IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PFIZER INC., WARNER-LAMBERT COMPANY L.L.C., C.P. PHARMACEUTICALS INTERNATIONAL C.V., and NORTHWESTERN UNIVERSITY,	)	
Plaintiffs,	)	
v.	)	C.A. No. 09-cv-307 (GMS) (Consolidated)
TEVA PHARMACEUTICALS U.S.A., INC., and TEVA PHARMACEUTICAL INDUSTRIES, LTD., et al.,	)	
Defendants.	)	

MEMORANDUM

I. INTRODUCTION

In this consolidated patent infringement action, plaintiffs Pfizer Inc., Warner-Lambert Company, L.L.C., C.P. Pharmaceuticals International C.V., and Northwestern University (collectively, "the plaintiffs") allege that pharmaceutical products proposed by defendants Actavis Elizabeth, L.L.C., Actavis, Inc., Alphapharm Pty. Ltd., Mylan Pharmaceuticals, Inc., Cobalt Laboratories, Inc., Lupin Ltd., Sandoz, Inc.,[1] Sun Pharma Global, Inc., Sun Pharmaceutical Industries, Ltd., Sun Pharmaceutical Industries, Inc., Teva Pharmaceuticals U.S.A., Inc., Teva Pharmaceutical Industries, Ltd., Wockhardt Limited, and Wockhardt U.S.A., L.L.C. (collectively, "the defendants") infringe the asserted claims of the patents-in-suit. (D.I. 1.) The court held a nine-day bench trial in this matter on October 11 through October 21, 2011. (D.I. 362-370.) Presently before the court are the parties' post-trial Findings of Fact and

[1] The plaintiffs stipulated to dismissal of Sandoz without prejudice on October 13, 2011. (D.I. 337.) As a result, the court does not include Sandoz in its discussion of "the defendants" in the "Discussion and Conclusions of Law" section.

Conclusions of Law concerning the validity of the patents-in-suit and whether the defendants' proposed products infringe the patents-in-suit. (D.I. 349-353.)

Pursuant to Federal Rule of Civil Procedure 52(a), and after having considered the entire record in this case and the applicable law, the court concludes that: (1) the asserted claims of the patents-in-suit are not invalid due to obviousness; (2) the asserted claims of the patents-in-suit are not invalid due to anticipation; (3) the asserted claims of the '819 and '175 Patents are entitled to a November 27, 1990 priority filing date; (4) the asserted claims of the '819 Patent are not invalid for written description[2]; (5) the asserted claims of the '819 Patent are not invalid due to improper inventorship; (6) the defendants' proposed products do not literally infringe claims 1 and 4 of the '819 Patent; (7) the defendants' proposed products infringe claims 1 and 4 of the '819 Patent under the doctrine of equivalents; (8) the '819 and '876 Patents' term extensions are not invalid under 35 U.S.C. § 156; and (9) each of the parties' Rule 52(c) motions are granted in part and denied in part. These findings of fact and conclusions of law are set forth in further detail below.

II. FINDINGS OF FACT[3]

A. The Parties

1. Plaintiff Pfizer Inc. ("Pfizer") is a corporation organized and existing under the laws of the State of Delaware, having a place of business at 235 East 42nd Street, New York, New York 10017.

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[2] The court notes that only defendant Sun Pharma raised the invalidity written description defense.

[3] Prior to trial, the parties submitted an exhibit of uncontested facts in conjunction with their Pretrial Order. (D.I. 324, Ex. 1.) The court takes most of its findings of fact from the parties' uncontested facts. Where necessary, the court has overruled objections to the inclusion of these facts. The court has also reordered and renumbered some paragraphs, corrected some spelling and formatting errors, and made minor edits for the purpose of concision and clarity that it does not believe alters the meaning of the paragraphs from the Pretrial Order. Otherwise, any differences between this section and the parties' statement of uncontested facts are unintentional.

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

2. Plaintiff Warner-Lambert L.L.C. ("Warner-Lambert") is a limited liability company organized and existing under the laws of the State of Delaware, having a place of business at 235 East 42nd Street, New York, New York 10017. Pfizer Inc. is the ultimate parent of Warner-Lambert Company L.L.C.

3. Plaintiff C.P. Pharmaceuticals International C.V. ("CPPI CV") is a limited partnership organized under the laws of the Netherlands, having its registered seat in Rotterdam, and is represented by its general partners, Pfizer Manufacturing L.L.C., a limited liability company organized under the laws of the State of Delaware and having a place of business at 235 East 42nd Street, New York, New York 10017 and Pfizer Production L.L.C., a limited liability company organized under the laws of the State of Delaware, and having a place of business at 235 East 42nd Street, New York, New York 10017, jointly acting, each in its capacity as a general partner for and on behalf of CPPI CV. Pfizer Inc. is a limited partner of and is the ultimate parent of all other partners of CPPI CV.

4. Plaintiff Northwestern University ("Northwestern") is an Illinois corporation, having its principal place of business at 633 Clark Street, Evanston, Illinois.

5. Defendant Actavis Elizabeth L.L.C. is a limited liability company organized and existing under the laws of the State of Delaware, having a principal place of business at 200 Elmora Avenue, Elizabeth, New Jersey. Actavis Elizabeth L.L.C. is a wholly owned subsidiary and agent of defendant Actavis, Inc.

6. Defendant Actavis, Inc. (together with Actavis Elizabeth L.L.C., "Actavis") is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 60 Columbia Road, Building B, Morristown, New Jersey.

7. Defendant Alphapharm Pty. Ltd. ("Alphapharm") is a corporation organized and existing under the laws of Australia, having a principal place of business at Chase Building 2, Wentworth Park Road, Glebe, NSW 2037, Australia.

8. Defendant Mylan Pharmaceuticals Inc. ("Mylan") is a corporation organized and existing under the laws of the State of West Virginia, having a principal place of business at 781 Chestnut Ridge Road, Morgantown, West Virginia 26505.

9. Defendant Cobalt Laboratories, Inc. is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 24840 South Tamiami Trail, Ste. 1, Bonita Springs, Florida.

10. Defendant Cobalt Pharmaceuticals, Inc. (together with Cobalt Laboratories, Inc., "Cobalt"), a sister company of Cobalt Laboratories, Inc., is a corporation organized and existing under the laws of Canada having a principal place of business at 6500 Kitmat Road, Mississauga, Ontario, Canada.

11. Defendant Lupin Ltd. is a company organized and existing under the laws of India, having a principal place of business at Laxmi Towers, B Wing, Bandra Kurla Complex, Bandra (East), Mumbai, Maharashtra 400 051, India.

12. Defendant Lupin Pharmaceuticals, Inc. (together with Lupin Ltd., "Lupin") is a corporation organized and existing under the laws of the State of Virginia, having a principal place of business at 111 South Calvert Street, Ste. 2150, Baltimore, Maryland. Lupin Pharmaceuticals, Inc. is a wholly-owned subsidiary of Lupin Ltd.

13. Defendant Sandoz, Inc. ("Sandoz") is a corporation organized and existing under the laws of the State of Colorado, having a principal place of business at 506 Carnegie Center, Ste. 400, Princeton, New Jersey.

14. Defendant Sun Pharma Global, Inc. is a company organized and existing under the laws of the British Virgin Islands, having a principal place of business at Akara Building, 24 De Castro Street, Wilkhams Clay 1 Road, Town Tartola, British Virgin Islands. Sun Pharma Global Inc. is a wholly-owned subsidiary of defendant Sun Pharmaceutical Industries Ltd.

15. Defendant Sun Pharma Industries Ltd. is a company organized and existing under the laws of India, having a principal place of business at Acme Plaza, Andheri Kurla Road, Andheri East, Mumbai 400 059, India.

16. Defendant Sun Pharmaceutical Industries, Inc. (together with Sun Pharma Global, Inc. and Sun Pharma Industries Ltd., "Sun Pharma") is a company organized and existing under the laws of the State of Michigan, having a principal place of business at 270 Prospect Plains Road, Cranbury, New Jersey 08512. Sun Pharmaceutical Industries, Inc. is a wholly owned subsidiary of defendant Sun Pharmaceutical Industries, Ltd.

17. Defendant Teva Pharmaceutical Industries, Ltd. ("Teva Ltd." and, together with Teva Pharmaceuticals U.S.A., Inc., "Teva") is a corporation organized and existing under the laws of Israel, having a principal place of business at 5 Basel Street, Petach Tikva 49131, Israel.

18. Defendant Teva Pharmaceuticals U.S.A., Inc. ("Teva U.S.A." and, together with Teva Pharmaceutical Industries, Ltd., "Teva") is a Delaware corporation having a principal place of business at 1090 Horsham Road, North Wales, Pennsylvania 19454.

19. Defendant Wockhardt Limited is a company organized and existing under the laws of India, having a principal place of business at Wockhardt Towers, Bandra Kurla Complex, Bandra East, Mumbai, 400 511, India.

20. Defendant Wockhardt U.S.A., L.L.C. (together with Wockhardt Limited, "Wockhardt") is a limited liability company organized and existing under the laws of the State of Delaware, having a place of business at 20 Waterview Boulevard, Parsippany, New Jersey 07054. Wockhardt U.S.A., L.L.C. is a wholly-owned subsidiary and agent of defendant Wockhardt Limited.

B. Background

21. 4-amino-3-(2-methylpropyl) butanoic acid is also known as "3-isobutylGABA" or "3IBG" and is used to treat seizures.

22. 3-isobutylGABA is a chiral compound: it exists in two different mirror-image orientations in space, called "enantiomers." 3-isobutylGABA has the structure of gamma-amino butyric acid ("GABA"), with a four-carbon isobutyl group added to the molecule in the "3-position."

23. A 50:50 mixture of enantiomers is called a "racemate" or a "racemic mixture."

24. Chemists distinguish between enantiomers by assigning an "R" or "S" prefix to the compound name depending on the "priorities of the substituents around the [chiral] carbon atom." These prefixes allow a chemist to immediately understand the three-dimensional structure of each enantiomer.

25. Chemists also designate enantiomers as (+) or (-) depending on the direction in which the enantiomer rotates polarized light, which is an inherent property of each enantiomer.

26. S-(+)-4-amino-3-(2-methylpropyl) butanoic acid (hereinafter, "S-3-isobutylGABA") is the S-enantiomer of 3-isobutylGABA, which is generally known as "pregabalin" and is the active ingredient in the product at issue, Lyrica®.

27. Pfizer, itself and through its wholly owned subsidiary, CPPI CV, holds approved New Drug Application ("NDA") Nos. 21-446, 21-723, and 21-724 for pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths, which Pfizer sells under the trade name Lyrica®.

28. Pfizer also holds NDA No. 22-488 for pregabalin oral solution containing 20 mg/mL of pregabalin.

29. Lyrica® is approved by the United States Food and Drug Administration (the "FDA") for adjunctive therapy of partial onset seizures, as well as for the treatment of neuropathic pain associated with diabetic peripheral neuropathy, postherpetic neuralgia, and fibromyalgia.

30. The FDA first approved Lyrica® in December 2004 for the treatment of neuropathic pain associated with diabetic peripheral neuropathy and post herpetic neuralgia.

31. In June 2005, the FDA approved Lyrica® as adjunctive therapy for the treatment of partial onset seizures and, in June 2007, the FDA approved Lyrica® for the treatment of fibromyalgia.

32. Pursuant to 21 U.S.C. § 355(b)(1) and attendant FDA regulations, U.S. Patent Nos. 6,197,819 ("the '819 Patent"), 5,563,175 ("the '175 Patent"), and 6,001,876 ("the '876 Patent"), as well as U.S. Reissued Patent No. RE 41,920 ("the RE '920 Patent") are listed in the FDA

publication, "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book"), with respect to Lyrica®. The RE '920 Patent is a reissue of the '876 Patent.

C. The Patents-in-Suit

27. The '819 Patent issued on March 6, 2001 and is entitled "Gamma Amino Butyric Acid Analogs and Optical Isomers." The '819 Patent lists two inventors, Dr. Richard Silverman and Dr. Ryszard Andruszkiewicz.

28. Northwestern holds title to the '819 Patent, and has granted Warner-Lambert an exclusive license to the Patent.

29. The '819 Patent claims priority to the following applications: U.S. Patent Application No. 07/618,692 ("Initial Application" or "the '692 application"), filed on November 27, 1990; U.S. Patent Application No. 07/886,080 ("First CIP" or "the '080 application"), filed on May 20, 1992 as a "continuation-in-part" of the Initial Application; U.S. Patent Application No. 08/064,285 ("Second CIP" or "the '285 application"), filed on May 18, 1993 as a "continuation-in-part" of the First CIP; and U.S. Patent Application No. 08/420,905 ("Final Application" or "the '905 application"), filed on April 11, 1995 as a "continuation" of the Second CIP.

30. The '175 Patent issued on October 8, 1996 and is entitled "GABA and L-Glutamic Acid Analogs For Antiseizure Treatment."

31. On February 22, 2005, the United States Patent and Trademark Office ("the PTO") issued a Certificate of Correction naming Richard B. Silverman, Ryszard Andruszkiewicz, and Po-Wai Yuen as inventors of the '175 Patent.

32. Northwestern holds title to the '175 Patent, and has granted Warner-Lambert an exclusive license to the Patent.

33. On March 1, 2011, the PTO issued a Certification of Correction, correcting the "Related Application Data" field on the '175 Patent to read "Divisional of Ser. No. 08/420,905, filed Apr. 11, 1995." With this correction, the '175 Patent claims priority to the '692 application, filed on November 27, 1990, through the '080, '285, and '905 applications.

34. The '876 patent issued on December 14, 1999 and is entitled "Isobutyl GABA and Its Derivatives for the Treatment of Pain." The sole inventor of the '876 Patent, Dr. Lakhbir Singh, assigned it to Warner-Lambert, which held title to the '876 Patent.

35. On November 9, 2007, Warner-Lambert filed Application No. 11/983,750 with the PTO, seeking reissue of the '876 Patent and, on November 9, 2010, the PTO reissued the '876 Patent as the RE '920 Patent.

36. At the time of its reissue, the RE '920 Patent was assigned to Warner-Lambert and Warner-Lambert continues to hold title to the RE '920 Patent.

37. The RE '920 Patent claims priority to U.S. Provisional Application No. 60/022,337, filed July 24, 1996.

38. On February 25, 2005, Pfizer applied for patent term extensions under 35 U.S.C. § 156 for the '819 Patent and for its '876 Patent (ultimately reissued as the RE '920 Patent), in view of the FDA's approval of two of its NDAs related to Lyrica®. Pfizer stated in its application that because the FDA approved the two Lyrica® NDAs on the same day, both patents were entitled to extensions under the statute. The PTO agreed and extended the term of both patents through December 30, 2018.

1. The Asserted Claims

39. The plaintiffs are asserting claims 1, 2, and 4 of the '819 Patent against all defendants.

40. The plaintiffs are asserting claim 1 of the '175 Patent against defendants Actavis, Cobalt, Lupin, and Sun (collectively, "the '175 Patent defendants").

41. The plaintiffs are asserting that: (1) Actavis' ANDA No. 91-025 infringes claims 2, 5, 13, 15-17, 19-22, and 24-25 of the RE '920 Patent; (2) Alphapharm and Mylan's ANDA No. 91-228 infringes claims 2, 5, 13, 15-17, 19-22, and 24-25 of the RE '920 Patent; (3) Lupin's ANDA Nos. 91-040 and 201989 infringe claims 2, 5, 13, 15-17, 19-22, and 24-25 of the RE '920 Patent; (4) Sandoz's ANDA No. 91-229 infringes claims 2, 5, 13, 16, 17, 19-22, and 24 of the RE '920 Patent; and (5) Teva's ANDA Nos. 91-219 and 91-224 infringe claims 2, 5, 13, 16-17, 19-22, and 24 of the RE '920 Patent.

i. *'819 Patent, Claim 1*

42. Claim 1 of the '819 Patent claims: "[a] compound of the formula (S)-(+)-4-amino-3-(2-methylpropyl) butanoic acid as a single optical isomer."

43. The court has construed the term "(S)-(+)-4-amino-3-(2-methylpropyl) butanoic acid as a single optical isomer," as used in claim 1, to mean 4-amino-3-(2-methylpropyl) butanoic acid "in single (S)-(+) isomer form only, free of the R-(-) isomer form."

ii. *'819 Patent, Claim 2*

44. Claim 2 of the '819 Patent claims "4-amino-3-(2-methylpropyl) butanoic acid, or a pharmaceutically acceptable salt thereof."

45. The court has construed the term "4-amino-3-(2-methylpropyl) butanoic acid" in claim 2 to cover "the chemical compound 4-amino-3-(2-methylpropyl) butanoic acid . . . without limitation as to sterochemical form."

iii. *'819 Patent, Claim 4*

46. Claim 4 of the '819 Patent claims "[a] pharmaceutical composition comprising a compound [of] any one of claims 1 or 3, together with a pharmaceutically acceptable carrier."

iv. *'175 Patent, Claim 1*

47. Claim 1 of the '175 Patent claims "[a] method of treating a patient having seizure disorders which comprises administering to said patient an effective amount of a substantially pure compound of the formula (S)-(+)-4-amino-3-(2-methylpropyl) butanoic acid."

48. The parties have construed "substantially pure" in claim 1 of the '175 Patent to mean "the compound [(S)-(+)-4-3-(2-methylproyl) butanoic acid] containing primarily the (S)-(+)-enantiomer."

v. *RE '920 Patent, Claim 2*

49. Claim 2 of the RE '920 Patent reads: "[a] method for treating pain comprising administering a therapeutically effective amount of [pregabalin], or a pharmaceutically acceptable salt thereof, . . . to a mammal in need of said treatment."

vi. *RE '920 Patent, Claim 5*

50. Claim 5 reads: "[a] method according to claim 2 wherein the pain treated is neuropathic pain."

vii. *RE '920 Patent, Claim 13*

51. Claim 13 reads: "[a] method according to claim 2 wherein the pain treated is acute herpetic and postherpetic pain."

viii. *RE '920 Patent, Claim 15*

52. Claim 15 reads: "[a] method according to claim 2 wherein the pain treated is idiopathic pain."

ix. *RE '920 Patent, Claim 16*

53. Claim 16 reads: "[a] method for treating pain comprising administering a therapeutically effective amount of [pregabalin], or a pharmaceutically acceptable salt thereof, to a human in need of said treatment."

x. *RE '920 Patent, Claim 17*

54. Claim 17 reads: "[a] method according to claim 16 wherein the compound administered is [pregabalin]."

xi. *RE '920 Patent, Claim 19*

55. Claim 19 reads: "[a] method according to claim 17 wherein the pain treated is chronic pain."

xii. *RE '920 Patent, Claim 20*

56. Claim 20 reads: "[a] method according to claim 17 wherein the pain treated is selected from the group consisting of inflammatory pain, neuropathic pain, cancer pain, postoperative pain, and idiopathic pain."

xiii. *RE '920 Patent, Claim 21*

57. Claim 21 reads: "[a] method according to claim 17 wherein the pain treated is neuropathic pain."

xiv. *RE '920 Patent, Claim 22*

58. Claim 22 reads: "[a] method according to claim 17 wherein the pain treated is diabetic neuropathic pain."

xv. *RE '920 Patent, Claim 24*

59. Claim 24 reads: "[a] method according to claim 17 wherein the pain treated is postherpetic pain."

xvi. *RE '920 Patent, Claim 25*

60. Claim 25 reads: "[a] method according to claim 17 wherein the pain treated is fibromyalgia pain."

2. <u>The Accused Products</u>

i. *ANDA No. 91-025 Submitted by Actavis*

61. Actavis submitted Abbreviated New Drug Application ("ANDA") No. 91-025 ("Actavis' ANDA") to the FDA on December 30, 2008, pursuant to 21 U.S.C. § 355(j), seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths ("Actavis' Proposed Product").

62. Actavis' ANDA refers to and relies upon the Lyrica® NDAs and contains data that, according to Actavis, demonstrates the bioequivalence of Actavis' Proposed Product and Lyrica®.

63. Actavis included certifications in its ANDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '819, '876, and '175 Patents are invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Actavis' Proposed Product.

64. On March 26, 2009, Actavis sent its Paragraph IV certifications to the plaintiffs, providing its asserted factual and legal bases for its contentions that the '819, '876, and '175 Patents are not infringed and are invalid or unenforceable.

65. In response to Actavis' Notice, on April 29, 2009, the plaintiffs brought suit against Actavis for infringement of the '819, '876, and '175 Patents, pursuant to 35 U.S.C. § 271(e)(2)(A).

66. On December 29, 2010, after the RE '920 Patent issued, Actavis sent another Notice of its Paragraph IV certification with asserted factual and legal bases for non-infringement and invalidity. The plaintiffs thereafter amended their complaint against Actavis to include claims for infringement of the '819, RE '920, and '175 Patents.

67. The plaintiffs have asserted infringement of claims 1, 2, and 4 of the '819 Patent, claim 1 of the '175 Patent, and claims 2, 5, 13, 15-17, 19-22, and 24-25 of the RE '920 Patent, against Actavis.

ii. *ANDA No. 91-228 Submitted by Alphapharm & Mylan*

68. Alphapharm submitted ANDA No. 91-228 to the FDA on December 30, 2008, pursuant to 21 U.S.C. § 355(j), seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths ("Alphapharm's Proposed Product" or "Mylan's Proposed Product"). Alphapharm designated Mylan as its U.S. agent for pregabalin ANDA No. 91-228 (hereinafter, "Mylan's ANDA").

69. Mylan's ANDA refers to and relies upon the Lyrica® NDAs and contains data that, according to Alphapharm and Mylan, demonstrates the bioequivalence of the generic product of Mylan's Proposed Product and Lyrica®.

70. Mylan's ANDA includes a certification, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '876 Patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Mylan's Proposed Product.

71. On April 29, 2009, the plaintiffs filed suit against Alphapharm and Mylan for infringement of the '876 Patent, pursuant to 25 U.S.C. § 271(e)(2)(A).

72. On March 1, 2010, Alphapharm filed a revised Patent Certification with the FDA and amended Mylan's ANDA to include a certification, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '819 Patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Mylan's Proposed Product..

73. On March 12, 2010, the plaintiffs sued Alphapharm and Mylan for infringement of the '819 Patent, pursuant to 35 U.S.C. § 271(e)(2)(A).

74. On January 26, 2011, after the RE '920 Patent issued, the plaintiffs amended their complaint against Alphapharm and Mylan to include claims for infringement of the RE '920 Patent.

75. On March 30, 2011, Mylan notified Pfizer and Warner-Lambert that Mylan had filed an amended certification with the FDA to include a certification, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the RE '920 Patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Mylan's Proposed Product.

76. The plaintiffs have asserted infringement of claims 1, 2, and 4 of the '819 Patent and claims 2, 5, 13, 15-17, 19-22, and 24-25 of the RE '920 Patent against Alphapharm and Mylan.

77. On March 21, 2011, Alphapharm and Mylan timely filed a Motion for Leave to File an Amended Answer, Defenses, and Counterclaims to the Amended Complaint to add an affirmative defense and counterclaim based on inequitable conduct.[4]

iii. *ANDA No. 91-221 Submitted by Cobalt*

78. Cobalt submitted ANDA No. 91-221 ("Cobalt's ANDA") to the FDA, pursuant to 21 U.S.C. § 355(j), seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths ("Cobalt's Proposed Product").

79. Cobalt's ANDA refers to and relies upon the Lyrica® NDAs and contains data that, according to Cobalt, demonstrates the bioequivalence of Cobalt's Proposed Product and Lyrica®.

80. Cobalt included certifications in its ANDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '819 Patent and the '175 Patent are invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Cobalt's Proposed Product.

81. On April 29, 2009, the plaintiffs filed suit against Cobalt alleging infringement of the '819 and '175 Patents, pursuant to 35 U.S.C. § 271(e)(2)(A).

82. The plaintiffs have asserted infringement of claims 1, 2, and 4 of the '819 Patent and claim 1 of the '175 Patent against Cobalt.

iv. *ANDA Nos. 91-040 & 201989 Submitted by Lupin*

83. Lupin submitted ANDA No. 91-040 ("Lupin's Capsule ANDA") to the FDA, pursuant to 21 U.S.C. § 355(j), seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths ("Lupin's Proposed Capsule Product").

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[4] The court notes that neither Alphapharm nor Mylan presented evidence related to inequitable conduct during trial. These defendants also did not address the issue of inequitable conduct in the defendants' Proposed Findings of Fact and Conclusions of Law. Consequently, the court does not address the issue of inequitable conduct in this Memorandum and Opinion.

84. Lupin included certifications in its Capsule ANDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '819 Patent and the '175 Patent are invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Lupin's Proposed Capsule Product.

85. On April 29, 2009, the plaintiffs sued Lupin for infringement of the '819 and the '175 Patents, pursuant to 35 U.S.C. § 271(e)(2)(A), based on Lupin's Capsule ANDA.

86. On May 20, 2009, the plaintiffs filed an amended complaint asserting infringement of only the '819 and '175 Patents, pursuant to 35 U.S.C. § 271(e)(2)(A), based on Lupin's Capsule ANDA.

87. By letter dated August 31, 2010, Lupin informed the plaintiffs that it had submitted ANDA No. 201989 ("Lupin's OS ANDA" and, together with Lupin's Capsule ANDA, "Lupin's ANDAs") to the FDA, pursuant to 21 U.S.C. § 355(j), seeking approval to market pregabalin oral solution, 20 mg/mL dosage strength ("Lupin's Proposed OS Product" and, together with Lupin's Proposed Capsule Product, "Lupin's Proposed Products").

88. Lupin included certifications in its OS ANDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)IV), that the '819, '876, and '175 Patents are invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Lupin's Proposed OS Product.

89. On October 6, 2011, the plaintiffs sued Lupin for infringement of the '819, '876, and '175 Patents, pursuant to 35 U.S.C. § 271(e)(2)(A), based on Lupin's OS ANDA.

90. On June 2, 2011, after the RE '920 Patent issued, the plaintiffs amended their complaint against Lupin to include claims for infringement of the '819, 'RE '920, and '175 Patents based on Lupin's OS ANDA.

91. The plaintiffs have asserted infringement of claims 1, 2, and 4 of the '819 Patent, claim 1 of the '175 Patent, and claims 2, 5, 13, 15-17, 19-22, and 24-25 of the RE '920 Patent, against Lupin.

v. *ANDA No. 91-229 Submitted by Sandoz*[5]

92. Sandoz filed ANDA No. 91-229 ("Sandoz's ANDA") with the FDA, pursuant to 21 U.S.C. § 335(j), on December 20, 2008, seeking approval to market 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage capsules ("Sandoz's Proposed Product").

93. Sandoz's ANDA refers to and relies upon the Lyrica® NDAs and contains data that, according to Sandoz, demonstrates the bioequivalence of Sandoz's Proposed Product and Lyrica®.

[5] As noted, the plaintiffs stipulated to the dismissal of Sandoz without prejudice on October 13, 2011. (D.I. 337.)

94. Sandoz included certifications in its ANDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '819, '876, and '175 Patents are invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Sandoz's Proposed Product.

95. On April 29, 2009, the plaintiffs sued Sandoz for infringement of the '819, '876, and '175 Patents, pursuant to 35 U.S.C. § 271(e)(2)(A).

96. On March 9, 2011, after the RE '920 Patent issued, the plaintiffs amended their complaint against Sandoz to include claims of infringement of the '819 and RE '920 Patents, and to drop the claims for infringement of the '175 Patent.

97. The Section viii statement in the November 12, 2010 Certification indicated that Sandoz is not seeking approval for the treatment of seizure disorder and fibromyalgia. Concurrent with the November 12, 2010 Patent Certification, Sandoz submitted an amended label in which all references to seizure disorder and fibromyalgia (or idiopathic pain) were deleted.

98. On March 30, 2011, Sandoz submitted a second revised Paragraph IV Patent Certification with the FDA indicating that the claims of the '876, '819, and RE '920 Patents are invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of the Sandoz pregabalin capsules; excepting where uses for which Sandoz is not presently seeking approval under Section viii.

99. The March 30, 2011, revised Patent Certification contained a Section viii statement that Sandoz "is not presently seeking approval" for uses for fibromyalgia in connection with the '876 and RE '920 Patents.

100. The plaintiffs have asserted infringement of claims 1, 2, and 4 of the '819 Patent and claims 2, 5, 13, 15-17, 19-22, and 24 of the RE '920 Patent against Sandoz. The plaintiffs withdraw without prejudice all allegations of infringement of claims 15 and 25 of the RE '920 Patent against Sandoz in view of Sandoz's proposed label amendment associated with ANDA No. 91-229, which does not indicate treatment of fibromyalgia. The plaintiffs reserve the right to reassert claims 15 or 25 of the RE '920 Patent if Sandoz amends the label associated with ANDA No. 91-229 to indicate treatment of fibromyalgia before the RE '920 Patent expires. Sandoz reserves the right to raise any defense should the plaintiffs reassert claims 15 or 25 of the RE '920 Patent in the future, but Sandoz would not contest the reassertion of those claims on any basis related to the plaintiffs' agreement to withdraw them now.

101. On March 21, 2011, Sandoz filed a motion to request leave to file amended affirmative defenses and counterclaims of inequitable conduct in its Answer to the plaintiffs' amended complaint.[6]

102. On April 5, 2011, the plaintiffs responded to Sandoz's March 21, 2011 motion, stating that they did not oppose the motion.

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[6] The court notes that Sandoz did not present evidence related to inequitable conduct during trial and the defendants did not address the issue in their Proposed Findings of Fact and Conclusions of Law. Consequently, the court does not address the issue of inequitable conduct in this Memorandum and Opinion.

vi. *ANDA No. 91-157 Submitted by Sun Pharma*

103. Sun Pharma submitted ANDA No. 91-157 ("Sun's ANDA") to the FDA, pursuant to 21 U.S.C. § 355(j), seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths ("Sun Pharma's Proposed Product").

104. Sun Pharma's ANDA refers to and relies upon the Lyrica® NDAs and contains data that, according to Sun, demonstrates the bioequivalence of Sun Pharma's Proposed Product with Lyrica®.

105. Sun Pharma included certifications in its ANDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '819 Patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Sun's Proposed Product.

106. On April 29, 2009, the plaintiffs sued Sun Pharma for infringement of the '819 Patent, pursuant to 35 U.S.C. § 271(e)(2)(A).

107. Pfizer and Northwestern received from Sun Pharma a letter, dated May 26, 2009, stating that Sun Pharma had included a certification in Sun Pharma's ANDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '175 Patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Sun Pharma's Proposed Product.

108. On June 15, 2009, the plaintiffs amended their complaint against Sun Pharma to include claims for infringement of the '175 Patent, pursuant to 35 U.S.C. § 271(e)(2)(A).

109. In January 2011, Sun Pharma sent samples of Sun Pharma's Proposed Product to SSCI (a division of Aptuit, Inc.) in West Lafayette, Indiana. SSCI received the samples.

110. The plaintiffs have asserted infringement of claims 1, 2, and 4 of the '819 Patent and claim 1 of the '175 Patent against Sun Pharma.

vii. *ANDA Nos. 91-219 & 91-224 Submitted by Teva*

111. Teva USA submitted ANDA Nos. 91-219 and 91-224 (collectively, "Teva's ANDAs") to the FDA, pursuant to 21 U.S.C. § 355(j), seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths ("Teva's Proposed Product").

112. Teva USA included certifications in its ANDAs, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '819 and '876 Patents are invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Teva's Proposed Product.

113. On April 29, 2009, the plaintiffs sued Teva for infringement of the '819 and '876 Patents, pursuant to 35 U.S.C. § 271(e)(2)(A).

114. On January 20, 2011, after the RE '920 Patent issued, the plaintiffs amended their complaint against Teva to include claims for infringement of the '819 and RE '920 Patents.

115. On January 25, 2011, Teva USA filed a Patent Amendment to ANDAs Nos. 91-219 and 91-224, which included certifications pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '819 and RE '920 Patents are invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Teva's Proposed Product.

116. The plaintiffs have asserted infringement of claims 1, 2, and 4 of the '819 Patent and claims 2, 5, 13, 16-17, 19-22, and 24 of the RE '920 Patent against Teva.

viii. *ANDA No. 91-222 Submitted by Wockhardt*

117. Wockhardt submitted ANDA No. 91-222 ("Wockhardt's ANDA") to the FDA, pursuant to 21 U.S.C. § 355(j), seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, 300 mg dosage strengths ("Wockhardt's Proposed Product").

118. Wockhardt's ANDA refers to and relies upon the Lyrica® NDAs and contains data that, according to Wockhardt, demonstrates the bioequivalence of Wockhardt's Proposed Product and Lyrica®.

119. Wockhardt included certifications in its ANDA, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that the '819 Patent is invalid, unenforceable, or will not be infringed by the commercial manufacture, use, or sale of Wockhardt's Proposed Product.

120. On April 29, 2009, the plaintiffs sued Wockhardt for infringement of the '819 Patent, pursuant to 35 U.S.C. 271(e)(2)(A).

121. The plaintiffs have asserted infringement of claims 1, 2, and 4 of the '819 Patent against Wockhardt.

D. Procedural History

122. The plaintiffs filed their complaint for patent infringement against Actavis (09-cv-311), Alphapharma (09-cv-308), Cobalt (09-cv-315), Mylan (09-cv-308), Lupin (09-cv-309), Sandoz (09-cv-310), Sun Pharma (09-cv-313), Teva (09-cv-307), and Wockhardt (09-cv-312) on April 29, 2009.

123. The parties filed a stipulation to consolidate the above-listed actions under case number 09-cv-307 on September 3, 2009. (D.I. 14.) The court approved the parties' consolidation stipulation on September 4, 2009. (D.I. 15.)

124. The plaintiffs filed a complaint for patent infringement against Lupin on October 6, 2010 (10-cv-853). This action was consolidated with the 09-cv-307 action on April 12, 2011.

125. The plaintiffs filed an amended complaint against: Actavis on January 6, 2011 (D.I. 151); Teva on January 21, 2011 (D.I. 159); Alphapharma and Mylan on February 1, 2011 (D.I. 164); and Sandoz on March 15, 2011 (D.I. 211).

126. The court held a nine-day bench trial in this matter on October 11 through October 21, 2011. (D.I. 362-370.)

127. On October 11, 2011, the first day of trial, the parties stipulated that: (1) to the extent the court finds the claim valid and enforceable, the defendants' respective ANDAs are covered by claim 2 of the '819 Patent under the court's claim construction; (2) to the extent the court finds it valid and enforceable, defendants Actavis, Cobalt, Lupin, and Sun Pharma's respective ANDAs are covered by claim 1 of the '175 Patent; (3) to the extent the court finds the claims valid and enforceable, defendants Actavis, Alphapharm, Mylan, Lupin, and Teva's respective ANDAs, as directed to post-herpetic neuralgia, are covered by claims 2, 5, 16-17, 19-21, and 24 of the RE '920 Patent; (4) to the extent the court finds the claims valid and enforceable, defendants Actavis, Alphapharm, Mylan, Lupin, and Teva's respective ANDAs, as directed to diabetic neuropathy, are covered by claims 2, 5, 16-17, and 19-22 of the RE '920 Patent; (5) to the extent the court finds the claims valid and enforceable, defendants Actavis, Alphapharm, Mylan, and Lupin's respective ANDAs, as directed to fibromyalgia, are covered by claims 2, 16-17, 19, and 25 of the RE '920 Patent; and (6) each of the foregoing individual patent claims shall automatically convert to a final judgment of infringement of the respective claim by each applicable defendant upon a final judgment of validity and enforceability regarding the particular claim. (D.I. 335.) To this end, should the court find that the asserted claims of the patents-in-suit are valid and enforceable, the defendants stipulate to infringement.

128. The defendants do not stipulate to infringement of claims 1 and 4 of the '819 Patent.

III. DISCUSSION AND CONCLUSIONS OF LAW

The court has subject matter over this matter pursuant to 28 U.S.C. §§ 1331, 1338, and 2201. Venue is proper in this court under 28 U.S.C. §§ 1391 and 1400(b). After having considered the entire record in this case, the substantial evidence in the record, the parties' post-trial submissions, and the applicable law, the court concludes that: (1) the asserted claims of the patents-in-suit are not invalid due to obviousness; (2) the asserted claims of the patents-in-suit are not invalid due to anticipation; (3) the asserted claims of the '819 and '175 Patents are entitled to a November 27, 1990 priority filing date; (4) the asserted claims of the '819 Patent are not invalid for written description; (5) the asserted claims of the '819 Patent are not invalid due to improper inventorship; (6) the defendants' proposed products do not literally infringe claims 1

and 4 of the '819 Patent; (7) the defendants' proposed products infringe claims 1 and 4 of the '819 Patent under the doctrine of equivalents; (8) the '819 and '876 Patents' term extensions are not invalid under 35 U.S.C. § 156; and (9) each of the parties' Rule 52(c) motions are granted in part and denied in part. The court's discussion of its findings of fact and conclusions of law are set forth in further detail below.

A. Obviousness

The defendants challenge the validity of many of the asserted claims as obvious in light of the prior art. Specifically, the defendants assert that claim 2 of the '819 Patent and each of the asserted claims of the RE '920 Patent[7] are invalid for obviousness under 35 U.S.C. § 103. The court finds, for the reasons that follow, that the defendants have failed to establish, by clear and convincing evidence, that the asserted claims of the patents-in-suit are, in fact, obvious.[8]

1. The Legal Standard

35 U.S.C. § 103(a) provides that a patent may not be obtained "if differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious to a person having ordinary skill in the art." 35 U.S.C. § 103(a). Obviousness is a question of law that is predicated on several factual inquiries. *See Richardson-Vicks v. Upjohn Co.*, 122 F.3d 1476, 1479 (Fed. Cir. 1997). Specifically, the trier of fact is tasked with assessing four considerations: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed subject matter and the prior

[7] As noted, the plaintiffs assert claims 2, 5, 16-17, 19-22, and 24-25 of the RE '920 Patent against the defendants identified in the Findings of Fact Section. *See supra* Section II.C.1 at ¶ 41.

[8] The court notes that, at the conclusion of trial, it ruled against the defendants on three defenses: (1) that claim 2 of the '819 Patent is invalid as obvious under 35 U.S.C. § 103; (2) claim 2 of the '819 Patent is invalid for inherent anticipation by U.S. Patent No. 4,123,438 (the "Geurts reference"); and (3) that the asserted claims of the RE '920 Patent are invalid for obviousness under 35 U.S.C. § 103. The court directed the plaintiffs to submit proposed Findings of Fact and Conclusions of Law consistent with these rulings. The plaintiffs submitted its proposed findings and conclusions in connection with these three defenses on December 19, 2011. (D.I. 353.) The court relies on these findings and conclusions in this obviousness section as well as in its anticipation analysis to follow. *See infra* Section III.B.

art; and (4) secondary considerations of non-obviousness, such as commercial success, long felt but unmet need, failure of others, acquiescence of others in the industry that the patent is valid, and unexpected results. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

A party seeking to challenge the validity of a patent based on obviousness must demonstrate by "clear and convincing evidence"[9] that the invention described in the patent would have been obvious to a person of ordinary skill in the art at the time the invention was made. Importantly, in determining what would have been obvious to one of ordinary skill in the art, the use of hindsight is not permitted. *See KSR Intern. Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007) (cautioning the trier of fact against "the distortion caused by hindsight bias" and "arguments reliant upon *ex post* reasoning" in assessing obviousness). In *KSR*, the Supreme Court rejected ridged application of the principle that there should be an explicit "teaching, suggestion, or motivation" in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art, in order to find obviousness. *See KSR*, 550 U.S. at 415. The *KSR* Court acknowledged, however, the importance of identifying "'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination." *Takeda Chem. Indus. v. Alphapharm Pty. Ltd.*, 492 F.3d 1350, 1356-57 (Fed. Cir. 2007) (quoting *KRS*, 550 U.S. at 418).

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

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

F.3d 1348, 1364 (Fed. Cir. 2007). Moreover, while the Federal Circuit has noted that pharmaceuticals can be an "unpredictable art" to the extent that results may be unexpected, it also recognizes that, per *KSR*, evidence of a "finite number of identified, predictable solutions" or alternatives "might support an inference of obviousness." *See Eisai Co. Ltd. v. Dr. Reddy's Labs. Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008).

The Federal Circuit has also clarified that, where the patented invention in question is a chemical compound, a court's assessment of "differences between the claim subject matter and the prior art" will involve examination of the compound and its properties, which are "inseparable." *See Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1087 (Fed. Cir. 2008). In this examination, the challenger initially bears the burden of proving a *prima facie* case of obviousness by showing: (1) that there is structural similarity between the claimed compound and the prior art "lead compound," which one skilled in the art would have selected for further research; and (2) that there was some reason in the art to make the "specific molecular modifications" to the lead compound necessary to arrive at the claimed compound." *Takeda Chem. Indus. Ltd.*, 492 F.3d at 1356-57. If the challenger fails to prove by clear and convincing evidence both that a person of ordinary skill in the art would have selected the alleged lead compound for further research, and that the prior art suggested the specific modifications needed to make the claimed invention, then the compound is not obvious. *See id.* at 1360. However, even if the challenger is able to establish the *prima facie* case of obviousness, the patentee may rebut it with evidence of "some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected. *See Procter & Gamble v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009).

1. <u>The Level of Ordinary Skill in the Art</u>

With regard to the asserted claims of the '819 Patent, a person of ordinary skill in the art would be a scientist with a Ph.D. in organic or medicinal chemistry with at least two years of experience in the synthesis of organic compounds or, alternatively, a master's degree in the same fields with at least five years of experience in organic synthesis.[10] (D.I. 349 at 24 (citing Tr. at 1171:16-1172:1 (Roush)).) A person of ordinary skill in the art with respect to the RE '920 Patent would be a physician trained in a clinical specialty focused on neuropathic pain management with drugs. (D.I. 353 at 18 (citing Tr. at 1396:3-8 (Loeser)).) The parties agree and the court concludes that the plaintiffs and defendants' definitions of a person of ordinary skill in the art do not differ in a meaningful way. (*Id.*; D.I. 353 at 9 (citing Tr. at 790:1-16 (Kupferberg); Tr. at 1284:24-1285:14 (White)).)

Moreover, the court concludes, with respect to the '819 Patent, that, for the reasons stated more fully in Section III.D, November 27, 1990, the filing date of the Initial Application that issued as the '819 Patent, is appropriate and is the date at which the level of ordinary skill in the art should be assessed.[11] The defendants' expert, Dr. Kupferberg, conducted his analysis of the prior art as of November 1990 and, therefore, his conclusions evaluate the prior art up to and including the appropriate priority date. (*Id.* (citing Tr. at 789:20-790:16 (Kupferberg)).) The court also finds, and the parties do not contest, that July 24, 1996[12] is the appropriate priority filing and prior art date for the RE '920 Patent. The court, therefore, assesses the parties' obviousness arguments in light of these findings. For the purpose of clarity, the court examines the defendants' arguments with respect to the '819 Patent and RE '920 Patent separately below.

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[10] The plaintiffs specifically state that a person of ordinary skill in the art with respect to the '819 Patent would be "a scientist with at least a Ph.D. in pharmacology and at least [five] years of experience working with various animal models for epilepsy and seizures, or a highly skilled technician lacking a Ph.D., but with at least [ten] years of experience working with various animal models for epilepsy and seizures." (D.I. 353 at 9.)

[11] *See infra* Section III.D.

[12] As noted, the RE '920 Patent is a reissue of the '876 Patent and claims priority to U.S. Provisional Application No. 60/022,337, which was filed on July 24, 1996. This priority filing date is not in dispute and, therefore, the parties agree that the prior art should be assessed as of this 1996 date.

2. The '819 Patent: The Scope and Content of the Prior Art and Differences Between the Claimed Subject Matter and the Prior Art

As noted, the defendants contend that claim 2 of the '819 Patent is invalid as obvious. Claim 2 of the '819 Patent recites 3-isobutylGABA, which the court has construed to include individual isomers (i.e., S-3-isobutylGABA and R-3-isobutylGABA), racemic mixtures, and non-racemic mixtures having unequal proportions of isomers, because the claim does not limit as to stereochemical form. At trial, the defendants focused their obviousness argument on the assertion that the PTO Examiner was incorrect in deciding, during prosecution of the '819 Patent, that comparative data overcame a rejection that the structure of 3-isobutylGABA was *prima facie* obvious based on the disclosure of homologous compounds in three prior art references: Fish, Shashoua, and Colonge. (D.I. 353 at 8 (citing Tr. at 794:13-18, 796:10-797:2, 800:11-805:25, 806:25-807:10, 812:4-815:16 (Kupferberg); DTX-820; DTX-1767; DTX-2406; DTX-2408. Specifically, the defendants' expert, Dr. Kupferberg, testified that the anticonvulsant test data the plaintiffs submitted in the application and in declarations filed under 37 CFR § 1.1.32 relied on "flawed procedures" and were "imprecise" and/or "meaningless." (*Id.* (citing Tr. at 791:20-792:4, 819:10-24, 849:1-12 (Kupferberg); DTX-836).) For the reasons that follow, the court finds that the defendants have failed to show, by clear and convincing evidence, that claim 2 of the '819 Patent is obvious in light of the prior art as of November 27, 1990.

a. Prior Art Addressing the Use of 3-isobutylGABA to Improve Seizure Treatment

In response to the defendants' arguments, the plaintiffs assert that the defendants did not introduce any evidence to support why a person of ordinary skill in the art in 1990 would have identified 3-isobutylGABA as an anticonvulsant treatment, other than to show that certain "homologous compounds were known to have anticonvulsant activity" and that homologous

series "should have similar properties."[13] (*Id.* (citing Tr. at 789:20-25, 791:2-10, 806:6-807:10 (Kupferberg)).) The court agrees and concludes that the evidence presented is insufficient to show clearly and convincingly that skilled artisans would have known to select 3-isobutylGABA in November 1990 based simply on the fact that it is a homologous compound.

Specifically, the plaintiffs' experts, Drs. White and Bazil, explained, in testimony the court finds credible, that identifying improved anticonvulsant drugs in 1990 was a complicated and unpredictable and was largely conducted through trial and error. (*Id.* (citing Tr. at 1277:18-1278:1 (White); Tr. at 1612:23-1615:2 (Bazil)).) In fact, by 1990 only one drug, vigabatrin, had been successfully developed by targeting a mechanism known to be related to epilepsy. (*Id.* at 10 (citing Tr. at 1276:18-1277:17 (White)).) Dr. White further testified that anticonvulsant drug discovery remains unpredictable today. Indeed, while almost 34,000 investigational drugs have been tested as potential anticonvulsants as part of an NIH screening program at the University of Utah, only fifteen new drugs have been approved in the United States for seizure treatment since 1993. (*Id.* (citing Tr. at 1269:18-1270:11 (White); Tr. at 851:15-852:4 (Kupferberg)).)

Moreover, the defendants did not identify any teachings from the Colonge, Fish, and Shashoua references, which, individually or combined, would have directed one of skill in the art to select 3-isobutylGABA. Specifically, and as the plaintiffs correctly note, the defendants did not point to any evidence in the prior art indicating that a particular compound or class of compounds, including alkyl-substituted GABA analogs, a broad class of compounds including 3-isobutylGABA, would improve anti-seizure treatment. (*Id.*) The defendants also failed to identify any teachings as of the filing date that would have directed a skilled artisan to substitute

[13] For instance, Dr. Kupferberg testified that the compounds claimed in Dr. Silverman's application are members of the same homologous series disclosed in the Fish reference. Tr. at 806:19-807:10 (Kupferberg). Dr. Kupferberg further stated that the Examiner rejected the Initial Application as obvious due to this similarity and only approved the application when Dr. Taylor submitted two declarations, which the court will discuss in the subsection to follow.

with an isobutyl group, as opposed to any other alkyl group, in the event that alkyl-substituted GABA-analogs were selected. (*Id.*)

In view of the foregoing and, in particular, in consideration of the unpredictability of anticonvulsant drug discovery and the absence of information detailing what structures were important for anticonvulsant activity in 1990, the court finds that the prior art did not direct skilled artisans to select 3-isobutylGABA or to anticipate its anticonvulsant activity.[14]

b. Prior Art Addressing 3-isobutylGABA's Anticonvulsant Activity Compared to Homologous Compounds

In support of their argument that the superiority of 3-isobutylGABA was known in the art in 1990, the defendants cite the testimony of their expert, Dr. Kupferberg, for the proposition that Dr. Taylor's declarations to the PTO regarding 3-isobutylGABA's superiority were based on "unreliable" and/or "meaningless" data. The court disagrees. During prosecution of the '819 Patent, the applicants submitted two declarations by Dr. Taylor, pursuant to 37 CFR § 1.1.32, and, based at least in part on these declarations, the Examiner concluded that 3-isobutylGABA's anticonvulsant activity was unexpectedly superior to compounds identified in the prior art. PTX-7A. Dr. Taylor, a pharmacologist at Parke-Davis who supervised preclinical screening of new anticonvulsant drug candidates, summarized in his declarations the preclinical anticonvulsant test data for 3-isobutylGABA as well as its closest prior art analogs and provided ED_{50} values[15] for the data. (D.I. 353 at 11 (citing Tr. at 965:6-967:12 (Taylor)).) In light of the testimony adduced at trial, the court finds the data underlying Dr. Taylor's declarations and his conclusions reliable.

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[14] The defendants' agreement with and reference to the Examiner's initial finding of obviousness is insufficient to establish a *prima facie* obviousness case. *See Applied Materials*, 98 F.3d at 1570. Rather, the defendants must present clear and convincing evidence that the claimed invention was obvious in light of the prior art. For the reasons stated, the court finds that the defendants have failed to do so.

[15] As explained at trial, ED_{50} values are commonly used to identify the potency of a compound; it is the dose that will protect (i.e., prevent seizures) in fifty-percent of the animals tested. Tr. at 823:12-824:13 (Kupferberg).

Specifically, Dr. Taylor's declarations explained how the estimated and calculated ED_{50} values were derived and referenced the data underlying their findings. The plaintiffs note that this data was already known to the Examiner because it was included in Table 2 of the original application that resulted in the '819 Patent. (*Id.* (citing Tr. at 1295:16-1296:19 (White)).) Dr. White, an expert who has supervised the screening of over 34,000 investigational drugs during his twenty-five years at the Anticonvulsant Screening Program at the University of Utah, testified that Dr. Taylor's underlying testing was appropriate, including the time point chosen, the number of animals tested, and the decision not to determine the time-to-peak effect for each compound—all decisions the defendants challenge as undermining the reliability of his data and conclusions. (*Id.* (citing Tr at. 1269:5-1271:12, 1295:16-1296:19, 1297:4-22, 1297:23-1299:8, 1299:9-16, 1300:2-9 (White)).) In consideration of the record before it and the testimony of Drs. Taylor and White, which the court finds credible, the court concludes that Dr. Taylor's testing and summary of the Table 2 data in his declarations did not rely on flawed procedures and was, in fact, appropriate. (*Id.* at 12 (citing Tr. at 1296:17-1297:3, 1299:17-1300:1 (White)).)

Dr. Taylor explained in his declarations and confirmed at trial that the data in Table 2 of the original application demonstrates that 3-isobutylGABA is "clearly superior to other compounds." (*Id.* (citing Tr. at 1288:8, 1286:22-1290:6 (White); Tr. at 984:11-986:11 (Taylor)).) Dr. Taylor reached this conclusion for three reasons. First, the data showed a dose-dependent anticonvulsant effect, which is considered in the art a critical pharmacological attribute. (*Id.* (citing Tr. at 1289:9-13 (White)).) Second, the data also showed that 3-isobutylGABA was substantially more potent than the other compounds to which it was compared. (*Id.* (citing Tr. at 1289:18-22 (White)).) Third, while many of the tested compounds did not protect one hundred-percent of the animals tested at any dose, 3-isobutylGABA

successfully protected all of the animals, indicating that it had "good efficacy." (*Id.* (citing Tr. at 1289:14-17, 1289:23-1290:2 (White)).) In sum, Drs. Taylor and White testified that the data outlined confirmed that 3-isobutylGABA was unexpectedly and significantly superior to 3-isopropylGABA and that, per Dr. White, "anyone looking at this kind of data would consider that isobutylGABA would be clearly superior to isopropyl." (*Id.* (citing Tr. at 1292:23-1294:23 (White)).) Dr. Taylor further testified that 3-isobutylGABA even "stood out [from] most of the compounds that [he] had ever screened in [his] laboratory." (*Id.* (citing Tr. at 985:16-986:5 (Taylor); Tr. at 892:22-893:23 (Silverman)).)

In view of the foregoing, the court concludes that the data in Dr. Taylor's declarations and Table 2 of the original application, demonstrate the unexpected superiority of 3-isobutylGABA and its (S)-3-isobutylGABA over the closest prior art analogs, including 3-isopropylGABA and other structurally close compounds not in the prior art. (*Id.* at 12-13 (citing Tr. at 1286:22-1291:6, 1292:23-1294:23 (White)).) In particular, the court finds the data presented to the Examiner and the comparisons between compounds made in the declarations to be reliable and agrees that it demonstrates that 3-isobutylGABA was unexpectedly and significantly superior to the prior art compounds. (*Id.* at 13 (citing Tr. at 1296:20-1300:9 (White)).) Thus, based in part on the data summarized in the declarations, the court agrees with the plaintiffs that the Examiner properly concluded that 3-isobutylGABA's unexpected superiority over the prior art was sufficient to rebut any *prima facie* case of obviousness.[16]

3. <u>The '819 Patent: Secondary Considerations</u>

In addition to the findings outlined above, the court also finds that the plaintiffs have presented evidence of secondary considerations sufficient to rebut a *prima facie* case of

[16] The court notes that, though it reached the same conclusion based on the evidence presented, the Examiner's decision is entitled to "added deference." *See Polaroid Corp.*, 789 F.2d at 1560.

obviousness. The court examines these secondary considerations—namely, unexpected results, long felt but unmet need, commercial success, and industry recognition—separately below.

a. Unexpected Beneficial Properties

The plaintiffs maintain that 3-isobutylGABA's "unexpected superiority derived from its unexpected inherent properties" and, as a result, that persons of skill in the art would not have anticipated its beneficial properties. In support of this contention, the plaintiffs note that 3-isobutylGABA binds to what was a then-unknown binding site in the brain, is able to cross into the brain by active transport, and is able to treat chronic pain—characteristics that were unknown to the inventors and those of ordinary skill in the art. Specifically, per the testimony of Dr. Silverman, he and Dr. Andruszkiewicz initially believed that the series of 3-alkylGABA analogs they synthesized, including 3-isobutylGABA, could be improved anticonvulsant agents because they activated an enzyme known as glutamate decarboxylase ("GAD"), which produces gamma aminobutyric acid ("GABA"), a compound preventing seizures. (D.I. 353 at 13-14 (citing Tr. at 869:19-875:24, 884:6-885:20 (Silverman)).) 3-isobutylGABA, however, was one of the weaker GAD-activators that they synthesized, which made it surprising to the inventors that 3-isobutylGABA was the most potent anticonvulsant of those compounds *in vivo*. (*Id.* (citing Tr. at 892:22-893:23 (Silverman)).)

Notably, the inventors ultimately discovered that 3-isobutylGABA's anticonvulsant activity was not attributed to activating GAD or inactivating GABA-aminotransferase ("GABA-AT"), the other enzyme the inventors targeted in their research, but by antagonizing a calcium channel in the brain, which indirectly leads to increased GABA levels and decreased seizures. (*Id.* at 14 (citing Tr. at 905:11-906:11 (Silverman)).) Dr. Silverman testified that this mechanism of action was completely unexpected in 1990. (*Id.*) The inventors were also surprised to learn

that, of all the 3-alkylGABA analogs they synthesized, only 3-isobutylGABA bound with high affinity to the specific channel binding cite. (*Id.* (citing Tr. at 1412:2-11 (Enna)).)

In addition, the inventors explained that 3-isobutylGABA's ability to pass through the blood brain barrier was unexpected, as compared to other analogs, and rendered this compound potentially more effective than other anticonvulsants. (*Id.* (citing Tr. at 874:19-23 (Silverman)).) Specifically, and as Dr. Silverman described, while anticonvulsant agents must enter the brain to be effective, amino acids like GABA are generally unable to cross the barrier. (*Id.* (citing Tr. at 874:13-875:15, 877:9-878:11 (Silverman)).) Dr. Silverman speculated that GABA analogs with lipophilic substituents might be "greasy" enough to pass the blood brain barrier, but was "skeptical" that 3-isobutylGABA would enter the brain without further modification of its structure to increase its lipophilicity. (*Id.* (citing Tr. at 889:3-890:4 (Silverman)).) The inventors were, therefore, surprised to discover that 3-isobutylGABA passed through the blood brain barrier without additional modifications. (*Id.* (citing Tr. at 906:12-907:5 (Silverman)).) The inventors learned that 3-isobutylGABA passes through the barrier via an unanticipated mechanism—active transport via the "System L" transporter for the amino acid leucine, which is not normally associated with alkyl or gamma amino acids. (*Id.* at 15 (citing Tr.at 906:12-907:5 (Silverman)).)

Finally, the inventors learned that 3-isobuytlGABA also possesses a number of surprising and beneficial pharmacokinetic properties. First, unlike most amino acids, which are "metabolized and excreted very readily," 3-isobutylGABA is not readily broken down into metabolites when ingested and, therefore, is "excreted intact." (*Id.* at 15 (citing Tr. at 907:6-11 (Silverman)).) Second, 3-isobutylGABA is ninety-percent orally bioavailable, meaning that ninety-percent of an oral dose is absorbed into and distributed throughout the body. To this end,

it does not interact with potassium channels to cause arrhythmia or with enzymes in the liver to cause negative drug-drug interactions. (*Id.* (citing Tr. at 907:14-17 (Silverman)).) Third, 3-isobutylGABA was shown to display linear pharmacokinetics, such that as dosage is increased, the amount absorbed in the intestines increases proportionally.

In view of the foregoing and in consideration of Drs. Silverman's testimony, which the court finds credible, the court concludes that the inventors and persons of skill in the art would not have expected 3-isobutylGABA to possess the beneficial properties and attributes detailed above. Thus, the court finds that the plaintiffs have produced evidence sufficient to show this secondary consideration and to support the court's conclusion that the asserted claim of the patent-in-suit is not obvious.

b. Long Felt, Unmet Need

The plaintiffs contend that, as of the early 1990s, there was a long felt need for anticonvulsants that had a linear pharmacokinetic profile, did not have significant protein binding, induce hepatic enzymes, or interact with other drugs, would prove effective in patients who were refractory to other anticonvulsants, and were not associated with the significant side effects common to many anticonvulsants at the time. (D.I. 353 at 15 (citing Tr. at 1615:3-1618:10 (Bazil)).) In support of this argument, the plaintiffs note that, in the 1990s, many anticonvulsants were associated with increased liver metabolism, because they induced hepatic enzymes, which could result in adverse side effects. (*Id.* at 16 (citing Tr. at 1615:22-1616:8 (Bazil)).) For instance, levels of warfarin, which is used to reduce blood clotting, may be reduced from increased liver metabolism and could cause a heart attack or stroke. (*Id.* (citing Tr. at 1615:22-1616:16 (Bazil)).) 3-isobutylGABA, however, is not known to metabolize in the

liver and, as a result, largely eliminates problems associated with drug interaction because its metabolization does not affect any other drug. Tr. at 1618:16-1619:9 (Bazil).

The plaintiffs' expert, Dr. Bazil, explained that 3-isobutylGABA's ability to metabolize without interfering with other drugs distinguished it from other drugs in the prior art directed to seizure treatment. *Id.* at 1619:1-25. Specifically, many anticonvulsants were known to have significant protein binding, such that careful monitoring and titration were necessary and there was no predictable dose-response relationship. *Id.* at 1616:17-1617:20. Unlike these drugs, Dr. Bazil testified that 3-isobutylGABA possesses a predictable dose-response relationship and does not bind significantly to proteins. *Id.* at 1618:1-1619:1, 1620:1-4. To this end, the plaintiffs assert that 3-isobutylGABA met a long felt but unmet need, in that it offered improved anticonvulsant treatment by successfully addressing the needs of refractory patients and offering superior properties over then-existing therapies, such as a lack of drug-drug interactions, good pharmacokinetics, and a lack of protein binding. *Id.* at 1618:11-1620:23. Neither side presented evidence of any other drug able to treat seizures without such adverse side effects or drug-drug complications. In consideration of the evidence presented, the court finds Dr. Bazil's testimony persuasive and agrees with the plaintiffs that, based on the record before it, 3-isobutylGABA met a long felt, but unmet need. Thus, the court finds that evidence of this secondary consideration also supports its conclusion that claim 2 of the '819 Patent is not obvious.

c. Commercial Success

The plaintiffs assert that the commercial success of Lyrica® is evidence of the non-obviousness of the patents-in-suit. Importantly, commercial success is "only significant if there is a nexus between the claimed invention" and the secondary consideration at issue. *See, e.g.*, *Ormco Corp. v. Align Tech., Inc.*, 463 F.3d 1299, 1311-12 (Fed. Cir. 2006). Moreover, "the

asserted commercial success of the product must be due to the merits of the claimed invention beyond what was readily available in the prior art." *See J.T. Eaton & Co. v. Atlantic Paste & Glue Co.*, 106 F.3d 1563, 1571 (Fed. Cir. 1997). In view of record before it, the court concludes that the plaintiffs have demonstrated commercial success.

As noted above, the S-enantiomer of 3-isobutylGABA is the active ingredient in Lyrica® and is one embodiment of the compound claimed in claim 2 of the '819 Patent. In addition, the RE '920 Patent claims the invention of using this compound for the treatment of diabetic peripheral neuropathy, post-herpetic neuralgia, and fibromyalgia pain. The plaintiffs presented evidence that, between 2008 and 2010, prescriptions for Lyrica® generated an average annual net revenue of nearly $600 million and over $2.3 billion in net revenue since Lyrica® was introduced in the United States in 2005. *See* PTX-1419; Tr. at 1512:7-1513:2 (Vellturo).

While the defendants attempted to challenge the plaintiffs' evidence regarding commercial success with the argument that Lyrica®'s success is not attributable to its patented features and/or is not as commercially successful as the plaintiffs maintain, the court is not persuaded. Rather, the court finds credible the testimony of the plaintiffs' expert, Dr. Velltura, who explained that Lyrica® has the largest share of prescriptions for branded products to treat diabetic peripheral neuropathy and posterpetic neuralgia combined in the United States and is one of the two leading branded products prescribed for the treatment of fibromyalgia. *See* PTX-1359; PTX-1365; Tr. at 1517:21-1519:15, 1521:25-1522:25 (Velltura). Dr. Velltura also testified, as evidence of Lyrica®'s commercial success, that Lyrica® shares the market with many competing products as well as with low-cost generic gabapentin alternatives, yet maintains considerable net sales and market shares. Tr. at 1523:1-12 (Velltura). In light of these figures, Dr. Velltura's examination of competitors in the market, and the evidence in the record, the court

concludes that the plaintiffs have presented evidence sufficient to demonstrate commercial success attributable to Lyrica®'s patented features.

d. Industry Recognition

A court assessing secondary considerations in an obviousness analysis may consider evidence of substantial industry recognition where it is presented to rebut the defendants' *prima facie* case of obviousness. *See Ortho McNeil Pharm., Inc. v. Mylan*, 520 F.3d 1358, 1365 (Fed. Cir. 2008). Here, the plaintiffs presented persuasive evidence of industry recognition at trial. Specifically, the plaintiffs presented testimony of '819 Patent co-inventor Dr. Silverman who explained that he received the Perkin Medal from the Society of Chemical Industry, the E.B. Hirschberg Award for important discoveries in medicinal substances from the American Chemical Society, and was inducted into the American Chemical Society's Medicinal Chemistry Hall of Fame for his invention on 3-isobutylGABA. Tr. at 909:1-16 (Silverman). The court agrees with the plaintiffs that this evidence demonstrates recognition from the scientific community of the inventors' work and, considered in concert with the other secondary consideration factors examined above, combine to support the court's finding of non-obviousness.

4. <u>The RE '920 Patent: The Scope and Content of the Prior Art and Differences Between the Claimed Subject Matter and Prior Art</u>

The court again notes that the RE '920 Patent[17] covers methods of treating various types of pain with 3-isobutylGABA.[18] Specifically, the asserted claims cover the treatment of such pain as: neuropathic, acute herpetic, postherpetic, idiopathic, chronic, diabetic neuropathic, and

[17] As noted in the Findings of Fact section, the RE '920 Patent is a reissue of the '876 Patent and claims priority to U.S. Provisional Application No. 60/022,337. *See* II.C at ¶¶ 34-36.

[18] *See supra* Section II.C.1 for a recitation of the types of pain treatment covered by the RE '920 Patent's asserted claims. *See* Section II.C.1 at ¶¶ 49-60.

fibromyalgia pain, among others.[19] The asserted claims, and claims 16 and 17 specifically, call for the administering of a therapeutically effective amount of pregabalin to provide pain treatment. *See generally* RE '920 Patent.

At trial, the defendants focused their obviousness arguments in connection with the RE '920 Patent on the assertion that the use of 3-isobutylGABA to treat neuropathic pain was obvious as of the relevant July 24, 1996 prior art date. (D.I. 353 at 17 (citing Tr. at 1396:9-1397:6 (Loeser); Tr. at 1422:8-1423:25 (Enna)).) Specifically, the defendants allege that, as of July 1996, it would have been obvious to a person of ordinary skill in the art that: (1) anticonvulsants were generally effective in the treatment of neuropathic pain; (2) gabapentin was effective in the treatment of neuropathic pain; and (3) gabapentin and pregabalin share a common binding site and mechanism of action, such that pregabalin would also be known to demonstrate analgesic properties. (*Id.*)

Conversely, the plaintiffs assert that the defendants' arguments were considered and rejected by the PTO and, further, that persons of skill in the art would not have had a reasonable expectation of success that pregabalin could effectively treat neuropathic pain based on case reports and the ineffectiveness of other anticonvulsants. (*Id.* at 18 (citing PTX-10 at PFE_LYR_0000791597)).) Thus, while the court concludes that the prior art renders every element of asserted claims non-obvious,[20] it will focus its discussion on how pregabalin and/or other anticonvulsants were viewed as an effective treatment for neuropathic pain by persons of ordinary skill in the art as of July 1996. For the reasons that follow, the court agrees with the

[19] *See id.*

[20] The court examined each asserted claim of the RE '920 Patent and concludes that the defendants have failed to establish obviousness as to each. The court is persuaded in this finding by the testimony of Drs. Clauw, Taylor, and Woolf.

plaintiffs that, in consideration of the record before it, the asserted claims of the RE '920 Patent are not obvious.

As noted, the patent at issue here is a reissue of the '876 Patent and was reissued from Reissue Patent Application No. 11/983,750. During the prosecution of this Reissue Patent Application, the plaintiffs submitted the prior art identified in the notices the defendants filed pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV). (*Id.* at 18.) Upon consideration of this prior art, the Examiner rejected the defendants' argument that the RE '920 Patent is obvious, stating: "given the structural differences between gabapentin and the instantly claimed compound [S-3-isobutylGABA], and further finding that *other* anticonvulsants (i.e., anticonvulsants other than gabapentin) are *not* effective in the treatment of pain" it is "considered persuasive that the skilled artisan would not have administered the instantly claimed compound(s) for the treatment of pain *with a reasonable expectation of success*." (*Id.* (citing PTX-10 at PFE_LYR_0000791597 (emphasis in original)).) While the court recognizes that the Examiner's finding is not dispositive in the obviousness assessment,[21] it agrees with the essence of the Examiner's findings based on the evidence presented at trial and, specifically, for the reasons that follow.

a. Prior Art Addressing Whether Anticonvulsants Were Understood to be Effective Analgesics

First, the court disagrees with the defendants' assertion, via the testimony of their expert, Dr. Loeser, that "anticonvulsants were generally known to be useful for neuropathic pains" as of the relevant 1996 prior art date. (*Id.* (citing Tr. at 1396:18-19 (Loeser)).) As the plaintiffs correctly note, while some anticonvulsants demonstrated success as analgesics as of 1996, the most commonly used anticonvulsants at the time, such as phenytoin, benzodiazepines,

[21] *See Applied Materials, Inc. v. Advanced Semiconductor Materials Am., Inc.*, 98 F.3d 1563, 1570 (Fed. Cir. 1996); *see also In re Rinehart*, 531 F.2d 1048, 1052 (CCPA 1976) ("Though the tribunal must begin anew, a final finding of obviousness may of course be reached, but such finding will rest upon evaluation of all facts in evidence, uninfluenced by any earlier conclusion reached by an earlier board.")

phenobarbital, and valproic acid, had limited, if any, efficacy in treating neuropathic pain. (*Id.* (citing Tr. at 1355:9-1356:21 (White); Tr. at 1477:24-1478:22 (Clauw); Tr. at 1571:13-1572:7 (Woolf)).) Notably, even the defendants' witness, Dr. Mellick, testified that some anticonvulsants, such as phenobarbital, were actually known in the art to enhance pain. (*Id.* (citing Tr. at 1355:16-1356:1 (Mellick)).)

Moreover, the plaintiffs' expert, Dr. Clauw, whose testimony the court finds credible, stated that while some anticonvulsants, such as carbamazepine, were known to affect neuropathic pains characterized by sharp, stabbing, or lancinating pain, such as trigeminal neuralgia, they were generally not effective in treating other types of neuropathic pain. (*Id.* at 19 (citing Tr. at 1478:8-1479:20 (Clauw); Tr. at 1571:13-1572:19 (Woolf)).) This conclusion is likewise supported by contemporary literature, which reflected concerns as to anticonvulsants' limitations as analgesics. For instance, a March 1984 article in *Clinical Neuropharmacology*[22] cautioned the use of anticonvulsants due to their lack of efficacy in the treatment of burning and aching pain, as opposed to lancinating pain. (*Id.* (citing DTX-2224).)

In view of the foregoing, the court rejects the defendants' assertion that those of ordinary skill in the art in 1996 would have viewed anticonvulsants "generally" as "useful for neuropathic pains," as Dr. Loeser opined. Rather, the court finds, based on the evidence presented at trial, that skilled artisans in 1996 would have recognized that many anticonvulsants would prove ineffective in treating and, in some instances would in fact worsen, a patient's pain. Thus, the court concludes that the defendants have failed to show by clear and convincing evidence that the use of anticonvulsants to treat pain was obvious as of July 24, 1996.

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[22] Mark Swedlow, *Review: Anticonvulsant Drugs and Chronic Pain*, CLINICAL NEUROPHARMACOLOGY Vol. 7, No. 1, at 31-82 (1984).

b. Prior Art Indicating That Pregabalin and Gabapentin Share Pharmacological Activity and That Pregabalin Would Prove Effective in Treating Pain

The defendants also assert that various case reports available in 1996 indicated that gabapentin, a compound sharing some similarities with pregabalin, was known to be an effective analgesic. (*Id.* (citing Tr. at 1391:24-1393:21 (Loeser)).) Specifically, Dr. Loeser testified that, as of 1996, there were at least "half a dozen" case reports[23] detailing gabapentin's successful treatment of patients with neuropathic pain, even where the treatment of such patients was ineffective using other compounds. Tr. at 1391:3-1395:5 (Loeser). Dr. Loeser further testified that these gabapentin results could be used to predict pregabalin's effectiveness in treating neuropathic pain because it "was known to have similar anticonvulsant activities to gabapentin." *Id.* In particular, Dr. Loeser noted that skilled artisans in 1996 could reliably make this prediction because: (1) it was known that both gabapentin and pregabalin bound to a binding site in the brain determined to be the α2δ subunit of voltage-gated calcium channels (D.I. 353 at 20 (citing DTX-1104; DTX-1090; Tr. at 1051:12-16, 1056:16-1057:2 (Taylor)); (2) the R-enantiomer of 3-isobutylGABA and the amino acid L-leucine also bound to the α2δ subunit (*id.* (citing DTX-1104; DTX-1090; Tr. at 1583:10-1585:5, 1579:14-1580:28 (Woolf)); and (3) "it was known that anticonvulsant activity was proportional to the binding affinity to that site, all of which suggested that this was a drug that was, in many ways, similar to gabapentin" and would have the same mechanism of action (Tr. at 1395:10-18 (Loeser)).

Conversely, the plaintiffs presented evidence challenging the contention that gabapentin's success in treating neuropathic pain was considered by persons of ordinary skill in the art in 1996 to mean that pregabalin would also prove effective in pain treatment. First, the plaintiffs note

[23] In particular, Dr. Loeser identified the following as case reports on which he relied in forming his conclusion that gabapentin was an effective analgesic: DTX-1978; DTX-468; DTX-2213; DTX-1030; DTX-2173; DTX-2394; DTX-1589.

that none of the case reports Dr. Loeser referenced mentioned pregabalin and, further, that skilled artisans in 1996 would have "no expectation that pregabalin would be an effective analgesic," as it was known that "even a very small difference in the structure of a chemical can result in a complete failure" and lead to dramatic differences in therapeutic outcomes.[24] Tr. at 1570:10-1571:4 (Woolf); *id.* at 1361:12-14, 1364:13-15 (Mellick).

Second, the plaintiffs argue that gabapentin and pregabalin sharing a common binding site would not indicate to a skilled artisan in 1996 that they would have the same mechanism of action and would prove effective in treating pain. Specifically, the plaintiffs' expert, Drs. Taylor and Woolf, testified that, in 1993, Parke-Davis discovered that gabapentin and pregabalin "bound to an undefined, uncharacterized binding site in the brain." (D.I. 353 at 20 (citing Tr. at 1051:12-16 (Taylor)).) In 1996, Parke-Davis discovered that the undefined binding site was the $\alpha 2\delta$ subunit. (*Id.* (citing Tr. at 1056:16-1057:2 (Taylor)).) However, while the identification of this subunit was an "exciting finding," Dr. Woolf explained that the discovery "raised many issues" as to the subunit's possible role in mediating the anticonvulsant action of gabapentin. (*Id.* (citing Tr. at 1577:10-1578:15)).) Chief among them: (1) whether, in this instance, the common binding site indicated that the site is responsible for the pharmacological actions of the drug because, generally speaking, this was not the case; and (2) whether the binding site was

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[24] Specifically, Dr. Woolf stated, in testimony the court finds credible, that:

Q: In general, can you draw conclusions about the effectiveness of one compound based on case reports about another compound?

A: No, for two reasons. One is, case reports by themselves do not constitute, in my opinion, evidence of efficacy. But in any case, even more important, each compound is nnique. Even if they have structural similarities, the way that a compound works pharmacologically is like a lock and key. It has to fit exactly into the lock in order to function. Even a very small difference in the structure of the chemical can result in a complete failure for the compound to interact with its target.

As of July, 1996, there was no means to determine, for example, whether pregabalin would have an identical structural shape to fit into its binding partner.

Q: Specifically, what could be predicted about pregabalin's analgesic potential based on case reports about gabapentin?

A: In my opinion, nothing could be predicted.

Tr. at 1570:10-1571:4 (Woolfe).

relevant to the therapeutic actions of the two compounds, particularly in light of the fact that the R enantiomer of 3-isobutylGABA and the amino acid L-leucine also bound to the same site and were known to have little anticonvulsant activity in 1996. (*Id.* (citing Tr. at 1579:14-1580:18, 1583:10-1585:5 (Woolfe); DTX-1104; DTX-1090).)

Third, the plaintiffs further contend that, if anything, the location of the binding site on calcium channels and its distribution in the body taught away from the conclusion that the site was relevant to gabapentin's mechanism of action. (*Id.*) In particular, the plaintiffs note that, as of 1996, it had been shown that: (1) gabapentin had no effect on calcium currents in neuronal cells, such that it was unclear how the α2δ subunit could be related to pharmacological activity (*id.* (citing DTX-1090; PTX-702; PTX-714; Tr. at 1582:12-17, 1588:2-1589:6 (Woolfe); Tr. at 1434:14-1435:14 (Enna)); (2) gabapentin bound to the site most significantly in skeletal muscle with lesser binding in heart tissue and that skilled artisans would have assumed that, if the α2δ subunit were pharmacologically relevant, binding to the cerebellum and heart and skeletal muscle would lead to changes in motor function, coordination, and excitability of the heart, which it did not (*id.* (citing DTX-1090; Tr. at 1578:3-1579:13 (Woolfe)). In sum, the plaintiffs contend that persons of ordinary skill in the art in 1996 attributed gabapentin's effectiveness in treating pain to mechanisms other than the α2δ subunit, such as the GABAergic system. (*Id.* at 21 (citing DTX-1589; DTX-1660; DTX-2213; PTX-714; Tr. at 1362:14-1363:9 (Mellick); Tr. at 1402:21-1404:1 (Loeser); Tr. at 1481:12-1483:5 (Clauw)).)

Finally, the plaintiffs note that even the defendants' expert, Dr. Loeser, admitted on cross examination that, in the mid-1990s, the majority of skilled artisans did not know how gabapentin worked and often suggested other mechanisms of action. Tr. at 1403:20-1404:1 (Loeser); *id.* at 1429:9-1430:3 (Enna). In fact, the plaintiffs note that research into these other mechanisms

continued after the filing of the RE '920 Patent and that the defendants did not provide any prior art teaching that gabapentin's analgesic effects are related to its binding to the α2δ subunit. (D.I. 353 at 21 (citing PTX-714; Tr. at 1068:11-1069:4 (Taylor); Tr. at 1585:12-1586:8 (Woolf)).)

In view of the foregoing, and in consideration of the relevant law, the court agrees with the plaintiffs that the defendants have failed to show, by clear and convincing evidence, that the use of pregabalin to treat pain was obvious in light of gabapentin. Specifically, while the court does not agree with the plaintiffs that the prior art necessarily taught away from the use of pregabalin to treat pain because other α2δ subunit binding compounds showed little anticonvulsant activity, it finds that the prior art does not render the asserted claims of the RE '920 Patent obvious. The court is not persuaded, based on its review of the record and evaluation of expert testimony, that the prior art clearly and convincingly taught or suggested a reasonable expectation of success with the use of pregabalin for the treatment of pain as claimed in the RE '920 Patent.[25] This conclusion is further supported by the secondary considerations addressed below.

5. The RE '920 Patent: Secondary Considerations

The evidence in the record on secondary considerations weighs in favor of non-obviousness and, therefore, supports the court's finding above that the RE '920 Patent is not obvious in light of the prior art. As noted in connection with the '819 Patent secondary considerations examined above, secondary considerations can be evaluated where a defendant

[25] As noted, as of 1996: (1) anticonvulsants were not generally understood to be effective analgesics; (2) the pharmacological mechanism of action of gabapentin was not established and, as a result, one could not use gabapentin to predict pregabalin's pharmacological activity with any degree of certainty; and (3) it was not understood whether any known analgesic activity of gabapentin was attributable to any particular mechanism of action. Thus, the defendants have failed to prove by clear and convincing evidence that a person of ordinary skill in the art would have reason to try, with a reasonable expectation of success, S-3-isobutylGABA for the treatment of the chronic pain covered by the RE '920 Patent. Moreover, the Examiner's determination that the prior art related to gabapentin's use as an analgesic and its relationship to pregabalin did not render pregabalin's use in the treatment of various chronic pains obvious is entitled to deference. *See Polaroid Corp. v. Eastman Kodak Co.*, 789 F.3d 1556, 1560 (Fed. Cir. 1986).

has established a *prima facie* case of obviousness. In such an instance, the plaintiff can present evidence of secondary considerations to rebut or overcome this *prima facie* showing. *See, e.g.*, *In re Huang*, 100 F.3d 135, 139 (Fed. Cir. 1996). Here, the plaintiffs presented evidence of long felt but unmet need and of commercial success. Because the court addressed the commercial success secondary consideration above in connection with the '819 Patent,[26] it considers only evidence of long felt but unmet need in this subsection.

Specifically, the plaintiffs presented testimony, via its expert, Dr. Clauw, that, by the 1990s, chronic pain, such as neuropathic and fibromyalgia pain, was difficult to treat and that the treatments available suffered from significant problems including inconsistent efficacy, incidence of severe side effects, and the possibility of addiction and overdose. Tr. at 1467:4-1472:1 (Clauw). Dr. Clauw testified that, as of 1996, opioids, NSAIDS, and tricyclic antidepressants were frequently used for the treatment of chronic pain, but that each presented significant limitations with respect to their efficacy and safety profiles. *Id.* In support of its long felt but unmet need argument, the plaintiffs also highlight that Dr. Loeser, the defendants' expert, testified that, in 1996, gabapentin addressed this existing, unmet need. *Id.* at 1399:9-24 (Loeser).

The plaintiffs assert that Dr. Loeser's statement demonstrates that there was a long felt but unmet need as of 1996 for a chronic pain treatment. Expanding on Dr. Loeser's statement, the plaintiffs also contend, however, that pregabalin met this need because it has significant therapeutic benefits over gabapentin, in that its linear dose-response relationship requires lower doses for analgesic activity, has a shorter time to titrate to an effective dose, and exhibits a broader spectrum of efficacy in different pain types. To this end, the plaintiffs assert that pregabalin addressed a need unmet by gabapentin—namely, an effective and well-tolerated pain treatment. *Id.* at 1472:2-1473:3, 1474:10-1477:15 (Clauw). In light of the evidence in the

[26] *See supra* Section III.A.3.c.

record, the court finds Dr. Clauw's assessment of pregabalin's effect on the treatment of chronic pain to be persuasive and agrees that the plaintiffs have presented evidence sufficient to show that pregabalin met a long felt but unmet need.[27] Thus, the court concludes that the secondary considerations evidence the plaintiffs presented at trial supports its finding of non-obviousness with respect to the RE '920 Patent.

B. Anticipation

The defendants assert, as one of their invalidity defenses, that claim 2 of the '819 Patent is invalid for inherent anticipation by U.S. Patent No. 4,123,438 ("the Geurts reference" or "Geurts").[28]

1. The Legal Standard

"[I]nvalidity by anticipation requires that the four corners of a single[] prior art document describe every element of the claimed invention, either expressly or impliedly, such that a person of ordinary skill in the art could practice the invention without undue experimentation." *Advanced Display Sys. Inc. v. Kent State Univ.*, 212 F.3d 1271, 1282 (Fed. Cir. 2000). The Federal Circuit recently discussed the standards for inherent disclosure in *Verizon Services Corp. v. Cox Fibernet Virginia, Inc.*, 602 F.3d 1325 (Fed. Cir. 2010):

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[27] Specifically, Dr. Clauw testified that pregabalin met a long felt but unfilled need, because:

> [Prior drug treatments], at best, worked in 50 percent of individuals, and then and now, the overwhelming majority of individuals with chronic pain, we can't treat their pain well enough that we would like them to or that they would like to get improvement. . . . [Pregabalin, however,] had at least as good efficacy and significantly less toxicity than these drugs that are listed here, opioids, nonsteroidal anti-inflammatory drugs, and tricyclics. And, in fact, for fibromyalgia, it was really only one of those classes of drugs that was at all helpful, which were the tricyclic drugs. . . . So one of the ways that it met this unmet need is that it had at least as much efficacy, significantly less toxicity than these commonly used analgesics [and] [e]ven after gabapentin appeared on the market, there were significant clinical advantages of pregabalin over gabapentin.

Tr. at 1472:2-1473:9 (Clauw).

[28] *See supra* note 6. The court notes that the defendants also raise an anticipation defense in connection with claim 4 of the '819 Patent. The court does not address this contention here, however, because it is related to the defendants' inventorship argument and, therefore, is more appropriately addressed in that section. *See infra* Section III.D.3.

> "[A] prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." However, a patent claim "cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled." "The standard for what constitutes proper enablement of a prior art reference for purposes of anticipation under section 102, however, differs from the enablement standard under section 112." It is well-settled that utility or efficacy need not be demonstrated for a reference to serve as anticipatory prior art under section 102.

Id. at 1337 (internal citations omitted). Moreover, inherent anticipation, which the defendants assert here, requires that every element of the claim be "necessarily and inevitably" present in the anticipating reference, even though those elements are not expressly disclosed. *See Schering Corp. v. Geneva Pharms.*, 339 F.3d 1373, 1378 (Fed. Cir. 2003). Whether a prior art reference anticipates a patent claim is a question of fact and must be established by clear and convincing evidence. *Advanced Display Sys.*, 212 F.3d at 1281; *see also AstraZeneca LP v. Apotex*, 633 F.3d 1042, 1055 (Fed. Cir. 2010).

2. The Parties' Contentions & Discussion

The defendants contend that claim 2 of the '819 Patent is inherently anticipated by U.S. the Geurts reference[29] because 3-isobutylGABA would be necessarily synthesized when a person of ordinary skill in the art conducted the chemical reaction disclosed in Example 6 of that reference. (D.I. 353 at 3.) To support this argument, the defendants offered the testimony of their expert, Dr. Atwood, who explained that he reproduced the chemical process described in Guerts Example 6 and identified 3-isobutylGABA in the products of that reaction. (*Id.* (citing Tr. at 675:9-15, 676:1-12, 718:14-21 (Atwood)).) The plaintiffs, however, challenge Dr. Atwood's adherence to Geurts Example 6 and assert that his analytical data does not, in fact, demonstrate the presence of 3-isobutylGABA, such that the Geurts reference cannot anticipate

[29] *See* DTX-1157. The court notes that DTX-1157 is also referenced as PTX-650 in the trial transcript.

claim 2. In view of the evidence presented at trial and the record before it, the court finds, for the reasons that follow, that claim 2 of the '819 Patent is not anticipated by the Geurts reference.

First, the court concludes that Dr. Atwood did not adhere to the requirements of Example 6 when he attempted to reproduce the chemical process described therein. Specifically, and as explained by the plaintiffs' expert, Dr. Bannister, Guerts Example 6's first step calls for the use of ammonia. Dr. Bannister explained, in testimony the court finds credible, that the term "ammonia" would be understood by a person of ordinary skill in the art to mean pure ammonia without water, which is otherwise known as "anhydrous" or "liquid ammonia." (*Id.* (citing DTX-1157, col. 2, ll. 43-46; Tr. at 1082:3-8 (Bannister)).) Ammonia with water, which is the type of ammonia Dr. Atwood used in his experiment, is generally described by skilled artisans and chemists as "aqueous ammonia" or "ammonium hydroxide," rather than simply as "ammonia." (*Id.* (citing Tr. at 1082:9-14, 1081:21-22 (Bannister)).)

As additional evidence to show that Geurts Example 6 calls for the use of anhydrous, not aqueous, ammonia, the plaintiffs note that Column 2 of the Geurts reference states that "preferably the hydrogenation is conducted in the presence of an inert solvent such as pyridine, pyrrolidone[,] or toluene," and water is not an inert solvent. *See* DTX-1157, col. 2, ll. 2-6; *see also* Tr. at 1084:5-15 (Bannister). Moreover, Dr. Bannister noted that there were numerous publications in the literature prior to the Geurts reference that showed the use of anhydrous ammonia in hydrogenation reactions similar to that disclosed in Geurts.[30] *See, e.g.*, PTX-644; *see also* Tr. at 1082:15-1084:4 (Bannister). The plaintiffs further presented evidence that Dr. Atwood's reaction itself demonstrates why a person of ordinary skill in the art would have

[30] Specifically, Dr. Bannister noted that:

> Ammonia has been used to describe anhydrous ammonia for a long time, going back to, I think, at least the 1930s and beyond. Liquid ammonia, anhydrous ammonia has been used and described in the literature as ammonia. And I think one example [PTX-644] brought up in my deposition was that there is a very old reaction from the thirties called a metal ammonia reaction.

Tr. at 1082:18-24 (Bannister).

understood Geurts Example 6 to mean anhydrous ammonia. Specifically, Dr. Bannister explained that substituting aqueous ammonia for anhydrous ammonia in conducting Example 6 would result in "multiple dead-end reaction pathways, would greatly reduce the overall efficiency of the intended reaction, and could prevent formation of the desired end products." (D.I. 353 at 4 (citing PTD-840A; Tr. at 1087:12-1088:07 (Bannister); Tr. at 1206:20-1209:15 (Roush)).) In fact, as the plaintiffs' expert, Dr. Roush, explained, the only compound that Dr. Atwood identified from his reaction could only result from a dead-end pathway, which would not have been intended by Geurts.[31] Tr. at 1206:20-1209:15 (Roush).

The plaintiffs also contend, and the court agrees, that Dr. Atwood's use of aqueous ammonia cannot be reconciled with the guidance of the Geurts reference or principles of organic chemistry and, further, that Dr. Atwood's failure to confirm whether he ran the reaction properly undermines the reliability of his results and his anticipation opinion generated from those results. The Geurts reference identifies two pyrrolidones as the expected and intended products of the Example 6 reaction and provides the expected yields of those intended products. *See* DTX-1157 at col. 3, ll. 40-46; *see also* Tr. at 1094:17-1095:6 (Bannister). However, despite the fact that Dr. Atwood had the capability to detect these products in the amounts and ratios detailed in Geurts

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[31] In particular, Dr. Roush explained:

Q: Now, what do you take from the presence of this product in Dr. Atwood's experimental work?

A: This product is evidence that having water in the initial hydrogenation step is actually detrimental to that process. . . . This material only arises by hydrolysis, and it occurs during the first step of the overall sequence. We heard Dr. Bannister earlier today testify that water in the hydrogenation step could lead to side reactions. Well, here is one such side reaction. And Dr. Atwood provides evidence of the side reaction.

Q: Could this compound have been produced if water was not present in the first hydrogenation step?

A: No, it could not be produced if water was not present in that first step.

Q: Does this compound appear anywhere in the Geurts patent?

A: No, it does not.

Tr. at 1208:9-1209:19 (Roush).

Example 6 to determine if the reaction was completed properly,[32] he did not do so. Tr. at 1106:21-1107:5 (Bannister); *id.* at 720:19-721:9, 721:10-21 (Atwood).

Based on the evidence before it, the court finds that Dr. Atwood did not accurately reproduce the reaction described in Geurts Example 6 because he used aqueous ammonia instead of anhydrous ammonia and did not attempt to confirm that this decision was correct or that he properly executed the reaction. Conversely, Dr. Bannister conducted the reaction using anhydrous ammonia and determined that he obtained the intended products of Example 6 in the ratios described in the patent, thus confirming that he ran the experiment properly. Tr. at 1092:12-19, 1094:4-1095:6 (Bannister). Moreover, the plaintiffs note that the Geurts reference does not concern pharmaceutical compounds or processes and does not identify or refer to 3-isobutylGABA at all. *Id.* at 1081:1-4. Consequently, the court concludes that Dr. Atwood's detection of 3-isobutylGABA during his reaction is not reliable to establish inherent anticipation by clear and convincing evidence.

Second, the court further concludes that Dr. Atwood's analytical data does not demonstrate the presence of 3-isobutylGABA in his reaction results. Specifically, Dr. Atwood testified that he attempted to identify 3-isobutylGABA in his reaction products using High Performance Liquid Chromatography ("HPLC") and X-ray Power Diffraction ("XRPD"). *Id.* at 699:17-700:7, 710:3-7 (Atwood). According to Dr. Atwood's testimony, his HPLC traces show a peak attributable to the presence of 3-isobutylGABA in the sample. *Id.* at 709:7-22. Dr. Bannister explained that, to confirm the presence of one compound in a mixture of other compounds using HPLC, it is important to use complementary methods, such as mass

[32] The plaintiffs correctly note that Dr. Atwood had the ability to confirm his results because he used NMR analysis at the outset to confirm the reaction he used to prepare his starting materials. Tr. at 720:19-721:9 (Atwood). Dr. Atwood also acknowledged that he did not use any other method by which to confirm successful replication of Geurts Example 6. *Id.*

spectroscopy, NMR, and control compounds to authoritatively determine that an HPLC peak results from the compound-in-question. *Id.* at 1107:6-1108:13 (Bannister). Dr. Atwood, however, admitted that his HPLC traces contained "somewhere between four and six peaks" and that "each of those peaks correspond[s] to the compound." *Id.* at 700:9-21 (Atwood). Dr. Atwood did not obtain HPLC traces for his reference standards and did not identify which compound was associated with each peak. *Id.* at 1107:25-1108:13 (Bannister). Therefore, Dr. Bannister concluded, and the court agrees, that the peaks Dr. Atwood attributes to 3-isobutylGABA may, in fact, be attributed to another compound.

This conclusion is further supported by the results of Dr. Atwood's HPLC "spiking experiments" and XRPD. With regard to the former, spiking experiments involve tests in which one compound is added to a sample. If the spiking experiment is reliable, a single spiked peak will increase in size and will be associated with the compound added to the sample. *Id.* at 1211:8-1212:7 (Roush). If the spiking experiment is unreliable, the sample will show changes in the size or movements in the retention time of other peaks. *Id.* Here, Dr. Atwood added a standard of 3-isobutylGABA to his sample, but observed that several different peaks changed in the spiked HPLC traces—some increased or decreased in size and others were no longer present. *Id.* at 706:21-707:7 (Atwood); *id.* at 1211:8-1212:7, 1212:18-1215:18 (Roush). Thus, because Dr. Atwood did not observe a single peak change upon adding 3-isobutylGABA to the sample, the court agrees with Dr. Roush's opinion, developed through testimony the court finds credible, that Dr. Atwood's spiking experiment was not reliable. *Id.*

Dr. Atwood's XRPD results from his samples likewise suffer in their reliability. Specifically, and as the plaintiffs' expert, Dr. Myerson, testified, the use of XRPD to identify a single compound in a mixture of unknown compositions is an atypical use of this type of testing.

Id. at 1151:24-1152:5 (Myerson). XRPD is commonly used to characterize a particular crystalline form in a known sample and it is difficult to use the testing to show the presence of one compound in a mixture of unknown compounds because any given peak may be shared by more than one compound resulting in overlapping or interfering peaks. *Id.* at 1149:23-1150:12, 1150:13-1151:23. To this end, only when the XRPD diffractogram for each compound in the mixture is known may a scientist say with certainty that one peak or set of peaks is unique to a particular compound for identification purposes. *Id.* at 1150:13-1151:23. Here, Dr. Atwood did not determine the composition of the sample he tested by XRPD and did not possess diffractograms for every compound in the sample. Moreover, of the eighty XRPD diffractograms Dr. Atwood provided, each of which was an image corresponding to an individual XRPD test, there is only one that he claims shows the presence of 3-isobutylGABA. Notably, none of the other diffractograms, including those from other experimental runs, indicate the presence of 3-isobutylGABA. *Id.* at 1161:15-1164:6. Based on this evidence, the court concludes that Dr. Atwood's analysis does not reliably demonstrate that 3-isobutylGABA was present in the sample.

In view of the foregoing, the court concludes that the defendants have failed to show that the Geurts references anticipates claim 2 of the '819 Patent. This finding is further reinforced by the fact that the plaintiffs' expert, Dr. Bannister, properly carried out Geurts Example 6. Specifically, Dr. Bannister analyzed the products of the reaction using HPLC and confirmed his analysis with two spectroscopic techniques—mass spectroscopy ("mass spec") and nuclear magnetic resonance spectroscopy ("NMR"). *See* PTX-1391; Tr. at 1093:22-1094:3 (Bannister). Through these tests Dr. Bannister identified the expected ratios of each of the expected products of Geurts Example 6 in his final material using HPLC and confirmatory mass spec and NMR

analysis. Tr. at 1094:4-1095:6, 1103:15-1104:9 (Bannister). Dr. Bannister also found that, through each of his analytical techniques, 3-isobutylGABA did not appear in any of his experimental samples, such that the Geurts reference does not "necessarily and inevitably" produce this compound. Thus, claim 2 of the '819 Patent is not invalid as inherently anticipated by the Geurts reference. *See AstraZeneca LP*, 633 F.3d at 1055; *Schering*, 339 F.3d at 1378.

C. Priority & Enablement

The parties contest the priority date to which claims 1, 2, and 4 of the '819 Patent and claim 1 of the '175 Patent are entitled. For the reasons that follow, the court finds that the asserted claims of the '819 Patent and claim 1 of the '175 Patent are entitled to priority filing dates of November 27, 1990. For the purpose of clarity, the court evaluates the priority date of each patent separately below and, in each section, addresses the impact of those priority dates on the defendants' validity defenses, which the court rejects based on its priority findings.

1. The Legal Standard[33]

To establish that an asserted claim of a patent-in-suit is entitled to the priority filing date of an earlier parent application, the application must provide a sufficient disclosure of the claimed invention under 35 U.S.C. § 112. *Waldemar Link v. Osteonics Corp.*, 32 F.3d 556, 558 (Fed. Cir. 1994). Section 112 requires the application's disclosure to describe the claimed invention and enable a person of ordinary skill in the art to make and use it. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1342-55 (Fed. Cir. 2011) (en banc). To satisfy the enablement requirement of § 112, the disclosure in a parent application, coupled with the knowledge generally available in the art at that time, must enable a person skilled in the art to

[33] The court outlines the relevant legal standards for priority and enablement in this section. The court notes, however, that it does not include the legal standards for obviousness and anticipation—defenses addressed in this section in connection with the defendants' priority and enablement related validity defenses—because these standards were recited in the preceding sections. *See supra* Sections III.A.1 and III.B.1.

make and use the claimed invention without "undue experimentation" as of the filing date of the earlier application. *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988); *see also Genetech, Inc. v. Novo Nordisk A/S*, 108 F.3d at 1361, 1368 (Fed. Cir. 1997). To this end, enablement is "not precluded where a 'reasonable' amount of routine experimentation is required to practice the claimed invention.'" *See ALZA Corp. v. Andrx Pharms., L.L.C.*, 603 F.3d 935, 941 (Fed. Cir. 2010). However, while the knowledge generally available in the art can supplement an application's specification, "[i]t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute adequate enablement." *Genetech, Inc.*, 108 F.3d at 1366.

Notably, the "dispositive question of enablement does not turn on whether the accused product is enabled," but, instead, on whether the specification teach[es] those skilled in the art how to make and use the full scope of the claim without undue experimentation." *Durel Corp. v. Osram Sylvania Inc.*, 256 F.3d 1298, 1306 (Fed. Cir. 2001). In determining whether "undue" experimentation is required to make and use a claimed invention, courts may, but are not required to, consider such factors as: (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. *See In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Federal Circuit has also instructed that "[i]t is unnecessary to spell out every detail of the invention in the specification" to satisfy the enablement requirement and the patent application does not need to disclose specific examples corresponding to every claimed embodiment. *See Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006). On the

contrary, § 112 requires only a "reasonable correlation" between the disclosure and the claims. *Invitrogen Corp v. Clontech Labs., Inc.*, 429 F.3d 1052, 1071 (Fed. Cir. 2005). Importantly, the Federal Circuit has established that an issued patent is presumed valid by statute. *See* 35 U.S.C. § 282. That presumption can be overcome only by clear and convincing evidence, which is defined as evidence that "proves in the mind of the trier of fact an abiding conviction that the truth of [the] factual contentions [is] highly probable." *Intel Corp. v. U.S. Int'l Trade Comm'n*, 946 F.2d 821, 830 (Fed. Cir. 1991).

2. The '819 Patent's Priority Filing Date/Enablement

The plaintiffs assert that claims 1, 2, and 4 of the '819 Patent are entitled to a priority date of November 27, 1990, the date of U.S. Patent Application No. 07/619,692, the Initial Application that led to the '819 Patent, because the '692 application would have enabled persons of ordinary skill in the art to make S-3-isobutylGABA and its single optical isomers without undue experimentation, by a variety of methods. (D.I. 351 at 3.) Conversely, the defendants challenge that claims 1, 2, and 4 of the '819 Patent are entitled only to a priority filing date of May 20, 1992, the date of the first continuation-in-part of the Initial Application, U.S. Patent Application No. 07/886,080, because the '692 application did not enable the S enantiomer of 3-isobutylGABA as a single optical isomer. (D.I. 352 at 2; D.I. 349 at 24.)

a. The Defendants' Contentions

The defendants maintain that, at the time of the '692 application, the plaintiffs had only enabled a racemic mixture of 3-isobutylGABA and that, because claim 2 requires enablement of both racemic mixtures and of the individual R and S enantiomers in isolation, claim 2 is not entitled to a November 1990 priority filing date. (D.I. 349 at 24.) In support of this argument, the defendants note that Dr. Silverman, the first named inventor, admitted that the '692

application does not disclose a method to make either the individual enantiomers of 3-isobutylGABA or non-racemic mixtures containing varying proportions of the two. (*Id.* (citing Tr. at 921:16-22, 929:14-930:4 (Silverman); Tr. at 532:23-533:10 (Andruszkiewicz)).) Instead, the '692 application states that "[t]he single diastereomers or enantiomers may be prepared or isolated by methods already well known in the art." (*Id.* at 25 (citing DTX-863 at PFE_LYR_1961).) The defendants note that the '692 application fails to specify starting materials or reaction conditions to make the R or S enantiomer of any non-racemic mixtures thereof and that the Examiner initially rejected claims to single enantiomers in the application as non-enabled because "no reference is made to the preparation of specific optical enantiomers." (*Id.* (citing PTX-9 at PFE_LYR_1993).)

In making this argument, the defendants reject the notion that the R and S enantiomers of 3-isobutylGABA were enabled by the '692 application because they could be "prepared or isolated by methods already well known in the art," as the application stated. (*Id.*) The defendants' expert, Dr. Davies, testified that, as of November 1990, there were three techniques that could be used to attempt to obtain a single enantiomer: (1) classical resolution by making diastereomeric salts or derivatives; (2) chiral chromatography; and (3) chiral synthesis.[34] (*Id.* (citing Tr. at 603:23-604:19, 612:5-14, 612:22-613:2 (Davies)).) The defendants assert that three highly skilled scientists, all employing each approach, attempted and failed to isolate the S enantiomer of 3-isobutylGABA contemporaneously with the filing of the '692 application and

[34] Dr. Davis explained that classical resolution by making diastereomeric salts or derivatives involves reacting a chiral resolving agent with a target to form a mixture of either diastereomeric salts or covalently bonded derivatives, both of which contain each of the individual enantiomers connected to the resolving agent. (D.I. 349 at 25.) The diastereomeric salts or derivatives are then separated based on differences in their physical properties. (*Id.* (citing Tr. at 610:9-611:10, 612:5-14 (Davies)).) Chiral chromatography involves separating R and S enantiomers by exploiting their different propensities for binding to chiral column substrates. (*Id.*) Finally, enantiomeric synthesis involves making a single enantiomer of a compound using a series of reactions that employ a chiral starting material or a chiral catalyst such as pig liver esterase ("PLE"). (*Id.* (citing Tr. at 613:3-18, 614:1-21, 615:13-616:5, 616:11-19 (Davies)).)

after, such that the '692 application's description that the S enantiomer could be resolved by routine methods known in the art was incorrect and, therefore, not enabled. (*Id.*)

Specifically, the defendants, rely upon the testimony of their expert, Dr. Davies, to argue that Drs. Andruszkiewicz, Pavia, and, at the outset, Yuen, were unable to make the individual enantiomers of S- and R-3-isobutylGABA or non-racemic mixtures of the two. First, the defendants note that while Dr. Andruszkiewicz was able to separate enantiomers of 3-methylGABA, he failed, after extensive experimentation with classic resolution and PLE, to separate the enantiomers of 3-ethylGABA and did not attempt separation of 3-isobutylGABA because he believed that the available techniques would not work. (*Id.* (citing Tr. at 624:10-625:25, 626:20-629:2, 629:3-630:12 (Davies); Tr. at 529:25-530:6, 530:13-20 (Andruszkiewicz); DTX-1887; DTX-2741).) In particular, the defendants charge that despite Dr. Andruszkiewicz's success using PLE on 3-methylGABA, his 3-ethylGABA work convinced him that PLE would not prove successful in separating 3-isobutylGABA. (*Id.* at 27 (citing Tr. at 529:25-530:20 (Andruszkiewicz)).)

Second, the defendants argue that Dr. Pavia, a chemist enlisted by Pfizer to separate the enantiomers of 3-isobutylGABA, was also unable to do so using routine resolution methods known in the art at the time of the '692 application. The defendants note that Dr. Pavia used chiral synthesis employing PLE, classic resolution, and chiral chromatography and ultimately failed to separate the enantiomers using all three methods. While Dr. Pavia was able, using PLE, to obtain a 75:25 mixture of a precursor of non-racemic 3-isobutylGABA, the defendants assert that this mixture was "far short of the level of purity required by the patented claims," rendering him unsuccessful in making the R or S enantiomer. (*Id.* (citing Tr. at 631:21-632:1, 636:17-638:14, 638:24-639:8 (Davies); Tr. at 545:12-20 (Pavia); Tr. at 554:3-13 (Yuen); DTX-925A at

PFE_LYR_68151-68152).) The defendants also state that Dr. Pavia did not know the precise identity of the precursor he did make and told Dr. Yuen that he considered his work a failure. (*Id.* (citing Tr. at 1190:25-1191:1 (Roush); Tr. at 639:2-8 (Davies); Tr. at 554:3-13 (Yuen)).)

Third, the defendants argue that the work of Dr. Yuen, a chemist who was instructed by Pfizer to separate 3-isobutylGABA's enantiomers and successfully did so, establishes by clear and convincing evidence that separation of the R and S enantiomers could not be accomplished by routine methods available in the 1990 prior art. Specifically, Dr. Yuen testified that, upon reviewing Dr. Pavia's work, he concluded that the classic resolution and PLE methods would prove ineffective. (*Id.* at 28 (citing Tr. at 552:6-554:17, 564:22-565:4, 569:20-570:10 (Yuen); Tr. at 639:18-25 (Davies); DTX-817 at PFE_LYR_1153).) Based on this finding, and as he explained in a declaration submitted in connection with the '819 Patent,[35] Dr. Yuen decided to attempt to make S-3-isobutylGABA and R-3-isobutylGABA using a chiral auxiliary. (*Id.* (citing Tr. at 558:21-25 (Yuen)).) The defendants note that, despite his four to five years of experience with chiral synthesis, Dr. Yuen was unable to make S-3-isobutylGABA and R-3-isobutylGABA on his first attempt. Dr. Yuen ultimately prevailed and obtained R-3-isobutylGABA after carrying out thirty-five reactions and "overcoming numerous challenges along the way." (*Id.* (citing Tr. at 641:23-642:22, 644:7-648:13 (Davies); Tr. at 556:15-22, 557:12-558:20 (Yuen); DTX-968A; DTX-817 at PFE_LYR_1153).) Dr. Yuen subsequently obtained S-3-isobutylGABA on September 30, 1991, ten months after the filing of the '692 application. (*Id.* (citing Tr. at 580:19-581:6 (Yuen); DTX-968A at PFE_LYR_0097732).)

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[35] Dr. Yuen submitted a declaration to the PTO during the prosecution of the '819 Patent wherein he stated:

> Knowing that Dr. Pavia's work had failed . . . and knowing that finding a resolving agent that would effectively separate the R and S enantiomers of [3-isobutylGABA] could be very difficult, I believed the best way to make the individual R and S enantiomers was to develop a chiral synthesis.

(*Id.* at 28 (citing DTX-817 at PFE_LYR_1153; Tr. at 640:1-21 (Davies)).)

The defendants argue that Dr. Yuen's chiral synthesis was "innovative" because it resulted in a "β-stereocenter," which would have been unexpected using this type of synthesis, as it was often used as a way of generating an α-stereocenter. (*Id.* at 29 (citing Tr. at 647:7-648:23 (Davies); DTX-2707; DTX-2708).) The defendants assert that this contention is supported by the '819 Patent, the '080 application, and statements the plaintiffs made to the Examiner during the prosecution of 08/420,905 ("the '905 application"), a continuation-in-part of the '080 application. With regard to the '819 Patent, the defendants note the Patent states that the available literature teaches toward α-stereocenters and away from β-stereocenters, thus conveying the novelty of Dr. Yuen's method. (*Id.* (citing Tr. at 648:17-23 (Davies); DTX-1 at 5:59-65).) Regarding the '080 application, which was filed as a continuation-in-part to the '692 application on May 20, 1992—the date the defendants assert is the appropriate priority filing date for the asserted claims—that application removed the '692 application's statement that the "enantiomers may be prepared or isolated by methods already well known in the art" and replaced it with twelve pages detailing Dr. Yuen's work, including a full page of complex chemical reactions conceived of solely by Dr. Yuen. (*Id.* (citing PTX-8 at PFE_LYR_001744, 1778-786; PTX-8 at 001759-62).)

Finally, the defendants highlight several statements Pfizer made to the Examiner during prosecution of the '905 application. For instance, in a July 2, 1998 amendment, Pfizer argued that Dr. Yuen's chiral synthesis of S-3-isobutylGABA was not routine, stating that:

> [r]egarding claim 38, directed to the preferred S-(+) stereoisomer of the 3-(2-methylpropyl) substituted compound [a.k.a. S-31BG], Applicants wish to make clear that . . . the preparation of the compound was *not* routine; rather preparation of the stereoisomer clearly required invention on the part of Dr. Yuen. Applicants submit that Poi-Wai Yuen is properly named an inventor because there was no routine way to produce the now-claimed enantiomer at the time that Richard B. Silverman and Ryszard Andruszkiewicz invented the racemic material.

(*Id.* at 29-30 (citing PTX-7b at PFE_LYR_1147-49 (emphasis in original)).) In addition, the defendants argue that Pfizer acknowledged that PLE was not a viable method for making the individual enantiomers of 3-isobutylGABA, stating that "all of Assignee's attempts to obtain the enantiomer by enzymatic resolution using pig liver esterase were unsuccessful," and, further, that classic resolution was not a "routine way to produce" S-3-isobutylGABA. (*Id.* at 30 (citing PTX-7b at PFE_LYR_1147-49).) With regard to the latter, the defendants cite Pfizer's statement that:

> Assignee attempted to resolve the racemic material using a trial of [fourteen] standard resolving acids. Of these agents, three (including mandelic acid worked). Therefore . . . Applicants submit that Poi-Wai Yuen is properly named as an inventor because there was no routine way to produce the now claimed enantiomer.

(*Id.* (citing PTX-7b at PFE_LYR_1149).)

Though the defendants cite these statements in connection with their inventorship argument, addressed *infra*,[36] they argue that they are similarly relevant here in demonstrating that the applicants acknowledged that separation of the R and S enantiomers of 3-isobutylGABA could not be achieved through routine methods known in the art. The defendants assert that the plaintiffs' acknowledgements were consistent with what was known by those of skill in the art in 1990 as to the difficulty in separating enantiomers. (*Id.* at 31.) Specifically, Dr. Davies testified that, as of November 1990, there was nothing in the literature describing the resolution of 3-isobutylGABA or the broader class of 3-aklylGABA compounds and that separating enantiomers

[36] *See infra* Section III.E. As will be examined in greater detail below, the defendants contend that the plaintiffs removed Dr. Yuen as an inventor because the Examiner issued a prior art rejection based on an article by Drs. Andruszkiewicz and Silverman that disclosed racemic 3-isobutylGABA. The defendants note that, according to the Examiner, the article was prior art because the inventive entity (Drs. Andruszkiewicz, Silverman, and Yuen) differed from the authorship of the 1989 article (Drs. Andruszkiewicz and Silverman). (D.I. 349 at 30.) The plaintiffs thus deleted Dr. Yuen, the defendants assert, to get over this prior art. (*Id.*) The defendants include this argument here, however, in an effort to demonstrate that, before the plaintiffs had a motivation to remove Dr. Yuen as an inventor, they acknowledged that his separation of 3-isobutylGABA's enantiomers was achieved through non-routine methods and, therefore, was not enabled by the '692 application. (*Id.*)

using classic resolution "can often be quite difficult," is a "challenging system," and is "notoriously unpredictable." (*Id.* (citing Tr. at 610:9-611:10, 611:11-24, 612:15-21 (Davies)).) Dr. Davies also identified a 1990 article by Drs. Andruszkiewicz and Silverman,[37] wherein they criticized use of resolution of diastereomeric salts to isolate enantiomers of 3-alkylGABA analogs. (*Id.* (citing Tr. at 611:11-612:3, 617:4-9; DTX-822 at NU036182-83).) Dr. Davies opined that this article would have taught skilled artisans away from employing classic resolution methods. (*Id.*)

In addition, the defendants contend that the nature of prior art in 1990 demonstrates that the resolution Dr. Yuen accomplished was not, and would not have been viewed as, routine. Dr. Davies testified that enantiomers of γ-amino acids, such as 3-isobutylGABA, are more difficult to resolve than either α- or β- amino acids because "certain chemical structures on 3-isobutylGABA hinder access of the resolving agent to the third carbon on the GABA backbone containing the isobutyl group." (*Id.* at 32 (citing Tr. at 606:19-609:19 (Davies)).) Likewise, Dr. Davies cited a 2008 Pfizer paper stating that "[t]he direct separation of pregabalin from its enantiomer has proven difficult because pregabalin is a γ-amino acid with both the amine and carboxylic functionalities separated from the chiral center by a methylene group." (*Id.* (citing DTX-1200 at SAND_PREG 153172).) Dr. Davies also noted that, as of November 1990, there were no references containing examples of separating 3-alkylGABA derivatives using chiral chromatography nor were there any reports of successful direct synthesis of the individual enantiomers of GABA compounds with functional groups at the third carbon on the GABA backbone other than methyl, including 3-ethylGABA and 3-isobutylGABA. (*Id.* (citing Tr. at 613:19-25, 614:22-615:3, 616:6-10 (Davies)).) Rather, only one article reported an enzymatic

[37] Andruszkiewicz, R. et al., *Chemoenzymatic Synthesis of (R)- And (S)-4-Amino-3-Methylbutanoic Acids*, SYNTHETIC COMM. 20(1):159-66 (1990).

synthesis of 3-methylGABA, the simplest of the GABA compounds, but did not report success with 3-isobutylGABA or any 3-alkylGABA analog. In addition, the 1989 Lam and Jones paper characterized PLE as more difficult with larger carbon side chains like 3-isobutylGABA. (*Id.* (citing Tr. at 616:20-617:3 (Davies); DTX-822).)

Thus, the defendants argue, in sum, that the '819 Patent is not entitled to the priority filing date of the '692 application, November 27, 1990, because that application provides no direction, guidance, or working examples concerning how to make individual enantiomers or non-racemic mixtures of 3-isobutylGABA other than to state that "[t]he individual diastereomers or enantiomers may be prepared or isolated by methods already well known in the art." Because, the defendants argue, separation of the R and S enantiomers could not be accomplished by methods already known in the art without "undue experimentation" and required Dr. Yuen's invention, the '692 application is not enabled and the appropriate priority filing date for the '819 Patent is May 20, 1992. Here, the defendants rely on the Federal Circuit's direction in *Genentech, Inc. v. Novo Nordisk A/S* that the enablement requirement "cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art" where the specification fails to supply the "novel aspects of the invention." *Genentech, Inc.*, 108 F.3d at 1266. Instead, the application must, the defendants argue, set forth the starting materials or conditions under which the process can be carried out. *Id.* at 1266.

b. The Asserted Claims of the '819 Patent: Discussion & Conclusions of Law

In light of the evidence adduced at trial and in consideration of the relevant law, the court disagrees and finds that the plaintiffs have produced evidence entitling the asserted claims of the '819 Patent to a priority filing date of November 27, 1990 and the defendants have not shown, by

clear and convincing evidence, that the '692 application does not enable each of these claims. The court reaches these conclusions for the reasons that follow.

i. *Claim 2 of the '819 Patent*[38]

Initially, with respect to claim 2, the plaintiffs argue that the defendants' validity defense is misguided, as it misconstrues the court's claim construction of that term. Specifically, the plaintiffs maintain that the defendants' enablement argument centers on the assertion that claim 2 is not entitled to a priority filing date of November 1990 because the '692 application does not explain how to separate the R and S enantiomers of 3-isobutylGABA and such separation could not be achieved using methods known to those of ordinary skill in the art. (D.I. 351 at 4.) In light of the arguments detailed above and the defendants' own statements,[39] the court agrees with the plaintiffs' characterization of the defendants' claim 2 enablement argument.

The plaintiffs charge that this argument fails because claim 2 is "narrowly directed to nothing more than the same compound described in the application—3-isobutylGABA—without any qualification as to enantiomeric forms. (*Id.*) The court agrees. As explained in its Order Construing the Terms of U.S. Patent No. 6,197,819, the court's construction with respect to claim 2 states: "[t]he term '4-amino-3-(2-methylpropyl) butanoic acid" as used in claim 2 is construed to mean 'the chemical compound 4-amino-3-(2-methylpropyl) butanoic acid.'" (D.I. 100.) The court further specified that construing the disputed term in claim 2 to mean 4-amino-3-(2-methylpropyl) butanoic acid is consistent with its conclusion that:

> There is no basis in the specification for the defendants' suggestion that the absence of an (R) or (S) prefix specifically signals the racemate, rather than the compound without limitation as to stereochemical form. Indeed, when the

[38] The court addresses the priority and enablement of claim 2, which claims 3-isobutylGABA, before examining the priority and enablement of claim 1, which claims S-3-isobutylGABA.

[39] The court notes that the defendants state in their Proposed Findings of Fact and Conclusions of Law that "[b]ecause claim 2 of the '819 Patent covers all forms of [3-isobutylGABA] and because Pfizer only enabled one—the racemic mixtures, claim 2 is not entitled to priority to the '692 application." (D.I. 349 at 24.)

> applicants identified the racemate in the specification of the '819 Patent, they used a prefix ("R, S") that does not appear in the disputed claim. The court further agrees with the plaintiffs that the prosecution history behind this claim term does not evince a disclaimer of non-racemic forms of the compound.

(*Id.* at n.2.)

As the plaintiffs correctly highlight, while the court construed claim 1 to mean "4-amino-3-(2-methylpropyl) butanoic acid in the single S-(+) isomer form only, free from the R-(-) isomer form," the court did not construe claim 2 to include this limitation with respect to purity. (*Id.* at 40.) Rather, the court's construction does not require the '692 application to enable each conceivable mixture of 3-isobutylGABA's enantiomers—including "single optical isomer forms" or any other composition of that compound—in order to satisfy the requirements of § 112. (*Id.*) Contrary to the defendants' assertions, where a court, as it has here, construes a claim to cover a chemical compound, the specification is not deficient merely because it does not disclose how to prepare a particular form of that compound.[40] *See In re Hogan*, 559 F.2d 595, 606 (C.C.P.A. 1977) (noting that requiring a specification to disclose how to make each particular form of a compound would "impose an impossible burden on inventors and thus on the patent system" and concluding that "[t]here cannot, in an effective patent system, be such a burden placed on the right to broad claims"). To this end, the court finds that the defendants' enablement argument conflates claim 1, which covers 3-isobutylGABA's S-enantiomer as a "single optical isomer," with claim 2, which covers 3-isobutylGABA "the chemical compound." As a matter of law, claim 1 and claim 2 are separate inventions that are each independently presumed valid and, accordingly, their validity must be considered separately. *See* 35 U.S.C. §

[40] The Federal Circuit's holding in *AK Steel Corp. v. Sollac* is inapplicable in this case based on the scope of claim 2. *See* 344 F.3d 1234 (Fed. Cir. 2003). In that case, the Federal Circuit explained that, where "a range is claimed, there must be reasonable enablement of the scope of the range." *Id.* at 1244. The court notes that, because it does not construe claim 2 to include a range of 3-isobutylGABA or a range with respect to purity, the specification does not need to detail how to make each form of the compound included in that range. *Id.* Rather, claim 2 covers a specific chemical compound and, therefore, the requirements of *AK Steel Corp.* are inapplicable here.

282; *see also Amazon.com Inc. v. Barnesandnoble.com*, 239 F.3d 1343, 1351 (Fed. Cir. 2001) (requiring the validity analysis to be conducted on a "claim-by-claim basis").

In view of the foregoing, the court concludes that claim 2 is enabled by the '692 application. As noted, claim 2 covers 3-isobutylGABA, a chemical compound, which, it is undisputed, was invented by Drs. Silverman and Andruszkiewicz. (D.I. 351 at 16 (citing Tr. at 657:14-18 (Davies); Tr. at 900:8-12 (Silverman); Tr. at 1186:16-1187:2 (Roush); PTX-9a at PFE_LYR_0000001961-63).) The defendants also do not dispute that the '692 application teaches how to make a racemic 3-isobutylGABA and the inventors did in fact do so. (*Id.* (citing Tr. at 658:13-659:11 (Davies)).) Thus, because a person of skill in the art could have relied upon the '692 application's disclosure to prepare 3-isobutylGABA as of November 27, 1990, and no more than routine experimentation in accordance with the specification would have been required to do so, the '692 application enables the invention of claim 2. The court recognizes as well that the Examiner reached the same conclusion, which is entitled to deference.[41] *See Polaroid*, 789 F.2d at 1560. For the reasons discussed below in connection with the enablement of claim 1, the court also finds the individual enantiomers of 3-isobutylGABA enabled by the '692 application, such that even if claim 2 required a teaching of how to make and use purified S-3-isobutylGABA to enable it, these requirements would be met.

ii. *Claims 1 & 4 of the '819 Patent*

[41] The plaintiffs note that, during prosecution of the '819 Patent, the Examiner considered whether the '692 application enabled a claim containing identical language to claim 2, and he concluded that it did. In the first office action after the '692 application was filed, the Examiner rejected all the original claims under § 112, because the application "[f]ailed to adequately teach one how to prepare the instant compounds." (D.I. 351 at 16 (citing PTX-9 at PFE_LYR_0000001993).) Claim 3, which, like claim 2, covers 4-amino-3-(2-methylpropyl) butanoic acid, was originally rejected. (*Id.* (citing PTX-9 at PFE_LYR_0000001969).) In response to the rejection, the applicants showed that the routine synthesis was "known in the art" and that the synthetic steps were "notoriously old." (*Id.*) The Examiner ultimately agreed and withdrew the § 112 enablement rejection. (*Id.* (citing PTX-9 at PFE_LYR_0000002021).)

With respect to the enablement of claim 1, the plaintiffs argue that a person of ordinary skill in art in November 1990 could have made S-3-isobutylGABA as a single optical isomer without undue experimentation by a variety of methods. (D.I. 351 at 3.) Thus, the plaintiffs assert, in response to the defendants' charge that the '692 application is non-enabling, that the application does, in fact, enable S-3-isobutylGABA, satisfying § 112. To support this contention, the plaintiffs presented the testimony of their expert, Dr. Roush, who explained, in testimony the court finds credible, that the resolution of enantiomers was systematic, routine, and well-known to organic chemists in November 1990. (*Id.*) The plaintiffs also note, in support of this contention, that the PTO considered the question of whether claim 1 was enabled in the context of determining if Dr. Yuen's work constituted inventive contribution to that claim and concluded both that the '692 application was enabling and that preparing 3-isobutylGABA's enantiomers was a matter of routine science. The plaintiffs assert that this finding is entitled to some deference and, moreover, that it is confirmed by the evidence presented at trial. (*Id.* at 32.)

As noted, the '692 application states that "[t]he individual diastereomers or enantiomers [of the claimed compounds, including 3-isobutylGABA,] may be prepared or isolated by methods already well known in the art." (*Id.* (citing PTX-9A at PFE_LYR_0000001961; Tr. at 1186:16-1187:7 (Roush)).) With regard to the plaintiffs' argument that resolution of 3-isobutylGABA's enantiomers did not require undue experimentation, Dr. Roush and others testified that this resolution is a "classical technique" that was known in the art for over a century and was used to prepare many different enantiomers. (*Id.* at 32 (citing Tr. at 1172:2-17 (Roush); Tr. at 414:14-25 (Williams); Tr. at 531:6-15 (Andruszkiewicz)).) Dr. Roush testified that it was known in the art that the "venerable old technique" of enantiomer resolution was a "predictable" practice likely to prove successful and that, by 1990, it would have been routine practice for a

person of ordinary skill to systematically screen various well-known resolving agents to determine which ones would resolve a chiral compound's enantiomers. (*Id.* (citing Tr. at 1172:2-1178:19 (Roush); PTX-844; PTX-1388).) This, Dr. Roush concluded, would not have required undue experimentation. (*Id.* (citing Tr. at 1176:17-1177:18 (Roush)).)

The court agrees. As Dr. Roush explained, by 1990 there was literature available in the prior art teaching the resolution of enantiomers. For instance, a 1977 review article by Wilen, Collet, and Jacques, entitled "Strategies for Optical Resolution," described a variety of methods and techniques relevant to the resolution of racemates and explained that it was "possible to carry out resolutions of organic compounds bearing functional groups quite rationally and with a high probability of success." (*Id.* at 33 (citing PTX-844 at PFE_LYR_0000824556; Tr. at 1172:18-1174:15 (Roush)).) These authors also published a 1981 monograph entitled, "Enantiomers, Racemates, and Resolution," which, Dr. Roush explained, "is essentially the Bible, the gold standard in the field." The monograph detailed, in seven chapters, "a wide range of techniques and discussions of how one would accomplish the separation of enantiomers" and, combined with the 1977 article, would, the court concludes, have provided guidance regarding how to resolve the 3-isobutylGABA enantiomers.

This conclusion finds further support in Parke-Davis' ability to make S-3-isobutylGABA with what the court finds to be less than undue experimentation. Specifically, the evidence presented at trial indicates that Parke-Davis successfully prepared 3-isobutylGABA's enantiomers using the classic resolution technique. (*Id.* (citing Tr. at 1196:20-24, 1197:9-19 (Roush); PTX-7b).) Parke-Davis screened fourteen standard resolving agents and found that three could be used to resolve the enantiomers. (*Id.*) In fact, one of these resolving agents, mandelic acid, is the resolving agent that Cobalt and Mylan used to prepare pregabalin as a

single optical isomer for their proposed products. (*Id.* (citing Tr. at 345:24-25 (Wolf); Tr. at 391:5-6, 414:17-25 (Williams)).) Dr. Roush testified that Parke-Davis' finding that three of the fourteen resolving agents could be used to successfully resolve a chiral compound's enantiomers was "well within the norm of what one would anticipate being able to accomplish using resolution technology." (*Id.* (citing 1198:10-19 (Roush)).)

In addition, the court finds credible Dr. Roush's testimony that there were separate chemoenzymatic synthesis techniques for preparing 3-isobutylGABA's enantiomers available in the art in November 1990, such that they could be employed to separate the enantiomers without undue experimentation. As Dr. Roush testified, chemoenzymatic synthesis is a technique that was well known in the art and disclosed in the literature by the 1970s. (*Id.* at 35 (citing Tr. at 1178:24-1179:13 (Roush)).) The '819 Patent inventors used a chemoenzymatic technique to prepare the enantiomers of 3-methylGABA and 3-ethylGABA and, in January 1990, published an article describing this technique. (*Id.* (citing 1179:10-1182:17, 1187:8-1188:12 (Roush); Tr. at 622:15-624:9 (Davies); Tr. at 894:19-896:10 (Silverman); DTX-822).) The article detailed that "the methodology given here should be useful for the syntheses of either enantiomer of 3-substituted 4-aminobutanoic acids," like 3-isobutylGABA. (*Id.* (citing DTX-822 at NU036183; Tr. at 895:21-896:9 (Silverman)).) The Parke-Davis scientists successfully used the method described in this January 1990 article to prepare S-3-isobutylGABA. (*Id.* (citing Tr. at 1204:9-1206:1 (Roush)).) These scientists subsequently described their chemoenzymatic synthesis, as well as five other distinct syntheses of S-3-isobutylGABA in a 1997 article. (*Id.* (citing PTX-197).) Dr. Roush testified that each of the synthetic techniques described in the 1997 article were well known in the art in 1990. (*Id.* (citing Tr. at 1203:4-1206:19 (Roush)).)

The defendants argue that the credibility of Dr. Roush's testimony that the S enantiomer of 3-isobutylGABA could be resolved in 1990 through "general techniques" known in the art is undermined by: (1) the fact that Dr. Andruszkiewicz rejected the use of classical resolution followed by either one or both of crystallization and chiral chromatography and Dr. Pavia tried classical resolution and failed (D.I. 349 at 33); (2) Dr. Pavia's statement to Dr. Yuen that he regarded his work as a failure (*id.*); (3) Dr. Yuen's need to overcome challenges in making S-3-isobutylGABA; and (4) the plaintiffs' statements to the PTO that resolution of S-3-isobutylGABA was not routine (*id.*). For the reasons that follow, the court disagrees and concludes, based on the evidence in the record, that resolution of the S enantiomer did not require undue experimentation and, therefore, was enabled by the '692 application.

First, and with respect to Dr. Andruszkiewicz, the plaintiffs challenge that Dr. Andruskiewicz's work resulted in his 1990 article describing the enzymatic method of preparing enantiomers and explaining that it could be used in the synthesis of 3-substituted GABA analogs. (D.I. 351 at 10 (citing DTX-822 at PFE_LYR_0000818512).) The plaintiffs also note that Dr. Andruskiewicz returned to Poland before he had the opportunity to synthesize 3-isobutylGABA's enantiomers and, therefore, that his reason for not doing so was not his belief that the enantiomer synthesizing was difficult or impossible. The court agrees that the defendants have not established that Dr. Andruszkiewicz's "reject[ion] of classical resolution techniques out of hand" necessarily leads to the conclusion that Dr. Andruszkiewicz believed the resolution of 3-isobutylGABA's enantiomers was beyond the realm of the prior art or that his rejection of classical resolution meant that separation of the enantiomers would require undue experimentation. In fact, Dr. Andruszkiewicz testified that, while he did not believe that chemoselective synthesis would prove effective with GABA analogs, he also stated that he

would likely have tried other methods with the GABA analogs had he had more time to do so before returning to Poland. Tr. at 530:13-532:15 (Andruszkiewicz).

Second, the court disagrees with the defendants' characterization of Dr. Pavia's work as unsuccessful as well as their conclusion, derived from this characterization, that his work demonstrates that the prior art did not teach separation of 3-isobutylGABA's enantiomers. Specifically, the defendants base their arguments on Dr. Yuen's testimony that Dr. Pavia regarded his own work as a failure because he was unable to separate the R or S enantiomer with PLE and classical resolution. (D.I. 349 at 33 (Tr. at 1231:3-1232:3 (Roush)).) However, in view of the evidence before it, the court does not find that Dr. Pavia's alleged statement[42] supports the conclusion the defendants reach. Indeed, a review of Dr. Pavia's work details that, using Dr. Andruszkiewicz's 1990 resolution method, he was able to obtain a 75:25 ratio of certain common chiral intermediates, which could have been converted into 3-isobutylGABA's enantiomers had he not stopped working on the project and completed the reaction. Dr. Pavia was able to achieve this ratio despite having no experience preparing enantiomers and having limited experience in conducting laboratory experiments. Moreover, while Dr. Pavia's work spanned a total of twelve days, he only worked to make 3-isobutylGABA's enantiomers on four of those days, and successfully produced crystals with three of his four attempts. (*Id.* (citing Tr. at 1193:16-23 (Roush)).) In fact, the defendants' expert, Dr. Davies, agreed that Dr. Pavia "just

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[42] While the defendants assert that Dr. Pavia told Dr. Yuen that he regarded his work as a failure, Dr. Yuen's testimony as to this conversation was fairly limited and did not detail specifics of the interchange:

> Q: He indicated to you that he had tried the enzynamtic techniques in Dr. Silverman's paper and they had failed?
>
> A: The paper reported Dr. Silverman's successful attempt in resolving the 3-methylGABA instead of 3-isobutylGABA, so he extended that method, using enzymatic resolution under similar conditions to try to resolve the key intermediate that would lead to 3-isobutylGABA.
>
> Q: And he indicated to you that those efforts had failed?
>
> A: Yes, he did.

Tr. at 554:3-13 (Yuen).

[did] what Dr. Andruszkiewicz did," as described in his 1990 article, and achieved the 75:25 mixture "the first time" after only three days of experimentation. (*Id.* (citing Tr. at 662:12-24 (Davies)).)

In light of this evidence, Dr. Roush testified that he could not agree with the characterization of Dr. Pavia's work as unsuccessful in resolving the enantiomers, a point with which the Examiner agreed. Specifically, the '080 application[43] prosecution Examiner, concluded, based on his review of Dr. Yuen's declaration describing Dr. Pavia's work, that Dr. Pavia had "successfully carried out" the enantioselective hydrolysis step of the Andruszkiewicz 1990 method, that his work was not a failure, but was instead incomplete, and that "one could prepare the single isomers based on the [Andruszkiewicz 1990] process." (*Id.* at 14 (citing PTX-7 at PFE_LYR_0000001291; Tr. at 1201:2-5 (Roush)).) The court finds the foregoing evidence and Dr. Roush's conclusions persuasive.

Third, the court similarly disagrees with the defendants' argument that Dr. Yuen's resolution of S-3-isobutylGABA demonstrates clearly and convincingly that separation of the enantiomers was outside the scope of the prior art in 1990. Specifically, the evidence at trial shows that Dr. Yuen, despite being entirely unfamiliar with 3-isobutylGABA before April 1991, when he was asked by Parke-Davis to prepare the enantiomers, successfully prepared the R enantiomer on his second attempt. (*Id.* (citing Tr. at 549:19-550:4, 555:12-14, 556:23-558:20 (Yuen)).) In particular, Dr. Yuen testified that "[t]he second attempt was successful, but for the synthesis of the R-enantiomer you have to go through a sequence of reactions, so during the sequence there are reactions that failed and I ha[d] to do slight modifications on trying to make the compound." Tr. at 558:3-8 (Yuen). Dr. Yuen further testified that once he successfully achieved the R enantiomer and "work[ed] out [its] synthetic route," synthesis of the S

[43] As noted, the '080 application was filed as a continuation-in-part of the '692 application.

enantiomer was "straightforward." *Id.* at 557:12-21. In fact, Dr. Yuen, in response to the question of whether he would characterize the synthesis of 3-isobutylGABA as "difficult," stated that he did not "think it [was] any easier or more difficult than any other synthesis [he had] taken on over [his] career." *Id.* at 567:4-10.

In view of the combined work of Drs. Pavia and Yuen detailed above, the court finds unavailing the defendants' expert, Dr. Davies', conclusion that classical resolution in November 1990 was viewed as "challenging," "notoriously unpredictable," and particularly difficult with respect to enantiomers of γ-amino acids or that resolution of S-3-isobutylGABA required undue experimentation. The court also notes that while Dr. Davies evaluated the success of Drs. Andruszkiewicz, Pavia, and Yuen in formulating his conclusion that the resolution of S-3-isobutylGABA was not routine, his discussion of the prior art was largely limited to noting that no prior art reference disclosed the resolution of 3-isobutylGABA specifically or using chiral chromoatography to separate 3-alkylGABA derivatives. *Id.* at 613:19-25, 614:22-615:3, 616:6-10, 616:20-617:3 (Davies). Based on the evidence in the record and the testimony presented at trial, the court finds Dr. Roush's assessment of the prior art and of Drs. Andruszkiewicz, Pavia, and Yuen's attempted resolution of S-3-isobutylGABA persuasive.

Finally, the court's conclusion is again supported by the finding of the Examiner who, in considering whether claim 1 of the '819 Patent was enabled by the '692 application, concluded that preparing 3-isobutylGABA's S enantiomer could be accomplished through "routine" methods and, specifically, through employing Dr. Andruszkiewicz's method. The Examiner reached this determination after assessing: (1) Dr. Yuen's declaration; (2) Dr. Pavia's notebook documenting his efforts to prepare the enantiomers; and (3) the chemoenzymatic method disclosed in Andruszkiewicz's 1990 article. The Examiner subsequently questioned, expressly,

whether the '692 application enabled S-3-isobutylGABA as a "single optical isomer," a point the defendants reference as reason for the court to afford diminished weight to the Examiner's finding. (D.I. 349 at 43 (citing PTX-7 at PFE_LYR_1289, 1484-85; PTX-9 at PFE_LYR_1993).)

However, the applicants noted, in response, that the Examiner had already determined that it did "since the Examiner explicitly found the Applicants' resolution of the enantiomers was routine" and, therefore, that the Initial Application "necessarily enabled the present invention." (D.I. 351 at 36 (citing PTX-7 at PFE_LYR_0000001289, 1310).) In particular, the Examiner concluded, in view of Parke-Davis' successful resolution of 3-isobutylGABA's enantiomers with three of fourteen standard resolving agents, that "[i]t is well within the skill of the artisan to obtain the individual enantiomers by known methods. Applicants admit that the racemic mixture can be resolve[d] by some standard resolving agents." (D.I. 351 at 34 (citing PTX-7b at PFE_LYR_0000001149).) The Examiner agreed, and found that the '692 application enabled 3-isobutylGABA as a single optical isomer under § 112. (*Id.* (citing PTX-7 at 0000001546; Tr. at 1202:9-1203:3 (Roush)).)

Thus, although the '692 did not provide working examples of how to resolve the S enantiomer or starting materials and reaction conditions, the Examiner concluded, as the court does here, that a person of skill in the art could resolve the enantiomers based on the prior art available detailing classical resolution and chemoenzymatic synthesis without undue experimentation.[44] The court notes that this finding is not undermined by the defendants'

[44] The defendants have not shown, by clear and convincing evidence, that the absence of such instructions compels a finding of non-enablement. (D.I. 349 at 39-41.) Rather, the evidence produced at trial demonstrates that, per Dr. Roush's credible testimony, the prior art available taught methods to resolve enantiomers and that could be used by skilled artisans and applied in the resolution of S-3-isobutylGABA. Indeed, the Examiner concluded, as the court does here, that Dr. Andruszkiewicz's 1990 method could be used in this resolution, and Dr. Pavia was able to make a 75:25 ratio in four days of experimentation despite not having attempted enantiomer resolution prior to his efforts at Parke-Davis. Likewise, Dr. Yuen was able to make R-3-isobutylGABA on his second attempt, despite his

assertion that, to be enabled, the '692 application was required to detail starting materials and reaction conditions. To support this argument the defendants rely, as noted above, on *Genetech, Inc.* and *Alza Corp.*'s instruction that applicants "must supply the novel aspects of an invention in order to constitute adequate enablement," rather than relying on the disclosure that "the process is within the skill of the art."[45] Here, however, the asserted claims cover a compound and the enantiomers of that compound, rather than a "novel" method or process. Thus, the court concludes that because the process to resolve the enantiomers was known in the art, as found by the Examiner, and was not the "novel" aspect of the invention it did not require a more specific disclosure to meet the enabling requirement. Moreover, Dr. Pavia's relative success in resolving the enantiomers and Dr. Yuen's ability to do so, confirm that such resolution was possible without undue experimentation. *See Monsanto Co. v. Scruggs*, 459 F.3d 1328, 1338 (Fed. Cir. 2006) (concluding that a disclosure is not insufficient simply because "some experimentation may be necessary to produce the invention"). The fact that the enantiomers were resolved after the filing of the '692 application does not impact this analysis. *See Brunning v. Hirose*, 161 F.3d 681, 686 (Fed. Cir 1998) (noting that production of the invention after the application filing date does not render the invention non-enabled).

The court also notes that its conclusion is not undermined by the applicants' statements to the PTO in connection with the '905 application, that the resolution of 3-isobutylGABA's enantiomers was not routine and that Dr. Yuen was appropriately named as the inventor. Although the court examines the defendants' inventorship arguments separately, it notes here that the Examiner expressly considered the questions of whether resolution of S-3-

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unfamiliarity with 3-isobutylGABA, and was able to resolve the S enantiomer with simple modifications to his R enantiomer resolution process. In consideration of this and other evidence discussed above, the court finds the defendants' non-enablement argument unavailing.

[45] *See Genetech, Inc.*, 108 F.3d at 1368; *ALZA*, 603 F.3d at 931.

isobutylGABA was routine and enabled and answered both in the affirmative after reviewing Dr. Yuen's declaration, Dr. Pavia's work, Dr. Andruszkiewicz's 1990 method, and Parke-Davis' success in resolving S-3-isobutylGABA using three of fourteen standard resolving agents. While the applicants' statements certainly may raise a question as to whether the applicants believed resolution of the S enantiomer was, in fact, routine, the defendants have not proved the conclusion they advance by clear and convincing evidence for the reasons examined above. *See Polaroid*, 789 F.2d at 1560 (concluding that where the PTO has considered a question and resolved it in favor of the applicants, there is an "added burden" on the defendants of "overcoming the deference" afforded the PTO).

In fact, even Sun Pharma's expert, Dr. Agranat, agreed, in connection his opinion as to the '692 application's written description, that a person of ordinary skill in the art could resolve 3-isobutylGABA's enantiomers using routine methods. (D.I. 351 at 34 (citing Tr. at 774:18-775:6 (Agranat)).) Dr. Agranat formed his opinion relying on references published prior to 1990 and concluded that methods existed that could be applied to enantiomer resolution by those of skill in the art.[46] (*Id.* (citing Tr. at 777:3-9, 777:15-778:8, 778:17-19 (Agranat)).)

In view of the foregoing, the court concludes that the defendants have not shown, by clear and convincing evidence, that claim 1 of the '819 Patent was not enabled by the '692 application. Rather, the court finds, based on the record before it, that preparing the S enantiomer of 3-isobutylGABA as a single optical isomer would not have required undue experimentation at the time of the '692 application. Because the application enables claim 1, it also enables claim 4, which covers pharmaceutical compositions containing the compound of

[46] The court notes that the defendants objected to Dr. Agranat providing his opinion on this question because he testified in connection with Sun Pharma's written description defense. However, the court allowed Dr. Agranat to testify on this issue at trial and considers his opinion here because, as the plaintiffs correctly stated at trial, the written description defense necessarily implicates consideration of the level of skill in the art as written description may be supplemented by the level of knowledge in the prior art field. Thus, the court concludes that Dr. Agranat's opinion is appropriately considered here.

claim 1. Thus, having found claims 1, 2, and 4 enabled by the '692 application, the court concludes that the asserted claims of the '819 Patent are entitled to a priority filing date of November 27, 1990.

3. The '819 Patent: The Defendants' Claim 2 Anticipation Defense

The defendants assert that, given the 1992 priority filing date of the '080 application, claim 2 of the '819 Patent is anticipated by Dr. Andruszkiewicz's 1989 article and Drs. Silverman and Andruszkiewicz's 1990 article, both of which independently disclose racemic 3-isobutylGABA and how to make the compound. (D.I. 349 at 34 (citing DTX-711 at 22290; DTX-724 at NU14882).) However, because the court finds that the appropriate priority filing date for claim 2 is November 27, 1990, it concludes that this claim is not anticipated by Drs. Andruszkiewicz or Silverman's articles. Specifically, neither article was published more than one year before the claim's priority date and, therefore, neither can anticipate claim 2 under Section 102(b). *See Finisar Corp. v. DirecTV Group, Inc.*, 523 F.3d 1323, 1334 (Fed. Cir. 2008) (directing that a reference must be published over one year before a filing date in order to constitute prior art under Section 102(b)). In view of the foregoing, the court finds that claim 2 is not invalid as anticipated.

4. The '175 Patent's Priority Date & Anticipation: Parties' Contentions & Discussion

The defendants challenge that claim 1 of the '175 Patent is invalid as anticipated by WO 93/23383,[47] which was published November 25, 1993. (D.I. 349 at 48-51.) Specifically, the defendants, in making this assertion, maintain that the plaintiffs' Certificate of Correction, which allowed it to claim the priority filing date of the '692 application, November 27, 1990, is invalid and, as a result, the '175 Patent is entitled to a priority filing date of April 12, 1995. The parties

[47] *See* DTX-1168.

have stipulated that, if the '175 Patent's priority filing date is April 12, 1995, WO 93/23382 would invalidate claim 1 as anticipated because the reference discloses and enables every element of that claim. (*Id.* at 49; D.I. 338.) The defendants assert that the April 12, 1995 priority filing date is appropriate for the reasons that follow.

The parties do not dispute that the '175 Patent, U.S. Patent No. 08/420,575 ("the '575 application"), was filed on April 12, 1995 as a divisional application of the '285 application. (D.I. 349 at 48 (citing PTX-5 at PFE_LYR_1-5).) On April 11, 1995, Pfizer filed a File Wrapper Continuing Application ("FWC") of the '285 application, pursuant to 37 C.F.R. § 1.62(g). (*Id.* (citing PTX-7 at PFE_LYR_867-68).) As a result of this FWC, the '285 application was abandoned, such that it was no longer pending and could not be relied upon for a claim of priority for the '575 application. (*Id.*) On March 25, 2009, Pfizer received notice that the '175 Patent was only entitled to the April 12, 1995 priority date and was, therefore, anticipated by WO 93/23383. (*Id.* (citing PTX-29 at 11).) Pfizer initiated the above-captioned action against the defendants on April 29, 2009. On September 29, 2010, Pfizer filed a Request for Certificate of Correction of Patent for Patentee's Mistake asserting an error in priority under 35 U.S.C. § 120. (*Id.* at 49 (citing PTX-11).) In this request, Pfizer acknowledged that it expressly abandoned the '285 application, causing a gap in co-pendency. (*Id.* (citing PTX-11 at PFE_LYR_0000794866).) On March 1, 2011, the PTO granted Pfizer's request, pursuant to 35 U.S.C. § 255, to correct this gap and to change the priority filing date of the '175 Patent. (*Id.* (citing DTX-2 at 17).)

The defendants contend that Pfizer's Certificate of Correction changing the '175 Patent's priority date to November 27, 1990 is invalid because: (1) under 37 C.F.R. § 1.62, Pfizer's filing of an FWC in connection with the '285 application resulted in an express abandonment of the

application on April 11, 1995 (*id.* at 49); (2) the '575 application, filed on April 12, 1995, did not claim priority to a prior co-pending application, resulting in an effective priority filing date of April 12, 1995 (*id.*); (3) under 35 U.S.C. § 225, such certificate can only correct "a mistake of a clerical or typographic nature, or of minor character" and must not involve changes in the patent that would require reexamination (*id.* at 49-50 (citing 35 U.S.C. § 255; *Superior Fireplace Co. v. Majestic Prods. Co.*, 270 F.3d 1358, 1369-70, 1375 (Fed. Cir. 2001)); (4) an incorrect claim of priority is not a simple mistake or a clerical or typographical error because such a change alters the universe of prior art applicable against the claims, requiring reexamination (*id.* at 50 (citing *Simmons, Inc. v. Bombardier Inc.*, 328 F. Supp. 2d 1188, 1292 (D. Utah 2004)); (5) an error in priority is not an error the court can correct, as courts are limited to correcting "obvious minor typographical and clerical errors" that are "apparent from the face of the patent," which this is not (*id.* (citing *Novo Industries*, 305 F.3d at 1356-57; *Simmons*, 328 F. Supp. 2d at 1202); and (6) the Certificate of Correction, even if approved by the PTO, would not apply to this action because it is only operative for causes of action arising after its issuance (*id.* (citing *Novo Indus., L.P. v. Micro Molds Corp.*, 350 F.3d 1348, 1356 (Fed. Cir. 2003).

In response, the plaintiffs assert that '175 Patent is entitled to the November 27, 1990 priority filing date of the '692 application and, therefore, is not invalid as anticipated by WO 93/23383. (D.I. 351 at 52-53.) Specifically, the plaintiffs maintain that because the PTO can issue Certificates of Correction under 35 U.S.C. § 255 to correct a mistake "of a clerical or typographical nature, or of minor character" via 35 U.S.C. § 120, and did so in this case, its March 1, 2011 Certificate of Correction is considered part of the '175 Patent. (*Id.* at 51-52.) The plaintiffs further challenge that to prove that the PTO's approval of its Certificate of Correction is invalid, the defendants must demonstrate this invalidity by clear and convincing evidence and

have not done so in this case. Thus, relying on this Certificate of Correction, the plaintiffs do not ask the court to correct its priority filing date or address the defendants' contention that its Certificate is invalid because the altered priority date would impact the prior art assessment, requiring reexamination.

Instead, the plaintiffs maintain that, contrary to the defendants' assertions, its Certificate of Correction is applicable to this action because it applies prospectively to acts of infringement occurring after the certificate issues, regardless of whether the patentee filed the complaint before issuance.[48] (*Id.* at 52).) In support, the plaintiffs note that, pursuant to 35 U.S.C. § 271(e)(2)(A), the "filing of an ANDA is considered an act of infringement under § 271(e)(2)(A), but this 'act' is merely a vehicle 'to create case or controversy jurisdiction to enable a court to promptly resolve' a dispute concerning an infringement that will happen in the future." (*Id.* (citing *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1249 (Fed. Cir. 2000)).)

To this end, because infringement under § 271(e)(2) is a "hypothetical case that asks the factfinder to determine whether the drug that will be sold upon approval of the ANDA will infringe the asserted patent," the question before the court is whether, if the defendants' ANDAs are approved, the use of their products will infringe the '175 Patent. (*Id.* (citing *Sanofi-Aventis v. Apotex Inc.*, 659 F.3d 1171, 1180 (Fed. Cir. 2011) (citation omitted)).) Because this potential infringement will occur after March 1, 2011, the plaintiffs argue that its Certificate of Correction will apply and, therefore, that '175 Patent's November 27, 1990 priority filing date is applicable here. *See E.I. Du Pont De Nemours & Co. v. MacDermid Printing Solutions, L.L.C.*, 525 F.3d 1353, 1362 (Fed. Cir. 2008) (noting that "each act of infringement gives rise to a separate cause

[48] *See Lamoreux v. Anazaohealth Corp.*, 669 F. Supp. 2d 227, 236-37 (D. Conn. 2009) ("[T]he critical date for purposes of determining whether the certificate of correction applies is . . . the date the infringing conduct occurred, and not the date the complaint was filed."); *see also Masonite Corp. v. Craftmaster Mfg., Inc.*, No. 09-CV-2131, 2011 WL 1642518, at *3-4 (N.D. Ill. Apr. 29, 2011) (concluding that a certificate that issued after the complaint was filed applied to acts of infringement occurring after the certificate was issued).

of action" and concluding that, while a certificate of correction will not apply if it issues after the "cause of action arose," it can apply to future infringing conduct).

In light of the parties' arguments and the relevant law, the court concludes, for the reasons that follow, that the '175 Patent is entitled to a priority filing date of November 27, 1990 and Pfizer's Certificate of Correction applies in this action. First, and with respect to the defendants' argument that Pfizer's Certificate of Correction is invalid, the court notes that, as with all validity defenses, the defendants are required to prove invalidity by clear and convincing evidence. *See Superior Fireplace Co.*, 270 F.3d at 1367. Here, the defendants argue that Pfizer's Certificate of Correction is invalid because, by altering the '175 Patent's priority filing date, the Certificate corrects more than a mistake "of a clerical or typographical nature, or of minor character" and instead alters evaluation of the prior art and requires reexamination, which is expressly disallowed by § 255.[49] The defendants, however, do not support their contention that the PTO erred in granting Pfizer's Certificate of Correction. In fact, other than arguing generally that such a change will require reexamination, the defendants do not present any evidence to support the assertion that reexamination is required in this case or that the Examiner failed to consider this point. Indeed, the WO 93/23383 reference the defendants cite as invalidating claim 1 of the '175 Patent as anticipated should have been considered in the PTO's examination of the '175 Patent's prior art in the absence of a Certificate of Correction because the reference was published in 1993.

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[49] 35 U.S.C. § 255 reads:

> Whenever a mistake of a clerical or typographical nature, or of minor character, which was not the fault of the Patent and Trademark Office, appears in a patent and a showing has been made that such mistake occurred in good faith, the Director may, upon payment of the required fee, issue a certificate of correction, if the correction does not involve such changes in the patent as would constitute new matter or would require re-examination. Such patent, together with the certificate, shall have the same effect and operation in law on the trial of actions for causes thereafter arising as if the same had been originally issued in such corrected form.

35 U.S.C. § 255.

In addition, the cases on which the defendants rely to support their invalidity contention are distinguishable from the instant matter. Specifically, *Superior Fireplace Co.* and *Simmons, Inc.*, which the defendants cite to relay their argument that a change in priority date is not a minor correction allowable under § 255, involved consideration of (1) whether a correction can be made under § 255 if it broadens a patent claim and, if so, under what conditions and with how much support in the intrinsic record, and (2) whether a district court can correct mistakes in a patent that are "subject to reasonable debate," respectively. *See Superior Fireplace Co.*, 270 F.3d at 1369-70, 1375; *Simmons, Inc.*, 328 F. Supp. 2d at 1202. While the defendants are correct that, based on Pfizer's filing of an FWC, it does not appear that the Pfizer Certificate of Correction was approved as a clerical or typographical error, the defendants have not shown by clear and convincing evidence that the PTO corrected an error here that was not "minor" or that the gap in co-pendency to the '575 application was not a mistake that occurred in "good faith."[50] Importantly, these considerations are ones that the Examiner would have had to consider under § 255 in determining whether to grant approval. *See* 35 U.S.C. § 255. Thus, the court finds that the defendants have not shown by clear and convincing evidence that Pfizer's Certificate of Correction is invalid and, therefore, claim 1 of the '175 Patent is entitled to a priority filing date of November 27, 1990.[51]

Second, the court finds that Pfizer's Certificate of Correction is applicable in this action. As the plaintiffs correctly argue, relevant case law has instructed that, for purposes of determining whether a certificate of correction applies, the date on which the infringing conduct

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[50] *See supra* note 46.

[51] In light of this finding, the court does not address the defendants' argument that, because correction of a priority filing date is more than a minor typographical error apparent on the face of the application, the court could not alter this filing date. While the court agrees that such a correction would lie outside the scope of this court's authority to correct an application, the validity of Pfizer's Certificate of Correction negates any request for it to do so. *See Novo Indus., L.P.*, 350 F.3d at 1354 (concluding that a district court may correct an error in a patent by interpretation of that patent "where no certificate of correction has been issued," the "correction is not subject to reasonable debate," and "the prosecution history does not suggest a different interpretation of the claims").

will occur, rather than the date a complaint is filed, dictates. *See E.I. Du Pont De Nemours*, 525 F.3d at 1362; *Lamoreux*, 669 F. Supp. 2d at 236-37; *Masonite Corp.*, 2011 WL 1642518 at *3-4. While the defendants are correct that, generally speaking, a certificate of correction applies only to actions filed after that certificate issued, this rule does not preclude application of Pfizer's Certificate. Rather, because infringement under § 271(e)(2) is hypothetical and, therefore, cannot occur prior to the filing of a complaint, a certificate of correction can be applied where the defendants' ANDA products will prospectively infringe the patents-in-suit. Here, because the defendants' alleged infringement would occur after March 1, 2011, Pfizer's Certificate of Correction appropriately applies to this action.

In light of these holdings, the court further concludes that claim 1 of the '175 Patent is not invalid as anticipated by WO 93/23383 because this reference was published after the Patent's priority filing date.[52]

D. Written Description

Sun Pharma asserts that claims 1, 2, and 4 of the '819 Patent are invalid because the '692 application does not meet the written description requirement detailed in 35 U.S.C. § 112. (D.I. 350 at 1.) To this end, Sun Pharma argues that the plaintiffs are not entitled to a 1990 priority filing date and, as a result, claim 2 is anticipated by Dr. Andruszkiewicz's 1989 article and claims 1 and 4 are rendered obvious by Drs. Andruszkiewicz and Silverman's 1989 and 1990 articles. The other defendants do not join Sun Pharma in this defense and the parties submitted separate Proposed Findings of Fact and Conclusions of Law on this issue. (D.I. 350; D.I. 352.) For the reasons that follow, the court concludes that the asserted claims meet § 112's written description requirements and are not invalid as anticipated or obvious based on this finding.

[52] The court notes that, if Pfizer's Certificate of Correction did not apply to this action because it issued after the complaint was filed, it would agree with the defendants that WO 93/23383 invalidates claim 1 of the '175 Patent as anticipated.

1. Legal Standard

To establish that an asserted claim of a patent-in-suit is entitled to a priority filing date of an earlier parent application, the patentee has the burden of proving that the written description in that earlier application supports the later-filed claim. *See Tech Licensing Corp. v. VideoTek*, 545 F.3d 1316, 1327 (Fed. Cir. 2008). Continuation-in-part patent applications are entitled to the priority date of the parent application for those claims that have an adequate written description in the parent application. *See Go Med. Indus. Pty, Ltd. v. Inmed Corp.*, 471 F.3d 12 64, 1270 (Fed. Cir. 2006). To comply with the written description requirement of 35 U.S.C. § 112, the patent disclosure must convey with reasonable clarity to a person of ordinary skill in the art that the inventor was in possession of the claimed invention at the time of the earlier application. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

The test for "reasonable conveyance" is a flexible one, "requir[ing] an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art" to determine whether, by reading the original disclosure, that person could "immediately discern the limitation at issue in the claims." *Id*; *see also Perdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000). Importantly, however, *in haec verba* disclosures using the same language of the claim are not required. *Ariad Pharms, Inc.*, 598 F.3d at 1352. Moreover, the application "does not have to describe exactly the subject matter claimed." *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 2000). Rather, the requirement is met if a person of ordinary skill in the art would find it is "reasonably clear what the invention is and that the patent specification conveys that meaning." *All Dental Prodx, L.L.C. v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779 (Fed. Cir. 2002).

To this end, "a description that merely renders the invention obvious does not satisfy the requirement" and support in the written description must be based on what actually is disclosed, not on an "obvious variant" of what is disclosed. *See Ariad Pharms, Inc.*, 598 F.3d at 1352; *Lockwood v. American Airlines*, 107 F.3d 1565, 1571 (Fed. Cir. 1997). However, the failure to "specifically mention a limitation that later appears in the claims is not fatal when one skilled in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented." *All Dental Prodx, Inc.*, 309 F.3d at 774. In sum, the written description must "actually or inherently disclose each element of the claim." *Power Oasis, Inc. L.L.C. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1307 (Fed. Cir. 2008).

Whether the written description requirement is met is a question of fact. *See Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1369-70 (Fed. Cir. 2009) (citation omitted). Once the plaintiff has shown "not only the existence of [an] earlier application, but why the written description in the earlier application supports the claim," including all limitations, the burden resides with the proponent of invalidity, who must "convince the court that [the patentee is] not entitled to the benefit of the earlier filing date." *Tech. Licensing Corp.*, 545 F.3d at 1328. To meet this burden, the invalidity proponent must persuade the court, by clear and convincing evidence, that it is correct. *Id.* (the "ultimate burden[] of persuasion" never "shifts to the other party," and instead "the risk of decisional uncertainty stays on the proponent of the proposition").

2. <u>The Parties' Contentions & Discussion</u>

Sun Pharma contends that the asserted claims of the '819 Patent are invalid for lack of written description because the '692 application does not convey to one of skill in the art that the inventors were in possession of the individual S enantiomer of 3-isobutylGABA. (D.I. 350 at 1.) Specifically, Sun Pharma argues that the validity of claims 1, 2, and 4 of the '819 Patent turns on

whether those claims are entitled to the November 27, 1990 filing date of the '692 application. Sun Pharma notes that without this filing date, Dr. Andruszkiewicz's 1989 article disclosing 3-isobutylGABA would be considered prior art and this reference would anticipate claim 2, rendering claims 1 and 4 obvious. (*Id.*)

With respect to its written description argument specifically, Sun Pharma asserts, in the main, that the '692 application does not convey possession of S-3-isobutylGABA because it does not: "describe how to obtain the individual enantiomers of the disclosed racemates or provide certain experimentally derived information related to the individual [S] enantiomer"; detail "how to obtain any individual enantiomers"[53]; "contain any evidence of resolution"; and/or describe "the optical rotation of the individual enantiomer" or the "biological activity data for the individual enantiomer." (*Id.* at 1, 4, 10.) In addition, Sun Pharma notes that "[a]lthough the ['692 application] refers to the individual enantiomers, "the (R) and (S) descriptors are based on a naming convention" that allows designation "of individual enantiomers as (R) or (S)" but does not convey possession of it.[54] (*Id.* at 4.) Therefore, absent the information detailed above, Sun Pharma maintains that the inventions of the asserted claims, each of which covers S-3-isobutylGABA, would not be conveyed to a person of ordinary skill in the art. (*Id.* at 11.)

Moreover, Sun Pharma argues that the insufficiency of the '692 application's written description is further evidenced by the fact that the plaintiffs, during prosecution of the patent-in-

[53] With regard to this latter assertion, Sun Pharma notes that, per the court's *Markman* construction, claim 2 of the '819 Patent "encompasses all mixtures of enantiomers including a racemic mixture of the two enantiomers, pure enantiomers, and formulations containing [3-isobutyl GABA]." (D.I. 350 at 2.) To this end, Sun Pharma argues that the '692 application would have to disclose possession of S-3-isobutylGABA and does not do so. (*Id.*)

[54] Specifically, Sun Pharma explains that "the (R) and (S) descriptors are based on naming convention, the Cahn-Ingold-Prelog priority rules, which allows one to designate" (R) or (S) based on a drawing, but that "[a] person of ordinary skill in the art did not need an excess of one enantiomer of 3-isobutyl GABA to designate that enantiomer as either (R) or (S). (*Id.* at 4 (citing Tr. at 1255:22-1256:1 (Roush)).)

suit, described obtaining the S enantiomer of 3-isobutylGABA as "anything but routine."[55] (*Id.*) In sum, Sun Pharma maintains that these facts demonstrate that "there is no dispute that the ['692] application does not contain any of the information necessary to convey possession of the individual [S] enantiomer to a person of ordinary skill in the art." (*Id.* at 1-2.) Thus, Sun Pharma asserts that claims 1, 2, and 4 of the '819 Patent are not entitled to the benefit of the 1990 filing date because the '692 application "does not satisfy the written description requirement with respect to those claims" and "cannot serve as a constructive reduction to practice of the individual S enantiomer."[56] (*Id.* at 2, 10 (citing *Goeddel v. Sugano*, 617 F.3d 1350, 1353 (Fed. Cir. 2010)).) In keeping with this holding, Sun Pharma argues that the appropriate priority date for the asserted claims is May 20, 1992 and, as a result, each is invalid as anticipated. Specifically, Sun Pharma argues that claim 2 is anticipated under § 102(b) by Dr. Andruszkiewicz's 1989 article, which disclosed the racemate 3-isobutylGABA and that claims 1 and 4 are obvious under § 103 because, as the plaintiffs concede, a person of ordinary skill in the art would have been able to obtain S-3-isobutylGABA by May 1992 and would have known to pair it with a pharmaceutically acceptable carrier. (*Id.* at 12-13.)

In response, the plaintiffs assert that the '692 application does, in fact, satisfy the written description requirement with respect to S-3-isobutylGABA as a single optical isomer. (D.I. 352 at 1.) Specifically, the plaintiffs argue that Sun Pharma and its expert, Dr. Agarant, misinterpret

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[55] Here, Sun Pharma notes that the preliminary amendment the plaintiffs submitted to the PTO on June 25, 1998 characterizing Dr. Yuen's efforts in making the S enantiomer as "anything but routine," contradicts the statement made in the '692 application that "[t]he individual diastereomers or enantiomers may be prepared or isolated by methods already well known in the art." (*Id.* at 3-4 (citing PTX-0009A at PFE_LYR_0000001961, ll. 17-19).) Sun Pharma also notes that the latter statement is not included in the '819 Patent. (*Id.*)

[56] In support of this latter argument, Sun Pharma asserts that, to satisfy the written description requirement, a patent application must serve as a constructive reduction to practice. Sun Pharma also notes, however, that an application that merely renders the claimed invention obvious does not satisfy the written description requirement. (D.I. 350 at 10 (citing *Goeddel*, 617 F.3d at 1355-56).) To this end, Sun Pharma argues that the court should reject Dr. Roush's conclusion that the disclosure of the racemate in the '692 application, combined with methods known in the art, satisfies written description. (*Id.* (citing Tr. at 1206:9-19 (Roush)).)

written description to require that the claimed invention be described in such terms as to convince someone that the inventors had actually, physically reduced it to practice and had the invention "in their hands." (*Id.* (citing Tr. at 765:12-15 (Agranat)).) This, the plaintiffs argue, is not the written description standard. Rather, the plaintiffs assert that, to satisfy the written description requirement, they must simply describe the invention in such terms as to show a person of skill in the art that it was part of what the patentee claimed. (*Id.*) Here, the plaintiffs argue that the '692 application does so because it claims 3-isobutylGABA and expressly states that its "individual enantiomers" are part of the claimed invention. (*Id.*) For the reasons that follow, the court agrees.

First, the court finds that claim 2 of the '819 Patent is not invalid for lack of written description. As discussed in the preceding analyses, the '692 application expressly claimed 3-isobutylGABA in its racemic and non-racemic mixtures and detailed Dr. Andruszkiewicz's 1990 method for synthesizing 3-isobutylGABA. The application also disclosed 3-isobutylGABA as the most-preferred compound and included seven claims specifically directed to 3-isobutylGABA or its use in pharmaceutical compositions or methods of treatment.[57] (*Id.* (citing PTX-9A at PFE_LYR_0000001960, 1967-67, cls. 3, 5, 7-9, 12, 15).) Moreover, the defendants' expert on enablement, Dr. Davies, testified that claims 2 and 3 of the '692 application claimed 3-isobutylGABA in its R, S, and racemic forms and that chemists would understand what the disclosure meant. (*Id.* at 4 (citing Tr. at 659:19-660:5, 660:11-14 (Davies)).) Indeed, Sun Pharma did not seriously challenge the written description of claim 2, and their expert on this matter, Dr. Agranat, did not mention claim 2 in his testimony.

[57] Specifically, claims 2, 3, 11, and 12 cover 3-isobutylGABA and pharmaceutical compositions containing 3-isobutylGABA, "as an (R), (S), or (R, S) isomer." (D.I. 352 at 3 (citing PTX-9A at PFE_LYR_0000001960, 1967-68).) The '692 application also provides 3-isobutylGABA's structure, in vitro enzymatic activity, in vivo antiseizure activity, and a route of synthesis to obtain the compound. (*Id.* at 4 (citing PTX-9A).)

The court finds that this description is more than sufficient to convey to those of skill in the art the subject matter of the claimed invention and that the inventors were in "possession of it." *See Union Oil Co. of Ca. v. Atlantic Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000) (concluding that the application need only contain information sufficient for "persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"); *see also In re Wallach*, 378 F.3d 1330, 1333, 1335 (Fed. Cir. 2004) (noting that, for chemical compounds, the application is sufficient where it details "relevant identifying characteristics" such that the compound can be distinguished from other compounds). In light of this finding, the court concludes that November 27, 1990 is the appropriate priority filing date for claim 2 and, therefore, that there are no prior art references that would render this claim invalid as anticipated.[58] *See Finisar Corp.*, 523 F.3d at 1334 (directing that reference must be published more than one year before the filing date to qualify under § 102(b)).

Second, the court finds that claims 1 and 4 of the '819 Patent are also not invalid for lack of written description. Claims 2 and 3 of the '692 application specifically claim the S enantiomer of 3-isobutylGABA and claims 11 and 12 claim pharmaceutical compositions containing the S enantiomer. (*Id.* at 5 (citing PTX-9A at PFE_LYR_0000001969, 1971-72; Tr. at 1182:18-1183:21 (Roush)).) In addition to these claims, the '692 application discloses that "the invention includes the individual diastereomers or enantiomers" of 3-isobutylGABA. (*Id.* at 6 (citing PTX-9A at PFE_LYR_0000001961).) The plaintiffs' expert, Dr. Roush, testified that a person of ordinary skill in the art reading claims 2 and 3 would immediately understand S-3-

[58] As noted in the enablement priority date examination in Section III.C.2-4, the inventors published the Dr. Andruszkiewicz article in 1989 and the Dr. Silverman article in 1990. (*Id.* at 5 (citing PTX-7 at PFE_LYR_0000000830, 856-57; DTX-711 at 22288).) These articles are not prior art to claim 2 under § 102(b) because they were not published more than a year before claim 2's 1990 priority filing date. Nor are these articles prior art under § 102(a) because the authors, Drs. Andruszkiewicz and Silverman, are the named inventors of the '819 Patent and the publications describe the inventors own work. Because these articles are not prior art, they cannot anticipate claim 2. Thus, the defendants have not shown by clear and convincing evidence that claim 2 is invalid as anticipated under § 102(b).

isobutylGABA's chemical structure and Sun Pharma's expert, Dr. Aganat, agreed that such skilled artisans would recognize that 3-isobutylGABA possesses enantiomers. (*Id.* at 5 (citing Tr. at 1183:22-1184:10 (Roush); Tr. at 773:10-24 (Agarant)).)

Moreover, Dr. Davies similarly agreed that a chemist reading these claims would understand that they contain a description of 3-isobutylGABA's S enantiomer, separate from its R enantiomer. (*Id.* at 5-6 (citing Tr. at 659:19-660:14 (Davies)).) These skilled artisans would likewise understand, based on knowledge of 3-isobutylGABA's unexpectedly high anti-seizure activity and the '692 application's disclosure, that 3-methylGABA's enantiomers had differing pharmacological activities and one of 3-isobutylGABA's enantiomers would be more active than the other. (*Id.* (citing Tr. at 1185:23-1186:15 (Roush)).) In addition, the court finds credible Dr. Roush's testimony that the S enantiomer's physical properties, including its optical rotation, are inherent to its chemical structure and, as a result, did not need to be included in the '692 application as part of the S-3-isobutylGABA description. (*Id.* (citing Tr. at 1184:11-18 (Roush)); *see also Wallach*, 378 F.3d at 1335 (requiring identification of a compound's "relevant . . . characteristics," such that the compound can be distinguished from others).

Here, the '692 application discloses 3-isobutylGABA's name, structure, and chemical formula, indicates that the compound is chiral, states that the "invention includes [its] individual . . . enantiomers," and includes four claims covering the S enantiomer specifically. Moreover, as noted in the enablement examination above, Dr. Agranat testified on cross examination that the preparation of 3-isobutylGABA's enantiomers was within the level of skill in the art in 1990.[59] Thus, the court finds that the '692 application's disclosure, coupled with what was known in the

[59] *See supra* note 44 and accompanying text. Based on his review of the prior art, Dr. Agarant formed the opinion that one of skill in the art as of 1992 would be able to resolve the S enantiomer of 3-isobutylGABA. Tr. at 774:18-775:6 (Agarant). Dr. Agarant further testified that, in reaching this conclusion, he relied on prior art published before 1990, such that the prior art enabling resolution of S-3-isobutylGABA was available at the time of the '692 application. *Id.* at 777:3-778:19.

art, would lead a skilled artisan to conclude that 3-isobutylGABA's enantiomers were part of the invention. *See Boston Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366 (Fed. Cir. 2011).

The court notes that this conclusion is not undermined by Sun Pharma's assertion that the '692 application's written description is insufficient because the inventors did not actually synthesize each enantiomer, characterize their properties, collect biological data, or report the data in the application. (*Id.* at 7 (citing Tr. at 771:22-25, 772:16-773:3 (Agranat)).) Rather, because written description does not require reduction to practice, the inventors did not have to physically possess the invention or report such test results in the application. *See, e.g.*, *Pfizer, Inc. v. Ranbaxy Labs., Ltd.*, 405 F. Supp. 2d 495, 505 (D. Del. 2005), *rev'd in part on other grounds*, 457 F.3d 1284 (Fed. Cir. 2006) (concluding that an application was not invalid for written description where the specification contemplated the enantiomers, even though the reaction sequences and examples were racemic and the specific isomeric compounds were not individually described). Moreover, the court notes that, under § 112, the disclosure in a subsequent patent application of an inherent property of the invented product does not deprive that product of the earlier filing date, as Sun Pharma seems to advance here in connection with the '080 application. *See Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352 (Fed. Cir. 2011) (en banc); *Kennecott Corp. v. Kyocera Intern., Inc.*, 835 F.2d 1419, 1423 (Fed. Cir. 1987). Thus, the court concludes that the '692 application provides a sufficient written description for claim 1 of the '819 Patent based on the application's identification of S-3-isobutylGABA, its claims demonstrating that the inventors conceived of the invention of claim 1, and the information well known in the art. *See Boston Sci. Corp.*, 647 F.3d at 1366.

Finally, the court notes that Sun Pharma does not dispute that the '692 application provides a sufficient description of pharmaceutical compositions. Therefore, because the

application provides a sufficient description of the compound of claim 1, it also provides a sufficient description of claim 4, which covers pharmaceutical compositions containing S-3-isobutylGABA as a single optical isomer. In view of the foregoing conclusions, the court finds that claims 1 and 4 of the '819 Patent are not invalid as obvious under § 103. Specifically, because the '692 application satisfies the requirements of § 112 with respect to claims 1 and 4 and, as a result, their priority date is November 27, 1990, Drs. Andruszkiewicz and Silverman's 1989 and 1990 articles cannot provide a basis for obviousness under § 103, as both were published within a year of the '692 application's filing date.[60] Thus, claims 1 and 4 are not invalid as obvious.

E. Inventorship[61]

As noted, the defendants assert that claims 1, 2, and 4 of the '819 Patent are invalid under 35 U.S.C. § 102(f) because: (1) Dr. Yuen is the true inventor of the individual enantiomer of S-3-isobutylGABA as recited in these claims; and (2) Drs. Andruszkiewicz and Silverman derived their invention from Dr. Yuen. (D.I. 349 at 44.) The defendants also contend that these asserted claims are invalid under § 102(g)(2) because Dr. Yuen did not "abandon, suppress, or conceal" his invention of S-3-isobutylGABA. Based on these arguments, the defendants further assert that claim 4 is invalid as obvious in light of Dr. Yuen's invention. (*Id.* at 47.) For the reasons that follow, the court concludes that the defendants have not established by clear and convincing

[60] As noted, to constitute prior art under § 102(b), a reference must be published more than a year before an application's filing date.

[61] The court notes that, in the parties' Final Pretrial Order, the plaintiffs included, in their "List of Additional Evidentiary and Legal Issues," that they "intend to seek correction of inventorship of the '175 Patent by removing Po-Wai Yuen as an inventor under 35 U.S.C. § 256." (D.I. 322, Exh. 14 at ¶ 4.) However, because the plaintiffs did not present evidence in support of this assertion at trial and failed to discuss the request in their Proposed Findings of Fact and Conclusions of Law, the court does not reach findings of fact or conclusions of law on this issue. Moreover, the court notes that, as the defendants correctly highlight, the plaintiffs request in this regard is directly contradicted by their final interrogatory responses of December 7, 2009, wherein they stated that the inventorship of the '175 Patent is correct. (D.I. 349 at 35 (citing DTX-2081 at 16).)

evidence that: Dr. Yuen is the proper inventor of the asserted claims, Drs. Andruszkiewicz and Silverman derived the claimed invention from Dr. Yuen's work, or that claim 4 is obvious.

1. Legal Standard[62]

A person is entitled to a patent unless he himself did not invent the subject matter sought to be patented. 35 U.S.C. § 102(f). To be an inventor, one must contribute to the conception of the invention. *See Burroughs Wellcome Co. v. Barr Labs*, 40 F.3d 1223, 1227-28 (Fed. Cir. 1994). "Conception is defined as 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." *Stern v. Trustees of Columbia Univ.*, 434 F.3d 1375, 1378 (Fed. Cir. 2006) (citations omitted). "Conception is complete when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation." *Id.* (citing *Burroughs Wellcome Co.*, 40 F.3d at 1228). Beyond conception, the purported inventor must demonstrate that he made a "contribution to the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention, and [did] more than merely explain to the real inventors well-known concepts and/or the current state of the art." *Acromed Corp. v. Sofamor Danek Group, Inc.*, 253 F.3d 1371, 1379 (Fed. Cir. 2001).

To this end, reducing an invention to practice is not inventive if the reduction to practice is within the scope of the prior art and does not require undue experimentation. *See Vanderbilt Univ. v. Icos Corp.*, 601 F.3d 1297, 1301 (Fed. Cir. 2010) (citation omitted). Inventorship is a question of law based on underlying facts. *See Ethicon, Inc. v. United States Surgical Corp.*, 135 F.3d 1456, 1460 (Fed. Cir. 1998). Importantly, invalidity for failure to name an inventor must be

[62] The court does not define the legal standard for obviousness here, as it is fully outlined in the preceding sections. *See supra* Section III.A.

established by clear and convincing evidence and issued patents receive the presumption that its inventors are the true and only inventors. *See, e.g.*, *Acromed Corp.*, 253 F.3d at 1379.

Section 102(f) also prohibits the issuance of a patent to a person or persons who derive the conception of an invention from any other source or person. *See Price v. Symsek*, 988 F.2d 1187, 1190 (Fed. Cir. 1993). To prove derivation under § 102(f), the patent challenger must establish prior conception of the invention by another and communication of that conception to the patentee. *Id.* Moreover, § 102(g)(2) operates to ensure that a patent is awarded only to the "first" inventor in law. *See Apotex USA, Inc. v. Merck & Co.*, 254 F.3d 1031, 1035 (Fed. Cir. 2001). To this end, a person is not entitled to a patent if, "before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it." 35 U.S.C. § 102(g)(2). Invalidity under § 102(g)(2) is ultimately a legal conclusion based on underlying facts. *See Checkpoint Sys., Inc. v. United States Int'l Trade Comm'n*, 54 F.3d 756, 761 (Fed. Cir. 1995).

2. The Parties' Contentions & Discussion

The defendants assert that claims 1, 2, and 4 of the '819 Patent are invalid because Dr. Yuen is the proper inventor of these claims and/or because Drs. Andruszkiewicz and Silverman improperly derived their invention from Dr. Yuen.[63] In support of these assertions, the defendants argue, as detailed in the priority section above, that Drs. Andruszkiewicz and Silverman did not make S-3-isobutylGABA. (D.I. 349 at 44 (citing Tr. at 528:12-18 (Andruszkiewicz); Tr. at 915:5-19, 918:21-919:4 (Silverman)).) Specifically, the defendants note that while Drs. Andruszkiewicz and Silverman did make a racemic 3-isobutylGABA, they

[63] The defendants assert that Dr. Yuen cannot be a joint inventor because, despite his common goal with Drs. Silverman and Andruszkiewicz to obtain S-3-isobntylGABA, Dr. Yuen did not collaborate with them and spoke only once to Dr. Silverman before completing his synthesis of the S enantiomer. (D.I. 349 at 36 (citing Tr. at 551:1-9, 555:12-23, 562:3-6, 564:7-18, 568:24-569:5, 576:3-7 (Yuen)).) Moreover, the defendants note that Dr. Silverman does not remember this conversation with Dr. Yuen and did not have conversations with him about how to synthesize the individual enantiomers of 3-isobutylGABA. (*Id.* (citing Tr. at 922:3-9, 929:3-6 (Silverman)).)

did not separate the S enantiomer of it and, further, there were no known prior art methods for doing so as of the '692 application date. (*Id.* (citing Tr. at 611:11-22, 613:19-25 (Davies)).) To this end, the defendants contend that Drs. Andruszkiewicz and Silverman did not "conceive" of S-3-isobutylGABA as a single optical isomer, as required by § 102(f). (*Id.* at 45 (citing *Burroughs Wellcome*, 40 F.3d at 1229).) Dr. Yuen, the defendants argue, both conceived of S-3-isobutylGABA and developed an operative method of making it, such that he is its proper inventor under § 102(f). (*Id.*)

The defendants further argue that, because Dr. Yuen conceived of an operable method of making S-3-isobutylGABA in September 1991 and communicated this method to Dr. Silverman prior to Dr. Silverman's filing of the '080 application, Drs. Andruszkiewicz and Silverman improperly derived the invention from Dr. Yuen in violation of § 102(f). (*Id.* (citing Tr. at 551:14-22 (Yuen)).) The defendants assert that this position is supported by the detailed description of Dr. Yuen's method of making S-3-isobutylGABA found in the '080 application. (*Id.* (citing PTX-8 at PFE_LYR_1747).) Therefore, the defendants maintain that claims 1, 2, and 4 are invalid under § 102(f) because Dr. Yuen is the true inventor of the subject matter covered by these claims. (*Id.*) Moreover, the defendants contend that claims 1, 2, and 4 are invalid under § 102(g)(2) because, after inventing § 102(g)(2) in September 1991, Dr. Yuen did not abandon, suppress, or conceal his invention, as shown by his disclosure of his method in the '080 application and his publication of that method in a peer-reviewed journal. (*Id.* (citing DTX-968A at PFE_LYR_97732; PTX-8; DTX-1128).)

The defendants argue that their positions find further support in the fact that Dr. Yuen was listed as an inventor on the '080 application, which detailed his method of resolving the S enantiomer, as well as in the applicants' statements to the PTO that Dr. Yuen's method was "not

routine" and that he was properly named as an inventor. (*Id.* at 35 (citing PTX-7 at PFE_LYR_1147).) The defendants maintain that Dr. Yuen was removed as an inventor only because the Examiner issued a prior art rejection based on an article by Drs. Andruszkiewicz and Silverman that disclosed racemic 3-isobutylGABA. (*Id.* at 30 (citing PTX-7 at PFE_LYR_1288-89).) Specifically, the defendants note that the Examiner determined the article was prior art because the inventive entity of Drs. Andruszkiewicz, Silverman, and Yuen differed from Drs. Andruszkiewicz and Silverman's 1989 article. (*Id.* (citing PTX-7 at PFE_LYR_1288; Tr. at 950:6-21 (Silverman)).) The defendants argue that Dr. Yuen was removed as an inventor so that the article's authorship and the inventive entity were identical and the patent could be allowed. Thus, in sum, the defendants argue that the asserted claims of the '819 Patent are invalid under § 102(f) and § 102(g)(2) because Dr. Yuen conceived S-3-isobutylGABA as a single optical enantiomer and an operative method of making it before the named inventors and did not abandon, suppress, or conceal his invention.

Conversely, the plaintiffs maintain, for the reasons they advanced in connection with the defendants' priority date defense, that Drs. Andruszkiewicz and Silverman are the proper inventors of the asserted claims. Specifically, the plaintiffs argue that it is undisputed that Drs. Andruszkiewicz and Silverman first made and tested 3-isobutylGABA and conceived of its use as an anticonvulsant before the '692 application was filed in November 1990. Consequently, because Dr. Yuen was unaware of 3-isobutylGABA until April 1991, they argue that it is clear Drs. Andruszkiewicz and Silverman did not derive claim 2 from his work under Sections 102(f) and that Dr. Yuen is not an inventor under Section 102(g). *See Gambro Lundia AB v. Baxter Healthcare Corp.*, 110 F.3d 1573 (Fed. Cir. 1997) ("To show derivation, the party asserting invalidity must prove . . . prior conception of the invention by another.").

In addition, the plaintiffs argue that claims 1 and 4 are not invalid for improper inventorship, because Drs. Andruszkiewicz and Silverman conceived of 3-isobutylGABA, including its S enantiomer, as well as the operative method of making it. First, and with respect to the first inventorship requirement, the plaintiffs note that it is clear from the '692 application that Drs. Andruszkiewicz and Silverman conceived of S-3-isobutylGABA. Specifically, the '692 application details that the R and S enantiomers can be separated by methods well known in the prior art, demonstrating that they were aware of 3-isobutylGABA's enantiomers and the ability to resolve them. Second, the plaintiffs contend that, for the reasons detailed in the priority examination above, the operative method of making S-3-isobutylGABA was well within the knowledge and skill of the prior art in 1990, such that the absence of a specific method from the '692 application does not mean that Drs. Andruszkiewicz and Silverman failed to operate their invention.

In view of the record before it, the court concludes that the defendants have failed to demonstrate, by clear and convincing evidence, that Dr. Yuen is the proper inventor of claims 1, 2, or 4 of the '819 Patent. Specifically, and with regard to claim 2, the court agrees with the plaintiffs that Drs. Andruszkiewicz and Silverman conceived of 3-isobuytlGABA and its operative method by, at the latest, November 27, 1990, the date of the '692 application. As noted, the '692 application claimed 3-isobutylGABA, its individual enantiomers, and mixtures thereof, and disclosed that 3-isobutylGABA was the preferred embodiment of the invention. (*Id.* at 12 (citing PTX-9A at PFE_LYR_0000001969-73).) In addition, the '692 application set forth Dr. Andruszkiewicz's method of synthesizing a racemic mixture of the compound. (*Id.* (citing PTX-9A at PFE_LYR_0000001961-53; Tr. at 900:8-14 (Silverman)).) Thus, the court concludes that claim 2 is not invalid for improper inventorship under § 102(f) or § 102(g)(2).

Moreover, and with respect to claims 1 and 4, the court finds that Drs. Andruszkiewicz and Silverman are properly listed as the inventors of those claims. For the reasons explained in connection with the priority examination above, the court concludes that, as of November 1990, resolution of the S enantiomer of 3-isobutylGABA could be accomplished through the use of routine methods known in the prior art. This finding, coupled with the fact that Drs. Andruszkiewicz and Silverman claimed 3-isobutylGABA's individual enantiomers in the '692 application, lead to the conclusion that Drs. Andruszkiewicz and Silverman conceived of S-3-isobutylGABA and its operative method. The court notes that this conclusion is not undermined by the fact that the '692 application does not detail a specific method of resolution of 3-isobutylGABA's S enantiomer or that Dr. Yuen was the first to resolve the enantiomer. Indeed, the Federal Circuit has instructed that where, as here, a court finds that an "idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation," conception is complete. *See Stern*, 434 F.3d at 1378. Thus, the court finds that absence of a specific resolution method does not mean that Drs. Silverman and Andruszkiewicz did not conceive of S-3-isobutylGABA's operative method as required by § 102.

The court also notes that the fact that Dr. Yuen was the first to resolve S-3-isobutylGABA does not render him a proper inventor of claims 1 and 4. Instead, because the court concludes that methods to resolve the S enantiomer were within the 1990 prior art, it finds that Dr. Yuen was, at most, the first to do what one of ordinary skill in the art could do by physically preparing 3-isobutylGABA's S enantiomer. The Federal Circuit has directed that this level of contribution does not rise to inventorship. *See Vanderbilt*, 601 F.3d at 1031; *see also Burroughs*, 40 F.3d at 1223. In addition, because Dr. Yuen did not begin working on 3-

isobutylGABA until 1991, after the '692 application, he cannot be considered an inventor of the subject matter of claims 1 and 4 and Drs. Andruszkiewicz and Silverman could not have derived their invention from his work. *See Burroughs*, 40 F.3d at 1227-28. Consequently, Dr. Yuen's resolution of the S enantiomer does not render claims 1 and 4 invalid under § 102(f) or § 102(g)(2).

Finally, the court notes that the listing of Dr. Yuen as an inventor on the '080 application of the S-enantiomer resolution method and his subsequent removal from that application does not rise to the level of clear and convincing evidence necessary to invalidate the claims for improper inventorship. Specifically, while the defendants' argument that Dr. Yuen was removed as an inventor only so that Drs. Andruszkiewicz and Silverman could get over the prior art appears as a potentially compelling argument, the defendants did not present evidence to show his inventorship by the required standard. First, aside from the assertion that the applicants knew via their statements to the PTO, that Dr. Yuen was the inventor of S-3-isobutylGABA, the defendants did not show that he was removed from the '080 application for the reason they advance. In fact, the plaintiffs assert that Dr. Yuen was removed from the application in view of the Examiner's conclusion that preparing the invention of claim 1 was routine and note that the Examiner expressly stated in the '819 Patent Notice of Allowability that the applicants' initial inclusion of Dr. Yuen as an inventor was "through error and without deceptive intent." (D.I. 351 at 14 (citing PTX-7 at PFE_LYR_0000001550-51).) The defendants did not present clear and convincing evidence to the contrary.

Thus, in the view of the foregoing and for the reasons detailed in the priority examination and this section, the court concludes that the defendants have not shown by clear and convincing evidence that Dr. Yuen is the proper inventor of claims 1, 2, and 4 of the '819 Patent or that the

applicants derived their invention from his work. Therefore, the court finds that the asserted claims of the '819 Patent are not invalid for improper inventorship under § 102(f) or § 102(g)(2).

3. The Defendants' Inventorship-Related Claim 4 Obviousness Defense

The defendants assert that claim 4 of the '819 Patent is an obvious combination of Dr. Yuen's invention of S-3-isobutylGABA and prior art regarding pharmaceutical use of racemic 3-isobutylGABA and similar compounds and is, therefore, invalid. Specifically, the defendants contend that Dr. Yuen's invention of S-3-isobutylGABA as a single optical isomer became prior art under § 102(f) or § 102(g)(2) in 1991. (D.I. 349 at 37.) Thus, the defendants argue that the only difference between claim 4 and Dr. Yuen's invention is the presence of a pharmaceutically acceptable carrier. (*Id.*) According to the defendants, a person of ordinary skill in the art in May 1992, the date they assert is the appropriate priority filing date for the '819 Patent, would have known to combine Dr. Yuen's invention of S-3-isobutylGABA with a carrier based on the 1989, 1990, and 1991 articles published by Dr. Silverman and his colleagues. (*Id.*) These articles, the defendants allege, taught that racemic 3-isobutylGABA and similar compounds could be used as pharmaceutical agents. (D.I. 349 at 47 (citing DTX-711; DTX-724; PTX-820); *id.* at 37-38 (citing Tr. at 599:14-602:2 (Davies)).) Thus, the defendants assert that a "person of ordinary skill would have combined Dr. Yuen's invention with any of Dr. Andruszkiewicz's 1989 article, Dr. Andruszkiewicz's 1990 article, or Dr. Silverman's 1991 article to obtain the subject matter of claim 4." (*Id.* at 38.)

In light of this court's findings with respect to the priority filing date and inventors of the '819 patent, the court disagrees. Specifically, because the court has found that the '819 Patent's priority filing date is November 27, 1990 and that Drs. Andruszkiewicz and Silverman are the

inventors of claim 4, the articles the defendants reference would not be considered prior art to their own invention. Consequently, claim 4 is not invalid as obvious.

F. Infringement

The plaintiffs contend that the defendants literally infringe the asserted claims of the '819, '175, and RE '920 Patents. As noted, however, the parties filed a Stipulation and Order on October 11, 2011, wherein the defendants stipulated that, should the court find the asserted claims of the patents-in-suit valid, the defendants' proposed products would infringe all asserted claims of the patents-in-suit except claims 1 and 4 of the '819 Patent.[64] (D.I. 335.) Because the court has found the patents-in-suit valid, it examines literal infringement and infringement under the doctrine of equivalents only with regard to claims 1 and 4 of the '819 Patent. For the reasons that follow, the court concludes that: (1) each of the defendants' proposed products do not literally infringe the asserted claims; and (2) the defendants' proposed products infringe the asserted claims under the doctrine of equivalents because prosecution history estoppel does not preclude the plaintiffs from asserting this claim.

1. <u>The Legal Standard</u>

The court addresses the legal standards for literal infringement and infringement under the doctrine of equivalents separately.

a. Literal Infringement

The application of a patent claim to an accused product is a fact-specific inquiry. *See Kustom Signals, Inc. v. Applied Concepts, Inc.*, 264 F.3d 1326, 1332 (Fed. Cir. 2001). Specifically, the patent infringement analysis is conducted in two steps: (1) construction of the claims; and (2) comparison of the construed claim to the accused product. *Amgen, Inc. v. Hoescht Marion Roussel, Inc.*, 314 F.3d 313, 1324 (Fed. Cir. 2003). While claim construction is

[64] *See* Findings of Fact, Section II.D at ¶ 127-28.

a question of law, the application of a construed claim to an accused product is a question of fact. *Glaxo Group Ltd. v. Apotex, Inc.*, 376 F.3d 1339, 1345 (Fed. Cir. 2004). Literal infringement is present only when each and every element set forth in the patent claims is found in the accused product. *See Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1575-76 (Fed. Cir. 1995). The patent owner has the burden of proving infringement by a preponderance of the evidence. *See Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 758 (Fed. Cir. 1984) (citing *Hughes Aircraft Co. v. United States*, 717 F.2d 1351, 1361 (Fed. Cir. 1983)). To this end, a patent owner does not have to produce "definite" proof of infringement, but must instead demonstrate that "infringement was more likely than not to have occurred." *See Warner-Lambert Co. v. Teva Pharms., USA, Inc.*, 418 F.3d 1326, 1341 n.15 (Fed. Cir. 2005) (citing *Advanced Cardiovascular Sys., Inc. v. Scimed Life Sys., Inc.*, 261 F.3d 1329, 1336 (Fed. Cir. 2001)).

In Hatch-Waxman cases such as this, the infringement inquiry is "properly grounded in the ANDA application and the extensive materials typically submitted in support." *Ben Venue Labs., Inc. v. Novartis Pharm. Corp.*, 146 F. Supp. 2d 572, 580 (D.N.J. 2001). Because "drug manufacturers are bound by strict statutory provisions to sell only those products that comport with the ANDA's description of the drug, an ANDA specification defining a proposed generic drug in a manner that directly addresses the issue of infringement will control the infringement inquiry." *Abbott Labs. v. TorPharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002). Thus, where an ANDA specification requires the applicant to produce a product that falls within the asserted claim, the ANDA itself will answer the question of infringement. *See, e.g.*, *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1248-50 (Fed. Cir. 2000).

In the absence of a specification directly addressing the question of infringement, the court is directed to consider "the ANDA itself, the materials submitted by [the ANDA applicant]

to the FDA, and other pertinent evidence provided by the parties," such as, for instance, an ANDA filer's FDA product testing. *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1567-70 (Fed. Cir. 1997); *see also Ben Venue*, 146 F. Supp. at 580. Ultimately, "under [35 U.S.C.] § 271(e)(2)(a), a court must determine whether, if the drug were approved based upon the ANDA, the manufacture, use, or sale of that drug would infringe the patent in the conventional sense." *Glaxo, Inc.*, 110 F.3d at 1569. To prove this by a preponderance of the evidence, the patentee must show not simply that the ANDA specification "permits" the defendant to sell or that the defendant might sell an infringing product. *See id.* at 1567. Instead, the patentee must show that that the product the defendant "ultimately would put on the market would likely infringe" the patent-in-suit. *Id.* Importantly, this requirement does not require the patentee to show that the defendant's product will meet the claims "9 times out of 10," but, instead, that the product will more likely than not infringe. *See Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1287 (Fed. Cir. 2010).

b. Doctrine of Equivalents

The doctrine of equivalents prohibits one from "avoiding infringement liability by making only 'insubstantial changes and substitutions . . . which, though adding nothing, would be enough to take the copied matter outside the claim, and hence outside the reach of law." *Siemens Medical Solutions USA, Inc. v. Saint-Gobain Ceramics & Plastics, Inc.*, 637 F.3d 1269, 1279 (Fed. Cir. 2011) (quoting *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 607 (1950)). The doctrine has evolved to protect patentees "against efforts of copyists to evade liability for infringement by making only insubstantial changes to a patented invention." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Corp.*, 535 U.S. 722, 727 (2002). To this end, infringement may also be established under the doctrine of equivalents because the "scope of a

patent is not limited to its literal terms but instead embraces all equivalents to the claims described." *Id.* at 732. Thus, a product or process that "does not literally infringe upon the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused product or process and the claimed elements of the patented invention." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997). The doctrine of equivalents must be applied to the "individual elements of the claim, not to the invention as a whole." *Id.* at 29.

"An element of an accused [product] is equivalent to an element of the patented invention if the differences between them are insubstantial." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 520 F. Supp. 2d 537, 547 (D. Del. 2007) (quoting *Warner-Jenkinson*, 520 U.S. at 39). Alternatively, the accused product infringes under the doctrine of equivalents "if the element in the accused device performs substantially the same function in substantially the same way to obtain the same result as the claim limitation." *Id.* at 547-48. Regardless of whether the insubstantial differences or the function test is used, the patentee must provide "particularized testimony and linking argument" for each limitation invoking the doctrine of equivalents. *See Texas Instruments v. Cypress Semiconductor Corp.*, 90 F.3d 1558, 1567 (Fed. Cir. 1996).

However, the doctrine of prosecution history estoppel may bar a patentee from asserting as an equivalent subject matter that was surrendered during prosecution of the patent or that would vitiate a claim term. *Festo*, 535 U.S. at 729; *Warner-Jenkinson*, 520 U.S. at 30-31. The prosecution history estoppel doctrine serves a public notice function. Specifically, if a patentee clearly states during prosecution that certain subject matter is not claimed, the public and the patentee's competitors, may rely on that representation in making and using unclaimed subject matter without giving rise to an infringement action. *See Festo*, 535 U.S. at 727. To this end, if

the prosecution history shows that the patentee made a narrowing amendment for reasons related to patentability or there is no explanation regarding the amendment, then a presumption is raised that bars equivalents for the added limitations. *Id.* at 739-40. An amendment is made for the purpose of securing patentability if, without it, "the patent probably would not have been [issued]." *See K-2 Corp. v. Salomon S.A.*, 191 F.3d 1356, 1369 (Fed. Cir. 1999). To rebut this presumption of estoppel, a patentee must show that: (1) the alleged equivalent was unforeseeable; (2) the alleged equivalent bears no more than a tangential relation to the amendment; or (3) some other reason supporting rebuttal. *See Festo*, 535 U.S. at 740.

To "constitute a binding surrender of claim scope," however, the patentee must disavow the claim scope in such a way as to "cause a competitor to reasonably believe that the applicant had surrendered the relevant subject matter." *LG Electronics USA, Inc. v. Whirlpool Corp.*, No. 08-CV-0234(GMS), 2011 WL 2610177, at 17 (D. Del. July 1, 2011) (quoting *Cybor Corp. v. FA Techs., Inc.*, 138 F.3d 1448, 1457 (Fed. Cir. 1998) (en banc)). Put another way, exclusion of the particular equivalent in question must be "clear and unmistakable" to give rise to estoppel. *See Cordis Corp. v. Medtronic Ave, Inc.*, 511 F.3d 1157, 1177 (Fed. Cir. 2008). To determine whether prosecution history estoppel applies in a given case, the trial court tasked with this assessment "must look to the specifics of the amendment and the rejection that provoked the amendment to determine whether estoppel precludes the particular doctrine of equivalents argument being made." *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1291 (Fed. Cir. 2010). The Federal Circuit has instructed that, in this analysis, a patentee should not be estopped "beyond a fair interpretation of what was surrendered." *Id.* (quoting *Festo*, 535 U.S. at 737-38). Thus, if the "rationale underlying an amendment bore no more than a tangential relation to the equivalent in question," in that "the reason for the narrowing amendment was peripheral, or not directly

relevant, to the alleged equivalent," prosecution history estoppel will not preclude the patentee from asserting the doctrine of equivalents. *See Festo v. Shoketsu Kinzoku Kabushiki Co., Ltd.*, 344 F.3d at 1368-69 (Fed. Cir. 2003).

2. Literal Infringement: Parties' Contentions & Discussion

As noted, the plaintiffs contend that each of the defendants' proposed products will literally infringe claims 1 and 4 of the '819 Patent. (D.I. 351 at 18-28, 42-44.) In making this argument, the plaintiffs assert that they have shown, by a preponderance of the evidence, that the defendants' proposed products infringe the asserted claims because: (1) none of the defendants' original ANDAs specify a minimum required amount of R enantiomer, such that the products may be produced completely "free of" R enantiomer, infringing claim 1; and (2) the test data the defendants submitted to the FDA in connection with their ANDAs demonstrate that their proposed products will literally infringe claim 1, as they will not include R enantiomer.

With respect to the former argument, the plaintiffs contend that because each original ANDA specification defines the maximum amount of R enantiomer that may exist in the product,[65] but does not contain a lower limit requiring the presence of R enantiomer, the court should conclude, based on the ANDAs alone, that the defendants will sell a claim 1 infringing product. (*Id.* at 18.) The plaintiffs rest this assertion on the fact that the defendants' original ANDAs "encompass[] a composition that is completely free of" R enantiomer. (*Id.*) The plaintiffs further maintain that Actavis and Lupin's ANDA amendments requiring a minimum amount of R enantiomer in their proposed products do not negate this finding because the ANDA

[65] Specifically, the plaintiffs note that each of the defendants' ANDAs include a "not more than" ("NMT") percentage indicating how much R enantiomer can be included in their products. These figures are: (1) Actavis, NMT 0.15%; (2) Cobalt, NMT 0.25%; (3) Lupin, NMT 0.20%; (4) Mylan, NMT 0.15%; (5) Sun, NMT 0.15%; (6) Teva, 0.15%; and (7) Wockhardt, NMT 0.15%. (D.I. 351 at 18.)

amendments are highly unusual and, to date, have not been approved.[66] (*Id.* at 23-24, 27-28.) Thus, the plaintiffs argue that the court should consider the defendants' original ANDAs in its infringement analysis and that these ANDAs, on their face, demonstrate literal infringement.

Regarding the latter argument, the plaintiffs assert that the test data the defendants submitted to the FDA confirms, with respect to all defendants except Lupin and Wockhardt, that their products will literally infringe claim 1 and, therefore, claim 4, because this data shows the defendants' proposed products can be produced with no R enantiomer. (*Id.*) In view of the record before it and in consideration of the relevant law, however, the court finds, for the reasons that follow, that the plaintiffs have failed to show by a preponderance of the evidence that the defendants' proposed products will literally infringe claims 1 and 4.[67]

a. Consideration of the Defendants' Original ANDAs

Based on the evidence adduced at trial and guiding case law, the court disagrees with the plaintiffs' argument that literal infringement can be found based solely on the defendants' original ANDA specifications in this case. At trial, the plaintiffs' expert, Dr. Chyall, testified that, due to the fact that the defendants' original ANDAs do not specify a lower limit requiring the presence of some R enantiomer in their proposed products, the court can find literal infringement on this evidence alone, because the specifications "permit" the defendants to sell and the defendants might sell, literally infringing products containing no R enantiomer. (*Id.* at

[66] The plaintiffs note that Actavis filed an amendment to its original ANDA on June 3, 2011, seeking to add a lower limit of 0.02% to its R enantiomer specification. (*Id.* at 23.) Similarly, on September 21, 2011, Lupin filed an amendment seeking to include in its specification that R enantiomer must be in the range of 0.01 to 0.20%, thus requiring the presence of a minimum amount of R enantiomer in its proposed product. (*Id.* at 27.) On June 12, 2012, the FDA sent Actavis a minor deficiency letter, recommending that Actavis remove the 0.02% lower limit. (D.I. 381 at 2-1.) Actavis plans to challenge this recommendation, but, in light of it, has requested the court consider its API pregabalin test data in addition to its amended ANDA in deciding literal infringement. (*Id.* at 2.) The court does so in its analysis. The FDA has not approved or rejected Lupin's lower limit amendment.

[67] The court notes that because it concludes that the defendants do not literally infringe clam 1, they also do not literally infringe claim 4, which alternatively requires the presence of a compound of claim 1 or unasserted claim 3. *See* 35 U.S.C. § 112; *Wahpeton Canvas Co. Inc. v. Frontier, Inc.*, 870 F.2d 1546, 1552 n2. (Fed. Cir. 1989).

18, 43-44.) The plaintiffs contend it is of no moment that the defendants' specifications would also permit them to produce non-infringing products containing R enantiomer. (*Id.* at 43.) In support of this assertion, the plaintiffs cite the Federal Circuit's direction in *Adams Respiratory Therapeutics, Inc. v. Perrigo Co.* and *Bell Communications Research, Inc. v. Vitalink Communications. Corp.* that, as the patentee, they are not required to "prove that an ANDA-filer's proposed product will meet the claims '9 times out of 10'"[68] and, moreover, that "an accused product that sometimes, but not always, embodies a claim[] . . . nonetheless infringes."[69] (*Id.* at 43-44.)

The relevant law, as applied to the record before the court compels a contrary conclusion. Specifically, while the plaintiffs are correct that a patentee does not have to demonstrate that a defendant's product will infringe every time to establish infringement, this standard does not remove from the plaintiffs their burden to prove that the defendants' proposed products will more likely than not infringe claims 1 and 4.[70] In the court's view, examination of the defendants' original ANDAs alone does not demonstrate that the defendants' proposed products

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[68] *Adams Respiratory Therapeutics, Inc.*, 616 F.3d at 1287.

[69] *Bell Commc'ns Research, Inc. v. Vitalink Commc'ns. Corp.*, 55 F.3d 615, 622-23 (Fed. Cir. 1995).

[70] The court notes that the cases the plaintiffs cite in support of this argument are distinguishable from the facts in the instant examination. Specifically, in *Adams Respiratory Therapeutics, Inc.*, the Federal Circuit clarified that, where a claim was construed to have a 90% confidence interval, the patentee was not required to show that the defendant's product would infringe 90% of the time to prove literal infringement. *Adams Respiratory Therapeutics, Inc.*, 616 F.3d at 1287. Importantly, the Federal Circuit noted that the patentee was still required to prove that the defendant would more likely than not infringe the asserted claim. *Id.* Because the preponderance of evidence standard has never required a showing of absolute or 100% infringement and instead, sets forth a "more likely than not standard," the court does not find this case necessarily instructive when applied to these facts.

Similarly, the plaintiffs' reliance on *Bell Communications Research, Inc.* does not authoritatively guide its analysis. In that case, the Federal Circuit noted that courts should give "due attention to the principle that an accused product that sometimes, but not always, embodies a claimed method nonetheless infringes." *See Bell Commc'ns Research, Inc.*, 55 F.3d at 622-23. Here again, the plaintiffs ask the court to conclude, based on the defendants' original ANDA specifications, that their proposed products will more likely than not infringe claims 1 and 4 without evidence to support that their products will, in fact, infringe at all. The court is not convinced that the defendants' original ANDA specifications alone establish that the defendants' proposed products will sometimes—or will be more likely than not to—infringe. Thus, unlike in *Bell Communications Research, Inc.*, where correct performance of a claimed method would result in infringement, here, claim 1 covers the enantiomer of a compound rather than a method whereby infringement depends on how it was performed. Therefore, the court cannot, absent additional evidence, determine whether the defendants' products will literally infringe the asserted claims because it is the end product, rather than the method of producing the product, that determines infringement.

would infringe—or that they would be more likely than not to infringe—claims 1 and 4. In particular, the specification does not require the defendants' proposed products to be "free of" R enantiomer and instead, simply requires an upper limit on the amount of R enantiomer present.[71] *See Abbott Labs*, 300 F.3d at 1373 (concluding that literal infringement can be decided based on an ANDA specification where the specification "directly addresses the issue of infringement"). Thus, because the court concludes that the defendants' original ANDAs do not directly address whether their proposed products will infringe, it is necessary to consider the defendants' ANDAs in conjunction with the testing and other materials each submitted to the FDA to ascertain whether the plaintiffs can establish literal infringement by the required standard. *Glaxo, Inc.*, 110 F.3d at 1567-70.

b. Consideration of the Defendants' FDA-Submitted Tests

Having considered the defendants' testing of their proposed products,[72] the methods of testing used, and the defendants' ANDAs, the court concludes that the plaintiffs have not proved by a preponderance of the evidence that the defendants' proposed products will literally infringe claims 1 and 4. Before examining each of the defendants' proposed products below, the court notes that the plaintiffs generally agreed with the methods the defendants and their suppliers employed to determine if their pregabalin products contain R enantiomer. Specifically, the defendants and their suppliers used an analytical method called high performance liquid chromatography ("HPLC") to test the presence and amount of R enantiomer in their active pharmaceutical ingredient ("API"), pregabalin, and, for Actavis, Lupin, Mylan, and, Teva, in their finished products as well. (D.I. 351 at 19 (citing Tr. at 77:10-13 (Chyall)).) The plaintiffs

[71] The court notes that, because only two defendants submitted amendments to the FDA requiring a minimum presence of R enantiomer in their proposed products, the court will address these defendants' proposed amended ANDAs in the defendant-by-defendant examination below.

[72] The court notes that the plaintiffs did not conduct their own testing on the defendants' proposed products or their active pharmaceutical ingredients ("API") to determine whether these proposed products literally infringed claims 1 and 4 of the '819 Patent. (D.I. 349 at 5.)

agree that the defendants' HPLC test methods for determining the amount and presence of R enantiomer "are state-of-the-art in the pharmaceutical industry" and are "all sensitive, well-validated, [and] scientifically-acceptable methods." (*Id.* (citing Tr. at 92:13-24 (Chyall)).)

However, Dr. Chyall testified that while HPLC is an appropriate method, the test generally includes a small amount of "noise," which results in random fluctuations appearing in the baseline of the chromatogram that is the output of an HPLC test. (*Id.* (citing Tr. at 83:18-84:1 (Chyall)).) Dr. Chyall explained that to distinguish peaks attributable to noise from peaks generated by compounds in a sample, a "limit of detection" ("LOD") is assigned to a given HPLC method, corresponding to the size of a peak required to determine with scientific confidence that the peak represents a compound's presence in the sample, rather than noise. (*Id.* (citing Tr. at 84:7-14, 106:9-13 (Chyall)).) Dr. Chyall opined, in testimony the court finds credible, that HPLC data detections at the LOD are less reliable than those above the LOD, because these above-LOD readings are more distinguishable from the "noise" inherent in the test. (*Id.*) Moreover, Dr. Chyall and several of the defendants' experts, such as, Dr. Caldwell, agreed that because there is no test known to modern science that can prove there is no R enantiomer in any batch of pregabalin, the ability to detect R enantiomer will often depend on the sensitivity of the test method used and, therefore, the LOD. (*Id.* (citing Tr. at 230:1-231:2, 107:10-108:4 (Chyall); Tr. at 336:9-337:8 (Caldwell)).)

Based on its review of the defendants' FDA-submitted testing and the relevant law on literal infringement, the court concludes that the plaintiffs have not shown, by a preponderance of the evidence, that the defendants' proposed products literally infringe claims 1 or 4 of the '819 Patent. For the purpose of clarity, the court's reasoning and analysis with respect to each defendant is detailed separately below. The court also notes that it includes a recitation and

examination of each defendant's FDA testing here for consideration of literal infringement as well as the doctrine of equivalents analysis to follow.

i. *Actavis' Proposed Product*

Actavis submitted ANDA No. 91-02 to the FDA seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths. (D.I. 349 at 11.) In its ANDA, Actavis identified Teva as its API pregabalin supplier and detailed its HPLC analytical method as Teva's "RC1." (D.I. 351 at 22-23.) Teva assigned this method an LOD of 0.03%, which Actavis re-validated and assigned a lower LOD of 0.012%. (*Id.* at 23 (citing PTX-1471 at 41; PTX-168; PTX-169; PTX-170; PTX-171; Tr. at 129:11-22, 130:1-131:11 (Chyall)).) The plaintiffs note, and Actavis does not dispute, that using these methods, neither Actavis nor Teva detected any R enantiomer in the four exhibit batches of Teva's API that were tested. (*Id.* (citing PTX-1471 at 42; PTX-178 at ACTPG000107854; Tr. at 131:120133:17 (Chyall)).) In addition, Actavis tested sixteen samples of its finished product using the same HPLC method and detected no R enantiomer. (*Id.* at 23 (citing PTX-1471 at 43; Tr. at 133:18-135:7 (Chyall)).)

On June 3, 2011, Actavis filed an amendment to its ANDA with the FDA seeking to: (1) add MSN Pharmachem ("MSN") as a supplier of pregablin API; (2) add a lower limit of 0.02% R enantiomer to its specification; and (3) add a new HPLC method, "RC5," for testing its API, with a lower LOD of 0.005%. (*Id.* (citing PTX-1417 at 44; PTX-452).) This amendment did not seek to remove Teva as a supplier of the raw material for Actavis' product. (*Id.* (citing Tr. at 512:12-16 (Jadeja)).) The plaintiffs note that Actavis informed them of the filed amendment on March 11, 2011, the day fact discovery was set to close, and did not provide them with any documents related to the proposed amendment until June 13, 2011. (*Id.* (citing DTX-2601 at 5,

7-8; PTX-1481).) Actavis continued producing documents on its proposed amendment until September 15, 2011, less than a month before trial. (*Id.* (citing PTX-1487).)

The plaintiffs maintain that Actavis' amendment was "very unusual" and Dr. Chyall testified that the amendment in question was the first time he had seen a "minimum amount of impurity . . . required to be present in [a] drug substance." (*Id.* at 23-24 (citing Tr. at 138:19-24 (Chyall)).) For this reason, and because the FDA had not yet approved the amendment, the plaintiffs assert that the court should consider only Actavis' original ANDA. (*Id.* at 24.) Perhaps for this reason, the plaintiffs did not assert literal infringement with respect to Actavis' API obtained from MSN in the final Pretrial Order, though they do assert literal infringement with regard to the Teva API. (D.I. 349 at 12 (citing D.I. 322, Exh. 12 at ¶¶ 40-56).) For similar reason, the plaintiffs reject the results from Actavis' re-testing of its four exhibit batches using its new HPLC method. This re-testing reported detection of R enantiomer at 0.03%, 0.03%, 0.04%, and 0.03%. (D.I. 351 at 24 (citing PTX-1471 at 45; PTX-449 at ACTPG_000109573; Tr. at 497:16-25 (Liotta)).) Because these detection figures are higher than the RC1 method's 0.01% LOD, the plaintiffs argue that Actavis' new RC5 method "overreports" R-3-isobutylGABA. (D.I. 349 at 12 (citing Tr. at 92:11-24, 276:3-8 (Chyall)).)

However, based on the evidence presented, the court disagrees with the plaintiffs' contention that Actavis' RC5 method detecting R enantiomer is unreliable. Indeed, Dr. Chyall testified that the RC5 method is a "validated" method with a low level of detection and did not offer any basis as to why the method would overreport as he opined. (*Id.* (citing Tr. at 141:2-143:10 Chyall)).) Moreover, Dr. Chyall reported that, using this RC5 method, Actavis was able to detect R enantiomer in its Teva batches at 0.15%, 0.10%, 0.11%, and 0.10%, all values above the LOD. Tr. at 143:11-25 (Chyall). As noted, Dr. Chayll did not conduct his own testing in

reaching his conclusions. In contrast, Actavis' expert, Dr. Liotta, tested the RC5 method and testified that it was free of any impurity that could cause overreporting of R-3-isobutylGABA. (*Id.* (citing Tr. at 480:14-481:23, 485:7-487:17 (Liotta)).)

In light of this evidence and Dr. Chyall's testimony regarding scientists' inability to disprove the presence of R enantiomer,[73] the court concludes that the plaintiffs have not shown by a preponderance of the evidence that Actavis' Proposed Product is "free of" R enantiomer. Thus, the court finds that Actavis does not literally infringe claims 1 and 4 of the '819 Patent.[74]

ii. *Cobalt's Proposed Product*

Cobalt submitted ANDA No. 91-221 to the FDA seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths. (D.I. 349 at 8 (citing DTX-63).) Cobalt's pregabalin API supplier is Changzhou Pharmaceutical Factory ("Changzhou"). (*Id.* (citing DTX-63 at CBLT-PRGBN542).) Changzhou manufactured seven batches of pregabalin that were used in Cobalt's ANDA exhibit batches. (*Id.* (citing DTX-63 at CBLT-PRGBN619; Tr. at 346:16-348:21 (Wolf)).) Changzhou identified R enantiomer as one of five known impurities that may arise during the manufacturing process, an impurity that Cobalt also identified in its ANDA. (*Id.* (citing DTX-63 at CBLT-PRGBN6615; Tr. at 344:7-345:11 (Wolf); PTX-200).) Cobalt ultimately adopted Changzhou's limit that "not more than"

[73] *See infra* Sections III.F.2.b.iv-v.

[74] The court notes that because the evidence at trial demonstrates that R enantiomer was present in at least some samples of Actavis' API pregabalin batches and the plaintiffs have not offered convincing evidence challenging the validity of the RC5 method or demonstrating that R enantiomer was not present, it does not need to consider Actavis' proposed amendment requiring a minimum amount of R enantiomer in its analysis. Specifically, the court finds that, regardless of whether the FDA approves Actavis' lower limit R enantiomer requirement, the detectable presence of R enantiomer in Actavis' batches demonstrates that Actavis' Proposed Product does not literally infringe the asserted claims. Tr. at 142:13-144:5 (Chyall) (recognizing that, in addition to the R enantiomer detected via the RC5 method, R enantiomer was also identified in Teva's product using the RC1 method). Thus, because R enantiomer was detected in both Teva and MSN's batches, the court does not need to reach the plaintiffs' argument that Actavis' amendment should not be considered.

0.15% R enantiomer is allowed in its proposed product. (*Id.* (citing DTX-63 at CBLT-PRGBN629; PTX-200).)

Cobalt evaluated the enantiomeric purity of the API used in all seven ANDA batches, using an HPLC method that it developed and validated. (*Id.* (citing DTX-63 at CBLT-PRGBN619; Tr. at 346:16-348:21 (Wolf)).) Cobalt confirmed and Drs. Chyall and Wolf agreed that this HPLC method is a valid and reliable scientific method for detecting the presence of R enantiomer in a substance. (*Id.* (citing Tr. at 92:11-24 (Chyall); Tr. at 362:2-364-15 (Wolf); DTX-63 at CBLT-PRGBN717-754).) Cobalt reported that its HPLC analysis detected R enantiomer in all seven Changzhou API batches in amounts ranging from 0.003% to 0.006%. (*Id.* (citing DTX-63 at CBLT-PRGBN619, 802, 806, 810, 814, 818, 822, 826; PTX-142; DTX-94 at CBLT-PRGBN20151-57, 20163-69; DTX-100; Tr. at 346:16-348:21, 347:14-350:11 (Wolf); Tr. at 158:12-20 (Chyall)).) Cobalt detected these numbers with a 0.003% LOD. (*Id.* at 9 (citing Tr. at 343:2-344:6, 353:13-354:2 (Wolf); Tr. at Chyall 259:2-261:13; PTX-1472).)

While the plaintiffs do not dispute Cobalt's detection numbers, they do assert that its testing should be disregarded because Changzhou conducted its own testing on the seven API batches using an LOD of 0.01% and found no detectable R enantiomer. (D.I. 351 at 25-26 (citing Tr. at 156:22-157:5 (Chyall); PTX-1472 at 51; PTX-202A).) The plaintiffs argue that Changzhou's HPLC testing is more reliable than Cobalt's HPLC analysis because: (1) Cobalt's testing of a blank solution detected R enantiomer even though it was not present in that solution (*id.* at 26 (citing DTX-63 at CBLT-PRGBN000727)); (2) Dr. Wolf, Cobalt's expert, acknowledged that there was no R enantiomer in this blank solution (*id.* (citing Tr. at 358:24-359:16, 359:24-360:2 (Wolfe)); (3) Cobalt uses a "worst case or highest numerical value" reporting conversion, which could "round up" detection numbers and "artificially inflate the

amount of R enantiomer reported in a given test" (*id.*); and (4) three of Cobalt's seven detection figures were at the LOD and were, therefore, unreliable per Dr. Chyall's testimony (*id.* (citing Tr. at 158:12-20 (Chyall); PTX-1472 at 52; PTX-206B).) Relying on these alleged failings, the plaintiffs assert that they have proved by a preponderance of the evidence that Cobalt literally infringes claims 1 and 4 because Changzhou's HPLC testing did not detect R enantiomer in Cobalt's API samples. The court disagrees.

First, the court is unconvinced that Changzhou's HPLC method is more reliable. As noted, Cobalt's LOD is 0.003%, three times more sensitive than Changzhou's 0.01% LOD and, based on Changzhou's LOD, the latter would not have detected the R enantiomer values Cobalt was able to identify through its HPLC method. (D.I. 349 at 9 (citing Tr. at 343:2-344:6, 353:13-354:2 (Wolf); PTX-1472).) Second, Changzhou follows the ICHQ3A reporting convention, which requires amounts below 0.5% to be reported "undetected." (*Id.* (citing Tr. at 352:18-353:12, 354:5-355:7 (Wolf)).) Thus, even if the Changzhou HPLC method were able to detect the R enantiomer amounts Cobalt identified, it would have reported these figures as "undetected." (*Id.*) Third, the plaintiffs' argument that Cobalt's method was unreliable because its blank solution testing in one run detected R enantiomer is unavailing. Specifically, Dr. Wolf explained, in testimony the court finds credible, that he attributed the presence of R enantiomer in the blank test to "carryover" from the running of a previous sample, a common occurrence in this type of testing. Tr. at 360:14-361:12 (Wolf). Dr. Wolf testified that he reviewed the laboratory notebook information from before this blank sample and found that "right before the injection . . . several samples being labeled as systems were injected . . . [that] contained large amounts of the reference standard," which "is containing 50% of the R-enantiomer." *Id.* at 362:16-363:5. Finally, Dr. Wolf explained that, to cure this carryover, an analyst would inject

another blank to wash it out and noted that he "inspected every single blank that was collected right before the actual batch analyses were run" for Cobalt's HPLC testing and found that its method was reliable. *Id.* at 364:2-17.

In light of this testimony and, in particular, evidence that the Changzhou method's LOD would not have detected the R enantiomer in Cobalt's samples or would have reported it as "undetected," the court concludes that the plaintiffs have not shown by a preponderance of the evidence that Cobalt's proposed product will not contain R enantiomer and will literally infringe. Rather, the court is persuaded by Dr. Wolf's testimony that Cobalt's HPLC testing was reliable and, because it detected R enantiomer, the plaintiffs have failed to show Cobalt's product will, more likely than not, be "free of" R enantiomer. In reaching this conclusion, the court notes that, while Cobalt's R enantiomer values were lower than those of the other defendants, they were detected by a sensitive testing method and, as Dr. Chyall testified, any R enantiomer present in a pregabalin API will remain present in the final dosage form. (D.I. 349 at 9 (citing Tr. at 104:4-6 (Chyall)).) Thus, in view of the foregoing, the court concludes that Cobalt does not literally infringe claims 1 and 4 of the '819 Patent.

iii. *Lupin's Proposed Products*

Lupin submitted two ANDAs, Nos. 91-040 and 201989, seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths and a pregabalin oral solution, respectively. (*Id.* at 6.) Lupin's ANDAs each identify Lupin as the supplier of its pregabalin API and this API is made in accordance with Lupin's DMF No. 22330. (*Id.* (citing PTX-223 at LUPRE046657; DTX-490A at LUPROS7, LUPROS13).) Lupin's DMF, as originally submitted, included a specification defining an upper limit of 0.20% for the amount

of R enantiomer that can be present in its pregabalin. (*Id.* (citing PTX-232 at LUPROS808; PTX-376 at LUPRE046289).)

Lupin asserts, and the plaintiffs do not dispute, that the Lupin method of identifying R enantiomer in its pregabalin has an LOD of 0.01% and is a reliable scientific procedure appropriate to determine if Lupin's Proposed Products are free of R enantiomer. (*Id.* at 7 (citing Tr. at 163:8-24, 163:25-164:5 (Chyall); PTX-242A at LUPRE9255-9256).) Lupin reported that each batch of pregabalin, Batch Nos. 080730501, 080730502, 080730503, and 080730504, used to make the exhibit batches for its capsule ANDA contains a detectable amount of R enantiomer. (*Id.* (citing PTX-232 at LUPROS803-806, LUPROS808-811; PTX-376 at LUPRE046286, LUPRE046289-46296; PTX-1474 at 55).) Lupin also made a batch, Batch No. 080770101, using its DMF, which was not used to make exhibit batches. (*Id.* (citing Tr. at 209:11-210:1 (Chyall)).) While Lupin was unable to detect R enantiomer in this batch in its first test, it later detected between 0.01% and 0.03% during stability testing after 1, 3, 6, 9, 12, 18, and 24 months of storage. (*Id.* (citing PXT-337 at LUPRE041471; DTX-369).) Lupin attributed its inability to detect R enantiomer in this batch during its first test to too little sample being recovered from the column, an explanation they assert is supported by the order of magnitude lower pregabalin peak area. (*Id.* (citing Tr. at 208:10-210:15, 211:16-22 (Chyall); Tr. at 328:3-25, 330:20-332:6 (Caldwell)).)

The plaintiffs do not dispute that Lupin detected R enantiomer in all of its batches prepared as exhibits for its OS ANDA. Instead, the plaintiffs challenge Lupin's filing of an amendment to its ANDA on September 21, 2011, one month before trial, wherein it revised its DMF specification to require a minimum of 0.01% R enantiomer in its proposed product. (D.I. 351 at 27-28.) While the plaintiffs correctly note that Lupin's amendment has not yet been

approved and they have not amended their ANDA to include the revised specification, Lupin's amendment filing does not impact the court's conclusion here because Lupin determined, by reliable methods, that its proposed product would include detectable levels of R enantiomer. Thus, because the plaintiffs have presented no evidence to indicate that Lupin's products would more likely than not be "free of" R enantiomer, the court concludes that Lupin's Proposed Products do not literally infringe claims 1 and 4.

iv. *Mylan's Proposed Product*

Alphapharma, through its U.S. agent, Mylan, submitted ANDA No. 91-228 to the FDA seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths. (D.I. 349 at 9.) Mylan's ANDA identifies Matrix Labs., Ltd. ("Matrix") and Mylan Development Center Private Ltd. ("MDC") as suppliers of its pregabalin API. (*Id.* at 10 (citing DTX-694 at MylanC596).) Mylan's expert, Dr. Williams, testified that the Matrix and MDC API manufacturing methods cannot produce pregabalin free of R enantiomer because they employ methods involving classical resolution, wherein successive crystallization cycles reduce R-3-isobutylGABA while enriching S-3-isobutylGABA, but do not ultimately remove the R enantiomer. (*Id.* (citing Tr. at 398:16-23, 401:2-9, 390:17-22, 391:1-392:17, 399:21-400:8 (Williams); DTX-707C at MylanD31-41; DTX-708B at MylanE30-332).) Dr. Williams further testified that intermediate testing showed 11% R-3-isobutylGABA in the API, which, he concluded, confirms the classical resolution enrichment process, and noted that Mylan does not use any methods that would remove R-3-isobutylGABA even after the API is formed. (*Id.* (citing Tr. at 395:12-396:6, 397:8-22 (Williams)).)

Mylan argues that its HPLC testing confirms the presence of R enantiomer, even though its test method was developed for the purpose of ensuring compliance with Mylan's "not more

than 0.15%" R enantiomer requirement. (*Id.*) Specifically, Mylan asserts that the presence of R enantiomer was shown in several batches throughout testing and that even when no R enantiomer was detected, it was still present based on the techniques Matrix and MDC use. (*Id.* (citing DTX-706 at MylanC2038; DTX-700 at MylanC1267; DTX-2569; DTX-2568; Tr. at 407:2-7, 410:15-25 (Williams)).) To this end, Mylan argues that because the R enantiomer was detected intermittently in certain batches, even when it was not detected initially, this failure to detect the R enantiomer resulted from the statistical limitations in its method of analysis, not from the absence of R enantiomer in a batch. (*Id.* at 11 (citing Tr. at 408:12-409:4, 409:15-410:14 (Williams)).)

The plaintiffs assert that Mylan literally infringes claims 1 and 4 because: MDC tested six batches of its API using an HPLC method with an LOD of 0.0125% and found no R enantiomer in five of the six; Matrix tested four batches of its API using an HPLC method with an LOD of 0.004% and found no R enantiomer in any batch; and Mylan tested its finished product using an HPLC method with an LOD of 0.0075% and detected no R enantiomer. (D.I. 351 at 25.) While the plaintiffs are correct that, based on the evidence presented, R enantiomer was not found in all but one batch, it does not agree with the plaintiffs' assertion that they have met their burden of proving that Mylan's Proposed Product is "free of" R enantiomer and, thus, literally infringes the asserted claims for two reasons. First, Mylan produced evidence that R enantiomer was detected in its batches intermittently throughout its classical resolution process and that this process does not employ methods to remove R enantiomer. Thus, while Mylan's HPLC testing did not detect R enantiomer in the majority of its samples, the court does not find it more likely than not that Mylan's Proposed Product will be "free of" this enantiomer.

Second, and supporting this conclusion, the defendants adduced testimony from the plaintiffs' expert, Dr. Chyall, that the detection of R enantiomer depends on the sensitivity of the method used and, further, that the "absolute absence of something," such as the absence of R enantiomer, cannot be authoritatively demonstrated. Tr. at 259:4-19 (Chyall). Specifically, Dr. Chyall testified, in response to the question of whether, if the R enantiomer is below the level of detection, it can be identified:

> In a hypothetical sense, we don't—we don't have any scientific basis to say, yes, definitely, it's there, or, no, definitely, it's not there on the basis of that experiment. . . . Our ability—and this is something we learn in school. In science, you can't prove a negative. You can't prove a negative in the sense that you can't demonstrate the absolute absence of something, or in this case you can't demonstrate that the material is—is free of R to some lower level, but below the detection limit. We're constrained with the sensitivity of our instrument.

Tr. at 259:2-19 (Chyall). In addition, Dr. Chyall testified in response to the question of whether a "substance might be [an] infringing product or noninfringing product" depending on "who the defendant is and their levels of detection," that "[i]f we apply the—the standard of literal infringement, I can see why that may be the case, and that one test has not detected, but you use a more sensitive test and it's fair. However, it does not have any bearing at all on my opinion on equivalency." *Id.* at 263:19-264:3.

In light of the evidence Mylan produced with respect to the inability of its method to remove the R enantiomer and Dr. Chyall's testimony that the detection of R enantiomer is dependent on the sensitivity of the testing method used, such that the absence of R enantiomer cannot be proved, the court disagrees with the plaintiffs' argument that the absence of R enantiomer in Mylan's HPLC tests demonstrates that its product is more likely than not "free of" the enantiomer. Thus, the court concludes that the plaintiffs have not proved by the required standard that Mylan's Proposed Product would literally infringe claims 1 and 4.

v. *Sun Pharma's Proposed Product*

Sun Pharma submitted ANDA No. 91-157 to the FDA seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths. (D.I. 349 at 14.) Sun Pharma's ANDA includes a specification defining the upper limit of "not more than" 0.15% R enantiomer in its proposed product and, per the testimony of its expert, Dr. Agranat, its HPLC method was designed to determine whether the sample exceeds that requirement. (*Id.* (citing Tr. at 748:22-749:17 (Agranat)).) Sun Pharma detected the R enantiomer in one of twelve tests on its API using a method with an LOD of 0.0089%, as well as in its ANDA product using a method with an LOD of 0.004%. (*Id.* at 15 (citing Tr. at 100:8-102:4, 102:9-103:2 (Chyall)).) Sun Pharma also asserts that, because the individual enantiomers of 3-isobutylGABA do not inter-convert, its detection of the R enantiomer using a lower LOD demonstrates that the detected presence or absence of the R enantiomer depends on the sensitivity of the test method used. (*Id.*) Finally, Dr. Agranat testified that Sun Pharma's API is made through a process that produces an intermediate that leads to R-3-isobutylGABA and that its purification step does not eliminate the R enantiomer, as shown through the detectable amount of R enantiomer in its batch test. (*Id.* (citing Tr. at 751:21-752:24, 753:2-756:2; 758:1-12 (Agranat); PTX-294; PTX-296; PTX-297; PTX-298).)

Conversely, the plaintiffs argue that because R enantiomer was only detected in one batch at 0.022% and the R enantiomer was not present in any of the other tested batches, they have proved that Sun Pharma's proposed product would be "free of" R enantiomer and literally infringe claims 1 and 4. (D.I. 351 at 22 (citing Tr. at 102:9-103:2 (Chyall); PTX-1475 at 30; PTX-284).) However, as noted in his testimony with respect to Mylan's Proposed Product, Dr. Chyall again testified that his ability to "conclude the absolute absence of something" is not

available in the technology and that the conclusion that a "chemical is free of another chemical relates to our ability to detect it," such that "when a chemist says that a material is free of another chemical, they are saying that I can't detect it using an appropriate test." Tr. at 107:10-108:4 (Chyall). Thus, while Dr. Chyall questioned Sun Pharma's detection of 0.022% R enantiomer in one test "because [there were] conflicting result[s] with the other test done at the same site," he concluded this detection could infringe claim 1 and would certainly infringe under the doctrine of equivalents. *Id.* at 108:5-14. In light of this testimony and the evidence Sun Pharma presented indicating that its process of making S-3-isobutylGABA does not remove the R enantiomer, the court concludes that the plaintiffs have not shown by a preponderance of the evidence that Sun Pharma's Proposed Product would literally infringe claims 1 and 4.

vi. *Teva's Proposed Product*

Teva submitted ANDA Nos. 91-219 and 91-224 to the FDA seeking approval to market pregabalin capsules in 25 and 50 mg dosages strengths, and 75, 100, 150, 200, 225, and 300 mg dosage strengths, respectively. (D.I. 349 at 13.) Teva's ANDAs each identify two different manufacturing sites, Israel and India, as their suppliers of pregabalin API. (*Id.*) Each manufacturing site employs different processes, as described in Teva's DMF No. 22242. (*Id.* (citing Tr. at 436:3-22 (Padwa); DTX-1252 at TEV0206162-163, TEV0206166-201).) Per the testimony of Teva's expert, Dr. Padwa, the Israeli process is a racemate resolution, which involves the separation of racemic 3-isobutylGABA into S-3-isobutylGABA and R-3-isobutylGABA, such that the final product will always contain R-3-isobutylGABA. (*Id.* (citing Tr. at 437:3-11, 439:4-11 (Padwa); DTX-1252 at TEV0206166-201).) Teva's ANDA products are based on six batches of API made by the Israeli process, Batch Nos. 495600407, 495600507, 495600608, 495600808, and 495601008. (*Id.* (citing Tr. at 443:14-444:9 (Padwa); DTX-1208c

at TEV0001212-213; DTX-1234 at TEV0007300).) Dr. Padwa testified that, based on the chemistry of the Israeli process, each batch must contain R-3-isobutylGABA. (*Id.* (Tr. at 447:19-448:9 (Padwa)).)

Similarly, the Indian process, which involves asymmetric synthesis and uses an achiral starting material, produces R-3-isobutylGABA. Specifically, Dr. Padwa testified that the achiral starting material is reacted to form an intermediate with four possible isomers and two of the four are eventually converted into R-3-isobutylGABA. (*Id.* at 13-14 (citing 449:23-451:16, 451:17024, 453:1-16 (Padwa); DTX-1252 at TEV0206166-201; DTX-1244 at TEV0049101-107).) Teva argues that its certificates of analysis and chromatograms show that the Indian API batches contain R-3-isobutylGABA and that the plaintiffs presented no testimony regarding this process. (*Id* at 14 (citing Tr. at 453:17-458:21 (Padwa); Tr. at 265:19-25 (Chyall); DTX-1234 at TEV0007376-379).) Moreover, Teva argues that the plaintiffs did not present evidence indicating that either of its API produces S-3-isobutylGABA free of the R enantiomer. The court agrees.

To advance their argument that Teva's Proposed Products would literally infringe claims 1 and 4, the plaintiffs note that Teva tested its API and its finished product using an HPLC method having an LOD of 0.03% and did not detect R enantiomer in six of the eight batches and in any of its finished product batches. (D.I. 351 at 22 (citing Tr. at 113:10-116:8 (Chyall); PTX-1469 at 34-35; DTX-1208C; DTX-1234; PTX-333).) However, in view of the fact that R enantiomer was detected in two of Teva's API batches, the plaintiffs' failure to address its Israeli process, and Dr. Chyall's testimony, detailed above, that proof of an absence of R enantiomer is not possible, the court concludes that the plaintiffs have not demonstrated by a preponderance of the evidence that Teva's Proposed Products literally infringe claims 1 and 4.

vii. *Wockhardt's Proposed Product*

As noted, Wockhardt submitted ANDA No. 91-222 to the FDA seeking approval to market pregabalin capsules in 25, 50, 75, 100, 150, 200, 225, and 300 mg dosage strengths. (D.I. 349 at 5 (citing DTX-1265 at WO-13).) Wockhardt's ANDA names MSN Laboratories ("MSN") as the supplier of its pregabalin API and adopts MSN's HPLC method. (*Id.* (citing Tr. at 181:5-8 (Chyall)).) Wockhardt's ANDA testing indicates that MSN validated its HPLC method and identified an LOD of 0.004% and a limit of quantitation ("LOQ") of 0.015%. (*Id.* (citing Tr. at 184:5-11, 181:17-18 (Chyall); D.I. 331 at ¶¶ 3,4).) Wockhardt relied on MSN's LOD and LOQ when testing in its laboratory and the plaintiffs' expert, Dr. Chyall, agreed that MSN's HPLC method would be appropriate to detect R enantiomer if it appeared above the LOD. Tr. at 181:21-182:13, 184:22-185:1 (Chyall).

Wockhardt's ANDA includes HPLC data, collected separately by MSN and Wockardt, and obtained using MSN's method for three batches of API—Batch Nos. PB0080708, PB0070708, and PB0090708. (*Id.* at 6 (citing D.I. 331 at ¶ 7; Tr. at 185:6013 (Chyall); Tr. at 307:9-10 (Feldman)).) Wockhardt indicates, and the parties do not dispute, that the three API batches were made by MSN using the same process that it will use for future batches of Wockhardt's API. (*Id.*) Testing Wockhardt's API, MSN detected 0.04%, 0.09%, and 0.05% R enantiomer in its exhibit batches, Batch Nos. PB0080708, PB0070708, and PB0090708, respectively. (*Id.* (citing D.I. 331 at ¶ 8; PTX-1473; DTX-1269 at WO-958, 961, 964).) Wockhardt tested these same batches as well and obtained the following results for PB0080708, PB0070708, and PB0090708: 0.05%, 0.08%, and 0.04% R enantiomer, respectively. (*Id.* (citing D.I. 331 at ¶ 9; PTX-1473; PTX-1269 at WO-966, 969, 972).) Viewing these detection numbers in light of the LOD for MSN's HPLC test, it is clear that Wockhardt's API contains detectable

amounts of R enantiomer. The plaintiffs do not dispute that detectable R enantiomer was found in Wockhardt's sample. In light of these test findings, the court concludes that the plaintiffs have not shown, by a preponderance of the evidence, that Wockhardt's Proposed Product would literally infringe claims 1 and 4 of the '819 Patent.

3. The Doctrine of Equivalents

The plaintiffs contend that even if the court were to find, as it has, that the defendants' proposed products do not literally infringe claims 1 and 4 of the '819 Patent, the products do infringe the asserted claims under the doctrine of equivalents. (D.I. 351 at 19-21, 28-31, 45-48.) In response, the defendants argue, in the main, that the plaintiffs are precluded from asserting a doctrine of equivalents claim based on prosecution history estoppel. Specifically, the defendants assert that prosecution history estoppel applies in this case because: (1) the '819 Patent applicants made a series of narrowing claim amendments throughout prosecution that were expressly made for the purpose of patentability (D.I. 349 at 18); and (2) there is no basis for overcoming the presumption of surrender that applies, as a non-racemic mixture of 3-isobutylGABA containing S and R enantiomer was "reasonably foreseeable" and the plaintiffs' narrowing of claim 1 was directly, rather than "tangentially" related to patentability (*id.*). Thus, the defendants contend that their proposed products cannot infringe by equivalence. However, in view of the record before it and in consideration of the relevant law, the court concludes, for the reasons that follow, that the defendants' proposed products infringe claims 1 and 4 under the doctrine of equivalents.

a. Parties' Contentions: The '819 Patent Prosecution History

As noted, the defendants contend that the plaintiffs are barred from asserting a doctrine of equivalents claim because they narrowed claim 1 during the '819 Patent's prosecution history in

order to obtain patentability and, therefore, are estopped from asserting this claim. (*Id.* at 18-23.) In support of this argument, the defendants detail the following prosecution history of claim 1 in an effort to demonstrate that this claim's "single optical isomer" language is appropriately construed as "free of" R isomer and, therefore, that the 0.15% and 0.20% of R enantiomer contained in the defendants' proposed products cannot be argued to constitute "equivalence." Specifically, the defendants note that, in the original '692 application, the applicants included claim 3, which was directed to 3-isobutylGABA "as an (R), (S) or (R, S) isomer." (*Id.* at 18 (citing DTX-5 at PFE_LYR_1969).) This claim, the defendants assert, did not recite enantiomeric purity and covered R-3-isobutylGABA and S-3-isobutylGABA as single enantiomers as well as non-racemic and racemic mixtures. (*Id.*) The applicants ultimately abandoned this application and claim 3, in favor of the '080 application, which covered S-3-isobutylGABA in claim 5. (*Id.* (citing DTX-6 at PFE_LYR_1787).)

The Examiner, however, rejected claim 5 because it did not require any enantiomeric purity and, as such, was "open to any composition of matter containing the recited isomer including the prior art racemic mixtures." (*Id.* at 18-19 (citing DTX-6 at PFE_LYR_1809-1814).) Thus, the defendants assert that the PTO understood the claim to cover S-3-isobutylGABA in isolation as well as racemic and non-racemic mixtures of S- and R-3-isobutylGABA. (*Id.* at 19.) The defendants' expert on this claim, Dr. Feldman, testified that, in his assessment, a person of ordinary skill in the art would have understood the Examiner's rejection to be related to purity. (*Id.* (citing Tr. at 312:5-14 (Feldman)).)

The defendants further detail that the applicants later abandoned the '080 application in favor of the '285 application, wherein they reintroduced claim 5, which was eventually canceled in favor of claim 38. (*Id.* (citing DTX-9 at PFE_LYR_781, 815-21, 849).) The Examiner again

rejected claim 38, however, for lack of novelty. (*Id.* (citing DTX-9 at PFE_LYR_859-862).) In a subsequent filing, the '905 application, the applicants attempted to amend claim 38 to recite "substantially pure" S-3-isobutylGABA. (*Id.* (citing DTX-9 at PFE_LYR_905).) In support of this amendment to claim 38, Pfizer stated: "[r]eferring to all of the rejections, each one states that there is no recitation of any particular purity of the compounds. Applicant has amended the claims consistent with the specification and the previously pending claim to recite the substantially pure compound." (*Id.* (citing DT9 at PFE_LYR_900).)

In light of this statement, Dr. Feldman testified that he would view the applicants' amendment as responsive to the Examiner's rejection of prior claims for lack of a purity limitation. (*Id.* (citing Tr. at 351:5-13.) Despite this amendment, however, the defendants note that the Examiner rejected claim 38's "substantially pure" language because the term lacked support in the specification and was indefinite.[75] (*Id.* (citing DTX-9 at PFE_LYR_910).) Finally, the applicants amended claim 38 to recite S-3-isobutylGABA "as a single optical isomer," and claim 38 ultimately issued as claim 1 of the '819 Patent. (*Id.* (citing DTX-9 at PFE_LYR_1130, 1134, 1137; DTX-1).)

In view of the foregoing, the defendants assert that the plaintiffs should be barred from asserting infringement under the doctrine of equivalents based on prosecution history estoppel

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[75] Specifically, the Examiner noted that the applicants:

> [r]aise new issues that would require further consideration and/or search. The expression "substantially pure" was not present in the claims considered in the final rejection raising new issues as to whether the prior art rejections should be withdrawn or modified. Moreover, there is no apparent basis in the specification for the phrase and applicants do not point out any such basis. Finally, the term "substantially" does not appear to have a definite meaning and would fail to particularly point out the invention.

DTX-9 at PFE_LYR_910. The court notes that the plaintiffs, in their Proposed Findings of Fact and Conclusions of Law, assert that the Examiner "refused to enter the amendment" for the term "substantially pure" because "Applicants proposed it after a final office action" and, as a result, that "the Examiner never considered the amendment on the merits." (D.I. 351 at 29.) In light of the above-quoted passage from the Examiner, however the court disagrees with the plaintiffs' characterization of the Examiner's action as it appears that the Examiner did consider the addition of "substantially pure" language in claim 38. The PTO Director subsequently upheld the Examiner's refusal to enter the amendment. (*Id.* (citing PTX-7 at PFE_LYR_000000910, 921).)

and contend that no exception to estoppel applies in this case. First, and for the reasons identified above, the defendants assert that prosecution history estoppel applies because the applicants narrowed their claim for "reasons related to patentability" and, in so doing, "surrendered the full scope between original claim 3 in the '692 application, covering [S-3-isobutylGABA] including any amount of [R-3-isobutylGABA], and issued claims 1 and 4," covering S-3-isobutylGABA "free of" R enantiomer. (*Id.* at 21 (citing *Festo*, 535 U.S. at 735-37).) Second, the defendants contend that the "foreseeability" exception to prosecution history estoppel does not apply here because it was foreseeable that non-racemic mixtures of 3-isobutylGABA containing both S and R enantiomers could exist. (*Id.* (citing Tr. at 319:20-320:4 (Feldman)).) In fact, the defendants note that the applicants tried to claim such a mixture by amending claim 38 to read "substantially pure," but failed to gain approval for this amendment. Thus, the defendants argue that the plaintiffs surrendered the full scope between original claim 38 and issued claims 1, which claim S-3-isobutylGABA alone. (*Id.* (citing Tr. at 317:12-318:15 (Feldman)).)

Third, the defendants argue that the plaintiffs cannot satisfy the "tangential relation" exception, which asks "whether the reason for the narrowing amendment was peripheral, or not directly relevant to, the alleged equivalent" and is a "very narrow" exception. (*Id.* (citing *Cross Med. Prods., Inc. v. Medtronic Sofamor Danek, Inc.*, 480 F.3d 1335, 1342 (Fed. Cir. 2007)).) Here, the defendants contend that it is clear the Examiner rejected the applicants' S-3-isobutylGABA claim because, until it was approved with the language "single optical isomer," the claim did not limit the enantiomeric purity. (*Id.* at 22 (citing Tr. at 321:13-19 (Feldman); Tr. at 294:14-15 (Drivas)).)

The defendants further note that the applicants were aware that their lack of reference to enantiomerical purity was the reason for the rejections, as is evidenced by their statement to the Examiner, in connection with claim 38, that the rejections stated there was "no recitation of any particular purity of the compounds." (*Id.* at 19 (citing DT9 at PFE_LYR_900).) Thus, because the applicants added an enantiomerical purity to claim 1 as "a single optical isomer" to avoid an Examiner rejection, the defendants maintain that the plaintiffs cannot argue that their claim narrowing was not directly related to patentability.[76] Finally, the defendants assert that the plaintiffs cannot meet the tangential relation test because "the only reasons revealed by the prosecution history concern restricting and defining enantiomeric purity, the defining characteristic of the alleged equivalents." (*Id.* at 22.) To this end, the narrowing amendment was not, the defendants argue, peripheral to the alleged equivalent.

In response, the plaintiffs challenge the conclusions the defendants derive from the prosecution history. Specifically, the plaintiffs assert that they are not barred from their equivalents claim by the prosecution history of the '819 Patent because the applicants narrowed claim 1 simply to distinguish it from Dr. Andruszkiewicz's article disclosing racemic 3-isobutylGABA, a reference the Examiner considered prior art. (D.I. 351 at 29 (citing PTX-7 at PFE_LYR_000000888).) The plaintiffs note that the Examiner believed that Dr. Andruszkiewicz's article was prior art to claim 1 because the inventive entity, which included

[76] The court notes that it does not agree with the defendants that, at trial, Pfizer's counsel made a binding judicial admission that the '819 Patent applicants narrowed the claim with respect to the equivalent and, as a result, that prosecution history estoppel bars the plaintiffs' doctrine of equivalent claim. Specifically, the defendants note that Pfizer's counsel stated that claim 1 "was narrowed to encompass single optical isomer and distinguish it from the racemate," and that, "[a]s far as the prosecution history and prosecution history estoppel, we did narrow that claim." (D.I. 349 at 20 (citing Tr. at 294:11-15 (Drivas)).)

However, Mr. Drivas' statement, as quoted, is taken out of context and, in light of the plaintiffs' argument that they did not narrow claim 1 beyond distinguishing it from the 50:50 racemate identified in Dr. Andruszkiewicz's article, it is clear that Mr. Drivas did not agree that prosecution history estoppel bars their claim. Rather, Mr. Drivas noted, in the sentence immediately following the defendants' quoted passage of his remarks, that "w[e] never gave up that subject matter during prosecution. But the claim was narrowed to encompass single optical isomer and distinguish it from the racemate. It was never intended to give up that which we are now seeking to claim." Tr. at 294:11-17 (Drivas).

Dr. Yuen at the time, did not match the article's authorship. (D.I. 351 at 29 (PTX-7 at PFE_LRY_000000888).) Because the Examiner ultimately concluded that this article was not a prior art reference after Dr. Yuen was removed as an inventor, the plaintiffs argue that "the 'prior art' disclosure that prompted the amendment was not, in fact, a valid basis for rejecting the claim" and, therefore, could not have been necessary to secure patentability. (*Id.* at 31 (PTX-7 at PFE_LYR_0000001546-47, PFE_LYR_000001550).)

In addition, the plaintiffs argue that the applicants did not intend to, and did not, claim S-3-isobutylGABA free of R enantiomer because: (1) they were not required to do so to distinguish claim 1 from Dr. Andruszkiewicz's 50:50 mixture; and (2) in light of the fact that the Examiner cited only Dr. Andruszkiewicz's article as prior art, the applicants' competitors would not assume they were disavowing S-3-isobutylGABA with a minute amount of R enantiomer present. (*Id.* (citing PTX-7 at PFE_LYR_000000888).) With regard to this latter argument, the plaintiffs highlight that, when the applicants filed a draft Supplemental Preliminary Amendment in advance of their interview with the Examiner and proposed modifying claim 38 to include the "as a single optical isomer" language, they stated that they were doing so to address the Examiner's assessment that "the racemate disclosed in [Andruszkiewicz] anticipated the claim." (*Id.* at 30 (citing PTX-7 at PFE_LYR_0000001119, PFE_LYR_0000001130 n.2).) Indeed, the plaintiffs also note that the Examiner stated in the Interview Summary that the "[p]roposed language 'single isomer [sic] optical isomer' would not appear to read racemic mixture." (*Id.* (citing PTX-7 at PFE_LYR_0000001134).) Thus, the plaintiffs contend that the applicants' statements and actions throughout prosecution show that the addition of the phrase "as a single optical isomer" to claim 38, which later issued as claim 1, was intended only to make clear that

the claim did not cover racemate 3-isobutylGABA—specifically, the 50:50 mixture of R and S enantiomers disclosed in Dr. Andruszkiewicz's reference.[77] (*Id.*)

Finally, the plaintiffs assert that irrespective of the applicants' claim 1 narrowing during the '819 Patent's prosecution history, they are not estopped from asserting a doctrine of equivalents claim because: (1) interpreting claim 1 to mean "free of" R enantiomer, as the court has construed, the defendants' proposed products are equivalents, as the differences between them and S-3-isobutylGABA covered in claim 1 are "insubstantial" (*id.* at 20); and (2) this argument is supported by Dr. Chyall's testimony and the testimony of defendants' expert, Dr. Williams, that organic chemists "rarely concern themselves" with producing compounds that are more than 99.9% pure and, further, that the "minute" amount of R enantiomer in the defendants' proposed products would be considered "free of" R enantiomer (*id.* (citing Tr. at 427:8-18 (Williams); Tr. at 95:5-10 (Chyall))).

The plaintiffs argue that its position is supported by the ICH guidelines—guidelines issued to harmonize drug development activities in the pharmaceutical industry—which note that a chemical with "not more than" 0.15% of an impurity, such as R enantiomer, does not have to undergo toxicology studies because such levels are considered safe. (*Id.*) Indeed, the FDA approved Lyrica®'s NDAs, which conducted tests to determine that R enantiomer of "not more than 0.20%" is safe and does not require toxicology studies. (*Id.* at 21 (citing Tr. at 96:24-97:11 (Chyall)).) Thus, the plaintiffs argue that the maximum 0.20% of R enantiomer in the defendants' proposed products are considered "free of" R enantiomer and, therefore, infringe the asserted claims.

[77] The plaintiffs also note that, during their appeal of the final office action, and then again after prosecution was re-opened, the applicants repeatedly argued that claim 38 did not cover the racemic mixture disclosed in Dr. Andruszkiewicz's article. Specifically, the applicants stated that the Examiner was incorrect to conclude that the claim covered "the prior art racemic mixture," that the invention of claim 38 was "distinct from the prior art racemic homologues," and that the claim "could not include prior art racemic mixtures as suggested in the Office Action." (D.I. 351 at 29-30 (citing PTX-7 at PFE_LYR_0000001062, 1085-86, 1111).)

b. Discussion & Conclusions of Law

In view of the foregoing and in consideration of the relevant law, the court concludes that the plaintiffs are not estopped from asserting their doctrine of equivalents claim for the following reasons. First, and in light of the testimony presented, the court agrees with the plaintiffs that the difference between the defendants' proposed products and S-3-isobutylGABA, as covered by claim 1, are insubstantial. Specifically, the defendants' testing of their API pregabalin and the results they provided to the FDA, as recited in the preceding section, demonstrate that no product contains over 0.19% R enantiomer and, in fact, the defendants' ANDAs require that each contain "not more than" 0.20% of this impurity. (*Id.* at 20-21.) Based on these numbers and Dr. Chyall's credible testimony regarding detection of R enantiomer, the court agrees with the plaintiffs that a "composition of S-3-isobutylGABA that contains less than 0.20% R enantiomer performs the same function, in the same way, to achieve the same result as a composition literally, 'free of'" R enantiomer. (*Id.* at 21 (citing Tr. at 94:1-97:11 (Chyall)).)

To this end, and considering the evidence detailed in the preceding literal infringement section, the court finds that the plaintiffs have demonstrated that the differences between the defendants' proposed product and the product of claim 1 are "insubstantial" and that Dr. Chyall's testimony was sufficiently "particularlized" with respect to the plaintiffs' S-3-isobutylGABA product and each of the defendants' proposed products to link the "insubstantial" difference between each. *See Martek Biosciences Corp.*, 520 F. Supp. 2d at 547; *see also Texas Instruments*, 90 F.3d at 1567. The FDA's approval of Lyrica®'s "not more than" 0.20% R enantiomer specification and the teachings of the ICH guidelines, which defendants Actavis, Cobalt, Sun, and Teva's ANDAs adopt, lend further support to this conclusion.

Second, the court concludes that, while the defendants are correct that the '819 Patent applicants narrowed the enantiomeric purity of claim 1 during prosecution, the applicants did not "clearly and unmistakably" surrender the equivalence asserted here. Specifically, based on the record before it, it is the clear to the court that the applicants would not be viewed by those of skill in the art, the Examiner, their competitors, or the defendants as disavowing the inclusion of "not more than" 0.20% R enantiomer in its "single optical isomer" S-3-isobutylGABA. *See LG Electronics*, 2011 WL 2610177, at *17 (concluding that a patentee, for a "binding surrender of claim scope of apply, must "cause a competitor to reasonably believe that the applicant had surrendered the relevant subject matter"). Rather, the evidence presented makes clear that organic scientists and those in the field would view this percentage of impurity as "insubstantial" and, in fact, possibly undetectable, based on the sensitivity of the method used to measure its presence. The FDA's approval of Lyrica®'s ANDA reciting a "not more than" 0.20% impurity percentage and the ICH's guidelines, support that the percentage of R enantiomer detected in the defendants' proposed products would not have been considered "clearly and unmistakably" surrendered by the applicants' narrowing of S-3-isobutylGABA's purity.

Notably, the Supreme Court has clarified that a patentee should not be estopped "beyond a fair interpretation of what was surrendered." *See Festo*, 535 U.S. at 737-38; *see also Cordis Corp.*, 511 F.3d at 1177. The prosecution history here indicates that the applicants narrowed, through the applications detailed above, claim 1 to distinguish it from Dr. Andruszkiewicz's racemic mixture. To this end, the applicants added the language "single optical isomer," which the defendants contend would be vitiated—particularly the term "single"—if the court were to allow a doctrine of equivalents claim. In view of the 0.20% R enantiomer equivalent asserted here, the court cannot agree. The defendants' proposed products are not 50:50 racemic mixtures,

but instead are at least 99.8% pure S-3-isobutylGABA. As detailed in the literal infringement section above, the defendants' proposed products often exhibit purity nearing or more than 99.9% and, by virtue of their ANDAs, cannot be less than 99.8% pure.

The defendants have not identified evidence indicating that the Examiner required the applicants to distinguish their invention over prior art disclosures of extremely-pure forms of S-3-isobutylGABA, like their proposed products, such that they would have to surrender the equivalent argued here. Instead, the plaintiffs cite evidence in the prosecution history wherein the applicants explicitly noted, and the Examiner confirmed, that the narrowing of claim 1 was to distinguish its purity from the racemic mixture Dr. Andruszkiewicz developed.[78] This evidence from the prosecution history coupled with testimony adduced at trial indicating that 0.20% impurity in a compound would be viewed by organic chemists as insignificant and, often, undetectable, leads the court to conclude that the applicants did not surrender their equivalence argument[79] and prosecution history estoppel does not apply in this case.

In view of the foregoing, the court concludes that finding the applicants to have surrendered the presence of "not more than" 0.20% R enantiomer would misinterpret the narrowing of the applicants' purity claim and unfairly estop their doctrine of equivalence contention. *Festo*, 535 U.S. at 737-38. Thus, because the defendants' proposed products contain

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[78] The court notes that it also finds persuasive the plaintiffs' contention that, because the Examiner concluded that Dr. Andruszkiewicz's article was not prior art after Dr. Yuen was removed as an inventor and claim 1 was amended to distinguish it from this reference, the applicants' amendments cannot have been necessary to secure patentability. (D.I. 351 at 31 (citing PTX-7 at PFE_LYR_0000001546-47, 1550).)

[79] As explained in the examination above, the plaintiffs assert that: (1) the difference between the defendants' proposed products and the patented invention are "insubstantial" and, therefore, equivalent under the doctrine of equivalents; and (2) because the applicants' rationale for their claim 1 narrowing amendment was to make clear that the claim did not cover 3-isobutylGABA racemate, and this rationale bears no more than a tangential relation to the accused equivalent here—exceedingly pure S-3-isobutylGABA—they rebut any presumption of prosecution history estoppel under the tangential relation exception. (*Id.* at 45-48.) For the reasons detailed in this section, the court agrees.

0.20% or less of R enantiomer, the court concludes that each defendants' proposed product infringes claim 1 and, therefore, claim 4 of the '819 Patent.[80]

G. Other Statutory Stay & Patent Expiration Related Issues

In addition to the infringement, validity, and enforceability issues addressed in the foregoing analysis, the plaintiffs and defendants each ask the court to address statutory stay and patent expiration related matters in connection with the asserted claims of the patents-in-suit. Specifically, the plaintiffs ask the court to extend the 42-month statutory stay with respect to Actavis and Lupin[81] and to enjoin the defendants from marketing their proposed products until the patents-in-suit expire. The defendants request that the court invalidate the '819 and '876 Patents' term extensions that were granted by the PTO because they violate 35 U.S.C. § 156. The court addresses the relevant arguments separately below.

1. Enjoining the Defendants Until Expiration of the Patents-in-Suit

The plaintiffs assert that the defendants should be enjoined from marketing their proposed generic products until the patents-in-suit expire. (D.I. 351 at 54.) Specifically, the plaintiffs note that, pursuant to 35 U.S.C. § 271(e)(4), "the court shall order the effective date of any [FDA] approval of the drug . . . involved in the infringement to be a date which is not earlier than the date of expiration of the patent which has been infringed" and may grant "injunctive relief . . . against an infringer to prevent the commercial manufacture, use, offer to sell, or sale

[80] The court notes that its conclusion applies to Actavis and Lupin, the two defendants that amended their ANDAs to require the presence of R enantiomer in their proposed products. Specifically, and as detailed in this examination, Actavis and Lupin's proposed products will, despite their amendments, contain a minimum amount of R enantiomer and, at most, 0.20% of the impurity. Because the court concludes that products containing the maximum amount of R enantiomer permitted under the defendants' specifications would be equivalent to a product "free of" R enantiomer, these defendants will infringe claims 1 and 4 regardless of their amendments.

[81] In their Proposed Findings of Fact and Conclusions of Law, the plaintiffs ask the court to "extend the 42-month stay of ANDA approval applicable to Actavis and Lupin's ANDAs until the court issues a final judgment in this action." (D.I. 351 at 53-54.) Because this Memorandum, Opinion, and Order is accompanied by a Final Judgment Order, the plaintiffs' request is moot and, therefore, the court does not address this argument or its merits.

within the United States or importation into the United States of an approved drug." *See* 35 U.S.C. §§ 271(e)(4)(A), (B). In light of the findings detailed above, the court agrees.

Because the defendants' proposed products infringe, under the doctrine of equivalents, claims 1, 2, and 4 of the '819 Patent, all of which are valid and enforceable, the defendants are enjoined from commercially manufacturing, using, offering for sale, or selling their proposed products, and the FDA is enjoined from approving the defendants' ANDAs prior to expiration of the '819 Patent, including any associated extensions and exclusivities. Moreover, because the use of Actavis, Cobalt, Lupin, and Sun Pharma's proposed products infringe claim 1 of the '175 Patent, which is valid and enforceable, Actavis, Cobalt, Lupin, and Sun Pharma are enjoined from commercially manufacturing, using, offering for sale, or selling their proposed products, and the FDA is enjoined from approving their ANDAs, prior to the expiration of the '175 Patent, including any associated extensions and exclusivities.

2. The '819 and '876 Patent Term Extensions

The defendants challenge that the plaintiffs are not entitled to patent term extensions of the '819 and '876 Patents because such extensions would violate 35 U.S.C. § 156. (D.I. 349 at 53-54.) Specifically, the defendants note that the plaintiffs applied for patent term extensions in both the '819 and '876 Patents on February 25, 2005, asserting that each covered the active drug product Lyrica® containing the active ingredient in pregabalin. (*Id.* at 53.) On September 12, 2007, the PTO approved the plaintiffs' requests and issued a certificate extending the terms of both patents to December 30, 2018. (*Id.* at 54.) The defendants argue that the PTO issued the certificate for both patents in error because both applications were based on a regulatory review period that began on January 10, 1996 and ended on December 30, 2004, in violation of § 156 which dictates that "in no event shall more than one patent be extended under subsection (e)(1)

for the same regulatory review period for any product." *See* 35 U.S.C. § 156(c)(4). The defendants note that, although different NDA numbers (NDA No. 21-446 and NDA No. 21-72) form the basis of the applications, both NDA numbers originate from the same original NDA submission (No. 21-446), which the FDA divided into NDA No. 21-723 and two other NDAs based upon indication. (*Id.*)

For the reasons that follow, the court disagrees that the PTO issued the certificate in error. Per 37 C.F.R. § 1.765(a), a patentee, in applying for a patent extension, "has a duty of candor and good faith towards the PTO and must disclose any 'material information adverse to a determination of entitlement to the extension sought.'" 37 C.F.R. § 17.65(a). The Director of the PTO is charged with deciding whether the patent is entitled to a term of extension and the Federal Circuit has clarified that that decision is afforded "'great deference.'" *See Pfizer, Inc. v. Ranbaxy Labs, Ltd.*, 457 F.3d 1284, 1290 (Fed. Cir. 2006) (citation omitted). Moreover, the defendants are required to prove that the PTO's determination should be overturned by "clear and convincing" evidence. *Id.* at 1291.

Here, the applicants identified the issue now raised by the defendants to the PTO when it sought the patent term extension. In fact, the plaintiffs note that it was this issue that formed the grounds on which the applications were sought. (D.I. 351 at 54.) Specifically, Pfizer applied for patent term extensions under 35 U.S.C. § 156 for the '819 Patent and for its '876 Patent, which ultimately reissued as RE '920 Patent, in view of the FDA's approval of two of Pfizer's NDAs related to Lyrica®. (*Id.* at 7 (citing PTX-6 at PFE_LYR_0000000538-539; PTX-7 at PFE_LYR_0000001561-1562).) Pfizer stated in its application that because the FDA approved the two Lyrica® NDAs on the same day, both patents were entitled to extensions under the statute. (*Id.* at 7-8.) The PTO agreed. (*Id.* at 8 (citing PTX-6 at PFE_LYR_0000000700-701;

PTX-7 at PFE_LYR_0000001715-1716).) The defendants have not produced evidence to the contrary.[82] Thus, the PTO granted extensions for both patents with this knowledge. (*Id.* at 54.) In light of this finding and in consideration of the "great deference" afforded the PTO Director, the court concludes that the defendants have not presented clear and convincing evidence that the PTO's decision should be overturned. *Pfizer*, 457 F.3d at 1290.

IV. CONCLUSION

For the reasons stated above, the court concludes that: (1) the asserted claims of the patents-in-suit are not invalid due to obviousness; (2) the asserted claims of the patents-in-suit are not invalid due to anticipation; (3) the asserted claims of the '819 and '175 Patents are entitled to a November 27, 1990 priority filing date; (4) the asserted claims of the '819 Patent are not invalid for written description; (5) the asserted claims of the '819 Patent are not invalid due to improper inventorship; (6) the defendants' proposed products do not literally infringe claims 1 and 4 of the '819 Patent; (7) the defendants' proposed products infringe claims 1 and 4 of the '819 Patent under the doctrine of equivalents; (8) the '819 and '876 Patents' term extensions are not invalid under 35 U.S.C. § 156; and (9) each of the parties' Rule 52(c) motions are granted in part and denied in part.[83] An appropriate order will follow.

Dated: July 19, 2012

CHIEF UNITED STATES DISTRICT JUDGE

[82] Indeed, the only evidence the defendants present to support their violation of § 156 argument is that both NDA numbers originate from the same original NDA submission and, thus, that the PTO erred in granting the patent term extensions under this statute. (D.I. 349 at 53-54.)

[83] As noted, the parties submitted Proposed Findings of Fact and Conclusions of Law, requesting that the court find in its favor on the issues of obviousness, anticipation, priority based on enablement, written description, inventorship, literal infringement, infringement under the doctrine of equivalents, and the validity of the '819 and '876 Patents' term extensions. For the reasons stated above and based on the court's findings, the plaintiffs' Rule 52(c) motion is granted in part and denied in part and the defendants' Rule 52(c) motion is granted in part and denied in part. The court clarifies that defendant Sun Pharma's Rule 52(c) motion with respect to written description and anticipation is denied (D.I. 350), and the plaintiffs' Rule 52(c) motion on these issues is granted (D.I. 352).

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PFIZER INC., WARNER-LAMBERT COMPANY L.L.C., C.P. PHARMACEUTICALS INTERNATIONAL C.V., and NORTHWESTERN UNIVERSITY, Plaintiffs, v. TEVA PHARMACEUTICALS U.S.A., INC., and TEVA PHARMACEUTICAL INDUSTRIES, LTD., et al., Defendants.	)	C.A. No. 09-cv-307 (GMS) (Consolidated)

ORDER

At Wilmington this 19th day of July, 2012, IT IS HEREBY ORDERED THAT:

1. The asserted claims of the patents-in-suit are not invalid as obvious;

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

3. The asserted claims of the '819 and '175 Patents are entitled to a priority filing date of November 27, 1990;

4. The asserted claims of the '819 Patent are not invalid for written description;

5. The asserted claims of the '819 Patent are not invalid due to improper inventorship;

6. The defendants' proposed products do not literally infringe claims 1 and 4 of the '819 Patent;

7. The defendants' proposed products infringe claims 1 and 4 of the '819 Patent under the doctrine of equivalents;

8. The defendants are enjoined, based on this infringement, from commercially manufacturing, using, offering for sale, or selling their proposed products and the FDA is enjoined from approving the defendants' ANDAs prior to expiration of the '819 and '175 Patents;

9. The '819 and '876 Patents' term extensions are not invalid under 35 U.S.C. § 156;

10. The parties' Rule 52(c) motions (D.I. 349-353) are GRANTED IN PART AND DENIED IN PART.

11. The Clerk of Court is directed to enter final judgment in favor of the plaintiffs and against the defendants.

CHIEF, UNITED STATES DISTRICT JUDGE