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UPDATING THE PATENT SYSTEM'S NOVELTY REQUIREMENT TO PROMOTE SMALL-MOLECULE MEDICINAL PROGRESS

JASON BREWER*

I. INTRODUCTION

In 1928, the accidental contamination of a bacteria culture dish with a spore from *Penicillium Notatum* spawned the greatest life-saving drug that the world had ever seen, Penicillin.¹ The phenomenal discovery of the effect of small molecules, like penicillin, on biological systems ignited the pharmaceutical industry.² Like other inventive industries, the pharmaceutical industry protects its intellectual property investment under patent law.³ Specifically, patent law affords protection only for novel,

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1. David Ho, *Bacteriologist Alexander Fleming*, TIME, Mar. 29, 1999, at 117, *available* at <http://www.time.com/time/magazine/article/0,9171,990612,00.html>. Alexander Fleming left a culture dish of Staphylococcus bacteria out while he was gone over a two-week period. *Id.* Upon returning Fleming noted an area clear of Staphylococcus surrounding a mold contaminate. *Id.* The name Penicillin was derived from the name of the mold, *Penicillium Notatum*. *Id.*

2. *Id.* A wide range of penicillin derivatives now exist in the medicinal market place. See Gordon L. Coppoc, *Penicillin Derivatives*, PURDUE RESEARCH FOUNDATION (Mar. 27, 1996), <http://www.cyto.purdue.edu/cdroms/cyto2/17/chmrx/penems.htm> (providing descriptions of various penicillin derivatives and their uses). Some examples include: Penicillin G; Penicillin V; Ampicillin; Amoxicillin; Hetacillin; Methicillin; Cloxacillin; dicloxacillin; Nafcillin; Oxacillin; Azlocillin; Carbenicillin; Mezlocillin; Piperacillin; and Ticarcillin. *Id.*

3. See, e.g., U.S. Patent No. 5,559,111 (filed Apr. 4, 1995) (claiming Tekturna in claim 19); U.S. Patent No. 7,109,205 (filed June 24, 2003) (claiming Letaris as the racemate in claim 7); U.S. Patent No. 8,256,346 (filed Nov. 3, 1994) (claiming Clevidipine in claim 3); U.S. Patent 5,223,510 (filed July 26, 1991) (claiming Multaq in claim ten); U.S. Patent No. 7,160,870 (filed May 24, 2001) (claiming Promacta in claim one); U.S. Patent No. 7,101,866

useful, and non-obvious inventions.⁴ However, the novelty requirement may in fact stifle future drug discovery.

For example, researchers may have discovered a cure for cancer that will never be marketed.⁵ The obvious question is “Why not?” The answer consists of two parts: first, the enormous cost and risk associated with clinical trials prevent companies from pursuing such research without a stable benefit;⁶ and second, our current patent system does not provide enough protection to allow companies to benefit from research on a known chemical compound.⁷

This Comment briefly explains current patent law, and suggests changes that will provide incentive to pharmaceutical companies to pursue known small molecules. Section II introduces a brief background of patent law and its policies, along with the history behind its development. Section III analyzes the patent law and policies, focusing on its effect on small-molecule medicinal research. Specifically, Section III highlights several reasons that the patent system’s novelty requirement stifles medicinal progress. Section IV proposes changes to the patent law that will provide exclusivity for known compounds with new medicinal uses, as well as alternative legislation that will grant similar exclusivity outside patent law.

(filed Aug. 3, 2001) (claiming Veramyst in claim one); U.S. RE38,551 (filed Jan. 28, 2002) (claiming Vimpat in claim eight).

4. 35 U.S.C. §§ 102-03 (2012).

5. This is intended as a purely hypothetical statement. *But see The DCA Patents*, WWW.THEDCASITE.COM (Nov. 26, 2011), http://www.thedcasite.com/the_dca_patents.html (failing to find investors for a simple nonnovel compound, dichloroacetic acid, because a patent could cover only the method of treating cancer not the composition of matter).

6. *See* Dennis Fernandez et al., *The Interface of Patents with the Regulatory Drug Approval Process and How Resulting Interplay Can Affect Market Entry*, in INTELLECTUAL PROPERTY MANAGEMENT IN HEALTH AND AGRICULTURAL INNOVATION: A HANDBOOK OF BEST PRACTICES 965, 966 (A Krattiger et al., eds., 2007), available at <http://www.iphandbook.org/handbook/chPDFs/ch10/ipHandbook-Ch%2010%2009%20Fernandez-Huie-Hsu%20Patent%20and%20FDA%20Interface%20rev.pdf> (stating that the F.D.A. requisite clinical trials alone can cost up to \$500 million); *see also Global Pharmaceutical R&D Productivity Declining According to Thomson Reuters*, CMR International, PR NEWswire, <http://www.prnewswire.com/news-releases/global-pharmaceutical-rd-productivity-declining-according-to-thomson-reuters-cmr-international-97281019.html> (last viewed Sept. 24, 2012) (noting that only ten percent of new drug clinical candidates are marketed).

7. *See* 35 U.S.C. § 102 (stating that patent protection only extends to novel inventions).

II. BACKGROUND OF THE PATENT SYSTEM

A. Constitutional Authority for Patent Laws

Patent law is rooted in the Constitution.⁸ The Framers of the Constitution debated the advantages and disadvantages of patents before granting Congress the power to grant monopolies for the useful arts.⁹ In the end, the Constitution grants Congress the power “[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.”¹⁰

The new Congress quickly exercised this grant of power in the Patent Act of 1790.¹¹ In the Act, Congress first listed the requirements a patent petitioner must satisfy to obtain a patent,¹² including: (1) a specification that would enable one skilled in the art to practice the invention; (2) the invention must have utility; and (3) the invention must be novel.¹³ The requirements today are similar, except the novelty requirement has further narrowed patentable subject matter by excluding obvious improvements.¹⁴ The Supreme Court of the United States stated that the purpose of these requirements is “to find a balance between promoting innovation and allowing the public to use and perfect the invention for the good of the economy.”¹⁵

8. U.S. CONST. art. I, § 8, cl. 8.

9. Jefferson initially proposed that the bill of rights should completely restrict monopolies because “the benefit even of limited monopolies is too doubtful to be opposed to that of their general suppression.” Letter from Jefferson to Madison (Dec. 20, 1787), *in* 1 THE REPUBLIC OF LETTERS 511, 512 (James Morton Smith ed., 1995); Letter from Jefferson to Madison (July 31, 1788), *in* 1 THE REPUBLIC OF LETTERS at 545. However, in 1789 Jefferson seemingly changed his mind: “Monopolies may be allowed to persons for their own productions in literature and their own inventions in the arts for a term [of] years but no longer. . . .” Letter from Jefferson to Madison (Aug. 28, 1789), *in* 1 THE REPUBLIC OF LETTERS at 630. See Edward Walterscheid, *Patents and the Jeffersonian Mythology*, 29 J. MARSHALL L. REV. 269, 274-75 (1996) (reciting Jefferson’s participation in the development of the patent system).

10. U.S. CONST. art. I, § 8, cl. 8.

11. Patent Act of 1790, 1 Stat. 109 (1790).

12. *Id.* Inventions covered included “any useful art, manufacture, engine, machine, or device, or any improvement therein not before known or used.” *Id.* at 110.

13. *Id.* at 109. “The specification shall contain a written description of the invention, and of the manner and process of making and using it . . . to enable any person skilled in the art . . . to make and use the same” 35 U.S.C. § 112 (2012). An invention must be useful to obtain a patent. 35 U.S.C. § 101 (2012). An invention cannot be patented if it is known, published, or patented. 35 U.S.C. § 102(a).

14. 35 U.S.C. § 103(a) (2012).

15. *Bilski v. Kappos*, 130 S. Ct. 3218, 3252-53 (2010).

B. The Patent Right Is a Negative Right

A patent grants the patentee the right to exclude others from “making, using, offering to sell, or selling the invention in the United States” for a maximum period of twenty years.¹⁶ Possessing a patent does not grant the patentee the right to make, use, or offer to sell the invention.¹⁷ Therefore, if an inventor’s invention is an improvement on a patented item, she must obtain permission to use, make, or sell her invention from the original invention’s patent holder.¹⁸

C. Patentable Inventions: Everything Under the Sun Modified by Man

Today, patentable subject matter is broader than the original Patent Act of 1790. Originally, the Patent Act of 1790 afforded protection to “any useful art, manufacture, engine, machine, or device, or any improvement therein not before known or used.”¹⁹ Most notably, the Act did not include new methods of using old inventions.²⁰ However, Congress and the courts have since changed the law, and now it allows patents on new methods of using old inventions.²¹ Since the 1952 Patent Act, the courts have interpreted patentable inventions to include “anything under the sun that is made by man.”²² With the limitation of “made by man,”

16. 35 U.S.C. § 271(a) (2012). The unauthorized “mak[ing], us[ing], offer[ing] to sell, or sell[ing] any patented invention, within the United States” is said to infringe the patent. *Id.* The patent life for a utility patent will begin at issue and will end twenty years after the initial filing date. 35 U.S.C. § 154(a)(2) (2012). Design patents last for fourteen years from the date of grant. 35 U.S.C. § 173 (2012).

17. 35 U.S.C. § 271(a).

18. *Id.*

19. 1 Stat. 110.

20. *Id.* Thomas Jefferson disfavored new-use patents on old products. ROBERT MERGES & JOHN DUFFY, PATENT LAW AND POLICY: CASES AND MATERIALS 387 (LexisNexis, 4th ed. 2007). The Supreme Court of the United States would not allow new-use patents. *See Roberts v. Ryer*, 91 U.S. 150, 157 (1875) (recognizing using an old machine for a new purpose is not a new invention).

21. *See Ansonia Brass & Co. v. Elec. Supply Co.*, 144 U.S. 11, 19 (1892) (stating a new use of an old device or process may be patentable if the new use is not analogous to the old use, and the new use required inventive skill to produce). The Patent Act of 1952 codified new-use patentability as a new process. Patent Act of 1952, 66 Stat. 792 (1952); *see also* 35 U.S.C. § 100(b) (2012) (defining process as “process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material”). *See Pfizer Inc. v. Teva Pharma. USA Inc.*, 803 F. Supp. 2d 409, 457 (E.D. Va 2011) (finding that Pfizer did not commit inequitable conduct and that the Viagra patent for use of treating erectile dysfunction is valid and enforceable).

22. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980) (upholding a patent for a genetically modified bacteria capable of breaking down various elements of crude oil).

only laws of nature, natural phenomena, and abstract ideas are unpatentable.²³

D. The Required Specification

The patent process is a quid pro quo exchange.²⁴ A patentee must disclose how to make and use his invention as consideration for the limited monopoly.²⁵ This disclosure is the specification. Statutorily, the specification must satisfy four requirements.²⁶ It must: (1) enable one skilled in the art to make and use the invention; (2) contain a written description of the invention; (3) contain the inventor's best mode of practicing the invention; and (4) contain definite claims.²⁷ A failure to satisfy any one of these requirements will void the patent.²⁸

23. *Diamond v. Diehr*, 450 U.S. 175, 185 (1981). Laws of nature, natural phenomena and abstract ideas are the only categories of inventions that are not patentable in the United States. *Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc.*, 548 U.S. 124, 126 (2006). Therefore, Einstein could not patent $E=mc^2$ and Newton could not patent the law of gravity. *Diamond*, 447 U.S. at 309. Natural minerals cannot be patented. *Id.* Electromagnetism, steam, the heat of the sun, electricity and the qualities of metals are not patentable. *Funk Bros. Seed. Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948); *O'Reilly v. Morse*, 56 U.S. 62, 116 (1853). The patentability of these inventions is barred because protection of these inventions would impede rather than promote progress. *Lab. Corp. of Am. Holdings*, 548 U.S. at 126. However, practical application of the forbidden subject matter may be patentable. *Diehr*, 450 U.S. 187-88. *Compare id.* (holding a process for curing rubber that uses a mathematical equation is patentable), *with Gottschalk v. Benson*, 409 U.S. 63, 71-72 (1972) (voiding a claim for a formula because it "has no substantial practical application"), *and Bilski*, 130 S. Ct. at 3231 (ruling that a business method of hedging risk is an unpatentable abstract idea); *see also Telephone Cases*, 8 S. Ct. 778, 782 (1888) (ruling the telegraph machine's use of electricity is patentable); *see also O'Reilly*, 56 U.S. at 86 (sustaining the patentability of machinery that uses the qualities of electricity).

24. *J.E.M. Ag. Supply Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124, 142 (2001).

25. *See Grant v. Raymond*, 31 U.S. 218, 224 (1832) (stating that the monopoly "is the reward stipulated for the advantage derived by the public for the exertions of individuals"); Suzanne Scotchmer & Jerry Green, *Novelty and Disclosure in Patent Law*, 21 RAND J. ECON. 131 (1990) (discussing patent disclosures); Vincenzo Denicolo & Luigi Franzoni, *The Contract Theory of Patents*, 23 INT'L REV. L & ECON. 365 (2003) (discussing how patent law incentivizes disclosures); WILLIAM CALLYHAN ROBINSON, THE LAW OF PATENTS FOR USEFUL INVENTIONS: VOL. 1 23 (Little, Brown, & Co., 1890).

26. 35 U.S.C. § 112.

27. *Id.* Paragraph two requires that the specification concludes with claims "particularly pointing out and distinctly claiming the subject matter" of the invention. 35 U.S.C. § 112(b). These claims must be definite in order to inform the public of the features protected via the monopoly. *Permutit Co. v. Graver Corp.*, 284 U.S. 52, 60 (1931).

28. *See Consol. Elec. Light Co. v. McKeesport Light Co.*, 159 U.S. 465, 476 (1895) (invalidating indefinite claims); *In re Wands*, 858 F.2d 731, 740 (Fed. Cir. 1988) (holding the invention was enabled because it would not require

E. The Novelty Requirement

When The Patent Act of 1752 was passed, monopolies were very unpopular with the general public.²⁹ The cause of this general grievance related to previous monopolies granted by the English Crown for “royal favor[s].”³⁰ These monopolies often controlled entrance into certain industries and removed commodities from the open market.³¹ Most notably, the monopoly on tea helped ignite the Revolutionary War.³² The British Statute of Monopolies attempted to eliminate the abuse of monopolies by limiting the grant of monopolies to only “new manufactures.”³³

Likewise, the first Congress interpreted the constitutional grant to “promote progress” through monopolies as limited to novel inventions.³⁴ Statutorily, an invention cannot be patented if “the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention . . . by the applicant.”³⁵ When an invention fails the novelty test, it is said to be anticipated.³⁶

Interestingly, the conception of the invention is patentable, but the product of conception is not.³⁷ Accordingly, merely prophetic disclosure may anticipate.³⁸

In order for a printed disclosure to anticipate a later

undue experimentation to reproduce it); *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1480 (Fed. Cir. 1998) (invalidating a claim because it was not supported by the written description); *Chemcast Corp. v. Arco Indus.*, 913 F.2d 923, 930 (Fed. Cir. 1990) (invalidating a patent because the inventor’s best mode was not described).

29. MERGES & DUFFY, *supra* note 20, at 5.

30. *Id.*

31. See MERGES & DUFFY, *supra* note 20, at 5 (requiring a patent to run an ale house).

32. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 7 (1966).

33. MERGES & DUFFY, *supra* note 20.

34. 1 Stat. 109.

35. 35 U.S.C. § 102(a). An inventor can anticipate himself if “the invention was patented or described in a printed publication 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.” 35 U.S.C. § 102(b). Even if the invention falls outside of 102(a)-(b), the invention can be anticipated by an unpublished U.S. patent application. 35 U.S.C. § 102(e).

36. MERGES & DUFFY, *supra* note 20, at 360.

37. See *Telephone Cases*, 8 S. Ct. at 782-83 (ruling that Bell’s telephone patent is enforceable even though at the time of application the idea was not reduced to practice); see also *Pfaff v. Wells Elec.*, 525 U.S. 55, 62-63 (1998) (ruling that the mere conception of a computer chip, including an enabling description, anticipated the patent application); *Alexander Milburn Co. v. Davis-Bournonville Co.*, 270 U.S. 390, 401 (1926) (allowing a patent disclosure of a nonreduced to practice invention, where the invention was not claimed in the patent, to anticipate the latter patent).

38. See *Pfaff*, 525 U.S. at 62-63 (holding a description and drawings of an instrument to be patentable before being reduced to practice).

invention, the single disclosure must enable the invention,³⁹ and disclose each and every element of the invention.⁴⁰ Yet, an element may be inherent.⁴¹ An inherent element is “the natural result flowing from” the disclosure.⁴² Initially, the inherent element had to be recognized by a skilled artisan, but the recognition requirement is now arguable.⁴³ The policy behind the inherent anticipation doctrine is to prevent removal of inventions from the public.⁴⁴

But, even with strict novelty requirements, the Supreme Court of the United States carved out an exception, known as the accidental anticipation doctrine. This doctrine provides that it would be “absurd” for an accidental and unnoticed production of an invention to anticipate because the accidental production gave nothing to the world.⁴⁵ Thus, in order to promote progress the courts have applied the doctrine and upheld patents on non-novel inventions.⁴⁶

39. *Seymour v. Osborne*, 78 U.S. 516, 555 (1870); *Struthers Scientific & Int'l Corp. v. Rappl & Hoenig Co., Inc.*, 453 F.2d 250, 255 (2d Cir. 1972).

40. *Hoover Grp. Inc. v. Custom Metalcraft, Inc.*, 66 F.3d 299, 302 (Fed. Cir. 1995); *Structural Rubber Prod. Co. v. Park Rubber Co.*, 749 F.2d 707, 716 (Fed. Cir. 1984); *Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565, 1576 (Fed. Cir. 1991).

41. *See In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (reversing the trial court's ruling that a diaper with two fastening mechanisms inherently disclosed a diaper with three fastening mechanisms); *see also Cont'l Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269 (Fed. Cir. 1991) (vacating summary judgment because the issue of inherency required trial).

42. *Eli Lilly & Co. v. Barr Labs. Inc.*, 251 F.3d 955, 970 (Fed. Cir. 2001). The “natural result flowing from administration of fluoxetine hydrochloride is inhibition of serotonin uptake.” *Id.*

43. *Compare In re Robertson*, 169 F.3d at 745 (requiring recognition of inherency by one skilled in the art), *with Schering Corp. v. Geneva Pharma., Inc.*, 339 F.3d 1373, 1380 (Fed. Cir. 2003) (dismissing the requirement of one skilled in the art to recognize inherency to anticipate a metabolite).

44. *See Schering Corp.* 339 F.3d at 1380 (using the inherent anticipation doctrine to prevent a patent for a metabolite of Loratidine that would prevent commercializing a generic form of Loratidine); *see also SmithKline Beecham Corp. v. Apotex Corp.*, 365 F.3d 1306, 1313 (Fed. Cir. 2004) (denying SmithKline's attempt to patent a new isoform of paroxetine, a hydrochloride hemihydrate, that is produced when making previously patented paroxetine hydrochloride); *but see SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1328, 1329 (Fed. Cir. 2005) (Newman, J., dissenting) (expressing concern over the expansion of the inherent anticipation doctrine which may call into question many previous patents, and ignores the accidental anticipation doctrine).

45. *Tilghman v. Proctor*, 102 U.S. 707, 711-12 (1873); *Edison Elec. Light Co. v. Novelty Incandescent Lamp Co.*, 167 F. 977, 980 (3d Cir. 1909).

46. *See Tilghman*, 102 U.S. at 711-12 (ruling the accidental production of glycerin and amino acids in a steam cylinder from the lubricant does not anticipate an understood process for producing glycerin and amino acids); *see also Edison Elec. Light Co. v. Novelty Incandescent Lamp Co.*, 167 F. 977, 980 (3d Cir. 1909) (validating a patent for light bulbs where glass covers the

F. Obviousness: A Further Expansion of the Novelty Requirement

Obviousness expands the novelty requirement by allowing the combination of elements from multiple disclosures.⁴⁷ While reviewing the obviousness statute, the Supreme Court stated in dicta, “Congress may not authorize the issuance of patents whose effects are to remove existent knowledge from the public domain, or to restrict free access to materials already available.”⁴⁸ After reviewing the statute, the Supreme Court upheld it, but developed its own obviousness test.⁴⁹

In general, the “combination of familiar elements according to known methods is likely to be obvious when [the combination] does no more than yield predictable results.”⁵⁰ Yet, a different obviousness analysis has developed for chemical compounds.⁵¹ For

platinum even though such light bulbs were made prior on accident, and especially because the accidental light bulbs were actually thrown out); *see also Appl. of Seaborg*, 328 F.2d 996, 998 (Fed. Cir. 1964) (validating a patent although the isotope may have been produced in minute undetectable quantities via a known process).

47. *See Appl. of Winslow*, 365 F.2d 1017, 1018-19 (Fed. Cir. 1966) (combining multiple references to find the invention not patentable). An inventor is presumed to know all prior art references. *Id.* An invention is obvious “if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” 35 U.S.C. § 103(a).

48. *John Deere*, 383 U.S. at 6. The Court cited the constitutional requirement of “progress” as necessitating the limitation. *Id.* The Supreme Court of the United States’s first review of 35 U.S.C. § 103 obviousness occurred in *Graham v. John Deere*. *Id.* at 3. The Court recognized precedent for obviousness from *Hotchkiss v. Greenwood*. *Id.* at 10; *See generally Hotchkiss v. Greenwood*, 52 U.S. 248 (1851) (invalidating a patent on doorknobs where the only change from the prior art was the material from which the doorknob was made). In the epic case of *John Deere*, the invention in question was a simple plow that combined known mechanical elements to absorb shock and prevent breakage. *John Deere*, 383 U.S. at 4. The Court invalidated the patent because there were “no operative mechanical distinctions, much less nonobvious differences.” *Id.* at 26.

49. *Id.* at 17. One must determine (1) the scope and content of the prior art, (2) differences between the invention and the prior art, and (3) the level of ordinary skill in the pertinent art. *Id.* Secondary considerations such as “commercial success, long-felt but unresolved needs, and failure of others” are addition factors. *Id.*

50. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). *See id.* at 422 (voiding a claim because combination of prior art, a sensor and an adjustable pedal, would be obvious to one of skill in the art).

51. *See In re Hass*, 141 F.2d 122, 125 (Fed. Cir. 1944) (ruling that a homolog could not be patented unless it possessed some “unobvious or unexpected beneficial properties not possessed by a homologous compound disclosed in the prior art”). To avoid obviousness, and promote progress, the court directed its obviousness analysis to all properties of a compound and not just similarity of structure. *Appl. of Papesch* 315 F.2d 381, 385-86 (Fed. Cir. 1963); *see id.* at 383 (ruling that the compound was patentable over a homolog

chemical compounds, structural similarity only supports a prima facie case of obviousness and shifts the burden of proof to the applicant to show that the compound possesses unexpectedly improved properties.⁵² Indeed, one generally cannot predict the biological properties of a chemical compound based on similar compounds.⁵³ For example, an exchange of a deuterium for a hydrogen may provide the distinction required for patentability.⁵⁴ Therefore, the applicant may rebut obviousness simply by showing that the compound possesses unexpected properties that a structurally similar compound does not.⁵⁵

G. Small-Molecule Medicinal Progress

The overarching policy of patent law is to promote progress.⁵⁶ With this goal in mind, one should ask whether the patent system has promoted medicinal progress. Progress in the medicinal field can be measured by changes in life expectancy and improved quality of life. In the United States, the life expectancy of an

because it possessed anti-inflammatory activity and the homolog did not). Relying on the recent *John Deere* decision, the Court of Appeals for the District of Columbia ruled that all “relevant facts” *including a compound's beneficial properties*, must be considered in an obvious analysis. *Comm. of Patents v. Deutsche Gold-und-Siber-Scheikansalt Vormals Roessler*, 397 F.2d 656, 662 (D.C. Cir. 1968). Most interestingly, in *Appl. of Stremniski*, Stremniski did not bear the burden of proving unexpected differences between his compound and the prior art because the prior art showed no significant use or property and Stremniski showed a use for his compound. *Appl. of Stremniski*, 444 F.2d 581, 588 (Fed. Cir. 1971). The court reasoned its decision would satisfy the constitutional requirement to promote progress. *Id.*

52. *In re Grabiak*, 769 F.2d 729, 731 (Fed. Cir. 1985); *See id.* (finding no prima facie case because prior art did not teach similarity between a thioester and an ester group). *See Appl. of Wilder*, 563 F.2d 457, 459-60 (Fed. Cir. 1977) (finding prima facie case of obviousness for adjacent homologs and structural isomers); *see also Appl. of May*, 574 F.2d 1082, 1089 (Fed. Cir. 1978) (finding a prima facie case of obviousness for stereoisomers); *In re Hoch*, 428 F.2d 1341, 1343 (Fed. Cir. 1970) (finding a prima facie case of obviousness for an acid from an ethyl ester).

53. Kristen C. Buteau, *Deuterated Drugs: Unexpectedly Nonobvious?*, 10 J. HIGH TECH. L. 22, 38 (2009).

54. *Id.* Unexpected properties may relate to a pharmacokinetic property, such as a compound's toxicity profile, bioavailability, or stability. *Id.* at 39. *See* Liming Shao & Michael Hewitt, *The Kinetic Isotope Effect in the Search for Deuterated Drugs*, 23 DRUG NEWS & PERSPECTIVES 398, 398 (2010) (showing the exchange of a deuterium for a hydrogen may increase the metabolic stability of a compound).

55. *See Sanofi-Synthelabo v. Apotex Inc.*, 550 F.3d 1075, 1077, 1090 (Fed. Cir. 2008) (finding the dextrotary enantiomer of clopidogrel, Plavix, nonobvious due to unexpected potency and a preferable toxicity profile); *see also Appl. of May*, 574 F.2d at 1084, 1093-94 (concluding that the lack of the addictive effect of morphine analog enantiomers was unexpected and nonobvious).

56. U.S. CONST. art. I, § 8, cl. 8.

individual increased by more than twenty-seven years over the last century.⁵⁷ Examples of drugs that improve quality of life include drugs that control pregnancy and treatments for infections, pain, swelling, sinus allergies, nausea, and impotence. Obviously, medicinal drug technology has flourished in the United States positively affecting both life expectancy and lifestyle.

Again, “[t]he policy behind the patent system attempts to find a balance between promoting innovation and allowing the public to use and perfect the invention for the good of the economy.”⁵⁸ Accordingly, the initial invention should trigger other inventions and affect the economy. Promoting new small-molecule medicinal drugs does both.

Once pioneering discovery efforts blossom, and new medications are approved or new mechanisms of action are discovered, cheaper therapies may be developed.⁵⁹ For example, a drug may be repurposed to treat multiple diseases.⁶⁰ Alternatively, follow-on drugs allow the pioneer drug to provide the proof of concept or mechanism of action, and then improve on that drug or provide a cheaper alternative.⁶¹ In regards to affecting the economy, study results indicate that effective drug use may decrease overall health costs.⁶² In effect, promoting drug discovery affords other inventors with information, which allows them to create better inventions, and therefore affects the economy through lowering health care expenses.

57. Laura Shrestha, *Life Expectancy in the United States*, CRS REPORT FOR CONGRESS, CRS-2 (Aug. 16, 2006), <http://aging.senate.gov/crs/aging1.pdf>.

58. *Bilski*, 130 S. Ct. at 3252-53.

59. Hongyu Zhao & Zongu Guo, *Medicinal Chemistry Strategies in Follow-on Drug Discovery*, 14 DRUG DISCOV. TODAY 516, 516 (2009); Daniel Grau, M. Phil. & George Serbedzija, *Innovative Strategies for Drug Repurposing*, DRUG DISCOVERY & DEVELOPMENT (Sept. 6, 2007), <http://www.dddmag.com/innovative-strategies-for-drug.aspx>.

60. Grau, Phil & Serbedzija, *supra* note 59. A repurposing approach is less risky than a novel drug. *Id.* This is because it begins with a known safety profile. *Id.* It may begin by screening known drugs against a wide range of new targets. *Id.* For example, Finasteride was originally discovered to treat prostate enlargement, but was repurposed to treat male hair loss. *Id.*

61. Zhao & Guo, *supra* note 59. During a follow-on discovery program, scientists may analyze the information gathered from the pioneering drug to develop new leads. *Id.* at 517. There are multiple examples of follow-on drugs. *Id.* For example, although Atorvastatin, also known as Lipitor, was the fifth statin to reach the market and it became the best-selling drug in history. *Id.* However, follow-on programs still carry substantial risk. *Id.* at 521.

62. Yuting Zhang & Stephen B. Soumerai, *Do Newer Prescription Drugs Pay for Themselves? A Reassessment of the Evidence*, 26 HEALTH AFFAIRS 880, 880 (2007). Although new drugs are expensive, their use may reduce the total health care cost by replacing more expensive services. *Id.* However, more studies need to be done. *Id.* at 885.

III. THE NOVELTY REQUIREMENT STIFLES MEDICINAL PROGRESS

The United States Constitution grants Congress the power “[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.”⁶³ To this purpose, the patent laws must “find a balance between promoting innovation and allowing the public to use and perfect the invention for the good of the economy.”⁶⁴ It is historically true that the patent system has successfully promoted medicinal technological innovation to progress society as seen through the increase in life expectancy and the improvement in lifestyle.⁶⁵ This analysis will show that: (A) society needs further medicinal progress; (B) claiming compounds by structure is wasteful; and (C) novelty via structure will stifle medicinal progress.

A. *Progress Is Still Needed: The Risk-Benefit Imbalance*

There are many diseases and illnesses still plaguing the world for which there are no medicinal treatments.⁶⁶ In fact one could say “the ‘big cures’ have not been discovered [because] [n]eurological damage, . . . chronic heart failure, chronic obstructive pulmonary disease, many cancers, obesity and other chronic conditions have few or no treatment options.”⁶⁷ Furthermore, treatments for other diseases possess serious adverse side effects.⁶⁸ For example, 74% of persons who start taking antipsychotics for schizophrenia and bipolar mania quit taking the medication due to side effects.⁶⁹ Hence, there is much need for new treatments.

One major factor implicated in drug companies’ failure to develop needed treatments is the imbalance of risk and benefit.⁷⁰

63. U.S. CONST. art. I, § 8, cl. 8.

64. *Bilski*, 130 S. Ct. at 3252-53.

65. Shrestha, *supra* note 57.

66. Esther Schmid & Dennis Smith, *Pharmaceutical R&D in the Spotlight: Why Is There Still Unmet Medical Need?*, 12 DRUG DISC. TODAY 998, 998 (2007).

67. *Id.* at 998-99.

68. See Eric M. Snyder & Melanie Murphy, *Schizophrenia Therapy: Beyond Atypical Antipsychotics*, 7 NATURE REVIEWS DRUG DISC. 471, 471 (2008) (pointing out Zyprexa’s sideeffects).

69. *Id.* Schizophrenia affects 1% of the population and bipolar disorder affects 3% of the population. *Id.* Yet Zyprexa, “the most effective atypical antipsychotic on the market,” lost half its market share due to side effects. *Id.*

70. New drugs take about twelve to fifteen years and \$800 million to develop and get to market. *Frequently Asked Questions About Pharmaceutical Research*, GLAXOSMITHKLINE, <http://us.gsk.com/html/healthcare/health-care-common-questions.html> (last updated June 18, 2007). However, this drug was only one of a million compounds screened. *Id.* In 1995, only one in five drugs entering clinical trials entered the market. *Prescription Drug Costs*, KAISEREDU.ORG (Feb. 2010), <http://www.kaiseredu.org/Issue->

Legislation in the area of medicinal drugs affects both risk and benefit through F.D.A. regulation, patent grants and term, and promoting litigation.⁷¹ With the high unmet medical need for effective treatments, it is imperative that while the government

Modules/Prescription-Drug-Costs/Background-Brief.aspx; Di Masi & Joseph A., *Success Rates for New Drugs Entering Clinical Testing in the United States*, 58 CLINICAL PHARMACOLOGY AND THERAPEUTICS, 1 (1995). However by 2006 the success rate had dropped to one in ten. Zhao & Guo, *supra* note 59, at 516. Exemplifying the risk, between 1995 and 1999 fifty neuroprotective drugs were tested at a cost of “almost \$6 billion in clinical trial costs alone, without even counting the discovery and preclinical costs” and all failed to show efficacy. Schmid & Smith, *supra* note 66, at 998-99.

71. F.D.A. regulation has led to a “dramatic increase in costs” in the search for new drugs. Richard Cheung et al., *Orphan Drug Policies: Implications for the United States, Canada, and Developing Countries*, 12 HEALTH L. J. 183, 184 (2004). Drugs are regulated by the F.D.A. for both safety and efficacy. Food, Drug and Cosmetic Act, 21 U.S.C. § 355(a)-(b) (2012). Congress passed The Food, Drug, and Cosmetic Act of 1938 after 107 people died from a marketed toxic elixir. *Legislation*, U.S. FOOD AND DRUG ADMINISTRATION (Jul. 9, 2012), www.fda.gov/regulatoryinformation/legislation/default.htm. The Defauver-Harris Amendment of 1962, which requires drugs to be proven both safe and effective, was passed after the marketing of Thalidomide, a treatment for morning sickness, which caused the improper growth of fetuses. Cheung et al., *supra*, at 183-84; *Promoting Safe and Effective Drugs for 100 Years*, U.S. FOOD AND DRUG ADMINISTRATION (June 18, 2009), <http://www.fda.gov/AboutFDA/WhatWeDo/History/CentennialofFDA/CentennialEditionofFDAConsumer/ucm093787.htm>. The F.D.A. approval process costs between \$100 and \$500 million. Dennis Fernandez et al., *supra* note 6. Thus drug development is obstructed by legal requirements “for the very proper, laudable and desirable aim of making drugs as safe as possible.” Miles Weatherall, *Limitations on the Discovery and Supply of Medicines*, 67 PROC. ROYAL SOC. MED. 1287, 1288 (1974), <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1645783/pdf/procrsmed00313-0020.pdf>. There is no such thing as a perfectly safe drug, merely a statistical balance of risk. *Id.* at 1289. Instead the “[p]ublic demand for totally safe drugs has led to excessive, costly and misleading toxicity testing.” Miles Weatherall, *An End to the Search for New Drugs*, 296 NATURE 387, 387 (1982). This demand reduces the resources available to discover new drugs. *Id.* Further complicating the issue, the F.D.A. is more likely to deny market entry than allow entry in order to protect itself. *Limitations on the Discovery and Supply of Medicines, supra*, at 1289. The F.D.A. will get blamed if the drug has negative side effect, but if there is no drug then the public blames pharmaceutical companies. *Id.* Therefore, “we are wasting a large amount of labour and resources on collecting evidence which can only damn the drug and which will not add to its potential therapeutic use.” *Id.* The exclusivity period is expressly spelled out in the patent law. 35 U.S.C. § 154(a)(2). Historically the government extended the patent term for patent office and F.D.A. delays. 35 U.S.C. §§ 154(b)(1), 155. However, the patent will not be extended beyond fourteen years. Fernandez et al., *supra* note 6. The Hatch-Waxman Act actually *promotes litigation* by granting an exclusivity period to the first generic company to submit the first abbreviated new drug application (ANDA). Ashlee Mehl, Comment, *The Hatch-Waxman Act and Market Exclusivity for Generic Drug Manufacturers: an Entitlement or an Incentive?*, 81 CHI.-KENT L. REV. 649, 650 (2006).

strives to balance other social policies, it must also strive to uphold the constitutional mandate to promote medicinal progress.

B. Claiming Compounds by Structure Is a Loss to Society

Novelty is the quintessential requirement to obtain a patent.⁷² This requirement stems from an antiquated fear of misuse inherited from the English crown.⁷³ Consequently, the patent laws forbid composition-of-matter protection if “the invention was known or used . . . or patented or described in a printed publication . . . before the invention . . . by the applicant.”⁷⁴ Yet, when relating to chemical compositions, requiring novelty purely by chemical structure removes all incentive to develop known chemical entities and causes society to lose out on many small-molecule drugs.⁷⁵

1. Method Claims Are NOT the Answer

The 1952 Patent Act provided that a new method of use for an old invention could be patented, a “use patent.”⁷⁶ However, the scope of protection granted to a new use is less than that offered to a new composition of matter.⁷⁷ The risk associated with weakly-protected method of use patents is well recognized.⁷⁸

Due to this inherent risk companies may avoid investment in compounds protected only via method of use patents.⁷⁹ Weakness in method of use patents stems from case law and policy, enforcement problems, and easy work-arounds for would-be

72. 35 U.S.C. § 102.

73. See *John Deere*, 383 U.S. at 7 (stating the monopoly on tea “sparked” the Revolutionary War).

74. 35 U.S.C. § 102(a). An inventor can anticipate himself if “the invention was patented or described in a printed publication . . . or in public use or on sale . . . more than one year prior to the date of the application for patent.” 35 U.S.C. § 102(b). Even if the invention falls outside of § 102(a)-(b), the invention can be anticipated by an unpublished U.S. patent application. 35 U.S.C. 102(e).

75. *Supra* § III(B)(4)(c) and corresponding endnotes; see *The DCA Patents*, *supra* note 5 (discussing the difficulty to market a known compound).

76. See 35 U.S.C. § 100(b) (defining process as “process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material”).

77. Harold L. Marquis, *An Economic Analysis of the Patentability of Chemical Compounds*, 63 J. PAT. OFF. SOC'Y 3, 4 (1981).

78. See Phil Milford, *Pfizer Viagra Patent Ruled Valid by Judge in Loss for Teva*, BLOOMBERG BUSINESSWEEK (Aug. 15, 2011), <http://www.businessweek.com/news/2011-08-15/pfizer-viagra-patent-ruled-valid-by-judge-in-loss-for-teva.html> (voicing amazement that Pfizer's Viagra patent for treating impotence was held valid because method of use patents for small molecules usually “don't hold up that well in court”).

79. See *The DCA Patents*, *supra* note 5 (discussing the difficulty to market a known compound).

infringers. The court cases indicate either that the court disfavors method of use claims or that the claims are incredibly difficult to write.⁸⁰ Further, infringement is difficult to track because the “mere sale is not per se infringement.”⁸¹ Finally, because the base compound is not protected via a composition-of-matter patent, an infringer may avoid the patent by making different polymorphs.⁸² At bottom, because of the weak protection afforded a method of use patent, its benefit cannot balance the risk and cost of medicinal discovery.

2. *Prior Art by Structure Leads to Inefficient Use of Chemical Space*

A single published disclosure of an invention will prevent the inventor from obtaining a patent: the invention is anticipated.⁸³ For chemical entities, disclosure of a molecular structure will anticipate that structure.⁸⁴ But, disclosure of chemical entities occurs for many reasons other than their utility. For example, many compound structures are published for purely academic reasons, such as developing synthetic methodology, educational projects, synthetic dissertations, and unrepeatable disclosures caused by professors’ desperation to obtain tenure.⁸⁵

80. See *Sun Pharma. Indus. Ltd. v. Eli Lilly & Co.*, 611 F.3d 1381, 1389 (Fed. Cir. 2010) (invalidating a patent for a method of treating cancer with Gemzar).

81. MERGES & DUFFY, *supra* note 20, at 390. Tracking down users that infringe is incredibly expensive. *Id.* Additionally, other laws allow doctors to prescribe any “FDA approved drug for off label use.” *Id.*

82. See Sasha Coffiner, *Cephalon Settlemen with Generic Makers in Nuvigil Patent Suits Could Be Delayed by Ongoing Anti-Trust Litigation – Experts*, PHARMAWIRE (May 19, 2010) http://www.wolfgreenfield.com/files/cephalon_article_pdf.pdf (pointing out that generic manufacturers may work around the patent by making a different polymorph because there is not a composition-of-matter claim).

83. See 35 U.S.C. § 102(a) (stating inventions that are patented or published by another cannot be patented); see also 35 U.S.C. § 102(b) (stating an inventor’s own publication may anticipate); 35 U.S.C. § 102(e) (stating unpublished U.S. patent applications will anticipate later inventions).

84. See *Sun Pharma. Indus. Ltd.*, 611 F.3d at 1389 (ruling that the claim was anticipated by an earlier disclosure of the compound structure).

85. See generally Jason Brewer et al., *A Systematic Study of the Relationship Between Molecular and Crystal Structure Among 3,5-Diazabicyclo[2.2.2]octane-2,6-diones*, 4 CRYSTAL GROWTH AND DESIGN, 591 (2004), http://www.chem.uky.edu/xray/people_documents/parkin/Parkin_Papers_pdfs/93_CGDv4n3p591.pdf (showing my undergraduate synthetic work, where the major purpose was to obtain synthetic experience); see generally Ronald Have et al., *Novel Synthesis of 4(5)-Monosubstituted Imidazoles via Cycloaddition of Tosylmethyl Isocyanide to Aldimines*, 53 TETRAHEDRON 11355 (1997) (teaching a method to synthesize imidazoles, not a use for the compounds synthesized); see also Asher Mullard, *Reliability of ‘New Drug Target’ Claims Called into Question*, 10 NATURE R. DRUG DISCOVERY 643, 643 (2011); and John P. A. Ioannidis, *Why Most*

Another major form of disclosure includes patents and patent applications.⁸⁶ Markush claims allow inventors to make claims in the alternative.⁸⁷ For example, one part of the compound may be “selected from the group consisting of A, B and C.”⁸⁸ Notably, chemical composition-of-matter patents claim millions or billions of compounds through the use of Markush claims.⁸⁹

Simply, Markush claims are wasteful. Because the claim protects the invention, which is the concept, often the inventor never synthesizes or reduces to practice the majority of the claimed compounds.⁹⁰ Thus, the product itself is never really given to society. But, by utilizing Markush claims the inventor increases the protection surrounding his invention.⁹¹ Thus, this incentive causes inventors to claim too broadly.⁹² Although one may argue that a Markush claim *may* not completely prevent a patent on a specific species,⁹³ the fact remains that companies will avoid the

Published Research Findings are False, 2 PLOS MEDICINE 696, 696 (2005), available at <http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.0020124> (pointing out that the majority of published research data is false).

86. See 35 U.S.C. § 102(a), (e) (stating printed publications and unpublished patent applications will anticipate later inventions).

87. *Id.*; see generally *Ex Parte* Markush, 1925 C.D. 126 (Comm'r Pat. 1925) (discussing alternative claims).

88. *Markush Claims*, 803.02 MANUAL OF PATENT EXAMINING PROCEDURE R5, available at http://www.zpatents.com/mpep/documents/0800_803_02.htm.

89. Steve Gardner & Andy Vinter, *Beyond Markush – Protecting Activity not Chemical Structure*, 1 [http://www.cresset-group.com/publications/Beyond_Markush .pdf](http://www.cresset-group.com/publications/Beyond_Markush.pdf) (last visited Sept. 25, 2012).

90. See *Telephone Cases*, 8 S. Ct. at 782-783; *Pfaff*, 525 U.S. at 60; *Alexander Milburn Co.*, 270 U.S. at 402 (1926) (each showing that the invention is the concept and reduction to practice is not necessary for a patent); see generally PCT Patent App. No. 2010/124042 (filed Apr. 23, 2009); U.S. Patent No. 5,559,111 (filed Apr. 4, 1995); U.S. Patent No. 7,109,205 (filed June 24, 2003); U.S. Patent No. 8,256,346 (filed Nov. 3, 1994); U.S. Patent 5,223,510 (filed July 26, 1991); U.S. Patent No. 7,160,870 (filed May 24, 2001); U.S. Patent No. 7,101,866 (filed Aug. 3, 2001); U.S. RE38,551 (filed Jan. 28, 2002); PCT Patent App. No. 2010/124042 (filed Apr. 23, 2009) (each showing most of the Markush claimed compounds do not appear in the examples).

91. See 35 U.S.C. § 102 (stating an invention is not patentable if it is not novel; see also 35 U.S.C. § 103 (stating an invention is not patentable if it is an obvious variation of another invention)).

92. See generally PCT Patent App. No. 2010/124042 (filed Apr. 23, 2009); U.S. Patent No. 5,559,111 (filed Apr. 4, 1995); U.S. Patent No. 7,109,205 (filed June 24, 2003); U.S. Patent No. 8,256,346 (filed Nov. 3, 1994); U.S. Patent 5,223,510 (filed July 26, 1991); U.S. Patent No. 7,160,870 (filed May 24, 2001); U.S. Patent No. 7,101,866 (filed Aug. 3, 2001); U.S. RE38,551 (filed Jan. 28, 2002); PCT Patent App. No. 2010/124042 (filed Apr. 23, 2009) (each showing the breadth of Markush claiming beyond the reduced to practiced molecules).

93. See *Appl. of Petering*, 301 F.2d 676 (Fed. Cir. 1962) (creating the genus-species test by ruling that only the members of a genus that the inventor could “at once envisage” would be precluded from further patenting). This test remains in use today. See *Sanofi-Synthelabo*, 550 F.3d at 1084; *Eli*

risk associated with Markush anticipation, and avoid Markush claimed compounds.

As shown, many *non-useful* disclosures of chemical structures exist. These disclosures may comprise unrepeatable academic expenditures or broadened protection through Markush claiming.⁹⁴ Unfortunately, these nonuseful structural disclosures remove the molecules cited from composition-of-matter patentable space and remove the incentive for pharmaceutical companies to develop them.⁹⁵

3. Medicinal Chemical Space Is Finite

Different chemical structures possess different chemical properties. Some structures have been identified as possessing favored properties in medicinal drugs.⁹⁶ These compounds have been labeled “privileged structures.”⁹⁷ Because of previous work, there now exists very little patentable space around these biologically favored compounds.⁹⁸

Other compounds have been shown to be limited by their physicochemical properties.⁹⁹ Some of these properties include the number of hydrogen bond donors or acceptors, molecular weight, lipophilicity, and polar surface area.¹⁰⁰ According to Lipinski’s

Lilly & Co. v. Zenith Goldline Pharms., Inc., 471 F.3d 1369, 1376 (Fed. Cir. 2006) (citing *Appl. of Petering*).

94. Ioannidis, *supra* note 85; Mullard, *supra* note 85; *Markush Claims*, *supra* note 88; U.S. Patent No. 7,160,870 (filed May 24, 2001); U.S. Patent No. 7,101,866 (filed Aug. 3, 2001).

95. 35 U.S.C. § 102(a)-(b), (e).

96. R.W. DeSimone et al., *Privileged Structures: Applications in Drug Discovery*, 7 COMBINATORIAL CHEMISTRY & HIGH THROUGHPUT SCREENING 473, 473 (2004).

97. *Id.* “[P]rivileged structures are molecular scaffolds with versatile binding properties, such that a single scaffold is able to provide potent and selective ligands for a range of different biological targets through modification of functional groups.” *Id.* Privileged structures “generally contain two or three ring systems connected by single bonds or by ring fusion.” *Id.* at 474. For example, purines have been used in anticancer, antibiotic, antifungal and antiviral therapeutics. *Id.* at 477. 1,4-Dihydropyridines have also exhibited activity across a variety of receptors. *Id.* at 478. Additionally, indoles are “richly represented in marketed drugs.” *Id.* at 479. A few other examples include spiroperidines, benzimidazoles, benzofurans, and benzopyrans. *Id.* at 482-487.

98. *See generally* DeSimone et al., *supra* note 96 (citing a few examples of privileged structures in multiple drug compounds).

99. *See* M.A. Navia & P.R. Chaturvedi, *Design Principles for Orally Bioavailable Drugs*, 1 DRUG. DISC. TODAY 179, 181 (1996) (discussing availability of compound designs); W.M. Pardridge, *Transport of Small Molecules Through the Blood-brain Barrier: Biology and Methodology*, 15 ADVANCED DRUG DELIVERY REV. 5, 12 (1995) (indicating that high molecular weight limits intestinal and blood brain barrier permeability).

100. Christopher A. Lipinski et al., *Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and*

“rule of 5,” “poor absorption or permeability are more likely when” a compound’s molecular weight is “over 500,” the “LogP is over 5,” and there are more than ten hydrogen bond donors.¹⁰¹ A combination of two of these factors showed a less than 10% chance for the compound to enter clinical trials.¹⁰² Additionally, in a recent Pfizer paper, cLogP and polar surface area were correlated with toxicity.¹⁰³ In short, the correlation between physicochemical properties and successful drugs limits medicinal chemical space.¹⁰⁴

4. *Historic and Current Policies Support Expanding the Novelty Requirement for Medicinal Drugs*

The Constitution granted Congress the power “[to] promote the Progress of Science and useful Arts” through the patent system.¹⁰⁵ Congress then created the novelty requirement as protection from abuses of monopolies similar to those of the English Crown.¹⁰⁶ However, there have been exceptions to the novelty rule.

a. *The Doctrine of Accidental Anticipation Supports Patenting Useful Productions of Prior Art*

The Supreme Court of the United States created the doctrine of accidental anticipation. The doctrine provides an exception to the novelty requirement. The doctrine provides that it would be “absurd” for an accidental and unnoticed production of an invention to prevent patentability because the accidental production gave nothing to the world.¹⁰⁷ Case law provides several examples of the doctrine in chemical cases.

Examples include *Tilghman v. Proctor*¹⁰⁸ and *Application of Seaborg*.¹⁰⁹ In *Tilghman*, the Supreme Court held that the accidental production of glycerin and amino acids from the lubricant in a steam cylinder did not anticipate an understood process for producing glycerin and amino acids.¹¹⁰ Similarly, in *Seaborg*, the Court validated a patent even though the isotope may have been produced in minute, undetectable quantities via a

Development Settings, 46 ADVANCED DRUG DELIVERY REV. 3, 6-7 (2001); Jason Hughes et al., *Physicochemical Drug Properties Associated with In Vivo Toxicological Outcomes*, 18 BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 4872, 4872 (2008).

101. Lipinski et al., *supra* note 100, at 9.

102. *Id.*

103. Hughes et al., *supra* note 100, at 4875.

104. *Id.*

105. U.S. CONST. art. I, § 8, cl. 8.

106. *John Deere*, 383 U.S. at 7.

107. *Tilghman*, 102 U.S. at 711-12.

108. *Id.* at 707.

109. *Appl. of Seaborg*, 328 F.2d 996.

110. *Id.*

known process.¹¹¹ So a mere *unusable* previous production in the chemical arts does not necessarily anticipate a latter *useful* production.

b. In an Obvious Analysis, Chemical Properties Are the Patentable Invention

The nonobvious requirement expands the novelty requirement, allowing the combination of elements from multiple disclosures.¹¹² However, when patenting chemical compounds, structural similarity supports only a prima facie case of obviousness, and shifts the burden of proof to the applicant to show that the compound possesses unexpected, nonobvious, improved properties.¹¹³ If a compound does possess an unexpected property, then the compound is patentable.¹¹⁴ Interestingly, in *Application of Stemniski*,¹¹⁵ Stemniski did not even bear the burden of proving unexpected differences because the prior art did not show a significant use or property.¹¹⁶ The *Stemniski* court reasoned that allowing the patent would promote progress.¹¹⁷ Thus, courts have recognized that the properties and uses of chemical compounds are the actual patentable invention, not the molecular structure.

C. The Novelty Requirement Will Stifle Medicinal Progress

The patent system should promote innovation to cure the unmet medical need. But instead, the current system will stifle future drug discovery. Method of use patents do not offer strong enough protection to support the huge financial burden associated

111. *Appl. of Seaborg*, 328 F.2d at 998.

112. See 35 U.S.C. § 103(a) (stating that an invention is obvious “if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains”); see also *Appl. of Winslow*, 365 F.2d at 1018-20 (combining multiple references to find the invention not patentable).

113. See *In re Grabiak*, 769 F.2d at 731 (finding no prima facie case because prior art did not teach similarity between a thioester and an ester group); see also *Appl. of Wilder*, 563 F.2d at 459-60 (finding prima facie case of obviousness for adjacent homologs and structural isomers); see also *Appl. of May*, 574 F.2d at 1089 (finding a prima facie case of obviousness for stereoisomers); see also *In re Hoch*, 428 F.2d at 1342 (finding a prima facie case for an acid and an ethyl ester).

114. See *Sanofi-Synthelabo*, 550 F.3d at 1077, 1090 (finding the dextrotary enantiomer of clopidogrel, Plavix, nonobvious due to unexpected potency and a preferable toxicity profile); see also *Appl. of May*, 574 F.2d at 1084, 1093-94 (concluding that the lack of the addictive effect of a morphine analog enantiomer was unexpected and nonobvious).

115. *Appl. of Stemniski*, 444 F.2d 581 (Fed. Cir. 1971).

116. *Id.* at 588.

117. *Id.*

with drug discovery.¹¹⁸ The novelty requirement precludes many compounds of interest due to the expansive prior art, including prophetic Markush claims.¹¹⁹ Physicochemical properties and privileged structures further limit the medicinal chemical space.¹²⁰ Thus, current patent novelty requirements do not promote progress of small-molecule medications due to extremely inefficient use of the finite medicinal chemical space.

Some courts have recognized this fatal flaw in the patent system. The Supreme Court's accidental anticipation doctrine recognizes the absurdity of placing unrecognized inventions within the prior art.¹²¹ Obviousness cases have recognized that the properties of a compound are the patentable feature.¹²² Thus, the combination of the *absurdity of removing compounds with unrecognized properties* from the patentable pool with the fact that *chemical properties are the patentable invention* indicates a supreme failure of current patent law to promote small-molecule medicinal progress.

IV. ALTERNATIVES TO NOVELTY EXCLUSION VIA STRUCTURE

Drug companies are crumbling under the current patent regime.¹²³ The patent novelty requirement bears a portion of the blame.¹²⁴ The first Congress included the novelty requirement in the Patent Act because it feared removal of inventions from the

118. *Supra* § III(B)(1) (explaining why method claims are not the answer).

119. *Supra* § III(B)(2) (showing that prior art by structure leads to inefficient use of chemical space).

120. *Supra* § III(B)(3) (pointing out that medicinal chemical space is finite).

121. *Tilghman*, 102 U.S. at 711-12.

122. *Supra* § III(B)(4)(b) (pointing out that obviousness recognizes chemical properties as the patentable invention).

123. See Jim Edwards, *Yes, There Will be More Layoffs at Pfizer, as These Numbers Show*, CBS MONEY WATCH (June 8, 2011, 12:12 PM), http://www.cbsnews.com/8301-505123_162-42848659/yes-there-will-be-more-layoffs-at-pfizer-as-these-numbers-show/?tag=bnetdomain (predicting goliath pharmaceutical company Pfizer's action to become more efficient and pointing out that Pfizer laid off nearly 20,000 people in 2009 after acquiring Wyeth, another pharmaceutical company); see also Frank Jordans, *Novartis Pharmaceutical Giant Plans 2,000 Layoffs Despite Profit Increase*, HUFFINGTON POST BUS. (Oct. 25, 2011, 7:53 AM), http://www.huffingtonpost.com/2011/10/25/novartis-layoffs-profit_n_1030137.html (telling of Novartis' plan to cut jobs in the wake of price pressures); see also Tracy Staton, *Layoffs Return with Abbott's 3,000 Job Cuts*, FIERCEPHARMA (Sept. 22, 2010), <http://www.fiercepharma.com/story/layoffs-return-abbotts-3-000-job-cuts/2010-09-22> (reporting that Abbot Laboratories will cut three thousand jobs after acquiring Solvay). Maureen Martino, *Roche Plots Layoffs as it Focuses on R&D*, FIERCEBIOTECH (Sept. 3, 2010), <http://www.fiercebiotech.com/story/roche-plots-layoffs-it-focuses-r-d/2010-09-03> (indicating that Roche plans to cut jobs).

124. 35 U.S.C. § 102.

public.¹²⁵ Unfortunately, Congress failed to see the stifling effect of the novelty requirement on medical progress. This failure occurred primarily because today's technology driven medicinal chemical arts were not practiced or understood when Congress passed the initial Patent Act.¹²⁶ Yet, Congress still has not recognized the novelty problem associate with drug discovery. Simply put, small-molecule medicinal research is: (1) extremely costly;¹²⁷ (2) limited via chemical properties to a finite number of compounds;¹²⁸ and (3) prevented from efficiently utilizing the finite number of compounds with drug-like chemical properties because the novelty requirement prevents composition-of-matter protection that could balance the risk of development.¹²⁹ This wasteful practice must stop. Patent law should be reformed to promote the development of known small-molecule drugs.

There are at least three options that will provide incentive to develop known small molecules into medicines. These options include: (A) amending the current patent laws; (B) providing a simple common law fix; and/or (C) providing incentive for the development of new drugs outside of the current patent law.

A. Amending the Patent Laws to Promote Progress

The Constitution affords Congress the power to grant monopolies to promote progress, and thus the power to amend the current patent law to promote progress.¹³⁰ Specifically, two laws may be amended to provide composition-of-matter protection for known chemical entities with new medicinal uses. These laws include (1) 35 U.S.C. § 101 and (2) 35 U.S.C. § 102. These statutes should be amended to provide incentive to research compounds that are known in the literature, but are not in use.

125. 1 Stat. 109; MERGES & DUFFY, *supra* note 20; *see John Deere*, 383 U.S. at 7 (noting that tea was removed from the colonial public). However, the 1952 Act attempted to remedy the situation by allowing patents for new uses. *See* 35 U.S.C. § 100(b) (including a "new use for a known process" in the definition of process). Unfortunately, the attempt failed to act as an incentive because of the weak protection afforded method of use patents. Milford, *supra* note 78.

126. *Compare* 1 Stat. 109 (dating back to 1790) *with* Ho, *supra* note 1 (indicating penicillin was not discovered until 1928).

127. *See* Fernandez et al., *supra* note 6; (stating that the F.D.A. requisite clinical trials alone can cost up to \$500 million); *see also Global Pharmaceutical R&D Productivity Declining According to Thomson Reuters, CMR International*, *supra* note 6 (stating that only ten percent of new drug clinical candidates are marketed).

128. Lipinski et al., *supra* note 100, at 9; Hughes et al., *supra* note 100, at 4875; DeSimone et al., *supra* note 96; *supra* § II(B)(3).

129. *Supra* § II(B)(2).

130. U.S. CONST. art. I, § 8, cl. 8; *See generally* Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (showing Congress's willingness to pass new patent legislation).

1. Amending 35 U.S.C. § 101¹³¹

Similar to the 1952 attempt to broaden the patentable inventions, Congress may expand patent protection by amending 35 U.S.C. § 101.¹³² To promote patent protection for known small molecules with an F.D.A. approved use, the following should be added to the statute:¹³³

Additionally, a known, non-commercialized chemical compound, with a new F.D.A. approved use, that is not in public use, may obtain composition-of-matter protection.

The amendment would protect against the abuse of removing more than necessary from the public. In requiring F.D.A. approval for the provision to apply, the amendment will limit the expansion to medicinal chemical compounds, preventing chemical entities without F.D.A. approval and with less expensive development costs from public removal.¹³⁴ Additionally, the limitation of “non-commercialized” and “not in public use” will prevent the removal of compounds that are currently sold or in use.¹³⁵

131. See 35 U.S.C. § 100(b) (amending the definition of process to include a “new use for a known process”).

132. *Id.*

133. Thus the entire statute will read: “Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.” *Additionally, a known, noncommercialized chemical compound with a new F.D.A. approved use, that is not in public use, may obtain composition-of-matter protection.* 35 U.S.C. § 101 (suggested amendment emphasized).

134. See Food, Drug and Cosmetic Act, 21 U.S.C. § 355(a)-(b) (2011) (ordering that drugs must be shown to be both safe and effective before entering the market); F.D.A. regulation led to a “dramatic increase in costs” in the search for new drugs. Cheung et al., *supra* note 71. Now new drugs take about 12 to 15 years and \$800 million to get to market. *Frequently Asked Questions About Pharmaceutical Research*, *supra* note 70. Thus, allowing a patent on a known unused compound will not be like removing tea, a plant, from the market. See *John Deere*, 383 U.S. at 7 (stating that the monopoly on tea sparked the Revolutionary War).

135. See *Bilski*, 130 S. Ct. at 3252-53 (quoting *Bonito Boats Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, (1989), stating patent laws must find a “careful balance between the need to promote innovation” and allowing the public to use and perfect the invention “for the lifeblood of a competitive economy”).

2. Amending 35 U.S.C. § 102¹³⁶

35 U.S.C. § 102 is the patent law novelty provision. Currently the invention is anticipated if, it was known, used, patented or published prior to invention by the applicant.¹³⁷ To protect known small molecules with an F.D.A. approved use the following should be added to the statute:¹³⁸

A person shall be entitled to a patent unless . . . (h) In regard to known chemical compounds with a new F.D.A. approved use, the compound is currently in public use or commercialized.

The limitations included in the § 102 amendment resemble those suggested in the § 101 amendment. The limitation of “F.D.A. approved use” again limits the exception to medicinal compounds, and the limits of “public use” and “commercialized” prevents removal of currently used chemical compounds from the public.¹³⁹

B. A Simple Common Law Fix

A simple interpretation of the common law may provide the protection necessary for known small molecules with a new medicinal use. Obviousness expanded the novelty requirement by allowing the combination of elements from multiple disclosures.¹⁴⁰ However, a prima facie obviousness analysis will be defeated if a compound shows unexpected properties.¹⁴¹ Thus, a compound’s

136. The important parts of 35 U.S.C. § 102 for this discussion state:

A person shall be entitled to a patent unless—

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or

(b) the invention was patented or described in a printed publication 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, or . . .

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent. . . .

35 U.S.C. § 102(a)-(b), (e).

137. *Id.*

138. *See id.* (beginning “a person shall be entitled to a patent unless— . . .”).

139. *See Bilski*, 130 S. Ct. at 3252-53 (discussing the balance between innovation and public use).

140. *See Appl. of Winslow*, 365 F.2d at 1018-19 (combining multiple references to find the invention not patentable).

141. *See In re Grabiak*, 769 F.2d at 731 (finding no prima facie case because prior art did not teach similarity between a thioester and an ester group); *see*

properties are elements.

Recognizing a compound's properties as elements will deliver many compounds from anticipation. Under the case law interpretation of 35 U.S.C. § 102 a single disclosure must contain each and every element of the invention to anticipate another invention.¹⁴² Thus, if properties are determined to be elements, a compound is only anticipated if the disclosure describes the chemical structure and the compound's properties of interest.

At first glance this interpretation seems to cause inherent conflicts within § 102.¹⁴³ Under 35 U.S.C. § 102 an invention is anticipated if, it was known, used, patented, or published prior to invention by the applicant.¹⁴⁴ However, the elemental analysis proposed easily dodges the known and published prior art because *the properties are not known or described*. Of course, the use or patented limitations require interpretation.

A simple interpretation of "use" and "patented" can protect all parties, providing incentive to perform drug research and preventing unnecessary removal of inventions from the public.¹⁴⁵ Note, the public cannot use the compound as a medicine without F.D.A. approval.¹⁴⁶ So, without F.D.A. approval the public did not lose use of a drug. Further, the "use" limitation shall prevent composition-of-matter protection if the compound is commercially produced, or publicly used. Likewise, a new compound cannot supersede current patent claims.¹⁴⁷ However, under this interpretation if the compound is claimed for a *new property*, and the compound is not currently commercially produced, a new inventor may *re-patent* the compound with full composition-of-matter protection *after* the prior patent expires. Thus, this interpretation provides incentive to scientists to research known small molecules and promotes small-molecule medicinal progress.

C. A New Medicinal Innovation Act

Congress has used the monopoly power outside of patent law. Examples include the 180-day exclusivity in the Hatch-Waxman

also Appl. of Wilder, 563 F.2d at 459-60 (finding prima facie case of obviousness for adjacent homologs and structural isomers); *see also In re May*, 574 F.2d at 1089-90 (finding a prima facie case of obviousness for stereoisomers); *see also In re Hoch*, 428 F.2d at 1342 (finding a prima facie case for acid and ethyl ester).

142. *Hoover Grp. Inc.*, 66 F.3d at 302; *Structural Rubber Prod. Co.*, 749 F.2d at 716; *Scripps Clinic & Research Found.*, 927 F.2d at 1576.

143. *See generally* 35 U.S.C. § 102(a)-(c) (2011).

144. *Id.*

145. *See Bilski*, 130 S. Ct. at 3252-53 (discussing the balance between innovation and public use).

146. 21 U.S.C. § 355(a)-(b).

147. 35 U.S.C. § 102(a), (e).

Act¹⁴⁸ and F.D.A. granted exclusivity, such as The Orphan Drug Act.¹⁴⁹

Likewise, Congress may provide incentive to discover medical properties of known small molecules by enacting a New Medicinal Innovation Act. The act must possess: (1) a fourteen to seventeen year composition-of-matter exclusivity term, with the exclusivity term beginning after F.D.A. approval;¹⁵⁰ and (2) complete composition-of-matter protection if the compound is not produced commercially or publicly used. The removal of small-molecule medicines from the current novelty via chemical structure regime will promote small-molecule medicinal progress.

V. CONCLUSION

In conclusion, the current patent system fails to efficiently utilize the medicinal chemical space and to promote progress.¹⁵¹ The novelty provision prevents development of compounds known

148. Mehl, *supra* note 71.

149. See Michael Dunn, *Timing of Patent Filing and Market Exclusivity*, 10 NATURE REVIEWS DRUG DISC. 487, 487 (2011) (explaining that the F.D.A. “provides 5 years [exclusivity] for a new chemical entity (NCE), 3 years for a new formulation . . . and 7 years for an orphan drug”); see also Randy Osborne, *Brand Biologics Grab 12 Years’ Exclusivity, for Now*, 27 NATURE BIOTECHNOLOGY 677, 677 (2009) (noting twelve years data exclusivity for biologic drugs).

“The Orphan Drug Act (ODA) has been recognized as one of the most successful US legislative actions in recent history.” Marlene E. Haffner et al., *Two Decades of Orphan Product Development*, 1 NATURE REVIEWS DRUG DISC. 821, 821 (2002). Prior to the Act few companies worked on rare diseases because the small market could not balance the cost of drug development. *Id.* The ODA’s purpose is to “stimulate the development of drugs . . . for the treatment of rare diseases.” *Id.* The legislation offers drug developers a number of incentives including seven years of market exclusivity. Cheung et al., *supra* note 71, at 185. Unlike the exclusivity provided via patents, the ODA’s exclusivity does not initiate until the F.D.A. grants approval. *Id.* In addition, the F.D.A. may not admit another orphan drug for the rare disease for the seven-year period. *Id.* “Orphan exclusivity is often considered to be a more comprehensive incentive than a patent” because there are not novelty or obviousness requirements and the exclusivity begins at approval, not application. Haffner et al., *supra*, at 822-23. Other countries, including Japan and the EU, followed suit, passing ODA like legislation. Cheung et al., *supra* note 71, at 188.

150. See 35 U.S.C. § 154(a)(2) (granting patent protection for up to twenty years after filing a patent application); see also 35 U.S.C. § 154(b)(1)(B) (extending patent life for patent office delays beyond three years, leaving a seventeen year patent term); see also Dunn, *supra* note 146, at 488 (indicating that the Hatch-Waxman Act limits patent term extensions to a maximum of fourteen years); see also Cheung et al., *supra* 71, at 185 (noting the exclusivity of The Orphan Drug Act initiates post F.D.A. approval).

151. See *supra* § III and corresponding endnotes (showing that the novelty requirement stifles medicinal progress).

but never used.¹⁵² Simply, prior art via chemical structure instead of chemical properties is wasteful¹⁵³ because it pushes research away from compounds with drug-like properties.¹⁵⁴

Three propositions to promote medicinal progress are included in this Comment. The propositions include: (1) amending 35 U.S.C. § 101 and/or § 102; (2) providing a common law interpretation where courts must include a compound's properties in the invention's elements when determining anticipation; or (3) drafting new legislation that provides exclusivity and composition-of-matter protection for new drugs developed from known small molecules. If adopted, any of these proposals will promote small-molecule medicinal progress.

152. *See supra* § III(B)(2) and corresponding endnotes (declaring prior art by chemical structure leads to inefficient use of chemical space).

153. *Id.*

154. *See supra* § III(B)(3) and corresponding endnotes (showing that medicinal chemical space is finite).

