] built further on these teachings by testing EDTA concentrations as low as 0.00037 w/v% EDTA, and finding that even those very low concentrations increased corneal permeability to some degree. (JTX 51 at 5, 12, fig.9)

3. Aqueous quinolone ophthalmic compositions comprising disodium edetate

U.S. Patent No. 4,551,456 ("the '456 patent") issued on November 5, 1985, and teaches that then-known quinolones[19] are both "compatible with ocular tissue" and useful in treating bacterial ocular infections through topical administration. (JTX 10, the '456 patent, 1:13-17) One of two exemplary ophthalmic compositions disclosed by the '456 patent comprises an aqueous solution of 0.3 w/v% norfloxacin and 0.01 w/v% disodium edetate. The '456 patent discloses EDTA in a list of 8 excipients described as "conventional ingredient[s]" in ophthalmic compositions. (*Id.*, col. 2:5-10)

U.S. Patent No. 4,780,465 ("the '465 patent") issued on October 25, 1988, and

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[17]"Grass (1988 I)" is Grass et al., *Mechanisms of Corneal Drug Penetration 1: In Vivo and In Vitro Kinetics*, 77 Journal of Pharm. Sciences 3 (1988). (JTX 50) "Grass (1988 II)" is Grass et al., *Mechanisms of Corneal Drug Penetration II: Ultrastructural Analysis of Potential Pathways for Drug Movement*, 77 Journal of Pharm. Sciences, 15 (1988). (JTX 53) Collectively with Grass (1985), "Grass references."

[18]"Rojanasakul" is Rojanasakul et al., *Mechanisms of action of some penetration Enhancers in the Cornea: Laser Scanning Confocal Microscopic and Electrophysiology Studies*, 66 Int'l Journal of Pharm., 131 (1990). (JTX 51)

[19]The quinolones discussed by the '456 patent include norfloxacin, ofloxacin, perfloxacin, enoxacin and ciprofloxacin. (*Id.* at col. 1:30-36)

discloses aqueous compositions for the quinolone lomefloxacin; it likewise characterizes disodium edetate as a conventional excipient. (JTX 11, the '465 patent, 2:31-46) The '465 patent addresses the low solubility exhibited by lomefloxacin solutions containing sodium chloride, another common eye drop excipient. (3:7-20) The inventors of the '465 patent solve these solubility issues irrespective of the presence of disodium edetate in the composition. Two exemplary ophthalmic compositions described in the '465 patent, similar to the ophthalmic composition disclosed by the '456 patent, contain 0.3 w/ v% lomefloxacin and 0.01 w/v% disodium edetate. (4:1-23)

Consistent with the '456 and '465 patents, the '470 patent discloses that pharmaceutical formulations of gatifloxacin follow "the routes well known . . ." with respect to "oral [ ] and parenteral [ ]" administration, including "liquids [and] eye drops . . . ." (470 patent at col. 7:21-26) While the '470 patent does not provide any guidance regarding these formulations, the 1995 Physician's Desk Reference ("the PDR") provides several example formulations of then available quinolone ophthalmic solutions. (*See* DTX 1098)

III. CONCLUSIONS OF LAW

A. Claim Construction

1. Standard

Claim construction is a matter of law. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1330 (Fed. Cir. 2005) (en banc). Claim construction focuses on intrinsic evidence - the claims, specification and prosecution history - because intrinsic evidence is "the most

significant source of the legally operative meaning of disputed claim language." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996); *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). Claims must be interpreted from the perspective of one of ordinary skill in the relevant art at the time of the invention. *Phillips*, 415 F.3d at 1313.

Claim construction starts with the claims, *id.* at 1312, and remains centered on the words of the claims throughout. *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1331 (Fed. Cir. 2001). In the absence of an express intent to impart different meaning to claim terms, the terms are presumed to have their ordinary meaning. *Id.* Claims, however, must be read in view of the specification and prosecution history. Indeed, the specification is often "the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at 1315.

2. Analysis

The court construes the preamble of claim 6, "[a] method for raising corneal permeability of an aqueous pharmaceutical Gatifloxacin eye drop solution," to mean "[s]howing an increased concentration of gatifloxacin in the aqueous humor."[20] The specification supports this construction, clarifying that it is the pharmacological agent, gatifloxacin, whose corneal permeability is sought to be increased. ('045 patent, 1:27-33, 1:61-2:4) The examiner cited the increase in corneal permeability of gatifloxacin using the 0.01% EDTA as reason for allowance of the reexamined claim. (JTX 3 at

[20]Defendants' position that this construction does not distinguish eye drops from ear or nose drops is not convincing as increasing corneal permeability is logically limited to the eye. Also, the claim ends with "said Gatifloxacin eye drop solution."

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A. Infringement

1. Standard

A patent is infringed when a person "without authority makes, uses or sells any patented invention, within the United States . . . during the term of the patent." 35 U.S.C. § 271(a). A two-step analysis is employed in making an infringement determination. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995). First, the court must construe the asserted claims to ascertain their meaning and scope. *See id.* Construction of the claims is a question of law subject to de novo review. *See Cybor Corp. v. FAS Techs.*, 138 F.3d 1448, 1454 (Fed. Cir. 1998). The trier of fact must then compare the properly construed claims with the accused infringing product. *See Markman*, 52 F.3d at 976. This second step is a question of fact. *See Bai v. L & L Wings, Inc.*, 160 F.3d 1350, 1353 (Fed. Cir. 1998).

"Direct infringement requires a party to perform each and every step or element of a claimed method or product." *BMC Res., Inc. v. Paymentech, L.P.*, 498 F.3d 1373, 1378 (Fed. Cir. 2007), *overruled on other grounds by* 692 F.3d 1301 (Fed. Cir. 2012). "If any claim limitation is absent from the accused device, there is no literal infringement as a matter of law." *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1247 (Fed. Cir. 2000). If an accused product does not infringe an independent claim, it also does not infringe any claim depending thereon. *See Wahpeton Canvas Co. v. Frontier, Inc.*, 870 F.2d 1546, 1553 (Fed. Cir. 1989). However, "[o]ne may infringe an independent claim and not infringe a claim dependent on that claim." *Monsanto Co. v.*

Syngenta Seeds, Inc., 503 F.3d 1352, 1359 (Fed. Cir. 2007) (quoting *Wahpeton Canvas*, 870 F.2d at 1552) (internal quotations omitted). A product that does not literally infringe a patent claim may still infringe under the doctrine of equivalents if the differences between an individual limitation of the claimed invention and an element of the accused product are insubstantial. *See Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 24 (1997). The patent owner has the burden of proving infringement and must meet its burden by a preponderance of the evidence. *See SmithKline Diagnostics, Inc. v. Helena Lab. Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988) (citations omitted).

For there to be infringement under the doctrine of equivalents, the accused product or process must embody every limitation of a claim, either literally or by an equivalent. *Warner-Jenkinson*, 520 U.S. at 41. An element is equivalent if the differences between the element and the claim limitation are "insubstantial." *Zelinski v. Brunswick Corp.*, 185 F.3d 1311, 1316 (Fed. Cir. 1999). One test used to determine "insubstantiality" is whether the element performs substantially the same function in substantially the same way to obtain substantially the same result as the claim limitation. *See Graver Tank & Mfg. Co. v. Linde Air Products Co.*, 339 U.S. 605, 608 (1950). This test is commonly referred to as the "function-way-result" test. The mere showing that an accused device is equivalent overall to the claimed invention is insufficient to establish infringement under the doctrine of equivalents. The patent owner has the burden of proving infringement under the doctrine of equivalents and must meet its burden by a preponderance of the evidence. *See SmithKline*

Diagnostics, Inc. v. Helena Lab. Corp., 859 F.2d 878, 889 (Fed. Cir. 1988) (citations omitted).

2. Discussion

a. Claims 12-16

Plaintiffs presented evidence at trial showing that the ANDA products meet each element of claim 12 and its dependant claims. Although patent infringement and invalidity are separate and distinct issues, defendants presented no evidence of non-infringement at trial and their experts testified that they were not asked to opine on infringement of reexamined claims 12-16. (D.I. 172 at 33; D.I. 166 at 527:19-529:4 (Dr. Grass); D.I. 166 at 654:13-655:8 (Dr. Sherman)); *Medtronic, Inc. v. Cardiac Pacemakers, Inc.*, 721 F.2d 1563, 1583 (Fed. Cir. 1983) ("Though an invalid claim cannot give rise to liability for infringement, whether it is infringed is an entirely separate question capable of determination without regard to its validity.").

In response to plaintiffs' motion for judgment as a matter of law on the issue of infringement, defendants' counsel argued for the first time that the pH ranges described by the ANDA specifications actually allow the products to exceed a pH of 6. (D.I. 167 at 777:18-22) Therefore, "because it is possible for the parties to manufacture a product that's . . . compliant with their ANDA specifications . . . where there is not an overlap of the infringing range called for by the patent," some of defendants' products do not infringe. (*Id.* at 777:24-778:7) This argument only applies to Lupin 0.3% (pH 5.7-6.3) and Hi-Tech 0.3% (pH 5.5-6.5).[21] (JTX 5 LUGA669; JTX 7 at HITECHPHARM3007,

[21]The Lupin 0.5% has a pH range of 5.1 to 5.7 (JTX 4 at LUGA4517) and HiTech 0.5% has a pH range of 5.3 and 5.5 (JTX 6 at HITECHPHARM182).

3128) The court will not entertain this argument which, although creative, was not asserted by defendants prior to trial. There was no expert opinion offered to support it, nor was it vetted through discovery.[22] The court concludes that plaintiffs have demonstrated that the ANDA products infringe the composition claims 12-16 of the '045 patent.

b. Claim 6

Method claim 6 is directed towards an eye drop solution having all the claimed components of claim 12.[23] As the court has construed the language, this claim further requires plaintiffs to show that the solution "show[s] an increased concentration of gatifloxacin in the aqueous humor." Plaintiffs are not required to test defendants' proposed ANDA products, but instead "may prove infringement by any method of analysis that is probative of the fact of infringement, and circumstantial evidence may be sufficient." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1372 (Fed. Cir. 2009). Plaintiffs submit that *in vivo* rabbit eye corneal permeability testing by Senju ("the Senju studies") demonstrates that the addition of 0.01% EDTA increases corneal permeability of gatifloxacin in the proposed 0.3 w/v% and 0.5 w/v% products. The Senju studies, performed prior to the filing of the ANDAs, compared the corneal permeability of a 0.3 w/v% gatifloxacin eye drop solution with another solution identical

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[22]Moreover, this argument is largely contradicted by the evidence of record. The testimony and ANDAs show that 6.0 is the target pH for both the Lupin 0.3% and HiTech 0.3%, which would meet the claim element of about 5 to about 6. (*See e.g.* D.I. 165 at 239:8-240:19, 261:14-262:11; D.I. 165 at 288:3-21; JTX 5 at LUGA141, 661; JTX 7 at HITECHPHARM3040, 3086)

[23]As found above, defendants' products contain all the components of the product claims.

but for the additional inclusion of EDTA. (JTX 15; JTX 16) The results of these studies demonstrated that the gatifloxacin concentrations in the aqueous humor were significantly higher for the solution containing EDTA. (D.I. 165 at 336-339)

Defendants provide several reasons why this evidence cannot demonstrate that the ANDA products infringe claim 6. Defendants argue that, in contrast to the ANDA products, the formulations in the Senju studies did not contain benzalkonium chloride ("BAK"). (JTX 15 at 2; JTX 16 at 2-3) This results in a material difference, according to defendants, because BAK is a known corneal permeability enhancer. (D.I. 165 at 411:10-17 (Dr. Stella); D.I. 166 at 523:13-16; 650:5-653:15 (Drs. Grass and Sherman); *see also* DTX 1063; DTX 1064; DTX 1352) Plaintiffs maintain, based on internal testing, that the inclusion of 0.005 w/v% BAK would not increase, or would minimally increase, the corneal permeability of gatifloxacin. (D.I. 164 95:6-14; D.I. 165 at 346:24-347:6) Consistent with both parties' experts, the court agrees that the inclusion of BAK would not negate the increase in corneal permeability caused by 0.01 w/v% EDTA. (D.I. 165 at 347:12-16; D.I. 166 at 662:4-15)

Defendants criticize the Senju studies, arguing that the triplicate dosing protocol used in JTX 15 cannot provide reliable data for the addition of 0.01 w/v% EDTA and that, because of the low "n" number and the high degree of variability in the results, JTX 16 is not reliable. Further, defendants' expert opined that the studies were not hypothesis driven (the purpose of JTX 15 was to show that 0.01 w/v% EDTA prevents discoloration) and were not subject to peer review. Weighing these criticisms against the opinions of defendants' experts, Dr. Grass and Dr. Sherman, that these side-by-side comparison studies were a "fair" means of assessing the effect of EDTA on the

corneal permeability of gatifloxacin (D.I. 166 at 658:9-20, 491:10-22; D.I. 167 at 839:21-24), the court finds, similarly to *Apotex I*, that the Senju studies are probative and concludes that it is appropriate for the purposes of infringement to equate the 0.3% accused products with the 0.3 w/v% gatifloxacin solution containing disodium edetate from the Senju studies.

As to the 0.5% products, plaintiffs' expert testified that a parallel comparison of a 0.5 w/v% solution with and without 0.01 w/v% EDTA showed an increase in corneal permeability. (JTX 14; D.I. 165 at 408:12-409:1, 410:4-19) Defendants' expert, Dr. Sherman, agreed at deposition that, based on the prior art, he had no reason to think that the 0.01 w/v% EDTA would not increase corneal permeability. (D.I. 166 at 656:17-658:3) Although defendants argue that there is no evidence for Dr. Stella to reliably opine that the 0.05 %w/v solutions infringe, the court disagrees. Based on the testimony presented, there is support for the proposition that the use of EDTA in the 0.5% products also shows an increase in corneal permeability.

Defendants argue that Hi-Tech's addition of gatifloxacin to a solution containing EDTA precludes literal infringement of claim 6, which requires addition of EDTA to a gatifloxacin eye drop solution. (D.I. 179 at 28-29) Plaintiffs respond that the claim does not require the addition of EDTA in any particular order and that Hi-Tech's order of addition results in a bioequivalent solution and infringement under the doctrine of equivalence.[24] "Unless the steps of a method actually recite an order, the steps are not

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[24]Defendants' argument that plaintiffs waived any doctrine of equivalents argument is undermined by Dr. Stella's expert report, where he opines, although briefly, "that the case law permits the steps of a process (e.g. order of addition) to be changed and infringement to be found" and "that whether the addition of disodium edetate

ordinarily construed to require one." *Interactive Gift Express, Inc. v. Compuserve Inc.*, 256 F.3d 1323, 1342-43 (Fed. Cir. 2001). To determine whether the steps of a method claim that do not otherwise recite an order, must nonetheless be performed in the order in which they are written, a court should look to the claim language to determine if, as a matter of logic or grammar, the steps must be performed in the order written and next look to the rest of the specification to determine whether it "directly or implicitly requires such a narrow construction." *Id.* at 1343 (finding that neither the claim or specification required the steps be performed in order and holding that the claim was not limited to embodiments that performed the steps in order, but covered real-time transactions); *Loral Fairchild Corp. v. Sony Electronics Corp.*, 181 F.3d 1313, 1321 (Fed. Cir. 1999) (holding that the claim language itself indicated that the steps had to be performed in their written order because the second step required the alignment of a second structure with a first structure formed by the prior step); *Mantech Envtl. Corp. v. Hudson Envtl. Servs., Inc.*, 152 F.3d 1368, 1375-76 (Fed. Cir. 1998) (holding that the steps of a method claim had to be performed in their written order because each subsequent step referenced something logically indicating the prior step had been performed).

In this case, claim 6 "comprises incorporating about 0.01 w/v% disodium edetate into said Gatifloxacin eye drop solution." The examples in the specification recite formulations and specify that "aqueous liquid preparations of Gatifloxacin were

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occurs before or after the addition of Gatifloxacin, the same increased corneal permeability would be obtained over that identical solution but without disodium edetate, and would [sic] it would be achieved in the same manner by including disodium edetate in a eye drop solution containing Gatifloxacin." (D.I. 182, ex. 2 at ¶¶ 134, 141, 158, 162)

prepared" without describing or attributing any importance to the order of addition of the ingredients. ('045 patent, 4:24-27, tbl.3, 5:39-8:10) In one example, the gatifloxacin and EDTA were added at the same time. (*Id.* at 4:63-66) The court concludes that no order of addition is necessarily described or required.

For completeness, the court turns its attention to the doctrine of equivalents argument, wherein plaintiffs contend that

> Hi-Tech's inclusion of 0.01 w/v% EDTA prior to the addition of gatifloxacin has no effect on the final product's qualities and performs the same function (increasing corneal permeability of gatifloxacin), in the same way (by including 0.01 w/v% EDTA in the solution), and achieves the same result (increased concentration of gatifloxacin in the aqueous humor) as including 0.01 w/v% EDTA after the addition of gatifloxacin.

(D.I. 182 at 21 (citing D.I. 165 at 356:24-358:7, 285:8-286:7; D.I. 172 at 45-48) While "the bioequivalency of an accused product with a product produced from the patent at issue is not sufficient to establish infringement by equivalents," bioequivalence "may be relevant to the function prong of the function-way-result test. *Abbott Laboratories v. Sandoz, Inc.*, 566 F.3d 1282, 1298 (Fed. Cir. 2009). Here, Hi-Tech relied on the similarity of its products to plaintiff's products to obtain a bioequivalence waiver. (D.I. 179 at 30) Hi-Tech dissolves EDTA in purified water for the ease of manufacturing. No testimony was offered that the order of addition of the components is material to the properties of the eye drop solutions. The purpose of the patent is the **inclusion of EDTA** to increase the corneal permeability of gatifloxacin. Even if the court accepts defendants' argument that the function of the "incorporating" step is to incorporate EDTA into a gatifloxacin solution, the incorporation of EDTA into a solution is the

process step and this step is also accomplished in Hi-Tech's process, albeit that EDTA is added before the gatifloxacin.

As discussed above, defendants' products contain each of the components of claim 6. Further, the court is satisfied that the accused products additionally satisfy the limitation of increasing the corneal permeability of gatifloxacin. Therefore, the court concludes that plaintiffs have shown, by a preponderance of the evidence, that defendants' ANDA products infringe claim 6.[25]

c. Miscellaneous defenses to infringement

Lupin argues that its products are made in India; specifically, the "incorporation" step is performed in India and, therefore, it cannot be found liable under 35 U.S.C. § 271(a) or (g) for methods that do not occur in the United States. (JTX 4 at 77; JTX 5 at 75; D.I. 167 at 752:16-19; 761:11-14) Plaintiffs respond seeking a declaration that claim 6 is infringed under U.S.C. § 271(a) because Lupin's products are made by the process of claim 6. The court concludes that Lupin's sale within the United States of its ANDA products will infringe under § 271 (g) as it will "import[] into the United States or offer[] to sell . . . within the United States a product which is made by a process patented in the United States."[26]

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[25]The court declines to entertain defendants' defense that their products do not infringe because they are not seeking to use them to "raise corneal permeability." This defense was raised for the first time in the pre-trial order and was not vetted through discovery. (D.I. 136, ex. 5 at ¶¶ 59-62)

[26]Defendants' cited cases are inapposite. See *Joy Technologies, Inc. v. Flakt, Inc.*, 6 F.3d 770, 773-74 (Fed. Cir. 1993) (holding that the sale of equipment which performs a patented process is not itself direct infringement of the process); *NTP, Inc. v. Research In Motion, Ltd.*, 418 F.3d 1282, 1323-24 (Fed. Cir. 2005) (determining that email packets were not physical products, thus § 271 (g) could not apply).

B. Obviousness

1. Standard

"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." 35 U.S.C. § 103(a). Obviousness is a question of law, which depends on several underlying factual inquiries.

> Under § 103, 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.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 406 (2007) (quoting *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966)).

"[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *KSR*, 550 U.S. at 418. Likewise, a defendant asserting obviousness in view of a combination of references has the burden to show that a person of ordinary skill in the relevant field had a reason to combine the elements in the manner claimed. *Id.* at 418-19. The Supreme Court has emphasized the need for courts to value "common sense" over "rigid preventative rules" in determining whether a motivation to combine existed. *Id.* at 419-20. "[A]ny need or problem known in the field of endeavor at the

time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed." *Id.* at 420. In addition to showing that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed process, a defendant must also demonstrate that "such a person would have had a reasonable expectation of success in doing so." *PharmaStem Therapeutics, Inc. v. ViaCell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007). "Because patents are presumed to be valid, see 35 U.S.C. § 282, an alleged infringer seeking to invalidate a patent on obviousness grounds must establish its obviousness by facts supported by clear and convincing evidence." *Kao Corp. v. Unilever U.S., Inc.*, 441 F.3d 963, 968 (Fed. Cir. 2006) (citation omitted). In conjunction with this burden, the Federal Circuit has explained that,

> [w]hen no prior art other than that which was considered by the PTO examiner is relied on by the attacker, he has the added burden of overcoming the deference that is due to a qualified government agency presumed to have properly done its job, which includes one or more examiners who are assumed to have some expertise in interpreting the references and to be familiar from their work with the level of skill in the art and whose duty it is to issue only valid patents.

PowerOasis, Inc. v. T-Mobile USA, Inc., 522 F.3d 1299, 1304 (Fed. Cir. 2008) (quoting *Am. Hoist & Derrick Co. v. Sowa & Sons*, 725 F.2d 1350, 1359 (Fed. Cir. 1984)).

2. Discussion

The differences between the reexamined '045 patent claims and the prior art may be summarized as: (1) using 0.3 w/v% to 0.8 w/v% gatifloxacin; (2) having a pH of above 5 to about 6; and (3) using 0.01 w/v% EDTA to increase corneal permeability. (D.I. 178 at 29; D.I. 183 at 1) As the court recognized in its order on defendants' motion

for judgment on the pleadings, the court in *Apotex I* did not make specific findings for a claim with a limitation of 0.01 w/v% EDTA. (D.I. 135 at 7) While plaintiffs remain determined to reargue each limitation of the reexamined claims, the court will not entertain each of these as new arguments separate from its findings in *Apotex I*.

a. Claims 12-16

The court adopts its previous analysis of the use of gatifloxacin and EDTA. Specifically, the court concludes that "it would be obvious for one of ordinary skill to substitute the gatifloxacin of the '470 patent for any of the quinolones described by the '456 patent in the prior art quinolone compositions . . . ." *Apotex I*, 717 F. Supp. at 421. Thus, the use of gatifloxacin for an ophthalmic solution is obvious in view of the '456 and '470 patent. *Id.* at 420-21. Moreover, the court again declines to accept the characterization of the prior art disclosure of EDTA as among a laundry list of excipients, as EDTA is listed among eight "conventional ingredients" in the '456 patent and a similarly small group of excipients, making it not remotely approaching an infinite genus. ('456 patent, 2:1-16; '465 patent, 2:36-49); see *Apotex I*, 717 F. Supp. at 420 (citing *In re Baird*, 16 F.3d 380, 382 (Fed. Cir. 1994)). The court also adopts its conclusion that the use of gatifloxacin with EDTA would have been obvious to a person of skill in the art. With this preliminary guidance, the court turns its attention to the particular issues of the reexamined claims, specifically, narrower ranges for both gatifloxacin and EDTA.

The use of 0.3 to 0.8 w/v% of gatifloxacin is outlined in the prior art. ('456 patent, 1:37-43 ("from about 0.03 to 3%"); '465 patent, 2:22-25 ("preferably about 0.3%

to 5% w/v"). The court concludes that the concentration range of gatifloxacin in the reexamined claims is explicitly recited in the prior art. Moreover, the use of 0.01 w/v% of EDTA was also known:

> [T]he prior art reveals that disodium edetate is a conventional excipient with beneficial properties used in aqueous ophthalmic quinolone compositions. Multiple commercial and noncommercial quinolone compositions utilized disodium edetate **in an amount of 0.01 w/v%**, i.e., within the concentration range of 0.001 to 0.2 w/v% claimed by the '045 patent.

Apotex I, 717 F. Supp. at 421. Specifically, the '456 patent discloses an exemplary formulation of a 0.3% quinolone solution that incorporates 0.01 w/v% EDTA. (4:1-23)

Plaintiffs argue that the pH range from about 5 to about 6 distinguishes the claims from the prior art. The court disagrees. The prior art ophthalmic quinolone compositions included eye drops maintained at a pH of between 5 and 8. See *Apotex I*, 717 F. Supp. at 420. Specifically, the '456 patent teaches solutions with a pH of 5.2. (3:35-37; *see also* D.I. 166 at 591:19-592:4; 629:17-630:7) The '465 patent teaches solutions with pH ranges between 3 and 6.5 (2:32) and with the preferred range of 4 to 6.5 (2:32-33). (*See also* D.I. 166 at 593:1-6; 629:17-630:7; D.I. 167 at 799:1-2) The target pH in the examples of the '465 patent is 6.0. (*Id.* at 3:24-4:34) Therefore, the pH range does not distinguish the reexamined claims from the prior art.

The court concludes that the combination of the '456, '465 and '470 patents discloses each limitation of the product claims.[27] Defendants have presented a prima

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[27]Plaintiffs contend that these references do not address improving corneal permeability and, further, that the inventors of the '045 patent encountered challenges and "methodically experimented with various formulations for efficacy and stability before accidentally happening upon low concentrations of EDTA as a successful

facie case of obviousness with respect to claims 12-16. It would have been obvious for one of ordinary skill to arrive at the products of the reexamined claims 12-16 of the '045 patent, with the reasonable expectation that it would result in an aqueous formulation, by substituting the gatifloxacin of the '470 patent for any of the quinolones described by the '456 patent, in the prior art quinolone compositions comprising disodium edetate, as described in the '465 patent.

b. Claim 6

Defendants rely on the '456, '465, '470 patents, the Grass references, and Rojanasakul to argue that the method of claim 6 is obvious, i.e., to show that using 0.01 w/v% EDTA would result in an increase in corneal permeability. Plaintiffs argue that the prior art does not teach or suggest using the combination of 0.01 w/v% EDTA with a gatifloxacin ophthalmic solution at a pH of from about 5 to about 6 to create a stable solution with increased corneal permeability. The court begins with the reasoning from *Apotex I*, namely, that

> [w]ith respect to the . . . [EDTA] concentration range of 0.001 to 0.2 w/v%, the record demonstrates that one skilled in the art would understand [Grass (1985)] to suggest that EDTA concentrations lower than 0.5 w/v% would be effective in view of the increased corneal permeability of the 0.5 w/v% EDTA formulation to which calcium was added. Accordingly, one of ordinary skill would apply this teaching in conjunction with the pre-existing quinolone formulations, which incorporated between 0.05 and 0.1 w/v% EDTA, in arriving at a gatifloxacin formulation characterized by increased corneal permeability.

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excipient that unexpectedly increased the corneal permeability of the gatifloxacin." (D.I. 178 at 30-34) The court declines to address this argument with respect to claims 12-16, as the product claims do not include a limitation of increasing corneal permeability.

Apotex I, 717 F. Supp. 2d at 421-22. The court concluded that "the step of adding [EDTA] (even at a concentration as low as 0.1 w/v%) to a solution of gatifloxacin eye drops would demonstrate an increased concentration of gatifloxacin in the aqueous humor."

Plaintiffs assert that the prior art teaches that the use of 0.01 w/v% EDTA fails to increase corneal permeability of either of the polar compounds tested. (JTX 50 at tbl. XIII and JTX 53 at 5, 9) The record reflects otherwise. The prior art teaches that adding EDTA to any polar compound solution will increase corneal permeability dose-dependently. (D.I. 166 at 505:11-22; *see, e.g.*, the Grass references) After experimenting with higher concentrations, Grass (1988 I) tested 0.1, 0.05, and 0.01 w/v% of EDTA, finding that each concentration raised corneal permeability; however, the increases were not all statistically significant. (JTX 50 at tbl. XIII) Specifically using 0.01 w/v% EDTA, the researchers found a permeability coefficient for methanol of 99.5 (control was 91.3) and for glycerol, 4.53 (control was 4.47).[28] (*Id.*) Researchers

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[28]Table 50 is reproduced below:

Name	Added Agent	P x $10^{5, a}$	95% CL x $10^{5, b}$	Percent Change in Permeability over Control
Methanol	Control	91.3	9.4	—
Methanol	0.01% EDTA	99.5	6.0	0
Methanol	0.1% EDTA	108.9	14.0	0
Glycerol	Control	4.47	2.45	—
Glycerol	0.01% EDTA	4.53	1.61	0
Glycerol	0.05% EDTA	8.41	1.46	88
Glycerol	0.1% EDTA	18.2	7.4	307

[a]Permeability coefficient. [b]95% confidence limit.

calculated the percent change in permeability over the control, which was zero for both methanol and glycerol. (*Id.*) Plaintiffs focus on this percent change to conclude that the data showed no increase in corneal permeability. Defendants concede that the percent changes were not statistically significant; however, defendants' expert points out that a person of ordinary skill would have recognized from the data that the 0.01 w/v% EDTA would increase corneal permeability. (D.I. 166 at 622-624) This is also consistent with further research, such as Rojanasakul, which tested concentrations of EDTA as low as 0.00037 w/v% and confirmed a dose dependent relationship between EDTA concentration and corneal permeability. (JTX051 at 5, 12, fig.9; D.I. 166 at 513-515; D.I. 167 at 689:20-25) The court concludes that the prior art suggests the use of concentrations as low as 0.01 w/v% EDTA would be effective to increase corneal permeability.

Finally, and contrary to plaintiffs' contentions,[29] the prior art ophthalmic quinolone compositions included eye drops maintained at a pH of between 5 and 8; for example, the '456 patent used a pH of 5.2 and the '465 patent a target pH of 6.0. The court concludes that the prior art teaches the pH range of claim 6.

A finding of obviousness of claim 6 does not require that the prior art teach or suggest the formation "of a stable, highly permeable gatifloxacin solution . . . adding 0.01 w/v% EDTA to a gatifloxacin ophthalmic formulation at a pH of from about 5 to

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[29]Plaintiffs contend that gatifloxacin's corneal permeability dropped in tests where the pH was lowered from 7 to 5 and that the prior art teaches the use of higher pH, referencing Rojanasakul and Grass references using a pH of 7.4. (JTX 13 at 9; D.I. 164 at 94:20-23) Plaintiffs' contentions ignore the focus of the prior art and the '045 patent, increasing corneal permeability using EDTA.

about 6." (D.I. 172 at 18) Instead, the law of obviousness looks to the subject matter as a whole and the reason to combine the elements in the manner claimed. *See* 35 U.S.C. § 103(a); *KSR*, 550 U.S at 418-19. As the parties agree that corneal permeability is a desirable property of an ophthalmic drug formulation, one of ordinary skill would place value on references showing the use of EDTA and gatifloxacin. The record demonstrates that a person of ordinary skill in the art would have been motivated to use gatifloxacin and EDTA together. The pH and EDTA concentration limitations of plaintiffs' claim 6 are found in the prior art. The court concludes that defendants have met their burden of showing, by clear and convincing evidence, that method claim 6 is obvious in light of the '456, '465, '470 patents, the Grass references, and Rojanasakul.

Plaintiffs argue that, even if defendants meet their prima facia case of obviousness (which they have), claim 6 is not obvious because of the unexpected result of "dramatically increased corneal permeability of gatifloxacin."[30] (D.I. 178 at 37) Plaintiffs rely on their interpretation of Grass (1988 I), i.e., that zero increase in corneal permeability would be expected when using 0.01 w/v% EDTA. (*Id.* at 37-38) The court agrees with defendants' expert and finds this interpretation incorrect as explained above.[31] Based on the dose dependent correlation (lower amounts of EDTA give lower increases in corneal permeability), the raw data in Grass (1988 I) and the further research in Rojanasakul show that the use of 0.01 w/v% EDTA would still show an increase in corneal permeability.

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[30]While plaintiffs present this theory for all asserted claims, as previously noted by the court, increased corneal permeability is not a limitation of product claims 12-16.

[31]See analysis of infringement of claim 6 at Part B.2.b.

Plaintiffs' arguments that the magnitude of the increase in corneal permeability with 0.01 w/v% EDTA is unexpected are equally unavailing.[32] Plaintiffs assert that the small increase shown in the Grass (1988 I) data would lead a researcher to predict a smaller increase, if any, in corneal permeability. (D.I. 178 at 44) Therefore, according to plaintiffs, the 40% increase in corneal permeability measured over two hours in JTX 15 (using three instillations at 15 minute intervals) and the 29% increase in JTX 16 (single instillation) are "completely unexpected effect[s]." (*Id.*) Dr. Stella did not use a statistical analysis to arrive at this conclusion, but relied on the data points shown in the studies.[33] (*See* 167 at 828: 13-22)

In contrast, defendants argue that, even accepting these percent increases,[34] modifying the pH from 7 to 6 leads to a 30% change in permeability. (D.I. 165 at 404 (Dr. Stella)) The '045 patent shows an increase in corneal permeability from 1.30 to 1.93 µg/ml (67%) with the use of 0.05 w/v% EDTA. (D.I. 183 at 17 (citing JTX 1 at tbl.2)) Based on the record and testimony offered, the court concludes that the increase in corneal permeability shown by plaintiffs using a 0.01 w/v% EDTA is not unexpected or surprising.[35] Instead, it is a product of routine optimization that would

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[32]Although defendants argue that this argument was first presented at trial, as the "unexpected results" argument was vetted through discovery, the court will consider the additional argument.

[33]This is in contrast to plaintiffs' repeated arguments that the actual data points in Grass (1988 I) should be ignored.

[34]Plaintiffs did not account for the large error bars seen in the data. (D.I. 167 at 741:6-13)

[35]The court declines to consider plaintiffs' additional argument that the results were unexpected because of the "relative size" of the gatifloxacin molecule, as it was

have been obvious to one of skill in the art. *See Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364, 1370 (Fed. Cir. 2007) (finding that "case law is clear that 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"). For the foregoing reasons, the court finds that the asserted claims of the '045 patent are invalid for obviousness.[36]

D. Intervening Rights

1. Standard

The doctrine of intervening rights recognizes the public's right to use what is not specifically identified in a patent as originally filed. *See, e.g., Seattle Box Co., Inc. v. Indus. Crating and Packing Inc.*, 756 F.2d 1574, 1579 (Fed. Cir. 1985). Claims amended during reexamination, if they are legally "identical" to the claims of the original patent,[37] can be enforced for the period prior to the issuance of the reexamination certificate. *See, e.g., Minco, Inc. v. Combustion Eng'g, Inc.*, 95 F.3d 1109, 1115 (Fed. Cir. 1996); *Kaufman Co. v. Lantech, Inc.*, 807 F.2d 970, 976 (Fed. Cir. 1986). On the other hand, an infringer who was engaged in allegedly infringing activities (or "substantial preparation was made by the infringer" to do so) before a reexamination certificate issued may continue to infringe said claims, if the court determines that the

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presented for the first time at trial and is outside the scope of the expert report. (D.I. 178 at 42-43)

[36]As the court found in the pre-trial conference that enablement was not properly presented as a defense, the court declines to allow defendants to pursue this argument. (D.I. 142 at 53:22-55:4)

[37]"Identical" does not mean verbatim, but rather means without substantive change. *See e.g., Westvaco Corp. v. Int'l Paper Co.*, 991 F.2d 735, 741 (Fed. Cir. 1993).

reexamined claims are not "without substantive change" compared to the original claims, and to the extent and under such terms as the court deems equitable for the continued manufacture, use or sale of an allegedly infringing product. *See, Seattle Box*, 756 F.2d at 1579. Therefore, the doctrine of intervening rights is a defense to infringing activity occurring after reexamination. *See, e.g., Fortel Corp. v. Phone–Mate, Inc.*, 825 F.2d 1577, 1580 (Fed. Cir. 1987).

Equitable intervening rights are based in the second sentence of the second paragraph of 35 U.S.C. § 252 and concern the manufacture, use, or sale of specific things after the issuance of a reissued or reexamined patent. Under equitable intervening rights, an infringer may continue to manufacture, use or sell additional products covered by the reissued or reexamined patent when the infringer made, purchased, or used identical products, or made substantial preparation to make, use or sell identical products, before the issuance of the reissued or reexamined patent. Thus, under equitable intervening rights, a court may protect investments made before the grant of the reissued or reexamined patent, if the equities dictate such a result. *BIC Leisure Prods., Inc. v. Windsurfing Int'l Inc.*, 1 F.3d 1214, 1221 (Fed. Cir. 1993).

2. Analysis

The court agrees with defendants that the reexamined claims are new or amended and substantively changed. *See Bloom Eng'g Co., Inc. v. N Am. Mfg. Co.*, 129 F.3d 1247, 1249-50 (Fed. Cir. 1997) (an amendment which narrows the scope of the claim may be considered a "substantive change" sufficient to invoke the doctrine of intervening rights). As the court has found the reexamined claims infringed, but invalid,

defendants' intervening rights defense is moot. As such, the court declines to undertake an examination of this argument herein.

E. LPI is a proper party

LPI describes itself as "the U.S. wholly owned subsidiary of Lupin Limited, which is among the top five pharmaceutical companies in India." Further, LPI "intends to bring a portfolio of generics as well as branded products to the US market." *See*, http://www.lupinpharmaceuticals.com/about.htm. With these statements, the court declines to accept defendants' argument that LPI is not the ANDA applicant and will not benefit economically. Clearly, LPI served as an agent on its parent company's behalf and countersigned the ANDA application. (JTX 4; JTX 5) As its mission is to become a "transnational pharmaceutical company," LPI cannot argue that it will not benefit economically. Therefore, the court concludes that LPI is a proper party to the case at bar.

F. Attorney Fees and Costs

Pursuant to 35 U.S.C. § 285, "[t]he court in exceptional cases may award reasonable attorney fees to the prevailing party." In order to determine whether a case is exceptional and, therefore, eligible for an award of attorney fees, the court undergoes a two-step process. *See Eon–Net LP v. Flagstar Bancorp*, 653 F.3d 1314, 1323–24 (Fed. Cir. 2011). The district court must first "determine whether the prevailing party has proved by clear and convincing evidence that the case is exceptional." Id. (citing *Forest Labs., Inc. v. Abbott Labs.*, 339 F.3d 1324, 1327 (Fed. Cir. 2003)). "Second, if the district court finds the case to be exceptional, the court must then determine

whether an award of attorney fees is appropriate and, if fees are appropriate, the amount of the award." *Id.* (citing *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1460 (Fed. Cir. 1998)).

Plaintiffs assert that defendants increased the cost of litigation by refusing to stipulate to infringement of the reexamined claims and maintaining that LPI was not a proper party to the case. (D.I. 172 at 54-55) Defendants counter that plaintiffs should have stipulated to the invalidity of claims 12-16. The court denied Lupin's motion for judgment on the pleadings, wherein Lupin alleged that the narrower reexamined claims of the '045 patent were invalid for obviousness and plaintiffs should be collaterally estopped from relitigating these claims based on the finding in *Apotex II*. At the pre-trial conference and at trial, both parties advanced theories not vetted through discovery and beyond the scope of the expert reports. Thus, the court will not award attorney fees to either party.

IV. CONCLUSION

For the foregoing reasons, the court finds that defendants infringe claims 6, 12-16 and that claims 6, 12-16 of the '045 patent are invalid for obviousness. An appropriate order shall issue.