Patent Claim Construction of Enantiomers

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With a history of jurisprudence that encompasses over sixty years, the statement that an enantiomeric composition is patentable over its racemate does not reverberate as groundbreaking to the patent community. But maybe it should shake it a little. An enantiomer is a compound composed of one of a pair of isomers. Each enantiomer is a nonsuperimposable mirror image of the other. A racemate consists of equal parts of each enantiomer, and a formulation chemist conventionally generates a racemate prior to a synthesis of either enantiomer individually. An individual enantiomer that was previously a component in a patented racemic mixture is not patentable as a compound, because that enantiomeric compound was necessarily disclosed as a component of the racemate. Thus, while a claim to an enantiomer as part of a composition is patentable, a claim to an enantiomeric compound previously sold or disclosed as a component of the racemate is not patentable.

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I. INTRODUCTION

A claim to the enantiomeric compound is not patentable over its racemate. This Article asserts that an enantiomer is only patentable over its racemate if it is properly claimed as a composition. Enantiomers are significant in the pharmaceutical arts. An enantiomer is a compound composed of "one of a pair of optical isomers."[1] These isomers are nonsuperimposable mirror images of each other.[2] To formulate an enantiomer, an organic chemist will typically first generate its racemate. A racemate is a composition of equal parts of each enantiomer.[3] Advanced techniques permit separation of the racemate into its constituent enantiomers.

Patent claims have explored the subject of racemates and enantiomers for over sixty years.[4] Historically, courts have held enantiomers patentable over previous disclosures or sales of their racemates.[5] However, if the racemate was the subject of a patent, printed publication, or sale more than one year before the filing of an application claiming the enantiomeric compound, then the claim should be denied because the racemate necessarily disclosed the enantiomer as a compound of the racemate.[6] Therefore, while a claim to an enantiomer as part of a composition is patentable, a claim to an enantiomeric compound either previously sold or disclosed is anticipated and thus not patentable over its racemate.

Part II of this Article reviews enantiomers and stereochemistry and addresses their importance to the pharmaceutical industry. Part III applies patent law to enantiomers and introduces the art and science of proper enantiomer claiming. Part IV presents *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc.* (*Ortho-McNeil II*), in which the District Court for the Northern District of West Virginia found that a claim to an enantiomeric compound derived from a previously

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1. RICHARD J. LEWIS, SR., HAWLEY'S CONDENSED CHEMICAL DICTIONARY 441 (14th ed. 2001).
2. *Id.*
3. *See id.* at 952.
4. *See, e.g.*, *In re* Williams, 171 F.2d 319 (C.C.P.A. 1948).
5. *See, e.g.*, *In re* May, 574 F.2d 1082 (C.C.P.A. 1978); *see also In re Williams*, 171 F.2d 319.
6. 35 U.S.C. § 102(b) (2006).

disclosed racemic mixture was both novel and valid.[7] Part IV disputes this holding. The claim to the enantiomeric compound was anticipated by its racemate, and the court should have invalidated this claim. Further, Part IV contends that the court erroneously added an element to the claim during construction, and that this element was necessary to determining the validity of the claim. Finally, Part IV distinguishes the findings in *Ortho-McNeil II* from other cases that illustrate enantiomers that are properly claimed as compositions over previously disclosed racemates. Part V discusses the errors of the *Ortho-McNeil II* court, how proper drafting and prosecution of the claims would have resulted in a valid patent, and the potential consequences of the court's decision.

II. THE CHEMISTRY AND PHARMACOLOGY OF ENANTIOMERS

In chemistry, "[a]n isomer is one of several molecular entities that have the same atomic composition or molecular formula, but a different stereochemical formula, meaning the atoms are the same in number and type but different in their spatial arrangement."[8] Stereoisomers are isomers that have the same molecular formula and constitution, but have different three-dimensional orientations of atoms in space.[9] Stereoisomers include both diastereoisomers and enantiomers.[10] An enantiomer, of great interest to the pharmaceutical arts,[11] is one of a pair of stereoisomers with one or more stereogenic centers, referred to as chiral centers.[12] These chirals have a unique three-dimensional shape lacking an internal plane of symmetry, meaning that they are nonsuperimposable mirror images of each other.[13] In organic chemistry, the asymmetric center is a carbon atom with four different substituent atoms or groups of atoms.[14] Achiral carbons bearing two identical substituents can be

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7. 348 F. Supp. 2d 713 (N.D. W. Va. 2004).

8. Pfizer Inc. v. Ranbaxy Labs., Ltd., 405 F. Supp. 2d 495, 502 (D. Del. 2005), *aff'd in part, rev'd in part*, 457 F.3d 1284 (Fed. Cir. 2006).

9. *Id.*

10. Diastereoisomers are "isomers of drugs with more than one chiral center that are not mirror images of one another." *Development of New Stereoisomeric Drugs*, U.S. FOOD & DRUG ADMIN. (May 1, 1992), http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm122883.htm.

11. *See id.* (calling for single-enantiomer data to evaluate pharmacokinetics in a single enantiomer or composition through a policy statement).

12. *See* LEWIS, *supra* note 1, at 441.

13. Bingyun Li & Donald T. Haynie, *Chiral Drug Separation*, *in* 1 ENCYCLOPEDIA OF CHEMICAL PROCESSING 449, 449 (Sunggyu Lee ed., 2006).

14. *See* LEWIS, *supra* note 1, at 97.

superimposed upon their mirror images; however, it is impossible to align the carbon framework of two enantiomers without breaking bonds.[15]

Enantiomers usually "require specialized chiral techniques for their correct identification, characterization, separation and measurement."[16] As the United States District Court for the District of Delaware explained in *Pfizer, Inc. v. Ranbaxy Labs., Ltd.*, "Chemists name and describe racemates and enantiomers with certain symbols and designations."[17] A racemic mixture, also known as a "racemate," is a composition containing both of the enantiomers of a chiral molecule, present in a 1:1 equimolar mixture.[18] To distinguish between different enantiomers of a racemate, chemists label the asymmetric centers according to the Cahn-Ingold-Prelog priority rules; these rules assign priority based on the atomic number of the chiral center's substituents.[19] The center of one enantiomer of the pair is designated the (R)-enantiomer, and its opposite is the (S)-enantiomer.[20] A racemate has the designation "RS" because it is an equal mixture of both enantiomers.[21]

The process of producing a chiral compound by a nonstereospecific or nonstereoselective process will always yield a racemate.[22] The separation of a racemate into its component enantiomers is called a "chiral resolution" or a "resolution of a racemic modification," and it can be carried out by various methods, such as high performance liquid chromatography (HPLC), gas chromatography (GC), capillary electrophoresis (CE), and supercritical fluid chromatography (SFC).[23] "A racemic or chiral switch may be defined as the development of a single

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15. Li & Haynie, *supra* note 13, at 449.

16. U.S. FOOD & DRUG ADMIN., *supra* note 10.

17. 405 F. Supp. 2d 495, 502 (D. Del. 2005).

18. Li & Haynie, *supra* note 13, at 449.

19. R.S. Cahn, C.K. Ingold & V. Prelog, *The Specification of Asymmetric Configuration in Organic Chemistry*, 12 EXPERIENTA 81, 83-94 (1956). Each substituent is assigned a priority based on the molecular weight of the atom closest to the chiral center. If more than one substituent starts with the same type of atom, then the molecular weight of the next closest atom is used as a tiebreaker. The lowest priority substituent is pointed away from the viewer. If the remaining three substituents are arranged from highest priority to lowest priority in a clockwise direction, then the molecule is labeled "R." If counterclockwise, then it is labeled "S."

20. *Pfizer*, 405 F. Supp. 2d at 502.

21. *Id.*

22. *See* Alan G. Mitchell, *Racemic Drugs: Racemic Mixture, Racemic Compound, or Pseudoracemate?*, 1 J. PHARMACY & PHARMACEUTICAL SCI. 8, 9 (1998), *available at* http://www.ualberta.ca/~csps/JPPS1(1)/A.Mitchell/Mitchell.pdf.

23. *See* Li & Haynie, *supra* note 13, at 449; *see also* 10 PHYSICAL METHODS OF CHEMISTRY SERIES (Bryant W. Rossiter & Roger C. Baetzold eds., 2d ed. 2005); Craig White & John Burnett, *Integration of Supercritical Fluid Chromatography into Drug Discovery as a Routine Support Tool: II. Investigation and Evaluation of Supercritical Fluid Chromatography for Achiral Batch Purification*, 1074 J. CHROMATOGRAPHY A 175, 175-76 (2005).

enantiomer from a previously marketed racemate," as explained by Hutt and Valentova in *The Chiral Switch: The Development of Single Enantiomer Drugs from Racemates*, and is a critical process to the pharmaceutical business model.[24] According to Hutt and Valentova, "The chiral switch process provides a strategy to extend the profitable life of a pharmaceutical 'bestseller,' and may result in extended patent protection and provide an advantage against generic competition."[25] Enantiomers may also be produced by enantioselective synthesis; however, past practice has proven most successful when the enantiomer is resolved from its racemate.[26]

Racemates are distinct from their enantiomers, generally having different physical properties like solubility and melting point.[27] In contrast, enantiomeric pairs exhibit essentially identical physical and chemical properties as each other (in an achrial environment), including boiling point, density, and chemical reactivity.[28] However, enantiomers are distinguishable from each other in that frequently one enantiomer will exhibit substantially different pharmacology and toxicology from its mirror image.[29] Mirror image enantiomers often differ with respect to their biological properties because "chirality is related to the three-dimensional structure, and one form may be more suitable for specific interaction with a biological molecule, such as a receptor, enzyme, etc."[30] Most racemic pharmaceuticals have one major bioactive enantiomer, which is called an "eutomer."[31] The other enantiomer, known as a "distomer," is inactive, less active, or can be toxic by exerting different pharmacological properties.[32] Innovator pharmaceutical corporations strive to resolve the active enantiomer. Once resolved, the active enantiomer becomes the subject of the chiral switch.[33] The active

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24. A.J. Hutt & J. Valentová, *The Chiral Switch: The Development of Single Enantiomer Drugs from Racemates*, 50 ACTA FACULTATIS PHARMACEUTICAE UNIVERSITATIS COMENIANAE 7, 8 (2003).

25. *Id.* at 15.

26. *See* U.S. FOOD & DRUG ADMIN., *supra* note 10.

27. Pfizer Inc. v. Ranbaxy Labs., Ltd., 405 F. Supp. 2d 495, 502 (D. Del. 2005); *see, e.g.*, Sanofi-Synthelabo v. Apotex, Inc., 550 F.3d 1075, 1081 (Fed. Cir. 2008) (discussing possible differences among enantiomers and their racemates); Mitchell, *supra* note 22, at 9 (discussing the expansion "of the definition of racemate to include an equimolar mixture of enantiomers in any physical state").

28. *See* U.S. FOOD & DRUG ADMIN., *supra* note 10.

29. *Id.*

30. Li & Haynie, *supra* note 13, at 449.

31. Lien Ai Nguyen et al., *Chiral Drugs. An Overview*, 2 INT'L J. BIOMEDICAL SCI. 85, 87 (2006), http://ijbs.org/User/ContentFullText.aspx?VolumeNO=2&StartPage=85&Type=pdf.

32. *Id.*

33. *Id.*

enantiomer is then separately patented, effectively extending the innovator's pharmaceutical protection of the market share for this solution. Because neither the structure nor the behavior of the racemate is indicative of the activity of its individual enantiomers, it is necessary to discern each enantiomer from the racemate and the other enantiomers to evaluate its properties.[34]

Chiral pharmaceuticals are "quantitatively analyzed for the presence or absence of chiral impurities."[35] Chemists accomplish this analysis using the fact that enantiomeric pairs are distinguishable based on their optical activity, which is their "ability to rotate plane-polarized light."[36] As stated in the *Journal of Pharmaceutical and Biomedical Science*, "Every optically active substance has its own specific rotation (degree of rotation in polarized light) as defined by Biot's law:

$$[\alpha]_{\lambda}^{T} = \frac{\alpha_{\lambda}^{T}}{cl}$$

where $[\alpha]$ = specific rotation; l = optical path length in dm; λ = wavelength; T = temperature; α = optical rotation, and c = concentration in g/mL."[37] Optical rotation is an empirical measurement of the amount a given sample rotates plane-polarized light.[38] "A pure enantiomer rotates plane-polarized light in only one direction," either clockwise or counterclockwise, "to the maximal amount permitted by that [particular] molecule."[39] In enantiomeric pairs, the rotation for both mirror image compounds is of the same magnitude, but in opposite directions.[40] "If the light rotates clockwise, then that enantiomer is labeled '(+)' or 'd' for dextrorotatory; its counterpart will rotate the light counterclockwise and is labeled '(-)' or 'I' for levorotatory."[41] Importantly, the magnitude and

34. *See id.* at 85; Li & Haynie, *supra* note 13, at 449.

35. Mukesh C. Gohel, *Overview of Chirality and Applications of Stereo-Selective Dissolution Testing in the Formulation and Development Work*, DISSOLUTION TECHS., Aug. 2003, at 16, 17, *available at* http://www.dissolutiontech.com/DTresour/0803art/DT0803art2.pdf.

36. Pfizer Inc. v. Ranbaxy Labs., Ltd., 405 F. Supp. 2d 495, 502 (D. Del. 2005).

37. Laila Kott et al., *An Evaluation of Four Commercial HPLC Chiral Detectors: A Comparison of Three Polarimeters and a Circular Dichroism Detector*, 43 J. PHARM. & BIOMEDICAL ANALYSIS 57, 57 (2007).

38. LEWIS, *supra* note 1, at 822.

39. *See Pfizer*, 405 F. Supp. 2d at 502. For example, a specific rotation of -25° for [R] is complemented by a +25° for [S]. The e.e. of the racemate is 100 x (0°) / (25°) = 0%. *In the example*, if the measured specific rotation is +8°, then [S] is in excess and the optical purity is (100)(+8° / 25°) = 32% excess of [S] over [R] (absolute value). The remaining 68% is equal parts [S] and [R] or 34% of each. Therefore, resulting in 66% [S] and 34% [R].

40. *See* Pfizer Inc. v. Ranbaxy Labs., Ltd., 457 F.3d 1284, 1286 (Fed. Cir. 2006).

41. *Id.*

direction of the measured optical rotation is dependent on the experimental parameters, such as the nature of substance, concentration of the solution, temperature, wavelength of light, sample path length, and solvent.[42] Thus, "[t]here is no correlation between the configuration of enantiomers and the direction in which they rotate plane-polarized light."[43] Therefore, "each R- and S-enantiomers [sic] can rotate plane-polarized light" in either direction and "be designated as R(+) or R(-) and S(+) or S(-)."[44]

As the United States Court of Appeals for the Federal Circuit explained in *Pfizer*, "In a racemate, which is an equal mixture of two opposite enantiomers, the compound is not optically active."[45] This lack of optical activity occurs because the optical rotations of the enantiomers are of equal magnitude and opposite direction and therefore "cancel each other out."[46] "[C]hemists use the '±' to indicate a racemate."[47] A racemate is distinguishable from an unequal mixture of two opposite enantiomers because such a mixture possesses an optical rotation, making it optically active.[48] For such a mixture, "the degree of optical rotation reflects the percentage of each enantiomer present in the mixture."[49] This percentage, referred to as "enantiomeric excess" (e.e. %), is "a measure of the purity of one enantiomer expressed as a percentage of a 100% pure sample of that enantiomer."[50] Enantiomeric excess is calculated using the equation for optical purity, $[\alpha]_{mixture} / [\alpha]_{pure\ sample} \times 100$,[51] which may be rewritten as ([R]-[S]) / ([R]+[S]) x 100, where [R] is the concentration of the R-isomer and [S] is the concentration of the S-isomer.[52] In other words, chemists calculate e.e. % by dividing the observed optical rotation by the optical rotation of the pure enantiomer, then multiplying by 100 to obtain a percentage. Therefore, while enantiomers may be distinguishable from their racemates by physical

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42. Kott et al., *supra* note 37.
43. U.S. Patent No. 7,786,127 col. 8 ll. 25-27 (filed Aug. 28, 2006).
44. Nguyen et al., *supra* note 31, at 86.
45. Pfizer Inc. v. Ranbaxy Labs., Ltd., 405 F. Supp. 2d 495, 502 (D. Del. 2005).
46. *Id.*
47. *Id.*
48. *Id.*
49. *Id.*; *see also* G.P. Moss, *Basic Terminology of Stereochemistry*, 68 PURE & APPLIED CHEMISTRY 2193, 2207, 2212 (1996), *available at* http://www.iupac.org/publications/pac/1996/pdf/6812x2193.pdf.
50. AztraZeneca AB v. Dr. Reddy's Labs., Ltd, No. 05-5553(JAP), 2010 U.S. Dist. LEXIS 48844, at *7 (D.N.J. May 17, 2010) (internal quotation marks omitted).
51. *See* Robert E. Gawley, *Do the Terms "% ee" and "% de" Make Sense as Expressions of Stereoisomer Composition or Stereoselectivity?*, 71 J. ORGANIC CHEMISTRY 2411, 2411 (2006).
52. *Id.* For example, in a sample with 30% e.e. [R], the remaining 70% is racemic with 35% [R] and 35% [S], resulting in 65% total [R]).

characteristics, the only consistent method of discerning enantiomeric pairs is by optical rotation. Thus, pharmaceutical chemists can evaluate a mixture of enantiomers by analyzing its optical activity and thereby discern its enantiomeric composition.

III. CLAIMING ENANTIOMERS IN PATENTS

A. Novelty of Compounds

A compound that exists in at least a trace amount anticipates and invalidates a claim to that compound if it is either revealed in a prior art publication or present in a prior art composition.[53] In *SmithKline Beecham Corp. v. Apotex Corp.* (*SmithKline Beecham I*), the United States Court of Appeals for the Federal Circuit found that the claim language "crystalline paroxetine hydrochloride (PHC) hemihydrate" was not ambiguous and was in fact descriptive of a particular chemical structure.[54] Patent holder SmithKline Beecham alleged Apotex infringed because Apotex manufactured trace amounts of the patented PHC hemihydrate during production of PHC anhydrate.[55] However, Apotex's alleged infringement occurred while it practiced an expired prior art patent directed to the PHC anhydrate.[56] Further, production of PHC anhydrate according to the prior art patent resulted in formation of at least trace amounts of the PHC hemihydrate compound from the disputed claim.[57] A product manufactured according to a prior art reference that infringes a subsequent patent claim would also logically anticipate the claim.[58] Even though the PHC anhydrate patent does not disclose PHC hemihydrate, this patent is undisputed prior art to the PHC hemihydrate claim.[59] The court held the PHC anhydrate patent inherently anticipated the PHC hemihydrate compound claim under 35 U.S.C. § 102(b).[60] The court reasoned that invalidating the later claim furthers

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53. U.S. PATENT & TRADEMARK OFFICE, MANUAL OF PATENT EXAMINING PROCEDURE § 2185 (8th ed. Rev. 9, Aug. 2012), http://www.uspto.gov/RDMS/detail/manual/MPEP/e8r9/d0e18.xml (search "MPEP" for "2185"; then follow link "2100> 2185-Related Issues Under 35 U.S.C. 112, First or Second Paragraphs (e8r9)").

54. 365 F.3d 1306, 1313 (Fed. Cir. 2004), *vacated en banc*, 403 F.3d 1328 (Fed. Cir. 2005), *and superseded by* 403 F.3d 1331 (Fed. Cir. 2005).

55. *Id.* at 1308-09.

56. SmithKline Beecham Corp. v. Apotex Corp. (*SmithKline Beecham II*), 403 F.3d 1331, 1345-46 (Fed. Cir. 2005).

57. *Id.*

58. *Id.* at 1341; *see* Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1378 (Fed. Cir. 2001) (restating the axiom "that which would literally infringe if later anticipates if earlier" (citing Lewmar Marine, Inc. v. Barient, Inc., 827 F.2d 744, 747 (Fed. Cir. 1987))).

59. *SmithKline Beecham II*, 403 F.3d at 1343.

60. *Id.* at 1345.

the policy of "allowing the public to practice expired patents."[61] Therefore, the existence of at least trace amounts of a compound in a prior art publication or event, such as a chemical process, will anticipate a later claim to that compound.

B. Novelty of Enantiomers

When properly claimed as a composition, an enantiomer may be patentable in view of a previously disclosed racemate.[62] All inventions, including chiral compounds, must meet the statutory requirements of usefulness, novelty, and nonobviousness to be patentable.[63] While an enantiomer is distinct both from its mirror image counterpart and its racemate, knowledge of the structure of one necessarily suggests the structure of the other. Thus, the debate concerning the patentability of an enantiomer frequently centers on an obviousness inquiry.[64] In contrast to obviousness, objections based on the usefulness of chiral compounds are rare because these compounds generally exhibit desirable pharmacological activity.[65] Challenges based on novelty are also less frequent and are typically dealt with summarily when they are raised.

For example, in *In re Williams*, the leading case regarding patentability of enantiomers, the Patent Office rejected claims to a levorotatory compound because a prior art publication had disclosed its racemate.[66] The court stated that an enantiomer, "having existed as part of the racemic mixture, cannot be novel."[67] The U.S. Court of Customs and Patent Appeals reversed, announcing, "The existence of a compound as an ingredient of another substance does not negative novelty in a claim to the pure compound, although it may, of course, render the claim unpatentable for lack of invention," now known as the nonobviousness requirement under 35 U.S.C. § 103.[68]

In *Pfizer Inc. v. Ranbaxy Laboratories Ltd.*, a more recent example from the District of Delaware, the court held, "[A] prior art disclosure of

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61. *Id.* at 1346; *see* Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1348 (Fed. Cir. 1999) ("The public remains free to make, use, or sell prior art compositions or processes, regardless of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate.").

62. *SmithKline Beecham II*, 403 F.3d at 1343.

63. 35 U.S.C. §§ 101-103 (2006).

64. *Id.* § 103(a).

65. *Id.* § 101.

66. 171 F.2d 319, 320 (C.C.P.A. 1948).

67. *Id.*

68. *Id.*; *see In re* May, 574 F.2d 1082, 1090 (C.C.P.A. 1978) ("As recognized in *In re Williams* . . . the novelty of an optical isomer is not negated by the prior art disclosure of its racemate.").

a racemate does not anticipate the individual isomers of the racemate or render the individual isomers of the racemate obvious."[69] In *Ortho-McNeil Pharmaceutical, Inc. v. Lupin Pharmaceuticals, Inc.*, another recent example, "[A]n enantiomer has consistently been recognized, by the FDA and the PTO, as a different 'drug product' from its racemate."[70] Thus, while claims to enantiomers may be subject to objection under § 103, they are usually immune from challenge for lack of utility or anticipation.

Importantly, however, a new claim to an enantiomer must be directed to a composition in order to satisfy the novelty requirement.[71] A racemic mixture is an equimolar mixture of both enantiomeric compounds, so a claim directed to an enantiomeric compound will not be novel if the racemic mixture has previously been disclosed. However, a claim disclosing both enantiomeric compounds in a ratio is novel, because the claim is directed to a new composition and not the compound previously revealed in the prior art. Further, a claim directed to an unequal ratio of both enantiomeric compounds as elements of a composition is novel over a prior art racemic mixture, because the composition claim is not directed to the prior art equimolar racemic mixture. In sum, for the purposes of novelty, a claim disclosing a composition that reflects the percentage of each enantiomer present in a nonequimolar mixture may be distinguished from its previously existing racemate.

IV. ENANTIOMERS IN PATENT CLAIM CONSTRUCTION

A. Ortho-McNeil II

In *Ortho-McNeil I*, the court focused on claim 2 of United States Patent No. 5,053,407 (the '407 patent), which reads, "S(-)-9-Fluoro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid according to claim 1," ((S)(-) levofloxacin).[72] Claim 1 of the '407 patent claims "S(-)-pyrido-benzoxazine compound represented by the formula . . . [:]

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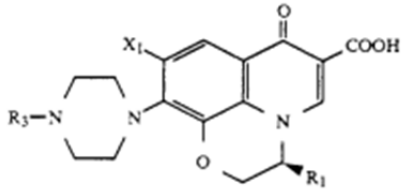
69. 405 F. Supp. 2d 495, 519 (D. Del. 2005) (citation omitted).

70. 603 F.3d 1377, 1380 (Fed. Cir. 2010).

71. *See SmithKline Beecham II*, 403 F.3d 1331, 1339-41 (Fed. Cir. 2005).

72. Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc. (*Ortho-McNeil I*), 267 F. Supp. 2d 533 (N.D. W. Va. 2003), *amended in part by* 348 F. Supp. 2d 713, 731-32 (N.D. W. Va. 2004); U.S. Patent No. 5,053,407 col. 23 ll. 29-32 (filed June 20, 1986).



wherein X_1 represents a halogen atom, R_1 represents an alkyl group having 1 to 4 carbon atoms, and R_3 represents an alkyl group having 1 to 3 carbon atoms."[73] The '407 patent issued to Hayakawa et al. on Oct. 1, 1991.[74] Levofloxacin received U.S. Food and Drug Administration (FDA) approval on December 20, 1996,[75] as the active ingredient in Ortho-McNeil's branded drug Levaquin®.[76] Ortho-McNeil sued Mylan for infringement of claim 2 from the '407 patent.[77] An aspect of the contention between Ortho-McNeil and Mylan rested on whether (S)(-) levofloxacin was novel or if it was anticipated by its racemate.[78]

The (S)(-) levofloxacin claim language is to a compound of an enantiomer.[79] As an enantiometric compound, (S)(-) levofloxacin was present in an equimolar ratio with its mirror image to form the racemate ofloxacin. As such, (S)(-) levofloxacin was necessarily present in the both the formulation of and the patent of ofloxacin. Ofloxacin, the subject of U.S. Patent 4,382,892, issued to Hayakawa et al. on May 10, 1983,[80] and is the active ingredient in Floxin®, which received FDA approval on December 28, 1990.[81] The earliest priority date that can be asserted for the claim to (S)(-) levofloxacin is in 1985.[82] Therefore, the ofloxacin patent issued more than one year prior to the (S)(-) levofloxacin application. Thus, both the racemic mixture itself and the ofloxacin patent are prior art references to the (S)(-) levofloxacin claim.

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73. '407 Patent ll. 14-28.

74. *Id.* at [45].

75. *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. FOOD & DRUG ADMIN. (current through Sept. 2012), http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=020635&TABLE1=OB_Rx.

76. *Ortho-McNeil I*, 267 F. Supp. 2d 533, 535-36 (N.D. W. Va. 2003).

77. *Id.*

78. *Id.* at 545.

79. *Id.* at 543.

80. U.S. Patent No. 4,382,892, at [45] (filed Sept. 2, 1981).

81. *Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*, U.S. FOOD & DRUG. ADMIN. (current through Sept. 2012), http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=019735&TABLE1=OB_Disc.

82. *Ortho-McNeil II*, 348 F. Supp. 2d 713, 731-32 (N.D. W. Va. 2004).

B. The Ortho-McNeil II *Court Found That Claim 2 Was Directed to a Compound*

The (S)(-) levofloxacin claim language is directed to a specific compound, described by Claim 2 of the '407 patent with nomenclature and a figure. The claim language recites "(S)(-) levofloxacin."[83] The claim also references a drawing of the molecule shown in a wedge configuration and depicting a single chiral center.[84] The "(S)(-)" designation and wedge configuration define the compound as an enantiomer and further describe the compound's structure and optical properties.[85] The classification used to label the chiral center of an enantiomer is based on the structure of the compound and the Cahn-Ingold-Prelog priority rules.[86] The structure for the claimed compound is to the (S) enantiomer, not the (R) enantiomer. As such, the compound could only be labeled using the levorotatory and not the dextrorotatory designation.[87] Thus, the claim language and the figure clearly describe the "(S)" levorotatory enantiomer of ofloxacin.

The nomenclature used to describe the optical rotation of a sample is based on empirical measurement and Biot's law.[88] The experimental parameters utilized to evaluate a sample will impact the resulting (±) nomenclature for the molecule.[89] Thus, either a (+) or a (-) can indicate the same enantiomer. "(S)(-) levofloxacin" describes a compound with specific spatial and optical orientation properties inherent to it as measured under a specific set of experimental circumstances. Therefore, if the compound of claim 2 was measured under different experimental conditions, it could have been designated (S)(+). However, in this case, the clear language claims the "(-)" configuration.[90]

According to the *Ortho-McNeil II* court:

> [T]he term "(S)(-)" clearly and plainly limits the claim language to the levorotatory enantiomer. Those skilled in the art clearly understand the term "(S)(-)" to affirmatively denote only the levorotatory enantiomer of a racemic compound, and not the racemic compound itself. Furthermore,

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83. *Id.* at 724.
84. U.S. Patent No. 5,053,407 col. 23 ll. 14-28 (filed June 20, 1986).
85. *See Ortho-*McNeil *I*, 267 F. Supp. 2d 533, 540 (N.D. W. Va. 2003), *amended in part by* 348 F. Supp. 2d 713.
86. *See* Cahn, Ingold & Prelog, *supra* note 19, at 81-94.
87. *See Ortho-McNeil II*, 348 F. Supp. 2d at 728.
88. *See supra* notes 37-44 and accompanying text.
89. *See* Li & Haynie, *supra* note 13, at 449.
90. *Ortho-McNeil II*, 348 F. Supp. 2d at 724.

> those skilled in the art clearly understand the terms "RS" or "(±)" to affirmatively denote a racemic compound.[91]

The court further supported this assertion with reference to the claims, specification, and prosecution history of the '407 patent, which clearly referenced the levorotatory enantiomer and did not claim or refer to the compound as a racemic mixture.[92] This finding agrees with *SmithKline Beecham I*, the Federal Circuit decision holding that a claim to a chemical formula was directed to a very specific compound.[93] The court did not specifically address it, but it should be noted that the claim solely defines the compound as (S)(-) and does not describe the compound in terms of the presence or absence of an (S)(+), (R)(+), or R(-) limitation.[94] Thus, the *Ortho-McNeil II* court found that the language claimed a compound by its chemical formula.[95]

C. The Court Incorporated an Element into the Claim

The district court construed claim 2 as "substantially pure levofloxacin" and subsequently held the claim as valid.[96] Prior to scrutinizing the claim language, the court reiterated the law under 35 U.S.C. § 282, which states that an issued claim deserves a presumption of validity.[97] The district court then approached construction as if the enantiomer's structure and its optical rotation exist independently of each other.[98] The court interpreted the "(S)(-)" designation from the claim language as two discrete elements or distinct limitations.[99] The court determined that the "(S)" described the spatial configuration of the compound, while the (-) indicated that the compound was an "optically active" levorotatory enantiomer that caused rotation of plane-polarized light in a counterclockwise direction.[100] The court went on and found "that more than a single molecule is required to manifest optical activity."[101] In other words, the court interpreted the "(-)" limitation of the

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91. *Id.* at 726.
92. *Id.*
93. *Id.* at 728 (citing *SmithKline Beecham I*, 365 F.3d 1306 (Fed. Cir. 2004)).
94. *See id.* at 724.
95. *See id.* at 728.
96. *Id.* at 730, 764.
97. *Id.* at 723; *see* 35 U.S.C. § 282 (2006).
98. *See Ortho-McNeil I*, 267 F. Supp. 2d 533 (N.D. W. Va. 2003), *amended in part by* 348 F. Supp. 2d 713; *Ortho-McNeil II*, 348 F. Supp. 2d at 724-30 (expending significant effort on construction of the (S)(-) limitation during two hearings).
99. *Ortho-McNeil II*, 348 F. Supp. 2d at 729.
100. *Id.* at 728-29 (defining the (-) limitation using the International Union of Pure and Applied Chemistry as an extrinsic source).
101. *Id.* at 729.

claim to require that sufficient molecules be present in the sample to rotate the plane of polarized light counterclockwise.

The court evaluated the formulation of the claimed product in light of the optical activity limitation and considered the examples in the specification, which contained sufficient molecules to rotate the plane of polarized light.[102] The court found that these examples were never optically pure, and "a person of ordinary skill in the art at the time of the filing of the '407 patent would have understood the claim to cover levofloxacin with a purity that was highly, but less than 100 percent, optically pure."[103] Significantly, the court then held that a formulation of pure (S)(-) levofloxacin in an adequate quantity to rotate the plane of polarized light counterclockwise could not be achieved because its enantiomeric pair, (R)(+) dextrofloxacin, would necessarily exist in at least trace amounts.[104] The court reasoned that this meant that the (S)(-) levofloxacin was merely present in excess relative to its enantiomeric pair.[105] The court then construed (S)(-) levofloxacin as "substantially pure levofloxacin."[106] This construction necessarily added the enantiomeric pair, the (R)(+) compound, as an element to the claim. The court then determined that the unexpected and superior results of the (S)(-) levofloxacin substantially separated from its other enantiomer were sufficient to overcome a prima facie challenge of obviousness in view of the racemate.[107] Finally, the court held defendant Mylan liable for infringement, and the Federal Circuit affirmed without written opinion.[108]

D. Significant Enantiomer Cases Illustrate Proper Composition Claiming

Courts have long construed enantiomers as patentable over their racemates.[109] *In re Williams* established this precedent.[110] A brief review of *In re Williams*, *In re May*, and several more recent decisions illustrates that courts have found enantiomer claims valid. However, these cases

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102. *Id.* at 728-29.

103. *Id.* at 729-30 (noting that Mylan expert, Dr. Mitscher, recognized Example 7 "may, in fact, not be 100 percent [pure], but it was 'the purest sample available' in the '407 patent").

104. *Id.* at 729-30.

105. *Id.* at 729.

106. *Id.* at 730.

107. *Id.* at 754-55, 760.

108. *Id.* at 764; Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc. (*Ortho-McNeil III*), 161 F. App'x 944 (Fed. Cir. 2005) (per curiam) (mem.).

109. *See In re* May, 574 F.2d 1082, 1090 (C.C.P.A. 1978); *In re* Williams, 171 F.2d 319, 320 (C.C.P.A. 1948).

110. 171 F.2d at 320.

also highlight the fact that the valid claims are directed to compositions, not compounds.

In *Williams*, the claim was to "the laevo rotary form 'substantially free from the dextro rotary form,'" and it was "evident that the laevo rotary form did not exist in this condition in the mixture of the [prior art] publications."[111] In *May*, the claim was to "[a] pharmaceutical composition for internal administration having an analgesic, non-addictive, morphine-antagonistic effect."[112] The *Williams* claim uses the "substantially free" language, and the *May* claim refers to a composition. Thus, neither claim in these leading cases is directed to a compound. The *Ortho-McNeil II* court addressed both *Williams* and *May*.[113] The court found these key limitations were merely sufficient but not necessary when claiming an enantiomer.[114] The court reasoned, "The inclusion of 'S(-)' in the claim language, coupled with the obvious exclusion of 'RS' or '(±),' militates against Mylan's assertion that an additional plain-English purity limitation is necessary to distinguish the patented invention over the prior art racemic ofloxacin."[115] In Mylan's prior claim construction, "The Court did not reference a minimum purity because no minimum purity was claimed or identified in the intrinsic record."[116] However, the court construed the claim to cover "substantially pure levofloxacin."[117] Thus, interestingly, in contrast to its declaration, the court incorporated a similar purity limitation on finding that it was necessary to properly define the claim. Many courts have interpreted enantiomers by following the guidelines provided by *In re Williams*.[118] Several more recent decisions highlighted below depict court holdings for a typical novelty challenge to a claim to an enantiomer.

In *Sanofi-Synthelabo v. Apotex, Inc.*, the claim at issue was to "[h]ydrogen sulfate of the dextro-rotatory isomer of methyl alpha-5(4,5,6,7-tetrahydro(3,2-c)thienopyridyl)(2-chlorophenyl)-acetate substantially separated from the levo-rotatory isomer."[119] The Federal Circuit found the claim valid because while the prior art references disclosed the racemate and suggested the enantiomers existed,

111. *Id.* at 319-20.
112. 574 F.2d at 1084.
113. *Ortho-McNeil II*, 348 F. Supp. 2d 713, 724-26 (N.D. W. Va. 2004).
114. *Id.* at 726.
115. *Id.*
116. *Id.* at 729.
117. *Id.* at 730.
118. *See* Sanofi-Synthelabo v. Apotex, Inc., 550 F.3d 1075, 1082-83 (Fed. Cir. 2008) (citing *In re* May, 574 F.2d 1082 (C.C.P.A. 1978)).
119. *Id.* at 1077.

"knowledge of the existence of enantiomers is not a description of a specific enantiomer 'substantially separated' from the other."[120] Of note, the claim includes language whereby the dextro-enantiomer is substantially separated from the levo-enantiomer.[121] This claim language specifically references both enantiomers and incorporates a purity limitation.[122] Therefore, this claim is distinct from the compound claim in *Ortho-McNeil II*.

In *Forest Laboratories, Inc. v. Ivax Pharmaceuticals, Inc.*, the disputed claim was directed to substantially pure (+)-citalopram.[123] The defendant challenged the compound on the basis of its novelty with a prior art reference that mentioned citalopram generally.[124] However, the United States District Court for the District of Delaware found the reference lacking: "[it] only disclose[d] the chemical structure of (R)-citalopram and [did] not disclose the chemical structure of (S)-citalopram, which corresponds to (+)-citalopram."[125] The court recognized that the cited reference did not "disclose anything with regard to the purity of the (S)(-) enantiomer."[126] Therefore, the *Forest* court interpreted the reference compound as the absolute chemical structure, and, as such, the reference compound cannot inherently disclose, as claimed, a composition with one enantiomer substantially separated from its counterpart.[127] The *Forest* holding is distinguishable from the *Ortho-McNeil II* holding. In *Ortho-McNeil II*, the claim was drafted to include the absolute chemical structure, (S)(-) levofloxacin, yet the court found that such a compound claim can disclose its counterpart enantiomer by incorporating a purity limitation through the "substantially pure" language.[128]

In *Pfizer Inc. v. Ranbaxy Laboratories Ltd.*, the disputed claim covered the active ingredient of the prescription drug Lipitor®.[129] Claim 1 only references a wedge and dash drawing of the structural formula of the compound, depicting two chiral centers without describing the structure using chemical nomenclature.[130] The compound "gives rise to

120. *Id.* at 1084, 1090.
121. *See id.* at 1077.
122. *See id.*; *Ortho-McNeil II*, 348 F. Supp. 2d at 724-25.
123. 438 F. Supp. 2d 479, 485-86 (D. Del. 2006).
124. *See id.* at 485.
125. *Id.* at 486.
126. *Id.*
127. *See id.*
128. *Ortho-McNeil II*, 348 F. Supp. 2d 713, 729-30 (N.D. W. Va. 2004).
129. 457 F.3d 1284, 1287-89 (Fed. Cir. 2006) (illustrating that claim 1 depicts a wedge projection the claimed compound).
130. U.S. Patent No. 4,681,893 col. 15 l. 68-col. 16 l. 11 (filed May 30, 1986).

four possible isomers, two of which are the R-cis- and S-cis-isomers and the other two of which are the R-trans- and S-trans-isomers."[131] Due to the ambiguity this drawing created, the court referred to the specification, which specifically states that the invention "contemplates only the trans-form."[132] However, there is no additional disavowal of claim scope limiting the trans-racemates only to either the R-trans or S-trans.[133] The court could have held that the absolute configuration shown in the wedge-dash projection was the only structure claimed. Instead, the court, relying on the intrinsic record, interpreted the claim to encompass both R-trans and S-trans isomers, reasoning that the absolute structure depicted by the wedge-dash projection is not the only orientation possible.[134]

This is unlike the (S)(-) levofloxacin claim from *Ortho-McNeil II*. The '407 patent claims the (S)(-) levofloxacin using claim language and the wedge projection.[135] As such, the claim specifies the enantiomer's structure and optical rotation without ambiguity. Extrinsic evidence may never be relied upon, however, to vary or contradict the clear meaning of terms in the claims.[136] Thus, seeking interpretation of the (-) as a separate limitation by resorting to an outside source to interpret the claim is inappropriate and unnecessary. Therefore, in contrast to *Pfizer v. Ranbaxy*, where resorting to the specification to limit the claim was proper, the court's interpretation beyond the language of the claim in *Ortho-McNeil II* was not necessary.

The court's construction and finding of validity and infringement was in error. A valid claim to an enantiomer derived from a previously disclosed racemate must be directed to a composition with the enantiomer described in a ratio relative to its enantiomeric pair.[137] In *Ortho-McNeil II*, however, the disputed claim is clearly directed to a

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131. *Pfizer*, 457 F.3d at 1287, 1289 (quoting '893 Patent col. 3 ll. 45-54) ("The terms 'cis' and 'trans' refer to the relative spatial arrangement of two particular substituents: 'cis' means they are on the same side of a plane, while 'trans' means they are on opposite sides . . . . If there are two chiral centers . . . , then there are four possible isomers: R-trans, S-trans, R-cis and S-cis. An equal mixture of R-trans and S-trans enantiomers is called the trans-racemate. An equal mixture of R-cis and S-cis enantiomers is called the cis-racemate.").

132. *Id.* at 1289.

133. *Id.*

134. *Id.*

135. U.S. Patent No. 5,053,407 col. 23 ll. 14-28 (filed June 20, 1986).

136. Markman v. Westview Instruments, Inc., 52 F.3d 967, 981 (Fed. Cir. 1995) (en banc) (citing U.S. Indus. Chems. Inc. v. Carbide & Carbon Chems. Corp., 315 U.S. 668, 678 (1942)), *aff'd*, 517 U.S. 370 (1996).

137. *See Pfizer*, 457 F.3d at 1285-89.

compound.[138] In light of *SmithKline Beecham II*, a claim directed to the enantiomeric compound (S)(-) levofloxacin is anticipated by both the presence of levofloxacin in the prior art racemic mixture and by the prior art patent disclosing the racemate ofloxacin.[139] While a claim to an enantiomeric composition is valid, the enantiomeric compound of claim 2 is invalid as anticipated by its racemate.

V. PROPER CLAIM CONSTRUCTION IN *ORTHO-MCNEIL II*

A claim to an enantiomeric compound is invalid as anticipated because the compound was necessarily present in the racemate. The primary statutory bar, 35 U.S.C. § 102(b), provides, "A person shall be entitled to a patent unless . . . the invention was patented . . . in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States."[140] In *Ortho-McNeil II*, the disputed patent claimed an enantiomer, (S)(-) levofloxacin.[141] However, the claim language did not define the enantiomer as part of a composition.[142] An enantiomeric compound is necessarily present as an equimolar component of its racemate. Instead, the claim recited a compound per se. Regardless, the court construed the claim as a composition and found it valid.[143]

Incorporating the (R)(+) element in the (S)(-) levofloxacin claim was erroneous. The findings of *Ortho-McNeil II* present several concerns with regard to enantiomer claims. Judicial rewriting of claims to preserve validity, even if done to save a valuable commercial patent, is improper. While a judge is the proper arbiter of claim language, a judge cannot construct a claim by adding an element to maintain validity of a patent.[144] The only route to adding an element to a claim in a previously issued patent is by reissue.[145] However, in a reissue, only the Director of the United States Patent and Trademark Office (USPTO), and not the court, is permitted to add elements to a claim.[146] A reissue was not conducted on the '407 patent.[147] Additionally, the court could have

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138. *See Ortho-McNeil II*, 348 F. Supp. 2d 713, 728 (N.D. W. Va. 2004), *aff'd per curiam*, 161 F. App'x 944 (Fed. Cir. 2005) (mem.).

139. 403 F.3d 1331, 1345-46 (Fed. Cir. 2005).

140. 35 U.S.C. § 102(b) (2006).

141. *Ortho-McNeil II*, 348 F. Supp. 2d at 721.

142. *See id.* at 723-24.

143. *Id.* at 730, 764.

144. U.S. PATENT & TRADEMARK OFFICE, *supra* note 53, § 1402 (search "MPEP" for "1402"; follow link for "1400> 1402-Grounds for Filing (e8r9)").

145. *Id.* § 1412.02.

146. *Id.* § 1401.

147. *See Ortho-McNeil II*, 348 F. Supp. 2d at 719, 721.

reasonably construed claim 2 to meet the (-) limitation, which requires that the compound rotate the plane of polarized light, without improperly adding an element to the claim; that is, the "substantially pure levofloxacin" construction was not necessary.[148] Furthermore, the court could have resolved the issue of novelty with respect to claim 2 simply by adopting the interference count. Finally, the holding, by adding an element to a claim, strips the claim of its ability to provide notice to the public of the claim's scope and reinforces improper claim drafting.

A. Incorporating an Element Is Beyond the Scope of Judicial Claim Construction

In *Ortho-McNeil II*, the court improperly added an element to claim 2. Claim construction determines not only whether a defendant has infringed the patent, but also whether the patent itself is valid or invalid.[149] According to the United States Supreme Court in *Markman v. Westview Instruments*, "[T]he construction of a patent, including terms of art within its claim, is exclusively within the province of the court."[150] "Claim interpretation, typically referred to as claim construction, is the crucial process of interpreting patent claims to determine their proper scope and meaning."[151] Claim 2 describes the S(-)-pyridobenzoxazine compound as "S(-)-9-Fluoro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-2,3-dihydro-7 H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid according to claim 1."[152] Thus, the claim language reads only to include the (S)(-) and not the (R)(+) enantiomer. However, through claim construction, the court defined this claim to mean "substantially pure levofloxacin," meaning "levofloxacin with a purity that was highly, but less than 100 percent, optically pure."[153] Optical purity of a single enantiomer is the percentage of one enantiomer in excess of another.[154] Thus, substantially pure levofloxacin is not optically pure and must necessarily include the (R)(+) dextrofloxacin enantiomer. Therefore, the district court added (R)(+) dextrofloxacin as an element to the claim.[155]

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148. *See id.* at 730 (construing claim to cover "substantially pure levofloxacin" incorporating the (R)(+) dextrofloxacin enantiomer).

149. Kimberly A. Moore, *Are District Court Judges Equipped To Resolve Patent Cases?*, 15 HARV. J.L. & TECH. 1, 2 (2001) ("[C]laim construction is the touchstone for any infringement or validity analysis . . . .").

150. Markman v. Westview Instruments, Inc., 517 U.S. 370, 372 (1996).

151. Thomas Chen, Note, *Patent Claim Construction*, 94 VA. L. REV. 1165, 1168 (2008).

152. U.S. Patent No. 5,053,407 col. 23 ll. 29-32 (filed June 20, 1986).

153. *Ortho-McNeil II*, 348 F. Supp. 2d at 729-30.

154. *See id.* at 734-35.

155. *Id.* at 730.

The Federal Circuit affirmed.[156] The Federal Circuit in a related case held that "with respect to enantiomers, . . . the PTO's determination that levofloxacin is a different 'product' than the racemate ofloxacin must be afforded 'great deference.'"[157]

An issued patent warrants a presumption of validity.[158] The Federal Circuit has held, "[C]laims should be so construed, if possible, as to sustain their validity."[159] However, the Federal Circuit later clarified, "[C]laims can only be construed to preserve their validity where the proposed claim construction is 'practicable,' is based on sound claim construction principles, and does not revise or ignore the explicit language of the claims."[160] Further, "[T]he phrase 'if practicable' cannot be ignored, and courts should not rewrite claims to preserve validity."[161] Historically, the Federal Circuit has admonished against judicial rewriting of claims to preserve validity.[162] In *Hoganas AB v. Dresser Industries, Inc.*, the court held: "It would not be appropriate for us now to interpret the claim differently just to cure a drafting error . . . . That would unduly interfere with the function of claims in putting competitors on notice of the scope of the claimed invention."[163] Moreover, according to the Federal Circuit in *SmithKline Beecham I*, "The scope of patent claims can neither be broadened nor narrowed based on abstract policy

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156. *Ortho-McNeil III*, 161 F. App'x 944, 944 (Fed. Cir. 2005) (per curiam) (mem.).

157. Ortho-McNeil Pharm., Inc. v. Lupin Pharms., Inc., 603 F.3d 1377, 1380 (Fed. Cir. 2010) (citation omitted).

158. 35 U.S.C. § 282 (2006).

159. ACS Hosp. Sys., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577 (Fed. Cir. 1984); *see also* Turrill v. Mich. S., & C., R.R. Co., 68 U.S. (1 Wall.) 491, 510 (1863) ("Patents for inventions are not to be treated as mere monopolies, and, therefore, odious in the eyes of the law; but they are to receive a liberal construction, and under the fair application of the rule, *ut res magis valeat quam pereat* [that the thing may rather have effect than be destroyed], are, if practicable, to be so interpreted as to uphold and not to destroy the right of the inventor."); *accord* Klein v. Russell, 86 U.S. (19 Wall.) 433, 466 (1873) ("The court should proceed in a liberal spirit, so as to sustain the patent and the construction claimed by the patentee himself, if this can be done consistently with the language which he has employed.").

160. Generation II Orthotics Inc. v. Med. Tech. Inc., 263 F.3d 1356, 1365 (Fed. Cir. 2001) (citing Rhine v. Casio, Inc., 183 F.3d 1342, 1345 (Fed. Cir. 1999)).

161. Nazomi Commc'ns, Inc. v. Arm Holdings, PLC, 403 F.3d 1364, 1368 (Fed. Cir. 2005) (citing *Rhine*, 183 F.3d at 1345 ("If the only claim construction that is consistent with the claim's language and the written description renders the claim invalid, then the axiom does not apply and the claim is simply invalid.")).

162. *See, e.g.*, Becton Dickinson & Co. v. C.R. Bard, Inc., 922 F.2d 792, 799 n.6 (Fed. Cir. 1990) ("Before us, both parties disclaim responsibility for the district court's misguided theory that it should or could rewrite the claims. Nothing in any precedent permits judicial redrafting of claims. At most there are admonitions to *construe* words in claims narrowly, if possible, so as to sustain their validity. Carman Indus. v. Wahl, 724 F.2d 932, 937 n.5 (Fed. Cir. 1983).").

163. 9 F.3d 948, 951 (Fed. Cir. 1993).

considerations regarding the effect of a particular claim meaning."[164] Further, the Supreme Court has stated:

> [W]e know of no principle of law which would authorize us to read into a claim an element which is not present, for the purpose of making out a case of novelty or infringement. The difficulty is that, if we once begin to include elements not mentioned in the claim, in order to limit such claim, and avoid a defense of anticipation, we should never know where to stop.[165]

In other words, unclaimed elements cannot be added to the claim language. In *Ortho-McNeil II*, claim 2 recites an enantiomeric compound that is anticipated by its racemate.[166] The district court interprets the compound as a composition and adds the (R)(+) dextrofloxacin element to the claim.[167] This element was not present in the claim prior to claim construction.[168] The court improperly read the (R)(+) element for the purpose of altering the claim's novelty. Thus, even though the '407 patent was commercially and highly valuable to Ortho-McNeil and warranted a presumption of validity as an issued patent,[169] the claim was improperly directed to the enantiomeric compound. This should not have been remedied from the bench.

After the issuance of the levofloxacin patent, the only way to properly add new matter to a claim would have been through a reissue of the patent.[170] A patentee may request the Director of the USPTO to reissue a patent.[171] The Director of the USPTO, not a district court judge, has the power to reissue.[172] Accordingly, only the Director, not the court, has the power to add elements to a claim of an already issued patent. Here, the court added the element to the claim, making the (R)(+) element of claim 2 an improper addition.[173]

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164. 365 F.3d 1306, 1314 (Fed. Cir. 2004), *vacated en banc*, 403 F.3d 1328 (Fed. Cir. 2005), *and superseded by* 403 F.3d 1331 (Fed. Cir. 2005) (citing Quantum Corp. v. Rodime, PLC, 65 F.3d 1577, 1584 (Fed. Cir. 1995) ("[I]t is well settled that no matter how great the temptations of fairness or policy making, courts do not redraft claims.")).

165. McCarty v. Lehigh Valley R.R. Co., 160 U.S. 110, 116 (1895).

166. 348 F. Supp. 2d 713, 721 (N.D. W. Va. 2004).

167. *See id.* at 729-30.

168. *See id.*

169. 35 U.S.C. § 282 (2006).

170. *Id.* § 251 ("Whenever any patent is . . . deemed wholly or partly inoperative or invalid, . . . by reason of the patentee claiming more or less than he had a right to claim in the patent, the Director shall, on the surrender of such patent . . . reissue the patent for the invention disclosed in the original patent . . . for the unexpired part of the term of the original patent.").

171. U.S. PATENT & TRADEMARK OFFICE, *supra* note 53, § 1402 (search MPEP" for "1402"; follow link for "1400> 1402–Grounds for Filing (e8r9)").

172. *Id.* § 1401.

173. *Ortho-McNeil II*, 348 F. Supp. 2d at 729-30.

B. Incorporating an Element Was Not Necessary for Proper Claim Construction

The compound was unambiguously claimed as (S)(-) levofloxacin.[174] The *Ortho-McNeil II* court could have properly construed the claim as such and found it invalid. In this case, the court construed the claim as "substantially pure levofloxacin" and added at least trace amounts of (R)(+) dextrofloxacin to the claim.[175] The court reached this conclusion following its holding that the (-) element in the claim language was distinct.[176] The court then found that the compound must be present in an amount sufficient to assess the (-) limitation of claim 2 and rotate polarized light in a counterclockwise direction.[177] As the Court of Customs and Patent Appeals has stated, "From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same thing."[178] Thus, the properties present in a compilation of the (S)(-) levofloxacin compound are present in every instance of this compound. The ability to discern the optical rotation of a sample is not relevant to the compound or its properties. Rather, the (-) limitation only indicates that under certain conditions the compound rotates plane-polarized light in a counterclockwise direction. Even though optical rotation may not have been measurable in a single instance of the molecule, it does not change the fact that this property is still present within that single molecule. Thus, the (-) limitation encompasses even a single instance of the (S)(-) levofloxacin molecule, and every instance of that molecule rotates the plane-polarized light in the counterclockwise direction.[179]

Further, the court did not need to examine the examples from the specification. Instead, the court could have reasoned that the claim limitation required an adequate amount of the (S)(-) levofloxacin be present to rotate the plane of polarized light. This conclusion would align with the court's reasoning and would not erroneously add an element to the claim. When the improper element is left out of the claim, the result is the enantiomeric compound.[180] A claim to (S)(-) levofloxacin indicates a molecule that rotates plane-polarized light in the counterclockwise direction. (S)(-) levofloxacin was present in the

174. U.S. Patent No. 5,053,407 (filed June 20, 1986).
175. 348 F. Supp. 2d at 730.
176. *Id.* at 728.
177. *Id.* at 728-29.
178. *In re* Papesch, 315 F.2d 381, 391 (C.C.P.A. 1963).
179. *Ortho-McNeil II*, 348 F. Supp. 2d at 726, 728.
180. *See* U.S. Patent No. 5,053,407 (filed June 20, 1986).

racemate. Whether the analysis, as the court suggests, requires a multitude of molecules or a single instance of the molecule, the properties of the compound are inherent. Thus, claim 2 would be barred under 35 U.S.C. § 102(b) because it would be anticipated by the presence of the compound in the racemate. Therefore, the court would have still invalidated the claim, even when considering the optical rotation limitation.

C. Ortho-McNeil's *Poor Drafting Could Have Been Cured by Adopting the Interference Count*

After prevailing during an interference proceeding, the inventor did not adopt the interference count, which would have resulted in a proper claim to (S)(-) levofloxacin.[181] The '407 patent was the subject of an interference proceeding before the USPTO Board of Patent Appeals and Interferences.[182] Junior party Schriewer et al. filed U.S. patent application 939,582 on December 9, 1986.[183] Senior party Hayakawa et al. filed U.S. patent application 876,623 on June 20, 1986.[184]

On February 26, 1991, the Board declared Hayakawa et al. the successful party in interference proceeding 102,168.[185] The examiner-in-chief presented the interference count.[186] A count is created to "defin[e] the interfering subject matter between two or more applications or between one or more applications and one or more patents," and each count corresponds to a separate patentable invention.[187] The count at issue read: "an enantiomerically pure 1,8-bridged 4-quinolone-3-carboxylic acid and derivatives thereof wherein said acid and derivatives

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181. "An *interference* is a proceeding instituted in the Patent and Trademark Office before the Board to determine any question of patentability and priority of invention between two or more parties claiming the same patentable invention." 37 C.F.R. § 1.601(i) (2004) ("interference" is not defined in subsequent code revisions). "Whenever an application is made for a patent which, in the opinion of the Director, would interfere with any pending application, or with any unexpired patent, an interference may be declared . . . . The Director may issue a patent to the applicant who is adjudged the prior inventor." 35 U.S.C. § 135(a) (2006).

182. *See Ex parte* Hayakawa, Interference No. 102,168, Paper No. 17, at 2 (B.P.A.I. June 28, 1989), *available at* http://portal.uspto.gov/external/PA_PeaiPair/view/BrowsePdfServlet?objectId=FPCL5IMZPPOPPY5&lang=DINO.

183. *Id.*

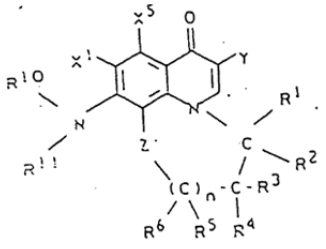
184. U.S. Patent No. 5,053,407 (filed June 20, 1986).

185. *Ex parte* Hayakawa, Interference No. 102,168, Paper No. 22, at 1 (B.P.A.I. Feb. 26, 1991), *available at* http://portal.uspto.gov/external/PA_PeaiPair/view/BrowsePdfServlet?objectId=FPCL5PZPPPOPPY5&lang=DINO.

186. *Id.*

187. 37 C.F.R. § 1.601(f) (2004) ("count" not defined in subsequent code revisions).

thereof are antibacterially more active than racemates thereof of the formula:"[188]



The examiner-in-chief further defined the functional groups identified by variables.[189] The "enantiomerically pure" limitation set out in the count results in the count being directed to a composition claim, not a compound. Therefore, had the prevailing inventors accepted and proceeded to patent claims of the same nature as the interference count, the claims would have been valid under 35 U.S.C. § 102(b).

D. Ramifications of the Ortho-McNeil II *Holding*

A claim to an enantiomer is not patentable given a previously disclosed racemate when the claim is strictly directed to the structure of the compound, following *SmithKline Beecham II*, because the subject matter is anticipated.[190] Proper claims for (S)(-) levofloxacin must distinguish the claimed enantiomer from the racemate by defining it in terms relative to its enantiomeric pair.[191] Valid claims to (S)(-) levofloxacin may include language such as "S(-) levofloxacin substantially free of (R)(+) dextrofloxacin," "S(-) levofloxacin substantially separated from (R)(+) dextrofloxacin," or "optically pure S(-) levofloxacin," all of which are similar to the claim posed by the interference count. A claim to optically pure or enantiomerically pure (S)(-) levofloxacin would be construed as 100% (S)(-) levofloxacin and 0% (R)(+) dextrofloxacin. Therefore, the claim would be directed to a composition covering both enantiomers, and it would have been possible for the court to construe the claim without introducing a new element.

The (R)(+) limitation added to the claim during construction produced several consequences. First, the (S)(-) levofloxacin claim language no longer provided notice of the metes and bounds of the right

188. *Ex parte* Hayakawa, Interference No. 102,168, Paper No. 22, at 1.
189. *Id.*
190. 403 F.3d 1331, 1341, 1345-46 (Fed. Cir. 2005).
191. *See Ortho-McNeil II*, 348 F. Supp. 2d 713 (N.D. W. Va. 2004).

to exclude.[192] Without a formal reissue of the patent, a new claim will not be granted. Claims provide public notice of an invention's subject matter.[193] The "public notice function . . . affects the interplay between competing firms in innovation markets."[194] A "patentee's competitors will consult and interpret the patent claims in order to assess their ability to design around or improve upon the claimed invention."[195] Further, "Claim construction similarly affects patent licensing negotiations, as parties must agree on patent claim scope when assessing the value of potential licenses."[196] Meanwhile, uncertainty will "either chill legitimate inventive activity or force competitors to engage in costly information gathering and/or litigation to assess the validity of the patent right."[197] Moreover, investors need to know the scope of a patent's exclusivity.[198] Investors want to assess the value that the patent and its claims produce because they desire either to invest in the patent holder's company or to purchase the patent.[199] Finally, the patentee must know the scope of protection possessed by her patented invention in order to understand the breadth of the market over which she has exclusivity.[200] The court in *Ortho-McNeil II* construed the claim with an additional element, the (R)(+) dextrofloxacin.[201] The issued claim does not contain this element.[202] Therefore, following *Ortho-McNeil II*, the (S)(-) levofloxacin claim does not provide the public notice of the subject matter and will significantly impact those relying on the claim text.

Second, because the USPTO did not grant a reissue of the '407 patent, reissue rights were not granted. Without a formal grant of reissue, there is no date to which infringement of the new claim

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192. *See* U.S. Patent No. 5,053,407 (filed June 20, 1986).

193. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1583 (Fed. Cir. 1996) ("In other words, competitors are entitled to review the public record, apply the established rules of claim construction, ascertain the scope of the patentee's claimed invention and, thus, design around the claimed invention."); *see also* Hoganas AB v. Dresser Indus., Inc., 9 F.3d 948, 951 (Fed. Cir. 1993) (noting "the function of claims in putting competitors on notice of the scope of the claimed invention").

194. Chen, *supra* note 151, at 1169.

195. *Id.*

196. *Id.*

197. Arti K. Rai, *Engaging Facts and Policy: A Multi-Institutional Approach to Patent System Reform*, 103 COLUM. L. REV. 1035, 1079 (2003).

198. *See* Clarisa Long, *Information Costs in Patent and Copyright*, 90 VA. L. REV. 465, 489-95 (2004) (classifying patent observers as avoiders, transactors, or builders).

199. *See id.*

200. 35 U.S.C. § 271 (2006) (defining activities that are considered patent infringement).

201. 348 F. Supp. 2d 713, 729 (N.D. W. Va. 2004) (stating that Mylan expert, Dr. Mitscher, recognized Example 7 "may, in fact, not be 100 percent [pure], but it was 'the purest sample available' in the '407 patent").

202. *See* U.S. Patent No. 5,053,407 col. 23 ll. 14-32 (filed June 20, 1986).

accrues.[203] As the Federal Circuit has noted, "Recapture through a reissue patent of what is dedicated to the public by omission in the original patent is permissible under specific conditions, but not at the expense of innocent parties."[204] The court has further stated that the "underlying rationale for intervening rights is that the public has the right to use what is not specifically claimed in the original patent."[205] If the claims of a patent change in scope or enforceability, then it would only be fair to allow infringing practices, for there would be no way to predict the final scope of the claims. Thus, if a court decides that equity dictates, an infringer may benefit from the right to continue an infringing activity after reissue.[206] Therefore, the rights of an alleged infringer regarding the new claim to substantially pure levofloxacin are not protected, because without the reissue, no reissue date was established.

Finally, the holding in the *Ortho-McNeil II* case impacts future prosecution, litigation, and counseling activities of the patent bar. Attorneys rely on court findings and holdings to dictate their practice.[207] As such, a claim interpretation directing practitioners towards drafting improper claims impacts decision making in all areas of patent law. The compound claim to (S)(-) levofloxacin was interpreted to mean substantially pure levofloxacin, a composition.[208] Any practitioner relying on this decision may consequently commit error in prosecuting or analyzing claims for counseling or litigation.

VI. CONCLUSION

Enantiomers are protected as compositions. They are significant compositions to both the pharmaceutical and healthcare industries. Valid enantiomer claims where the racemate was known in the prior art must

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203. U.S. PATENT & TRADEMARK OFFICE, *supra* note 53, § 1405 (search "MPEP" for "1405"; follow link for "1400> 1405-Reissue and Patent Term (e8r9)").

204. Seattle Box Co. v. Indus. Crating & Packaging Inc., 756 F.2d 1574, 1579 (Fed. Cir. 1985) (citing Sontag Chain Stores Co. v. Nat'l Nut Co., 310 U.S. 281, 290 (1940) (allowing the defendant to continue activity that was not covered by the original patent after the reissue, even though that activity infringed the reissue patent)).

205. *Seattle Box*, 756 F.2d at 1579.

206. *Id.*

207. The court in *Ortho-McNeil Pharmaceutical, Inc. v. Lupin Pharmaceutical, Inc.*, Civ. No. 06-4999(GEB), 2009 U.S. Dist. LEXIS 37049 (D.N.J. May 1, 2009), relied on the holding of *Ortho-McNeil II*, 348 F. Supp. 2d 713, 729-30 (N.D. W. Va. 2004). Further, law reviews particularly addressing obviousness have analyzed the *Ortho-McNeil II* decision and relied on the court's findings, including Miles J. Sweet, Note, *The Patentability of Chiral Drugs Post-KSR*, 24 BERKELEY TECH. L.J. 129 (2009), and Jonathan J. Darrow, *The Patentability of Enantiomers: Implications for the Pharmaceutical Industry*, 2007 STAN. TECH. L. REV. 2 (2007), http://stlr.stanford.edu/pdf/darrow-patentability.pdf.

208. *Ortho-McNeil II*, 348 F. Supp. 2d at 730.

recite a percentage, a purity limitation, or reference to enantiomeric excess to satisfy novelty. If not, then a claim to a pure enantiomer compound is anticipated by the existence of the racemic mixture as the subject of a patent, printed publication, or sale before a critical 35 U.S.C. § 102(b) date. *Ortho-McNeil II* highlights poor claiming, poor examination, and improper judicial interpretation of these important compositions. (S)(-) levofloxacin was drafted as a compound, so the compound claim should accordingly have been invalidated due to lack of novelty because it existed in the prior art racemate as part of a composition.