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FEDERAL CIRCUIT'S OBVIOUSNESS TEST FOR NEW PHARMACEUTICAL COMPOUNDS: GOBBLEDYGOOK?

DOUGLAS L. ROGERS*

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FEDERAL CIRCUIT'S OBVIOUSNESS TEST FOR NEW
PHARMACEUTICAL COMPOUNDS: GOBBLEDYGOOK?

Justice Scalia: "This is gobbledeygook. It really is, it's irrational." (Referring in 2007 during oral argument to the Federal Circuit's teaching, suggestion, motivation test to determine obviousness)¹

I. INTRODUCTION

In order to obtain a U.S. patent, an invention must not have been obvious to a person having ordinary skill in the art ("PHOSITA") at the time of the invention.² PHOSITA is not a real person, but a legal benchmark to use in determining whether an invention was obvious, much like the rea-

1. Transcript of Oral Argument at 41, *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2006) (No. 04-1350) [hereinafter Transcript]. Merriam Webster's online dictionary provides the following definition of "gobbledeygook:" "speech or writing that is complicated and difficult to understand." See gobbledeygook, MERRIAM-WEBSTER, <http://www.merriam-webster.com/dictionary/gobbledeygook> (last visited May 26, 2014).

2. The Leahy-Smith America Invents Act, Pub. L. No. 112-29, § 3(n), 125 Stat. 284, 293 (2011) (codified as amended in scattered sections of 35 U.S.C.), ("AIA") changed the date for determining obviousness or lack of obviousness from the date of the invention to the effective filing date of the patent claim for applications filed on and after March 16, 2013. See 2 DONALD S. CHISUM, CHISUM ON PATENTS §5.01 [hereinafter CHISUM ON PATENTS],

sonable man/person in tort law.³ Many scholars refer to obviousness as the fundamental gatekeeping requirement of patent law.⁴ The standard for obviousness determines how different an invention must be from “prior art” to obtain a patent.⁵ Starting as a judge-made concept in the 1800’s,⁶ Congress established obviousness as a statutory requirement in 1952 by adopting 35 U.S.C. § 103 (hereinafter “§ 103”), but obviousness has always been controversial.⁷

In 1966, the Supreme Court decided *Graham v. John Deere*, its first decision interpreting the obviousness statute.⁸ The Court held, “Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined.”⁹ In addition, the Court added, “Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. As indicia of obviousness or nonobviousness, these inquiries may have relevancy.”¹⁰

3. See Michael Abramowicz & John F. Duffy, *The Inducement Standard of Patentability*, 120 YALE L.J. 1590, 1605 (2011) [hereinafter *Inducement Standard*].

4. See, e.g., Robert P. Merges, *Commercial Success and Patent Standards: Economic Perspectives On Innovation*, 76 CALIF. L. REV. 803, 812 (1988) [hereinafter *Commercial Success*] (calling obviousness the “ultimate condition of patentability” and citing NONOBVIOUSNESS—THE ULTIMATE CONDITION OF PATENTABILITY, 5:101-5:111 (J. Witherspoon ed. 1980)); See also Mark D. Janis, *Tuning The Obviousness Inquiry After KSR*, 7 WASH. J. L. TECH. & ARTS 335, 336 (2012) [hereinafter *Tuning*] (“The obviousness doctrine is rightly considered one of the most crucial legal innovations in patent jurisprudence.”).

5. See Rebecca S. Eisenberg, *Pharma’s Nonobvious Problem*, 12 LEWIS & CLARK L. REV. 375, 381 (2008) [hereinafter *Nonobvious Problem*]; See also Jeanne C. Fromer, *The Layers of Obviousness in Patent Law*, 22 HARV. J.L. & TECH. 75, 76 (2008) (nonobviousness “requires that an invention represent a significant technological or scientific breakthrough compared to what is already known or doable”). § 103 does not define “prior art,” but the sources most often relied upon to show obviousness under § 103 have been those mentioned in § 102(a) (requiring that an invention be novel), such as patents and printed publications. See *infra* note 94 and JANICE M. MUELLER, PATENT LAW 284–93 (Wolters Kluwer Law and Business, 4th ed. 2013) 284–293 [hereinafter PATENT LAW]. However, other subsections of pre-AIA § 102 have also been the sources of prior art for determining if an invention was obvious. 2 CHISUM ON PATENTS, *supra* note 2, at §5.03[3]. Unless noted, in this article references to the patent statute refer to the pre-AIA versions of that statute.

6. For a history of the judge-made doctrine of obviousness, see 2 CHISUM ON PATENTS, *supra* note 2 at §5.02[1]–[3]; see also John F. Duffy, *Inventing Invention: A Case Study of Legal Innovation*, 86 TEX. L. REV. 1, 39–43 (2007) [hereinafter *Case Study*].

7. For a history of the passage of § 103, see CHISUM ON PATENTS, *supra* note 2 at §5.02[4]; see also *Case Study*, *supra* note 6, at 34–39. For a history of the predecessors to § 103 from 1790 through 1836, see *infra*, note 30.

8. *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1 (1966). See *infra* Part II of this article for a more detailed discussion of *Graham*.

9. *Graham*, 383 U.S. at 17.

10. *Id.* at 17–18. In *Graham*, the Supreme Court cited one law journal article on secondary considerations, Richard L. Robbins, *Subtests Of Nonobviousness: A Nontechnical Approach To Patent Validity*, 112 U. PA. L. REV. 1169 (1964) [hereinafter *Subtests*]. *Graham*, 383 U.S. at 18. The subtests

To implement this obviousness standard prior to 2007, the Federal Circuit¹¹ generally ruled that prior art had to teach, suggest or motivate PHOSITA (the “teaching, suggestion, motivation” or “TSM” test) to combine elements of prior art references before a court would hold the invention obvious.¹² However, during a 2007 oral argument before the Supreme Court, *KSR International Co. v. Teleflex, Inc.*, Justice Scalia referred to this test as “gobbledygook.”¹³ Earlier in the same argument, Chief Justice Roberts said, referring to the same test, “it seems to me that it’s worse than meaningless because it complicates the inquiry rather than focusing on the statute.”¹⁴ In its unanimous decision,¹⁵ discussed below in Part II–C, the Court in 2007 rejected the rigid application of the teaching, suggestion, motivation test and increased the likelihood that inventions would be found obvious.¹⁶ Professor Miller said then that it was “plain that, for the Su-

suggested by that article were long felt demand, commercial success, commercial acquiescence, simultaneous solution, professional approval and progress through the Patent Office. *Subtests*, at 117–18. The article emphasized the non-technical nature of these subtests. *Id.* at 1171–72. The Federal Circuit subsequently took the position that when secondary considerations are present, the court must take those into account. See Robert W. Harris, *The Emerging Primacy of Secondary Considerations as Validity Ammunition: Has the Federal Circuit Gone Too Far?* 71 J. PAT. & TRADEMARK OFF. SOC’Y 185, 189 (1989). A detailed analysis of secondary considerations is beyond the scope of this article. For more detailed discussions of secondary considerations, see *Commercial Success*, *supra* note 4 at 816–32; PATENT LAW, *supra* note 5, at 297–302; and 2 CHISUM ON PATENTS, *supra* note 2, at §5.05.

11. The Federal Circuit was created in 1982 by a “merger” of the U.S. Court of Claims and the Court of Customs and Patent Appeals. WILLIAM M. LANDES & RICHARD A. POSNER, *THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW*, 334 (The Belknap Press of Harvard University Press, 2003) [hereinafter *ECONOMIC STRUCTURE*]. Professor Landes and Judge Posner assert, “The Federal Circuit has indeed turned out to be a pro-patent court in comparison to the average of the regional courts that it displaced in the patent domain.” *Id.* at 335.

12. The Supreme Court said that under the TSM test, “a patent claim is only proved obvious if ‘some motivation or suggestion to combine the prior art teachings’ can be found in the prior art, the nature of the problem, or the knowledge of a person having ordinary skill in the art” (quoting in part *AI-Site Corp. v. VSI Int’l, Inc.*, 174 F.3d 1308, 1323–24 (Fed. Cir. 1999)). *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 407 (2006). Professor Underweiser argued, “The Federal Circuit’s strict application of the TSM test essentially reduced the test for obviousness to the test for novelty when all the elements of a claimed invention could be found in the prior art, since instructions for putting the pieces together needed to be found in the prior art as well.” Marian Underweiser, *Presumed Obvious: How KSR Redefines The Obviousness Inquiry To Help Improve The Public Record Of A Patent*, 50 IDEA 247, 258 (2010) [hereinafter *Presumed Obvious*]. For a detailed description of the TSM test before the Court’s decision in *KSR*, see Steven J. Lee & Jeffrey M. Butler, *Teaching, Suggestion and Motivation: KSR v. Teleflex and the Chemical Arts*, 17 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 915 (2007). Before the Supreme Court’s decision in *KSR*, “[t]he Federal Circuit had already begun to broaden its TSM test to allow ‘suggestion’ to combine prior art references to be implicit in the nature of the problem that the inventor was trying to solve.” Frederick G. Vogt, *Unexpected Results: the Current Status of Obviousness Determinations for Pharmaceutical and Biotechnology Patents*, 29 TEMP. J. SCI. TECH. & ENVTL. L. 305, 311–12 (2010) [hereinafter *Unexpected Results*].

13. See Transcript, *supra* note 1, at 40–41.

14. *Id.* at 40.

15. *KSR*, 550 U.S. at 404.

16. See Glynn S. Lunney, Jr. & Christian T. Johnson, *Not So Obvious After All: Patent Law’s Nonobviousness Requirement, KSR, and the Fear of Hindsight Bias*, 47 GA. L. REV. 41, 43 (2012) [hereinafter *Not So Obvious*] (the Supreme “Court both rejected some of the key restrictions the Federal Circuit had placed on the obviousness doctrine and broadened the circumstances under which obvious-

preme Court, a wrongful patent grant is more harmful than a wrongful denial.”¹⁷

It may be more plain now, because in the term ending June 30, 2014, the Supreme Court ruled on six patent cases (none involving obviousness), and in each one ruled unanimously against the patentee.¹⁸ In five of those cases the Supreme Court reversed the Federal Circuit.¹⁹ Also, since *KSR* but before the 2014 term, the Supreme Court held—three times—that the patented products or processes at issue did not constitute patentable subject matter, narrowing what patents claimants could obtain.²⁰ Recognizing potential harm from patent grants, the Court said that “patent protection strikes a delicate balance between creating ‘incentives that lead to creation, invention, and discovery’ and ‘imped[ing] the flow of information that might permit, indeed spur, invention.’”²¹

This article addresses whether the Federal Circuit has changed its test for obviousness since the Supreme Court’s decision in *KSR* to reflect the standard required by *KSR*. Since *KSR*, commentators have noticed flexibility in the TSM test and obviousness determinations for fields other than new pharmaceutical compounds, such as electrical and mechanical inventions.²² However, commentators have not noticed the same flexibility in the

ness could be found”); Ali Mojibi, *An Empirical Study of the Effect of KSR v. Teleflex on the Federal Circuit’s Patent Validity Jurisprudence*, 20 ALB. L. J. SCI. & TECH. 559, 581 (2010) (“studies of both the Federal Circuit and District court cases [after the Supreme Court’s *KSR* decision] reveal that the courts are more likely to find patents invalid for obviousness as a result of *KSR*.”).

17. Joseph Scott Miller, *Remixing Obviousness*, 16 TEX. INTELL. PROP. L.J. 237, 239 (2008) [hereinafter *Remixing*].

18. See, e.g., *Alice Corp. Pty. Ltd. v. CLS Bank Int’l.*, 134 S. Ct. 2347 (2014); (2014); *Limelight Networks, Inc. v. Akamai Techs. Inc.*, 134 S. Ct. 2111 (2014); *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S. Ct. 2120 (2014); *Highmark Inc. v. Allcare Health Mgmt. Sys., Inc.*, 134 S. Ct. 1744 (2014); *Octane Fitness, LLC v. Icon Health & Fitness, Inc.*, 134 S. Ct. 1749 (2014); *Medtronic v. Mirowski Family Ventures, LLC*, 134 S. Ct. 843 (2014).

19. See, e.g., *Limelight*, 134 S. Ct. 2111 (2014); *Nautilus*, 134 S. Ct. 2120 (2014); *Highmark*, 134 S. Ct. 1744 (2014); *Octane*, 134 S. Ct. 1749 (2014); *Medtronic*, 134 S. Ct. 843 (2014).

20. See, e.g., *Ass’n. for Molecular Pathology v. Myriad Genetics, Inc.* 133 S. Ct. 2107 (2013); *Mayo Collaborative Svcs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012); *Bilski v. Kappos*, 561 U.S. 593 (2010).

21. *Myriad*, 133 S. Ct. at 2116, (quoting in part *Mayo*, 132 S. Ct. at 1305).

22. *Presumed Obvious*, *supra* note 12, at 285–87, 302 (after *KSR*, the approach of the Federal Circuit in many cases “is essentially a ‘presumption of combinability’ False Not all Federal Circuit cases since *KSR* can be said to follow this pattern . . . in chemical cases the court looks for a ‘lead compound’ and requires ‘some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.’”). Professor Underweiser also said that “the Federal Circuit must inevitably revisit the law of obviousness in the chemical arts as it is currently doing in the electrical and mechanical fields.” *Id.* at 288; see also Jason Rantanen, *The Federal Circuit’s New Obviousness Jurisprudence: An Empirical Study*, 16 STAN. TECH. L. REV. 709, 752 (2013) (“the Federal Circuit has read *KSR* to expand the ways in which a patent can be obvious, permitting the use of common sense as well as the idea that predictable uses of prior art elements according to their established functions are de facto obvious.) But the question of “when something that is ‘obvious to try’ is ‘obvious’ . . . was not included in the study’s coding. The same was true

test for new pharmaceutical compounds.²³ This article therefore focuses on the Federal Circuit's test for new pharmaceutical compounds.

Part II discusses Supreme Court decisions on obviousness and the reasons for the obviousness requirement—to screen out trivial inventions. Part II explains that under *KSR*, an invention is obvious if PHOSITA would have readily developed the invention from prior art, based on her creativity and common sense, by taking recognized scientific paths to resolve known needs, even though the specific steps in and result of the path were not shown in advance in the prior art.²⁴ Part II also shows that the Federal Circuit has applied the *KSR* standard in the generally unpredictable area of nucleic acids that code for (create) certain proteins, to contrast that approach to the Federal Circuit's test new pharmaceutical compounds, another field considered generally unpredictable and discussed in Part III.

Part III explains how the Federal Circuit has departed from the Supreme Court's approach in *KSR* and applies instead a test for new pharmaceutical compounds that generally makes it more difficult than under *KSR* to prove obviousness. This Federal Circuit test requires a challenger to show that elements in prior art identified (i) the lead compound, (ii) each individual step thereafter and (iii) the resulting invention, even though the lead compound was not part of the patent claim. Part III notes that the Federal Circuit developed this test before *KSR* and continues to apply essentially the same test now, even though it is inconsistent with *KSR*.

Part IV points out that § 103 requires PHOSITA and the court to consider the claim “as a whole” rather than splitting up an invention into steps and determining if prior art predicted each step of the invention. Part IV argues that as a result the Federal Circuit's test for new pharmaceutical compounds is also inconsistent with § 103.

Part V concludes that the Federal Circuit's test for new pharmaceutical compounds “complicates the inquiry rather than focusing on the stat-

of the use of a ‘lead compound’ analysis, a particular obviousness framework developed for the chemical arts. False. These doctrinal components are left to future studies.” *Id.* at 760–61.

23. See Briana Barron, *Structural Uncertainty: Understanding The Federal Circuit's Lead Compound Analysis*, 16 MARQ. INTELL. PROP. L. REV. 401, 417 (2012) [hereinafter *Structural Uncertainty*] (“another problem which has been addressed, but only in a cursory fashion, is whether the lead compound analysis, which is highly rigid and formulaic, comports with the requirements for any obviousness analysis from *KSR*, which is that the approach must be flexible.”).

24. This naturally leads to the inquiry, if it would have been obvious to PHOSITA, why wasn't the invention discovered previously? Professor Duffy set forth considerations in answering that inquiry. John F. Duffy, *A Timing Approach To Patentability*, 12 LEWIS & CLARK L. REV. 343 (2008) [hereinafter *Timing*]. In that article, he also gives the following summary, focusing on secondary considerations: “An obvious innovation may not have been previously created because a recent change has yielded a new component necessary for the innovation (a supply-side change) or a new market demand (a demand-side change). Where no such change explains the emergence of the innovation—i.e., where supply and demand considerations have remained relatively static for some significant period of time—then the innovation was almost certainly nonobvious.” *Id.* at 346.

ute”²⁵ and that the Federal Circuit should adopt the obviousness test it uses for other products, consistent with *KSR* and § 103 and the general foundations of patent law.

II. THE STANDARD OF OBVIOUSNESS

A. Foundations of the Obviousness Requirement

The ultimate determination of whether or not an invention is obvious within the meaning of § 103 is a legal conclusion, and when the facts are not in material dispute, the court can grant summary judgment on whether an invention was obvious.²⁶ This ultimate legal decision has a “significant subjective component” and “allows section 103 to be used as a policy instrument to further the constitutional goal of promoting the progress of the useful arts.”²⁷ As Professor Duffy has said, “Courts will always find it necessary to create canonical verbal formulations to articulate what the law is False [T]hose verbal formulations do not themselves provide any intuition for why the law is,”²⁸ however, so it is necessary to be familiar with the foundations of the obviousness requirement to evaluate a court’s rulings on obviousness.

The Supreme Court established the predecessor to the obviousness requirement in 1850 in *Hotchkiss v. Greenwood*, a case involving a patent for a doorknob of clay and porcelain connected to a metal shank (each element had been known previously).²⁹ Holding the patent invalid, even though there was no statutory requirement that an invention be nonobvious,³⁰ the

25. See Transcript, *supra* note 1, at 40 (statement of Chief Justice Roberts during *KSR* oral argument).

26. *KSR Int’l v. Teleflex, Inc.*, 550 U.S. 398, 427 (2007).

27. CRAIG ALLEN NARD, *THE LAW OF PATENTS* 405 (3d. ed., 2014) [hereinafter *LAW OF PATENTS*]; See also *Nonobvious Problem*, *supra* note 5, at 390 (In *KSR* the Supreme Court “endorsed the Federal Circuit’s characterization of the ultimate determination of (non)obviousness as a question of law, leaving the Federal Circuit with considerable room for active appellate review of the issue”).

28. *Case Study*, *supra* note 6, at 72.

29. 52 U.S. 248, 266–67 (1850). In a sense, all inventions are a combination of existing elements. See *infra* note 74 and accompanying text.

30. § 1 of the Patent Act of 1790, ch. 7, 1 Stat. 109–112 (April 10, 1790), provided in relevant part, “That upon the petition of any person or persons. . . [who] have invented or discovered any useful art, manufacture, engine, machine, or device, or any improvement therein no before known or used. . . [any two of the Secretary of State, Secretary for the department of war, and the Attorney General shall granted a patent] if they shall deem the invention or discovery sufficiently useful and important.” *CHISUM ON PATENTS*, *supra* note 2, at App’x 9–1. Section 1 of the Patent Act of 1793, ch. 11, 1 Stat. 318–23 (February 21, 1793) provided in relevant part, “That when any person or persons, being a citizen . . . of the United States, shall allege that he or they have invented any new and useful art, machine, manufacture or composition of matter, not known or used before the application . . .” they may obtain a patent from the Secretary of State. The 1790 requirement of “sufficiently useful and important” was omitted. *CHISUM ON PATENTS*, *supra* note 2, at App’x 10–1. Section 6 of the Patent Act of 1836, ch. 357, 5 Stat. 117 (July 4, 1836) authorized the grant of patent “any person or persons having

Court said that “there was an absence of that degree of skill and ingenuity which constitute essential elements of every invention False [T]he improvement is the work of the skillful mechanic, not that of the inventor.”³¹ In the 1952 Patent Act, Congress enacted § 103, substituting for “invention” what was thought to be a more objective standard—“obviousness.”³²

The Supreme Court in *Graham* discussed the constitutional basis for the limited power of Congress to enact patent laws.³³ The Court said that the Patent Clause “is both a grant of power and a limitation. This qualified authority . . . is limited to the promotion of advances in the ‘useful arts.’ . . . The Congress in the exercise of the patent power may not overreach the restraints imposed by the stated constitutional purpose.”³⁴ The Court tied that limit to the public domain, stating, “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.”³⁵ The Court then mentioned the “underlying policy of the patent system that ‘the things which are worth to the public the embarrassment of an exclusive patent,’ as Jefferson put it, must outweigh the restrictive effect of the limited patent monopoly.”³⁶ The “inherent problem” in the patent system, the Court observed, “was to develop some means of weeding out those inventions which would not be disclosed or devised but for the inducement of a patent.”³⁷

In his seminal work on obviousness, Professor Merges said that the “conventional ideal standard of patentability is that patents should only be awarded to those inventions that would not have been made without the

discovered or invented any new and useful art, machine, manufacture, or composition of matter, or any new and useful improvement . . . not known or used by others. . . .” provided the inventor submitted an application meeting certain disclosure criteria to the Commissioner of Patents, and the Commissioner concluded the conditions for a patent had been met. CHISUM ON PATENTS, *supra* note 2, at App’x 11–6.

31. *Hotchkiss*, 52 U.S. at 267.

32. See, e.g., *Case Study*, *supra* note 6, at 2 (“in the United States, what is today called nonobviousness was for about a century known as the invention doctrine.”); Glynn S. Lunney, Jr., *E-Obviousness*, 7 MICH. TELECOMM. & TECH. L. REV. 363, 365 (2001), available at <http://www.mttr.org/volveven/lunney.html> (passage of § 103 in 1966 “effectively changed the name for this . . . substantive requirement for patentability from ‘invention’ to ‘nonobviousness’”). § 103(a) provided, “[a] patent may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102 [the statute requiring that a patent claim be novel], if the differences between the claimed invention and the prior art are such that the claimed invention 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. Patentability shall not be negated by the manner in which the invention was made.”

33. Article I, Section 8, Clause 8 of the U.S. Constitution provides, “The Congress shall have Power . . . To 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.”

34. *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 5–6. (1966).

35. *Id.* at 6.

36. *Id.* at 10–11.

37. *Id.* at 11.

availability of the patent.”³⁸ Stated slightly differently, he argued that the obviousness “standard insists that only the results from uncertain research should be rewarded with a patent.”³⁹ He argued for denial of a patent in close cases, reasoning, “[t]here are more projects with a high probability of promising results that would still be undertaken without a patent system than there are such projects that need the extra incentive of a patent.”⁴⁰

Professor Duffy argued that the obviousness doctrine performs four related functions restricting the possible grant of patents: (1) preventing “thickets” of economically trivial patents; (2) preventing the exploitation of technical developments achieved independently of the patent (which he referred to as exogenous developments); (3) allocating rewards among alleged inventors; and (4) limiting the scope of patent rights.⁴¹ Of those, he argued that the most important function was the second, namely to prevent the exploitation of inventions that are nonetheless obvious because they were responsive to exogenous developments.⁴²

Regardless of the point of emphasis, the obviousness requirement performs a “gatekeeping function”⁴³ that protects society from what would otherwise be excessive grants of patents excluding others from freely using the underlying ideas.⁴⁴ Professors Bohannon and Hovenkamp have written, “[w]hen patents are granted on obvious products or processes, we have effectively created an exclusive right over something that in the natural

38. Robert P. Merges, *Uncertainty and the Standard of Patentability*, 7 HIGH TECH. L. J. 1, 19 (1992) [hereinafter *Uncertainty*].

39. *Id.* at 2. Professor Merges’s article was written before the Supreme Court in *KSR* made the nonobvious requirement more difficult to satisfy.

40. *Id.* at 31.

41. *Case Study*, *supra* note 6, at 11–17.

42. *Id.* at 12.

43. *Uncertainty*, *supra* note 38, at 2.

44. See, e.g., ROBERT PATRICK MERGES & JOHN FITZGERALD DUFFY, PATENT LAW AND POLICY: CASES AND MATERIALS 606, 608 (Lexis-Nexis 6th ed., 2013) [hereinafter MERGES] (“Nonobviousness asks whether a development is a significant enough technical advance to merit the award of a patent. . . if an idea is so obvious that people in the field would develop it without much effort, then the incentives provided by the patent system may be unnecessary to generate the idea.”); Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698 (1998), available at <http://www.sciencemag.org/content/280/5364/698.full> (“A proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream in the course of research and product development”). Not everyone agrees with the proposition that patent grants for trivial improvements can inhibit competition. For instance, in dissent in *Momenta Pharms. Inc. v. Amphastar Pharms. Inc.*, 686 F.3d 1348, 1374–75 (Fed. Cir. 2012), then Chief Judge Rader said, “Too often patent law is misunderstood as impeding more than promoting innovation. This academic proposition, called the tragedy of the Anti-commons in some scholarly presentations, suggests that exclusive rights impede the flow of information and limit experimentation that might lead to the next generation of technological advance False The reason that patents have not been proven to impede more than stimulate technological advance is simple: it does not happen.”

course would have been developed independently by many different people.⁴⁵

With that as background, this article next examines the key Supreme Court decisions on the obviousness requirement, which did not establish or suggest a special test for new pharmaceutical compounds.⁴⁶

B. Graham v. John Deere: The Obviousness Standard

William T. Graham and his company, Graham Plow, Inc., sued John Deere Company of Kansas City and obtained an injunction in 1963 for defendants' infringement of the '798 patent for a vibrating shank plow.⁴⁷ The Eighth Circuit, however, found the '798 patent invalid and reversed the judgment.⁴⁸ The Supreme Court affirmed the Eighth Circuit's conclusion that the patent was invalid as obvious.⁴⁹

The Supreme Court examined § 103 and said obviousness referred to the difference between prior art—"what was known before as described in section 102"⁵⁰—and the "subject matter sought to be patented."⁵¹ In comparing prior art to the patent claim, the Court said, "[i]f this difference is

45. CHRISTINA BOHANAN AND HERBERT HOVENKAMP, CREATION WITHOUT RESTRAINT: PROMOTING LIBERTY AND RIVALRY IN INNOVATION 98 (Oxford University Press 2012) [hereinafter CREATION]; See also Gregory Mandel, *The Non-Obvious Problem: How the Indeterminate Nonobviousness Standard Produces Excessive Patent Grants*, 42 U.C. Davis L. Rev. 57, 89 (2008) [hereinafter *Indeterminate*] (too high a nonobvious standard reduces the incentives for individuals to invent but too low a standard "allows excessive patenting, resulting in inefficient patent thickets, anti-commons, minefields, hold-ups and other problems.").

46. Due in part to the great expense of developing new pharmaceutical compounds, there appears to be a consensus that patent protection is important as an incentive for the development of new pharmaceutical compounds. See, e.g., DAN L. BURK AND MARK A. LEMLEY, THE PATENT CRISIS AND HOW THE COURTS CAN SOLVE IT, 3 (University of Chicago Press 2011) [hereinafter PATENT CRISIS]. Still, that does not mean the obviousness requirement currently is at the right gatekeeping level for new pharmaceutical compounds. Whether special protection for the pharmaceutical industry (e.g., a longer period of exclusivity for marketing a new chemical) should be addressed under the Federal Food and Drug Act is beyond the scope of this article. See, e.g., Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503 (2009) ("The novelty and nonobviousness requirements make no concession for the development costs of inventions and thus cause patents to be withheld from drugs that are unlikely to reach the public without that protection. False Congress can easily avoid this problem by ensuring that the successful completion of the FDA's rigorous clinical-trial process is rewarded with a lengthy exclusivity period enforced by the FDA.")

47. *Graham v. John Deere Co. of Kan. City*, 216 F. Supp. 272, 280 (W.D. Mo. 1963), *rev'd*, 333 F.2d 529 (8th Cir. 1964), *aff'd*, 383 U.S. 1 (1966).

48. *John Deere Co. of Kan. City v. Graham*, 333 F.2d 529, 535 (8th Cir. 1964), *aff'd*, 383 U.S. 1 (1966). The Fifth Circuit had held the patent was valid (since it concluded that a combination that produced an old result in a "cheaper and otherwise more advantageous way" was patentable) and the Eighth Circuit had held the patent was not valid (there was no new result in the combination of elements). The Supreme Court concluded neither circuit had applied the correct test, but affirmed the judgment of the Eighth Circuit that the patent was not valid as obvious. 383 U.S. at 4.

49. *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 4 (1966).

50. § 102 contains the novelty requirement for patent law and sets forth what constitutes prior art for purposes of obviousness under § 103. See discussion *supra* note 5 and *infra* note 94.

51. *Graham*, 383 U.S. at 15.

such that the subject matter *as a whole* would have been obvious at the time to a person skilled in the art, then the subject matter cannot be patented.”⁵² The Court also said that there were a number of “basic factual inquiries” under § 103 to be determined and listed the three factors, plus the secondary considerations, mentioned above.⁵³

The Court noted that technology had progressed greatly over the years, and said, “[i]t is but an evenhanded application to require that those persons granted the benefit of a patent monopoly be charged with an awareness of these changed conditions.”⁵⁴ Put another way, the level of the applicable PHOSITA(s) was greater in 1966 than in 1916, and would be greater today than in 1966.

Rather than looking at individual steps in the invention, the Supreme Court looked at the ultimate difference between the prior art and the patent claim and observed, “[t]he sole element in patent ‘798 which petitioners argue before us is the interchanging of the shank and hinge plate and the consequences flowing from this arrangement.”⁵⁵ Without identifying the specific level of skill of PHOSITA, the Court concluded, “[c]ertainly a person having ordinary skill in the prior art, given the fact that the flex in the shank could be utilized more effectively if allowed to run the entire length of the shank, would immediately see that the thing to do was what Graham did, i.e., invert the shank and the hinge plate.”⁵⁶ The Court held that the ‘798 patent was obvious and thus invalid.⁵⁷

In a companion case, *United States v. Adams*, Adams had a patent on a nonrechargeable electrical battery with a magnesium electrode, a cuprous chloride electrode and a battery fluid using either plain or salt water.⁵⁸ Each of the elements of the battery were known in prior art, but the art at the time also indicated that “water-activated batteries were successful only when combined with electrolytes detrimental to the use of magnesium.”⁵⁹ Since Adams’ battery used water and magnesium, the Supreme Court said that prior art “would . . . deter any investigation into such a combination as is used by Adams.”⁶⁰ Holding that the patent was not obvious, the Court concluded that “known disadvantages in old devices which would naturally

52. *Id.* (emphasis added).

53. *Id.* at 17–18; *see supra* notes 9–10.

54. *Graham*, 383 U.S. at 19.

55. *Id.* at 23.

56. *Id.* at 25.

57. *Id.* at 25–26.

58. 383 U.S. 39, 42 (1966). Adams sued the United States under 28 U.S.C. § 1498 for infringing the patent. *Id.* at 41.

59. *Id.* at 51–52. Prior art also indicated that “batteries which continued to operate on an open circuit and which heated in normal use were not practical.” *Id.* at 52.

60. *Id.* at 51–52.

discourage [commonly referred to as “teaching away”] the search for new inventions may be taken into account in determining obviousness.”⁶¹ The Court in *Adams*, in other words, was saying that if the results expected by PHOSITA at the time of a prospective combination of elements would have been that such combination would fail to solve the problem, but the inventor went ahead anyway with the combination, then that result — unexpected by PHOSITA — would tend to indicate the combination was not obvious.⁶²

This article next discusses *KSR* and its significance to the obviousness analysis.

C. *KSR v. Teleflex: Filling in the Gaps Left by Graham*

1. Introduction

In *KSR*, the Supreme Court made the legal standard for proving obviousness easier to meet than it had been under the Federal Circuit’s teaching, suggestion, motivation test⁶³ by: (1) increasing what prior art to consider (C2 below), (2) making it easier to conclude that PHOSITA would have combined elements from prior art to create a new invention (C3 below), and (3) increasing the level of skill and creativity of PHOSITA (C4 below).

Teleflex was the exclusive licensee of a patent for an adjustable pedal assembly with electronic throttle control. Teleflex sued *KSR* for combining *KSR*’s patented adjustable pedal control with an off the shelf electronic throttle control sensor.⁶⁴ The district court granted defendant *KSR* summary judgment on the ground of obviousness,⁶⁵ but the Federal Circuit reversed.⁶⁶

61. *Id.* at 52. The Court further noted, “[n]or are these the only factors bearing on the question of obviousness. We have seen that at the time *Adams* perfected his invention noted experts expressed disbelief in it. Several of the same experts subsequently recognized the significance of the *Adams* invention, some even patenting improvements on the same system.” *Id.*

62. *See id.* at 51–52. In other words, the fact that an inventor might be a genius or otherwise know better than PHOSITA that such a combination would be favorable would not argue against patentability.

63. *See supra* note 12; *see also Not So Obvious, supra* note 16, at 43.

64. 550 U.S. at 405–06, 409–10. In the 1990’s car manufacturers increasingly used electronic throttles to manage the flow of fuel to the engine. That “demand-side change” resulted in demand to switch mechanical pedals to electronic pedals. “Because the ‘prior art taught a number of methods for achieving [the necessary update]’ multiple engineers across the industry were independently able to achieve the new combination in response to the market need. That is a classic situation in which granting exclusive patent rights is unnecessary.” *Timing, supra* =note 24, at 352–53.

65. *Teleflex, Inc. v. KSR Int’l Co.*, 298 F. Supp. 2d 581, 595–96 (E.D. Mich. 2003), *vacated and remanded*, 119 F. App’x 282 (Fed. Cir. 2005), *rev’d*, 550 U.S. 398 (2007).

66. *Teleflex, Inc. v. KSR Int’l Co.*, 119 F. App’x 282, 286 (Fed. Cir. 2005), *rev’d*, 550 U.S. 398 (2007).

In 2007 the Supreme Court reversed, holding that the “ultimate judgment of obviousness is a legal determination” and agreeing with the district court’s grant of summary judgment that the invention was obvious.⁶⁷ The Court repeated—as the standard for obviousness—the considerations set forth in *Graham*⁶⁸ and added, “[w]hile the sequence of these questions might be reordered in any particular case, the factors continue to define the inquiry that controls.”⁶⁹

Recognizing the danger of patent grants for obvious inventions, the Supreme Court cautioned against a patent that “diminishes the resources available to skillful men.”⁷⁰ The Court added, “[g]ranting patent protection to advances that would occur in the ordinary course without real innovation retards progress and may, in the case of patents combining previously known elements, deprive prior inventions of their value or utility.”⁷¹

In *KSR*, the Supreme Court said that “a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.”⁷² In one sense, of course, all inventions of products/compositions of matter are combinations of what was known at the time in prior art.⁷³ Even if an invention is a new chemical composition, the inventor created that new composition through some combination of existing elements (including perhaps heat, energy and other forces). Therefore, the statement that “a court must ask whether the improvement is more than a predictable use of prior art elements according to their established functions” is essentially a standard for all patent claims. The Supreme Court in *KSR* then went through an analysis of the *Graham* factors and the errors of the Federal Circuit. This article discusses that analysis next.⁷⁴

67. *KSR Int’l Co.*, 550 U.S. at 426–27 (“Nothing in the declarations proffered by Teleflex prevented the District Court from reaching the careful conclusions underlying its order for summary judgment in this case”).

68. 550 U.S. at 406.

69. *Id.* at 407.

70. 550 U.S. at 416 (quoting *Great Atlantic & Pacific Tea Co. v. Supermarket Equip. Corp. Co.*, 340 U.S. 147, 152–53 (1950)).

71. *Id.* at 419.

72. *Id.* at 417.

73. In *KSR*, the Court observed that “inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” *Id.* 418–19.

74. The Court did not add anything to *Graham* on secondary considerations. It said, “To this end, *Graham* set forth a broad inquiry and invited courts, where appropriate, to look at any secondary considerations that would prove instructive.” *Id.* at 415. The Court concluded that like the district court, “Teleflex has shown no secondary factors to dislodge the determination that claim 4 is obvious.” *Id.* at 426. In neither *Graham* nor *KSR* did the Supreme Court say that lower courts must consider the “secondary factors” mentioned in *Graham*, and in *Sakradia v. Ag Pro, Inc.*, 425 U.S. 273, 282–83 (1976), the Court said that at least commercial success by itself could not result in a conclusion of obviousness in certain cases.

2. First *Graham* Factor: Prior Art⁷⁵

The Supreme Court in *KSR* expanded the scope of prior art to consider. The Court said an error of the Federal Circuit “was . . . holding that courts and patent examiners should look only to the problem the patentee was trying to solve” and added that the Federal Circuit had “failed to recognize that the problem motivating the patentee may be only one of many addressed by the patent’s subject matter.”⁷⁶ The Supreme Court also said, “[o]ne of the ways in which a patent’s subject matter can be proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent’s claim.”⁷⁷ The crucial issue was “whether the combination was obvious to a person with ordinary skill in the art,” not the inventor.⁷⁸

Any art a PHOSITA would likely consider in addressing a “patent’s subject matter” is analogous art in determining obviousness.⁷⁹ Not limiting the applicable prior art to some rigid formula, the Supreme Court added, “Common sense teaches . . . that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle.”⁸⁰

75. This article discusses the elements in the order set forth in *Graham*. At least at times the Federal Circuit has given the elements a different order, switching PHOSITA with the difference between prior art and the patent claim. *See, e.g.*, *Eisai Co., Ltd. v. Dr. Reddy’s Labs. Ltd.*, 533 F.3d 1353, 1356 (Fed. Cir. 2008). However, as the Supreme Court said, the order of discussion is inconsequential, as long as one remembers the factors—other than secondary considerations—are from the point of view of PHOSITA. *KSR*, 550 U.S. at 407.

76. 550 U.S. at 420.

77. *Id.* at 419–20. The Court also said, “[u]nder the correct analysis, any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed.” *Id.* at 420. This statement appears focused on what may suggest a combination of elements, not what is analogous art that PHOSITA might consider. For a discussion of views on analogous art, *see* PATENT LAW, *supra* note 5 at 293–97.

78. 555 U.S. at 420.

79. *Id.* *See also*, *Icon Health & Fitness, Inc.*, 496 F.3d 1374, 1380 (Fed. Cir. 2007) (“an inventor considering a hinge and latch mechanism for portable computers would naturally look to references employing other ‘ housings, hinges, latches, springs, etc., ’ which in that case came from areas such as ‘ a desktop telephone directory, a piano lid, a kitchen cabinet, a washing machine cabinet, a wooden furniture cabinet, or a two-part housing for storing audio cassettes. ’”) (quoting *In re Paulsen*, 30 F.3d, 1475, 1481–82 (Fed. Cir. 1994)). It seems apparent that when the Federal Circuit referred to “an inventor” in the quoted part of the decision in *Icon* it was referring to PHOSITA rather than “the inventor,” since earlier in the same paragraph the Federal Circuit had referred to “the inventor.” *Id.* Analogous prior art is a broader concept than the lead compound approach taken by the Federal Circuit discussed in part IIIA. *See, e.g.*, David J. Martens et. al., *Lead Prior Art Methodology: Applying Lead Compound Case Law To Other Disciplines For Enhanced Objectivity*, 27 SANTA CLARA COMPUTER & HIGH TECH. L. J. 551, 616 (April 2011) (“under the Lead Prior Art methodology, sensible starting point will always be analogous prior art but analogous prior art will not always be a sensible starting point.”).

80. *KSR*, 550 U.S. at 420.

3. Second *Graham* Factor: Obvious to Try

The Supreme Court in *KSR* also made the obviousness standard easier to satisfy. The Court directly said, “the fact that a combination was obvious to try might show that it was obvious under § 103.”⁸¹ In discussing *KSR*, Professor Rai explained that an invention which is the result of some steps that are “‘obvious to try’ . . . can be obvious if the universe of possible solutions is finite and predictable.”⁸²

An invention can be obvious even if PHOSITA cannot predict the ultimate invention in advance of the steps taken to achieve the invention. The Supreme Court said, “When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp.”⁸³ The Court continued that if this obvious to try approach “leads to the anticipated success . . . [T]he fact that a combination was obvious to try might show that it was obvious under § 103.”⁸⁴ The statements about “predictable solutions” and “anticipated success” must refer to success in solving the problem, not being able to predict the solution in advance, because the Court also said that “a person of ordinary skill has good reason to pursue the known options [not the results] within his or her technical grasp.”⁸⁵

The reference to “finite” solutions was at least an implicit recognition by the Supreme Court that a court should take into account the ease of finding solutions, because otherwise — once it is recognized that every invention of a product is a combination of prior art — every product patent claim would be obvious through a perhaps infinite combination of elements.⁸⁶

81. *Id.* at 421.

82. Arti K. Rai, *Who’s Afraid of the Federal Circuit?*, 121 YALE L.J. 335, 342 (December 20, 2011) (citing *KSR*, 550 U.S. at 421).

83. *KSR*, 550 U.S. at 421. Earlier in *KSR*, the Court made other statements using “predictable”:
(1) “The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results” *Id.* at 416; (2) “when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result” *Id.* at 416; (3) “if a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability” *Id.* at 417.

84. *Id.* at 421. This does not answer how likely it must be that there will be a resolution, which must be taken into account. Discussing *KSR* and the likelihood of solving a problem through undertaking a research path, Professor Eisenberg explained, “The Supreme Court disapproved of the Federal Circuit’s focus on the problem that the patentee was trying to solve as the point of departure for figuring out whether the invention was obvious, preferring instead an ‘objective’ approach that asks whether the claimed invention was likely to come about as the obvious solution to any known problem in light of the prior art.” *Nonobvious Problem*, *supra* note 5 at 392. See also *infra* notes 85 and 96 and accompanying text.

85. *KSR*, 550 U.S. at 421.

86. This would be akin to the “infinite monkey theorem” that “a monkey hitting keys at random keys at random on a typewriter keyboard for an infinite amount of time will almost surely type a given text, such as the complete works of William Shakespeare.” INFINITE MONKEY THEOREM,

However, the Court did not set forth any outward limit to the number of possible paths to pursue before a patent claim was not obvious. Indeed, the Supreme Court has consistently favored broad standards over more specific rules announced by the Federal Circuit in patent law cases.⁸⁷

The Supreme Court rejected the Federal Circuit's principle, "[o]bvious to try has long been held not to constitute obviousness."⁸⁸ The Federal Circuit previously had elaborated on that principle by stating that "a general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out."⁸⁹ Rejecting the Federal Circuit's position that a PHOSITA would have to know in advance "a particular result" of the steps to be taken before an invention would be obvious, the Supreme Court called this a "constricted analysis."⁹⁰

Similarly, the Supreme Court rejected the Federal Circuit's standard that there had to be a teaching, suggestion or motivation identified in the prior art for the claimed invention to be obvious.⁹¹ The Supreme Court explained, "[t]he obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by over-emphasis on the importance of published articles and the explicit content of

https://www.princeton.edu/~achaney/tmve/wiki100k/docs/Infinite_monkey_theorem.html (last visited Jul. 29, 2014). Professor Mandel has argued, "Nonobviousness should depend on how probable the invention would have been for a person having ordinary skill in the art working on the problem that the invention solves." *Indeterminate*, *supra* note 45 at 116.

87. See John F. Duffy, *Rules and Standards on the Forefront of Patentability*, 51 WM. & MARY L. REV. 609, 611, 623 (2009) ("[c]lear rules can provide the certainty that encourages investment both in obtaining and developing the rights, but standards can provide the flexibility to accommodate the new and unpredictable wonders of human ingenuity. . . . [T]he law defining limits of patentability has generally been hostile to rule-based approaches, and that hostility has been especially apparent for rules of exclusions at the Supreme Court."); Rebecca S. Eisenberg, *Wisdom of the Ages or Dead-Hand Control? Patentable Subject Matter for Diagnostic Methods After In Re Bilski*, 3 CASE W. RES. J. INT'L L. 1, 14 (2012) ("the Federal Circuit often prefers bright-line rules that point towards clear outcomes in future cases over broad, open-ended standards that require the exercise of judgment and on which reasonable minds can differ. But Supreme Court precedents on patent law, including its decisions about patentable subject matter, more typically state broad, open-ended principles. The Supreme Court had repeatedly faulted and reversed the Federal Circuit for applying unduly rigid rules that departed from the flexibility of its own precedents") (footnotes omitted); and Craig Allen Nard, *Legal Forms and the Common Law of Patents*, 90 B.U. L. REV. 51, 53, 108 (2010). ("the patent code, much like the Sherman Act, is a common law enabling statute. . . . For more than two hundred years the courts have navigated the contours of the patent system, adeptly construing doctrine and interpreting elliptical statutory phrases. . . . This accretive process. . . possesses comparative advantages to congressional intervention. . . .").

88. *KSR*, 550 U.S. at 421 (internal quotation marks omitted);

89. *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995). The Federal Circuit in *Deuel* added, "[E]ven if, as the examiner stated, the existence of general cloning techniques, coupled with knowledge of a protein's structure, might have provided motivation to prepare a cDNA or made it obvious to prepare a cDNA, that does not necessarily make obvious a particular claimed cDNA." *Id.*

90. *KSR*, 550 U.S. at 421. Professor Eisenberg wrote, "The Federal Circuit noticeably softened its TSM rhetoric while *KSR* was pending on appeal." *Nonobvious Problem*, *supra* note 5, at 387.

91. 550 U.S. at 419. Professors Bohannon and Hovenkamp explained that "TSM became a recipe for granting patents on trivial innovations." *Creation*, *supra* note 45, at 108.

issued patents,”⁹² the primary sources of prior art.⁹³ The Court noted, “[i]n many fields it may be that there is little discussion of obvious techniques or combinations, and it often may be the case that market demand, rather than scientific literature, will drive design trends.”⁹⁴

KSR opened the door to a finding of obviousness with respect to inventions resulting from well-known scientific techniques that were obvious to try but for which the results were not known in advance.

4. Third *Graham* factor: PHOSITA

KSR elevated what had been the role of PHOSITA in the obviousness analysis.⁹⁵ The Supreme Court said that “a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.”⁹⁶ It gave the following example of common sense that a court should attribute to PHOSITA: “[c]ommon sense teaches . . . that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle.”⁹⁷ The Court also said, “[a] person of ordinary skill is also a person of ordinary creativity, not an automaton.”⁹⁸ These statements about the common sense and creativity of PHOSITA in choosing prior art references contrast with the Federal Circuit position that a court “cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.”⁹⁹

The Supreme Court also said that advances in science, “once part of our shared knowledge, define a new threshold from which innovation starts

92. 550 U.S. at 419.

93. 35 U.S.C. § 102(a) (2006) provided, “A person shall be entitled to a patent unless (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.”(amended by 35 U.S.C. § 102 (2012)) See also *supra* note. 5 on sources of prior art.

94. *KSR*, 550 U.S. at 419.

95. See Brenda M. Simon, *The Implications of Technological Advancement for Obviousness*, 19 MICH. TELECOMM. & TECH. L. REV. 331, 339 (2013) [hereinafter *Implications*] (“*KSR v. Teleflex* changed how the PHOSITA is viewed, transforming the PHOSITA from a mere ‘automaton’ to a person having ordinary skill and creativity in the art.”).

96. *KSR*, 550 U.S. at 418.

97. *Id.* at 420.

98. *Id.* at 421. Previously the Federal Circuit had ruled that PHOSITA was a person who only thought conventionally and did not attempt to innovate: “A person of ordinary skill in the art is also presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate, whether by patient, and often expensive, systematic research or by extraordinary insights, it makes no difference which.” *Standard Oil Co. v. American Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985).

99. *Ecolochem, Inc. v. Southern California Edison Co.*, 227 F.3d 1361, 1371 (Fed. Cir. 2000) (quoting *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988)).

once more.”¹⁰⁰ Acknowledging the harm to innovation caused by patent grants that did not recognize scientific advances, the Court said, “[w]ere it otherwise, patents might stifle, rather than promote, the progress of useful arts.”¹⁰¹ These statements fit well with Professor Eisenberg’s pre-*KSR* article arguing, “[t]he written record understates the technological know-how that active practitioners bring to bear upon a problem”¹⁰²

5. Summary

KSR made it more likely than under the Federal Circuit’s TSM test that a court would find a patent claim to be obvious:

First, *KSR* expanded what prior art a court should consider, from only art addressing the particular problem the inventor had been considering to any art PHOSITA would reasonably have considered in trying to address “the patent’s subject matter.”¹⁰³

Second, *KSR* expanded the focus of obviousness from (1) only searching prior art for a teaching, suggestion or motivation for a particular solution to the particular problem the inventor had been addressing to (2) also considering whether PHOSITA—responding to market pressures—would have used known research techniques that were obvious to try and that readily resulted in a solution of a recognized need, without knowing the particular result in advance.¹⁰⁴

Third, *KSR* recognized that the skill of PHOSITA was important not simply to explain prior art, but also to use her common sense and creativity to try reasonable research approaches to resolving recognized needs, and that such skill increased as science increased.¹⁰⁵

This article next discusses the Federal Circuit’s test for new pharmaceutical compounds, to compare that test to the *KSR* standard.

C. The Federal Circuit’s Analysis of Obviousness in In re Kubin

Before *KSR*, the Federal Circuit had said in *In re Deuel*, “[o]bvious to try’ has long been held not to constitute obviousness.”¹⁰⁶ *Deuel* involved

100. *KSR*, 550 U.S. at 427. The Court also said that “as progress beginning from higher levels of achievement is expected in the normal course, the results of ordinary innovation are not the subject of exclusive rights under the patent laws. Were it otherwise patents might stifle, rather than promote, the progress of useful arts.” *Id.*

101. *Id.* (citing Article I, § 8, clause 8 of the Constitution as the basis for the obviousness requirement). In addition, “These premises led to the bar on patents claiming obvious subject matter established in *Hotchkiss* and codified in § 103.” *Id.* See also *Case Study*, *supra* note 6 at 68 (“More important is the Supreme Court’s recognition that patents on obvious innovations could serve to stifle rather than promote progress.”).

102. Rebecca S. Eisenberg, *Obvious to Whom? Evaluating Inventions from the Perspective of PHOSITA*, 19 BERKELEY TECH. L. J. 885, 888 (2004) [hereinafter *To Whom*].

103. 550 U.S. at 420. See *supra* Part II.C.2.

104. See *supra* Part II.C.3.

105. See *supra* Part II.C.4.

106. *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995).

the issue of whether knowledge of (1) general methods of isolating DNA molecules, (2) cloning techniques and (3) a protein's structure made obvious the patent claim — the cDNA that coded for the protein.¹⁰⁷ The Federal Circuit held the known methods did not make the claimed invention, cDNA, obvious because “the combined references do not teach or suggest the claimed cDNA molecules”¹⁰⁸ In other words, even though PHOSITA would know what steps to take to achieve the sought after result (the cDNA sequence of nucleotides), she did not know the particular result in advance, so that result was not obvious.¹⁰⁹

After *KSR*, however, the Federal Circuit decided *In re Kubin*,¹¹⁰ which involved a claim for an isolated nucleic acid molecule encoding (creating) a certain protein.¹¹¹ The Federal Circuit said, “[i]nsofar as *Deuel* implies the obviousness inquiry cannot consider that the combination of the claim's constituent elements was ‘obvious to try,’ the Supreme Court in *KSR* unambiguously discredited that holding.”¹¹² Even though prior art did not supply the nucleotide sequence identified in the patent claim in *Kubin*, the Federal Circuit held that the claim was obvious, because “the prior art teaches a protein of interest, a motivation to isolate the gene coding for that protein, and illustrative instructions to use a monoclonal antibody specific to the protein for cloning this gene.”¹¹³ It added that “the claimed invention is ‘the product not of innovation but of ordinary skill and common sense.’”¹¹⁴ The scientists did not know the end result in advance, but knew how to discover what the end result would be by following known scientific methods. Thus the claim was obvious.

The Federal Circuit in *Kubin* declined to “cabin *KSR* to the ‘predictable arts’” and referred to the “well-known and reliable nature of the cloning and sequencing techniques in the prior art”¹¹⁵ In other words, consistent with the teaching of *KSR*, even if an inventor does not know the end

107. *Id.*

108. *Id.* at 1560. See also Thomas A. Isenbarger, *In re Kubin's Reinvigorated Nonobviousness Standard for DNA Patents*, 2009 WIS. L. REV. 1435, 1437 (2009) [hereinafter *Reinvigorated*] (“[T]he *Deuel* standard considers the obviousness of the DNA molecule's structure by the proxy of its sequence, and not the obviousness of the method used to isolate it”).

109. *In re Deuel*, 51 F.3d at 1559 (“the claims at issue define compounds, not methods”).

110. *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009).

111. *Id.* at 1353 (“An isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide at least 80% identical to amino acids 22–221 of SEQ ID NO:2, wherein the polypeptide binds CD48.”).

112. *Id.* at 1358.

113. *Id.* at 1360.

114. *Id.* (quoting *KSR*, 550 U.S. at 421).

115. *Id.* Professors Abramowicz and Duffy point out that in *Kubin* the Federal Circuit “specifically embraced the argument that, in determining obviousness of DNA sequences coding for a particular protein, the courts must take into account ‘the ease and predictability’ of techniques for isolating those DNA sequences.” *Inducement Standard*, *supra* note 3, at 1611.

result of a well-known method that was obvious to try to solve a need in the field, the result could be obvious.¹¹⁶

Although *Kubin* “raised the bar significantly for nonobviousness of genetic inventions”¹¹⁷ in light of the Federal Circuit’s previous decision in *Deuel*,¹¹⁸ in fact *Kubin* was a logical application of *KSR* to biochemical inventions. After all, the Supreme Court in *KSR* had said that “the fact that a combination was obvious to try might show that it was obvious under § 103.”¹¹⁹ The Court in *KSR* was clearly expanding the reach of the principle of “obvious to try” as a red flag for a possible conclusion of obviousness.¹²⁰

The level of the nonobvious gate under *KSR* is consistent with much scholarship on obviousness. For instance, Professor Barton discussed the costs to society of grants of patents not needed as incentives and said, “it is clearly essential to err on the cautious side rather than the generous side in interpreting the nonobviousness standard.”¹²¹ He added that “there is something unseemly about giving a patent to the product of a routine process or even of a machine—surely the sequencing machine is at the level of ordinary skill in the art!”¹²² Professor Dreyfuss concluded, “a procedure that promotes a very high level of inventiveness is likely superior to one that sets it too low. That, perhaps, is the essence of *KSR*.”¹²³ Professor Denicoló said that “economists have recognized that the fragmentation of patent rights increases transaction costs and may lead to pricing inefficiencies. This provides another potential source of externalities that an innovator

116. *Reinvigorated*, *supra* note 108, at 1448 (the analysis in *Kubin* “focused on the problem to be solved, the availability of methods to solve it, and a reasonable expectation of success”).

117. PATENT LAW, *supra* n. 5 at 333, note 49. Professor Mueller also wrote, “The *Kubin* decision signals that ‘classical’ biotechnology inventions (i.e., claims to isolated genes that encode particular proteins) may now routinely be characterized as ‘obvious to try’ in the *KSR* sense.” *Id.* at 312, n.159.

118. See *supra*, notes 106–08 and accompanying text.

119. 550 U.S. at 421. Discussing *KSR*, Professor Eisenberg said, “[t]he Supreme Court disapproved of the Federal Circuit’s focus on the problem that the patentee was trying to solve as the point of departure for figuring out whether the invention was obvious, preferring instead an ‘objective’ approach that asks whether the claimed invention was likely to come about as the obvious solution to any known problem in light of the prior art.” *Nonobvious Problem*, *supra* note 5 at 392.

120. See Janice M. Mueller, “Chemicals, Combinations, and ‘Commonsense’: How the Supreme Court’s *KSR* Decision Is Changing Federal Circuit Obviousness Determinations in Pharmaceutical and Biotechnology Cases,” 35 N. KY. L. REV. 281, 286 (2008) [hereinafter *Mueller*] (“*KSR* also gave new credence to so-called ‘obvious to try’ arguments, of particular relevance in chemical cases. . . . [*KSR*] re-frames the obvious to try inquiry. Applicants, examiners, litigants, judges and juries must now determine whether the prior art identified ‘predictable’ solutions, and whether such solutions were ‘finite’ in number. When these conditions are satisfied, obvious to try evidence may indeed establish the ultimate conclusion of obviousness.”)

121. John H. Barton, *Non-Obviousness*, 43 IDEA 475, 495 (2003).

122. *Id.* at 507.

123. Rochelle Cooper Dreyfuss, *Nonobviousness: A Comment on Three Learned Papers*, 12 LEWIS & CLARK L. REV. 431, 440 (2008) [hereinafter *Dreyfuss*].

may impose on others, and hence another possible motive for denying patentability to certain innovations.”¹²⁴

Part III of this article contrasts *KSR* with the test the Federal Circuit uses to determine obviousness of new pharmaceutical compounds and shows that the Federal Circuit’s test is not consistent with *KSR*.¹²⁵ After discussing the Federal Circuit’s contrasting approaches to determining obviousness of new pharmaceutical compounds and other products, Professor Marian Underweiser has suggested, “[t]he fact that the Federal Circuit opinions do not always appear to apply the same approach may reflect a distinction between focusing on the claimed invention as a combination of elements as opposed to understanding the invention as potentially resulting from a combination of the prior art. The latter is a more principled and universal way to view the obviousness analysis, as evidenced by the opinion in *Kubin*.”¹²⁶ The Federal Circuit’s obviousness test is a test that makes it more difficult (compared to *KSR* and *Kubin*) for a challenger to show that a patent for a new pharmaceutical compound is obvious.

III. THE FEDERAL CIRCUIT’S TEST FOR OBVIOUSNESS OF NEW PHARMACEUTICAL COMPOUNDS IS INCONSISTENT WITH *KSR*

Under *KSR*, an improvement in the treatment of a disease with one compound is likely to be obvious if PHOSITA would have “readily” created that improvement by modifying structurally similar compounds using known scientific techniques, even though the particular result of the techniques would not have been known in advance.¹²⁷ In contrast, under the Federal Circuit’s obviousness test for new pharmaceutical compounds,

124. Vincenzo Denicolò, *Economic Theories of the Nonobviousness Requirement for Patentability: A Survey*, 12 LEWIS & CLARK L. REV. 443, 455 (2008).

125. See, e.g., *Implications*, *supra* note 95 at 366–67 (“the Federal Circuit’s recent decisions seem to discount *KSR* with regard to combination claims in chemical formulation patents, an area fraught with unpredictability. . . . The focus should be on whether the invention would be predictable to the PHOSITA in light of technological advances, such as if the number of possible solutions is practical, even if the invention is in an unpredictable field.”).

126. *Presumed Obvious*, *supra* note 12, at 289, after discussing the test for new pharmaceutical compounds at 286–287. The Federal Circuit has recognized obvious to try in another case not involving a new pharmaceutical compound, a “cryopreserved therapeutic composition comprising viable human neonatal or fetal hematopoietic stems cells. . . .” *Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342, 1347 (Fed. Cir. 2007). In *Pharmastem* the Federal Circuit applied *KSR* and said that PHOSITA “would have had reason to attempt to make the composition . . . and would have had a reasonable expectation of success in doing so.” *Id.* at 1360 (citing *KSR*). The Federal Circuit concluded the invention was obvious and added, “the inventors merely used routine research methods to prove what was already believed to the case.” *Id.* at 1363.

127. The meaning of “readily” would be a question for the fact-finder. See *supra* notes 87–88, 116, and *infra* note 148 for a discussion of why an obvious invention may not have been developed earlier, see also *supra*, note 24 (discussing how supply side and demand side changes can make what had been a nonobvious invention obvious).

such improvement would not be obvious unless prior art had identified a lead compound and each step in making the improvement, including the final result, in advance, even though the lead compound was not part of the patent claim.

A. The Federal Circuit's Test for New Pharmaceutical Compounds

The Federal Circuit's test for new pharmaceutical compounds does not compare the applicable prior art to the whole patent claim to determine whether the claim is obvious. Instead, the test breaks apart the claim into what the court perceives are "historical" segments (such as a lead compound) preceding the invention and never puts the parts back together to compare the invention as a whole to prior art. The test generally makes it more difficult than under *KSR* for a party challenging a patent on obviousness to succeed.

Part 1 below describes two 2014 Federal Circuit decisions: *Pfizer, Inc. v. Teva Pharmaceuticals USA, Inc.* and *Bristol-Myers Squibb Co. v. Teva Pharmaceuticals USA, Inc.*¹²⁸ Part 2 shows that the test originated before *KSR* and that the Federal Circuit has only made cosmetic changes in its test after *KSR*. Part 3 shows that the Federal Circuit's attempts to distinguish *KSR* do not justify the Federal Circuit's disregard of *KSR*.

1. *Pfizer, Inc. v. Teva Pharmaceuticals USA, Inc.*¹²⁹ and *Bristol-Myers Squibb Co. v. Teva Pharmaceuticals USA, Inc.*¹³⁰

Pfizer

In *Pfizer*, the Federal Circuit used (1) the strict teaching, suggestion, motivation test the Supreme Court had rejected in *KSR* and (2) a test for obviousness of new pharmaceutical compounds — not suggested in either *Graham* or *KSR* but based on a pre-*KSR* Federal Circuit decision — to hold that a patent for a new chemical compound marketed by Pfizer under the name Lyrica® was not obvious.¹³¹ Pfizer had sued Teva and others for

128. *BMS* was reported in the Federal Reporter, whereas *Pfizer* was reported in the Federal Appendix. The Federal Appendix report states on the first page, "This case was not selected for publication in the Federal Reporter. Not for Publication in West's Federal Reporter." The Supreme Court changed the Federal Rules of Appellate Procedure in 2006 to provide in relevant part at Rule 32.1, "A court may not prohibit or restrict the citation of federal judicial opinions, orders, judgments, or other written dispositions that have been: (i) designated as 'unpublished,' 'not for publication,' 'non-precedential,' 'not precedent,' or the like; and (ii) issued on or after January 1, 2007."

129. 555 F. App'x 961 (Fed. Cir. 2014).

130. 752 F.3d 967 (Fed. Cir. 2014)

131. The compound was for treatment of seizures and certain types of pain. The district court had explained, "4-amino-3-(2-methylpropyl) butanoic acid is also known as '3-isobutylGABA' or '3IBG' and is used to treat seizures. . . . 3-isobutylGABA is a chiral compound: it exists in two different mirror-image orientations in space, called 'enantiomers.' . . . Chemists distinguish between enantiomers by

filing an abbreviated new drug application (“ANDA”) for the generic equivalent of Lyrica®, and the defendants alleged, among other things, that the patent was invalid as obvious.¹³²

The district court stated, and the parties agreed on, the level of skill of PHOSITA for the applicable patent: “a person of ordinary skill in the art would be a scientist with a Ph.D. in organic or medicinal chemistry with at least two years of experience in the synthesis of organic compounds or, alternatively, a master’s degree in the same fields with at least five years of experience in organic synthesis.”¹³³ The district court did not discuss the process of drug discovery in the pharmaceutical industry.¹³⁴ The district court concluded the defendants had not demonstrated clearly and convincingly that the claim was obvious and enjoined the defendants from manufacturing, selling or offering to sell the generic product.¹³⁵

The Federal Circuit affirmed, but in its opinion on obviousness did not cite either *Graham* or *KSR*.¹³⁶ In fact, the only Supreme Court decision cited on obviousness was the Supreme Court decision on a defendant’s burden of proof in challenging the validity of a patent, *Microsoft Corp. v.*

assigning an ‘R’ or ‘S’ prefix to the compound name depending on the ‘priorities of the substituents around the [chiral] carbon atom.’ . . . S-(+)-4-amino-3-(2-methylpropyl) butanoic acid is the S-enantiomer of 3-isobutylGABA, which is generally known as ‘pregabalin’ and is the active ingredient in the product at issue, Lyrica®.” *Pfizer, Inc. v. Teva Pharm. USA, Inc.*, 882 F.Supp.2d 643, 654 (D. Del. 2012).

132. *Id.* at 656. An ANDA is the application a manufacturer submits to the FDA seeking approval to market a generic version of a patented drug. *See* Abbreviated New Drug Application (ANDA): Generics, FDA, <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/>, (last visited Jul. 29, 2014). Under 35 U.S.C. §271, it is not an act of infringement for a manufacturer to make a drug patented by another company, “to the extent it is necessary for the preparation and submission of an ANDA.” *Bristol-Myers Squibb Co. v. Royce Labs, Inc.* 69 F.3d 1130, 1132 (Fed. Cir. 1995). However, the submission of the ANDA after such preparation is an act of infringement under §271(e)(2), and “the patent owner can seek to prevent approval of the ANDA by bringing a patent infringement suit.” *Id.* at 1302. *See also* PATENT LAW, *supra* note 5, at 508–12.

133. *Pfizer*, 882 F. Supp. 2d at 665–66.

134. This contrasts with BMS, discussed next, and may reflect that various litigants pursue the skill of PHOSITA as an issue more rigorously than others (of course, if you put five litigators in a room, there will likely be five different approaches of emphasis in any complex area). A court’s failure to discuss this area may not reflect any predisposition on the court, but simply the approach of litigants.

135. *Pfizer*, 882 F. Supp. 2d at 666–69, 732. The Supreme Court held that a defense of patent invalidity required by clear and convincing evidence. *Microsoft Corp. v. i4i Limited P’ship*, 131 S. Ct. 2238, 2242 (2011) In a concurring opinion joined by Justices Scalia and Alito, Justice Breyer said, “I believe it worth emphasizing that in this area of law as in others the evidentiary standard of proof applies to questions of fact and not to questions of law.” *Id.* at 2253.

136. The Federal Circuit’s failure to cite *KSR* has occurred before. Professor Eisenberg said, “The Federal Circuit may be off to a poor start in showing its respect for *KSR*. In three post-*KSR* (non)obviousness cases the Federal Circuit has not even cited *KSR*. *Forest Labs, Inc. v. Ivax Pharm., Inc.*, 501 F.3d 1263 (Fed. Cir. 2007); *Daiichi Sankyo, Co. v. Apotex, Inc.* 501 F.3d 1254 (Fed. Cir. 2007); *Frazier v. Layne Christensen Co.*, 239 Fed. App’x 604 (Fed. Cir. 2007).” *See Nonobvious Problem*, *supra* note 5, at 395 n.93.

i4i Ltd. P'ship.¹³⁷ Put another way, the Federal Circuit cited a Supreme Court decision that made it more difficult for a defendant to successfully challenge the validity of a patent (by confirming a high burden of proof to successfully challenge the validity of a patent), but did not cite *KSR*, the Supreme Court case making it easier for a litigant to successfully challenge patent validity.¹³⁸

In *Pfizer* the Federal Circuit said, “[w]hether a new chemical compound would have been prima facie obvious over particular prior art compounds follows a two-part inquiry under our precedent.”¹³⁹

(1) “First, the court determines whether a chemist of ordinary skill in the art would have selected the asserted prior art compound as a lead compound, or starting point, for further development”;¹⁴⁰

(2) “The second step of the obviousness analysis requires a showing that the prior art would have taught a skilled artisan to make ‘specific molecular modifications’ to a lead compound so that the claimed compound may be made with a reasonable expectation of success.”¹⁴¹

In addition, the Federal Circuit said:

(3) “A patent challenger . . . must demonstrate the selection of a lead compound based on its ‘promising useful properties,’ not a hindsight-driven search for structurally similar compounds.”¹⁴²

By requiring that a challenger not only show that prior art identified structurally similar compounds but also that prior art showed those compounds had similar, useful properties, the Federal Circuit was essentially disregarding the Supreme Court’s “promotion” of obvious to try in *KSR*.

137. *Microsoft*, 131 S.Ct. at 2242, cited at *Pfizer Inc. v. Teva Pharm. USA, Inc.*, 555 F. App’x 961, 969. (Fed. Cir. 2014). The substantive patent question in *Microsoft Corp.* was whether “the on-sale bar of § 102(b) precludes patent protection for any ‘invention’ that was ‘on sale in this country’ more than one year prior to the filing of a patent application.” 131 S.Ct. at 2242.

138. As noted, the Federal Circuit also did not cite *Graham*, but since it was the first Supreme Court case interpreting the obviousness requirement of § 103, it is difficult to say if *Graham* made the standard either higher or lower—it set the standard.

139. 555 F. App’x at 969.

140. *Id.* (emphasis added). Professor Eisenberg has written, “The focus on whether a PHOSITA would have selected the closest prior art molecule as a ‘lead compound’ is an interesting move that makes it easier to establish nonobviousness for new chemical entities that have not previously been developed as drugs. New drugs are often structurally similar to prior art compounds that, for one reason or another, have not been selected for development through clinical trials.” *Nonobvious Problem*, *supra* note 5, at 423. Professor Janis acknowledges that the lead compound analysis “also treads close to the forbidden territory of ‘rigid’ motivation rules, . . . and this concern would be heightened if the rule becomes the foundation for a formalized hierarchy of corollaries, or if the rule is invoked reflexively and woodenly to negate obviousness proofs irrespective of the factual context.” *Tuning*, *supra* note 4, at 345.

141. *Pfizer*, 555 F. App’x at 971 (emphasis added).

142. *Id.* at 970. (emphasis added).

KSR points to the conclusion that it can be obvious to try changing structurally similar compounds, even if they initially do not exhibit similar properties. In addition, in *Pfizer*, the Federal Circuit said:

(4) “the district court found Appellees to have credibly established that anticonvulsant drug discovery in 1990 was ‘complicated,’ ‘unpredictable’ and ‘largely conducted through trial and error.’ . . . This finding would have precluded any argument by Appellants that there would have been a ‘reasonable expectation of success.’”¹⁴³

The Federal Circuit did not discuss the level of skill of PHOSITA, which is perhaps not surprising, since the parties had no dispute about that.¹⁴⁴

In both (2) and (4) above, the Federal Circuit talked about “reasonable expectation of success.” Professor Mueller has written, “[t]he Supreme Court in *KSR* did not cite or directly address . . . the Federal Circuit’s requirement that the skilled artisan possess a reasonable expectation of success in modifying/combining the prior art disclosures.”¹⁴⁵ However, considering reasonable expectation of success seems at least implicit from the discussion in *KSR* of “a marketplace that a created a strong incentive to convert mechanical pedals to electronic pedals”¹⁴⁶ and “[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp.”¹⁴⁷

Put another way, the greater the reason (*e.g.*, billions of dollars in possible profits) to pursue a research path, the lower the expectation of success might need to be for PHOSITA to undertake the path. Conversely, the greater the expectation of success, the smaller the reasons to combine would need to be. Professor Duffy argued “[m]ixing economic considerations into the analysis — or better still, making economic factors the centerpiece of analysis rather than merely relevant factors — is desirable not only because it generates better patent policy but also because it represents the better interpretation of the statute and reconciles patent law with other areas of regulatory theory.”¹⁴⁸

143. *Id.* at 971 (emphasis added).

144. *See supra*, note 134.

145. *See* PATENT LAW, *supra* note 5, at 292.

146. *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 424 (2007).

147. *Id.* at 421.

148. *Inducement Standard*, *supra* note 3, at 1612. Professor Landes and Judge Posner similarly argue, “[a] more illuminating approach ties nonobviousness to uncertainty and cost.” *See* ECONOMIC STRUCTURE, *supra* note 11, at 304. The Federal Circuit agreed that courts must take into account “the ease and predictability” of research paths in determining whether an invention was obvious. *See In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009); *see supra*, notes 110–20 and accompanying text.

On the other hand, the fact that a particular field, such as chemistry, may generally be considered unpredictable does not warrant a conclusion that a particular research path in chemistry was not obvious to try or that the result was not obvious.¹⁴⁹ As Dr. Liang pointed out, “not all properties of chemical arts are equally unpredictable While scientists working in the field are embracing technologies that can predict properties of chemical compounds, perhaps, the court should do the same.”¹⁵⁰ Similarly, Professor Underweiser said, “KSR did not say that it only addressed the law of obviousness in predictable fields . . . broad characterization of any field must inevitably change as new technologies emerge and scientists become more comfortable with existing ones, so the Federal Circuit must inevitably revisit the law of obviousness in the chemical arts as it is currently doing in the electrical and mechanical fields.”¹⁵¹

The Federal Circuit in *Pfizer*, however, ruled that the district court did not err in concluding defendants failed to show that prior art identified the lead compounds or the necessary teachings to modify a lead compound to “improve anticonvulsant activity.”¹⁵² The court concluded by saying that since the defendants had not proven the claim at issue “would have been ‘prima facie obvious’¹⁵³ over the asserted prior art compounds, we need not address the court’s findings regarding secondary considerations of nonobviousness.”¹⁵⁴

149. For instance, through structure activity relationship (“SAR”) analysis and quantitative structure activity relationship (“QSAR”) models. See Guyan Liang, *The Validity Challenge To Compound Claims And The (Un?)predictability Of Chemical Arts*, 13 WAKE FOREST J. BUS. & INTELL. PROP. L. 38, 41, 74 (2012). Such “technologies and approaches used to predict properties of chemical compounds have grown out of the ivory tower of theoretical chemistry and become more and more accepted by the general scientific community” and “are firmly rooted in the knowledge of people having ordinary skill in the art and are often applied in their research.” *Id.* at 79–80.

150. *Id.* at 69, 80.

151. *Presumed Obvious*, *supra* note 12, at 288.

152. *Pfizer Inc. v. Teva Pharm. USA, Inc.*, 555 F. App’x 961, 971. (Fed. Cir. 2014).

153. “Prima facie obvious” here refers to cases where a patent has issued and the defendant has the burden to prove invalidity by clear and convincing evidence. 35 U.S.C. §282 (2012) and *Microsoft v. i4i Limited Partnership*, 131 S.Ct. 2238 (2011). In *re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litigation*, the Federal Circuit said that “a court inquires whether the party challenging validity has proven a ‘prima facie’ case of obviousness, based only on reference to the patent and the proffered prior art, and only then considers objective evidence, asking whether such evidence is sufficient to overcome the prima facie case.” 676 F.3d 1063, 1076 (Fed. Cir. 2012). The Federal Circuit said that using “prima facie obvious” or similar terms “should not be interpreted as establishing a formal burden-shifting framework” and that “the ‘prima facie’ and ‘rebuttal’ language generally have made clear that a fact finder must consider all evidence of obviousness and nonobviousness before reaching a determination.” *Id.* at 1077. Whether the issue is prima facie obviousness or obviousness after rebuttal evidence has been presented, the multi-part test for new pharmaceutical compounds remains the same, as set forth in *Pfizer* and, described next, *BMS*.

154. *Pfizer*, 555 F. App’x at 971. (emphasis added).

BMS

The Federal Circuit in 2014 used the same obviousness test for new pharmaceutical compounds it had used in *Pfizer* earlier in 2014. The representative claim was “directed to a nucleoside analog composed of two regions: a carbocyclic ring and a guanine base.”¹⁵⁵ BMS sued Teva for filing an ANDA for a generic version of entecavir.¹⁵⁶ In *BMS* the Federal Circuit’s obviousness test for new chemical compounds effectively precluded the analysis of much evidence that should have been relevant to PHOSITA in determining obviousness, as discussed below, making the decision seem arbitrary, regardless of whether one concludes the obviousness hurdle for the challenger was too high or too low.¹⁵⁷

The district court had made detailed findings of fact¹⁵⁸: four concerning three different approaches for the discovery of new drugs;¹⁵⁹ nine concerning the invention of entecavir, including detailed steps taken by the inventors;¹⁶⁰ seventeen concerning selection of the lead compound (2’CDG);¹⁶¹ twenty-three on the modification of the lead compound to create entecavir;¹⁶² and 8 on an ordinary medicinal chemist’s expectation of success in making entecavir.¹⁶³ The district court noted that the experts for both parties “stated that regardless of which definition of the person of

155. *Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, 752 F.3d 967, 969 (Fed. Cir. 2014). Entecavir was a compound used as a treatment for hepatitis B under the trade name Baraclude®. *Id.* at 969.

156. *Bristol-Myers Squibb Co. v. Teva Pharmaceuticals USA, Inc.*, 923 F. Supp. 2d 602 (D. Delaware 2013).

157. Although the test for new pharmaceutical compounds generally makes it easier to defend a claim of nonobviousness (*see supra*, note 137) than warranted by KSR, another problem is that the test would seem to improperly limit from consideration evidence that would otherwise seem relevant to PHOSITA on the issue of obviousness. *See infra*, text accompanying notes 178–179.

158. Of course, the district court in *Pfizer* made many findings of fact, but those findings did not discuss not the process used by *Pfizer* to invent the pharmaceutical compound. The district court instead focused on unpredictability, saying that “identifying improved anticonvulsant drugs in 1990 was a complicated and unpredictable and was largely conducted through trial and error . . . while almost 34,000 investigational drugs have been tested as potential anticonvulsants as part of an NIH screening program at the University of Utah, only fifteen new drugs have been approved in the United States for seizure treatment since 1993.” *Pfizer Inc. v. Teva Pharm. U.S.A., Inc.*, 882 F. Supp. 2d 643, 667 (D. Del. 2012).

159. *Bristol-Myers Squibb Co.*, 923 F. Supp. 2d at 613, findings of fact (“FOF”): (30) “modification of a known lead compound,” (31) “random screening of compounds against an *in vitro* assay to find a lead compound,” and (32) “the most difficult . . . learning about the biology of a disease and, from their, attempting to design drug that targets the disease.”)

160. *Id.* at 613-615, FOF 33-41 (“35 . . . the traditional drug discovery approach—making structural changes to lead compoundsFalse . . . 36. By 1989, after his team had failed to succeed using the traditional drug discovery approach, Dr. Zahler decided to try a different approach, which led to his conception of entecavir. . . . Dr. Zahler first came up with the idea for entecavir in his head and drew it out on paper. . . . 39. Dr. Zahler’s team selected several different compounds to compare to entecavir via computer modeling and to help ‘validate’ the computer model.”)

161. *Id.* at 620-624, FOF 78–94.

162. *Id.* at 626-630, FOF 100–122.

163. *Id.* at 630-631, FOF 123–130.

ordinary skill in the art is found to be correct, their opinions as to the validity of the patent would remain the same.”¹⁶⁴

The district court made detailed findings of fact concerning the differences between the claimed invention (entecavir) and 2'-CDG (the identified lead compound), including:

“94. Even if some evidence did exist prior to October 1990 indicating that 2'-CDG was associated with toxicity, such evidence was limited, and would not have discouraged the ordinary medicinal chemist from using 2'-CDG as a lead compound. Indeed, Dr. Slusarchyk [one of the inventors], the medicinal chemist who designed the synthesis for entecavir, testified that toxicity data about nucleoside analogs that he was making ‘wouldn't deter [him] from making more compounds in the area to investigate further’ as he was a ‘medicinal chemist,’ not a ‘toxicologist.’”^{False}

95. The only structural difference between entecavir and 2'-CDG is the addition of one carbon atom at the 5 prime position of the ribose portion of entecavir. 2'-CDG has a single carbon atom at the 5 prime position while entecavir has an exocyclic methylene group (a “carbon-carbon double bond”) at the 5 prime position.^{False}

97. ^{False} Through this computer modeling, Dr. Zahler [the other inventor] and his team confirmed that entecavir and 2'-CDG should have similar antiviral activity.^{False}

99. The most significant difference between 2'-CDG and entecavir is that the former is toxic while the latter is not (Tr. 252:8–13), although this difference was not clear as of October 1990, as explained above.”¹⁶⁵

The district court concluded that Teva had shown by clear and convincing evidence that PHOSITA “would have had a reason to select [2'-CDG] over other compounds in the prior art.”¹⁶⁶ The district court also concluded that PHOSITA “would have a reason or motivation to modify 2'-CDG by adding a carbon atom to arrive at entecavir with a reasonable expectation of success.”¹⁶⁷ The district court held the claim was invalid as obvious under § 103.¹⁶⁸

BMS appealed, and the Federal Circuit affirmed.¹⁶⁹ Although in *Pfizer* it did not, the Federal Circuit in *BMS* did cite *Graham* and *KSR*, but only in one sentence, essentially to repeat the *Graham* standard: “[o]bviousness requires assessing (1) the ‘level of ordinary skill in the pertinent art,’ (2) the ‘scope and content of the prior art,’ (3) the ‘differences between the

164. *Id.* at 616

165. *Id.* at 624–626.

166. *Id.* at 655.

167. *Id.* at 665.

168. *Id.* at 686.

169. *Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, 752 F.3d 967, 969 (Fed. Cir. 2014)), *petition for panel rehearing and rehearing en banc denied*, 769 F.3d 1339 (Fed. Cir. Oct. 20, 2014), *petition for cert. pending*.

prior art and the claims at issue,’ and (4) ‘secondary considerations’ of nonobviousness such as ‘commercial success, long-felt but unsolved needs, failure of others, etc.’”¹⁷⁰ The Federal Circuit did not discuss at all *KSR*’s guidance on obvious to try.

The Federal Circuit in *BMS* used the same multi-part test for the obviousness of new pharmaceutical compounds that it used in *Pfizer*:

(1) Select lead compound:

“Generally, an obviousness inquiry concerning such ‘known compounds’ focuses on the identity of a ‘lead compound.’ *Eisai Co. Ltd. v. Dr. Reddy’s Labs., Ltd.*, 533 F.3d 1353, 1359 (Fed.Cir.2008).”¹⁷¹

“[W]e therefore agree with the district court that those of ordinary skill in the art [PHOSITA] would have selected 2’-CDG . . . as a lead compound for further development efforts before BMS applied for the ‘244 patent.”¹⁷²

(2) Identify modifications to lead compound:

“BMS attacks the lower court’s obviousness determination by contending that a skilled artisan would have had to make too many decisions to arrive at entecavir. Those decisions include selecting (1) the class of nucleoside analog compounds, . . . (6) the type of carbon to carbon bond (single or double).”¹⁷³

“[W]e see no clear error in the district court’s finding that the modification required to transform 2’-CDG into the structurally similar entecavir is a minor one.”¹⁷⁴

Just as it did in *Pfizer*, the Federal Circuit in *BMS* also discussed the general topic of unpredictability. In *BMS*, the court discussed the higher degree of effectiveness of the compound than expected. However, it also said that “did not upset an already established motivation to modify a prior art compound based on the expected properties of the resulting compound.”¹⁷⁵ Adding further complexity, the court said, “[w]hile a ‘marked

170. *Id.* at 973. (internal citations omitted).

171. *Id.* (emphasis added).

172. *Id.* at 974. See also *Id.* at 973 (“the district court properly found strong evidence of obviousness, because the record shows that a skilled artisan would have selected 2’-CDG as a lead compound. . .”).

173. *Id.*

174. *Id.* at 975.

175. *Id.* at 976. The Federal Circuit treated unexpected results as a secondary consideration, although Professor Eisenberg argues, “Evidence of surprising or unexpected properties is unlike these other sources of market evidence that indicate obviousness only through a chain of inferences. It is primary, technological evidence going directly to the statutory inquiry as to the differences between the subject matter sought to be patented and the prior art. . . . The characterization of this evidence as secondary seems fundamentally confused. . . .” *Nonobvious Problem*, *supra* note 5, at 418 (internal quotations and citations omitted). Whether the Federal Circuit’s treatment of “unexpected results” is consistent with *Graham* and *KSR* is beyond the scope of this article.

superiority' in an expected property may be enough in some circumstances to render a compound patentable, a "mere difference in degree" is insufficient"¹⁷⁶

Donald Chisum has noted, "[u]nexpected results and properties have played an especially important role in assessing the patentability of new chemical compounds, compositions, and pharmaceutical methods."¹⁷⁷ However, in neither *Pfizer* nor *BMS* did unexpected results cause the Federal Circuit to reverse the district court's holdings on obviousness (in *Pfizer* a finding of not invalid for obviousness and in *BMS* a finding of obviousness). Chisum also said that "the courts tend to recite and rely upon secondary considerations when ruling in favor of patent claims and tend to disparage such considerations when ruling against patent claims."¹⁷⁸

Although in *BMS* the Federal Circuit did preface the first step of the test with the word "generally", the court did not suggest any other possible test. In fact the Federal Circuit stuck to the lead compound part of the test even though there were at least two alternative ways to view the facts. For instance, after four years of trying to identify a lead compound, Dr. Zahler, one of the inventors, and "his team had failed to succeed using the traditional drug discovery approach" of identifying a lead compound.¹⁷⁹ Dr. Zahler subsequently "came up with the idea for entecavir in his head and drew it out on paper Then, because he tended to think in 'three dimensions,' Dr. Zahler used what are known as 'Dreiding models' in order to further develop his ideaFalse"¹⁸⁰ If a claimant were not limited to the obviousness test for new pharmaceutical compounds, Dr. Zahler's failure over a four year period to identify a lead compound would seem to strongly support a conclusion that entecavir was not obvious.

Alternatively, what if PHOSITA focused on the differences found between the prior art and the patent claim at the time of the invention?

"95. The only structural difference between entecavir and 2'-CDG is the addition of one carbon atom at the 5 prime position of the ribose portion of entecavir. . . 2'-CDG has a single carbon atom at the 5 prime position while entecavir has an exocyclic methylene group (a "carbon-carbon double bond") at the 5 prime position. . .

176. *Bristol-Myers Squibb Co.*, 752 F.3d at 977 (internal citations omitted). The Federal Circuit also considered the secondary considerations of nonobviousness of commercial success and long-felt need found by the district court, but agreed with the district court that the "record demonstrates strong evidence of obviousness" and affirmed the legal conclusion of obviousness. *Id.* at 979.

177. CHISUM ON PATENTS, *supra* note 2 at §5.04[1][g].

178. *Id.* at §5.05.

179. *Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, 923 F. Supp. 2d 602, 614 (D. Del. 2013), FOF 36 ("By 1989, after his team had failed to succeed using the traditional drug discovery approach, Dr. Zahler decided to try a different approach, which led to his conception of entecavir. . . . Dr. Zahler first came up with the idea for entecavir in his head and drew it out on paper").

180. *Id.* at 614-36. (internal citations omitted).

97. . . . [t]hrough this computer modeling, Dr. Zahler [the other inventor] and his team confirmed that entecavir and 2'-CDG should have similar antiviral activity. . . .”¹⁸¹

Under these two findings of fact, the legal conclusion of obviousness under *KSR* would naturally seem to result.

The Federal Circuit’s new pharmaceutical compound test cabins the fact-finder by limiting the ability of the inventor to show how difficult her invention was to make at one end (favoring a finding of nonobviousness) and, on the other end, by preventing a challenger from arguing that regardless of whether or not a lead compound was identified from prior art, the small structural differences between prior art chemicals and the new pharmaceutical compound made the patent claim obvious (favoring a finding of not obvious). This apparent limitation of evidence to consider is consistent with Professor Rai’s argument that the Federal Circuit has adopted “formalist, bright-lined rules that leave inferior decision-makers little room for factual inquiry The court’s adoption of bright-line rules that are insensitive both to technological fact and to related issues of innovation policy is also suspect.”¹⁸²

Where and when did the Federal Circuit’s test for new pharmaceutical compounds originate? The next section traces the Federal Circuit’s development of this test to the strict teaching, suggestion, motivation test adopted by the Federal Circuit before *KSR* and subsequently rejected by the Supreme Court in *KSR*.

2. The Federal Circuit’s Test for New Pharmaceutical Compounds Relies on the Strict Teaching, Suggestion, Motivation Test Adopted Before/Rejected by the Supreme Court in *KSR*

In *Pfizer* the Federal Circuit cited in support of its test for new pharmaceutical compounds its earlier decision of *Eli Lilly and Company v. Zen-*

181. *Id.* at 624–25. In *Eisai Co. Ltd. v. Dr. Reddy’s Labs. Ltd.*, 533 F.3d 1353, 1357 (Fed. Cir. 2008) (internal citations omitted), the Federal Circuit said, “for a chemical compound, a prima facie case of obviousness requires ‘structural similarity between claimed and prior art subject matter . . . where the prior art gives reason or motivation to make the claimed compositions.’” For a discussion of prima facie obviousness, see *supra* note 154. Prima facie obvious can also be used to denote the burden the PTO has before rejecting a claim because of obviousness. See *In re Mayne*, 104 F.3d 1339, 1341–42 (Fed. Cir. 1997). There is no suggestion in *KSR* that in order for some path to be obvious to try, prima facie obviousness must first also have been established.

182. Arti K. Rai, *Engaging Facts And Policy: A Multi-Institutional Approach To Patent System Reform*, 103 COLUM. L. REV. 1035, 1037 (2003). She further argued that the Federal Circuit also pursued another strategy that appeared anomalous, “relatively vigorous de novo review . . . of technological fact.” *Id.* Professor Lee argued “[a] less appreciated facet of the TSM test is that it limits the range of technologically challenging inquiries that a court must make. Quite simply, the TSM test truncates the nonobviousness inquiry.” Peter Lee, *Patent Law and Two Cultures*, 120 YALE L. J. 2, 38 (2010) (hereafter *Two Cultures*).

ith Goldline Pharmaceuticals, Inc. [hereafter *Lilly*].¹⁸³ Eli Lilly had a patent for olanzapine to treat schizophrenia and sued Zenith and others for filing an ANDA for generic olanzapine and the use of the compound to treat schizophrenia.¹⁸⁴ The district court found Eli Lilly's patents valid and infringed, and in 2006, before the Supreme Court decided *KSR*, the Federal Circuit affirmed.¹⁸⁵

In *Lilly* the Federal Circuit held that prior art must have made obvious not only the lead compound, but the individual steps taken to change the lead compound into the claimed invention.¹⁸⁶ The Federal Circuit quoted its 2000 decision of *Yamanouchi Pharmaceutical Co., Ltd. v. Danbury Pharmacal, Inc.*, perhaps the earliest decision in which the Federal Circuit described this test for new pharmaceutical compounds:¹⁸⁷

“[The ANDA filer] did not show sufficient motivation for one of ordinary skill in the art at the time of invention to take any one of the following steps, let alone the entire complex combination: (1) selecting example 44 as a lead compound, (2) combining the polar tail from example 44 with the substituted heterocycle from tiotidine, and (3) substituting the carbamoyl (CONH₂) group in the intermediate compound with a sulfamoyl group (SO₂NH₂) to create famotidine.”¹⁸⁸

In *Lilly*, the Federal Circuit concluded that Zenith and other defendants similarly had failed the first part of the test (lead compound), because “the defendants have not shown that a person ordinarily skilled in this art would have selected Compound '222 as a lead compound because it contained hydrogen rather than fluorine or chlorine.”¹⁸⁹ The Federal Circuit also concluded the defendants had failed the second part of the test (steps

183. *Pfizer Inc. v. Teva Pharm. USA, Inc.*, 555 F. App'x 961, 969. (Fed. Cir. 2014).

184. *Eli Lilly and Co. v. Zenith Goldline Pharm. Inc.*, 471 F.3d 1369, 1373 (Fed. Cir. 2006), rehearing and rehearing en banc denied March 29, 2007.

185. *Eli Lilly and Co. v. Zenith Goldline Pharm., Inc.*, 364 F. Supp. 2d 820 (S.D. Ind. 2005), *aff'd* 471 F.3d 1369 (Fed. Cir. 2007).

186. *Lilly*, 471 F.3d at 1378–79, (citing *Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, 1344–45) (Fed.Cir.2000) (The ANDA filer “did not show sufficient motivation for one of ordinary skill in the art at the time of invention to take any one of the following steps, let alone the entire complex combination: (1) selecting example 44 as a lead compound, (2) combining the polar tail from example 44 with the substituted heterocycle from tiotidine, and (3) substituting the carbamoyl (CONH₂) group in the intermediate compound with a sulfamoyl group (SO₂NH₂) to create famotidine.”). *Yamanouchi* involved a challenge to a patent for famotidine, a drug used to treat heartburn and ulcers. *Id.* at 1341. The Federal Circuit in *Lilly* also said, “Beyond the nonobvious selection step, the prior art also did not suggest any of the other modifications necessary to reach olanzapine.” 471 F.3d at 1379.

187. *Yamanouchi*, 231 F.3d 1339; see *Structural Uncertainty*, *supra* note 23 at 405 (“The earliest case establishing the modern ‘lead compound’ analysis is *Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc.*”).

188. *Lilly*, 471 F.3d at 1378–79.

189. *Id.* at 1379.

taken to obtain the final compound), because, “the prior art also did not suggest any of the other modifications necessary to reach olanzapine.”¹⁹⁰

In both *Lilly* and *Yamanouchi*, the Federal Circuit employed a strict teaching, suggestion, motivation test before the Supreme Court’s subsequent rejection of such a test in *KSR*. Referring to this lead compound approach to obviousness in 2008, Professor Eisenberg wrote that the Federal Circuit “ha[d] articulated an approach to evaluating the (non)obviousness of chemical inventions, including pharmaceuticals, that sometimes seems as ‘rigid and mandatory’ as the TSM approach at issue in *KSR*.”¹⁹¹

Do *Pfizer* and *BMS* indicate the Federal Circuit changed its new pharmaceutical compounds test since *KSR*? The citation to *Lilly*, and *Lilly*’s reliance on *Yamanouchi*, would suggest the Federal Circuit has not changed its test. However, the Federal Circuit in *BMS* and *Pfizer* cited three post-*KSR* cases, *Otsuka Pharmaceutical Co., Ltd. v. Sandoz, Inc.* (hereafter *Otsuka*),¹⁹² *Eisai Co. Ltd. v. Dr. Reddy’s Laboratories, Ltd.* (hereafter *Eisai*),¹⁹³ and *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.* (hereafter *Takeda*)¹⁹⁴ in support of the new pharmaceutical compounds test.¹⁹⁵ In 2012 Professor Janis wrote that “post-*KSR* decisions appear to have put the Federal Circuit firmly back into the practice of invoking the TSM test, albeit flexibly.”¹⁹⁶ Therefore the next section of this article examines *Otsuka*, *Eisai* and *Takeda*.

3. The Federal Circuit’s Attempts to Distinguish *KSR*

Otsuka, *Eisai* and *Takeda* each involved patents for new pharmaceutical compounds, and in each the Federal Circuit attempted to distinguish *KSR*, apparently recognizing tension between the Federal Circuit’s test and the Supreme Court’s decision in *KSR*. However, the facts in those cases did not remove them from the *KSR* standard.

190. *Id.*

191. *Nonobvious Problem*, *supra* note 5, at 377. She continued, “Under this approach, a patent examiner (or a challenger of an issued patent) must first show that a claimed molecule is prima facie obvious by identifying a ‘structurally similar’ molecule in the prior art and by showing motivation to modify that prior art molecule to create the claimed invention.” She suggested that *KSR* “calls into question the Federal Circuits’ approach to chemical (non)obviousness.” *Id.*

192. *Otsuka*, 678 F.3d 1280 (Fed. Cir. 2012).

193. *Eisai*, 533 F.3d 1353. (Fed. Cir. 2008).

194. *Takeda*, 492 F.3d 1350 (Fed. Cir. 2007).

195. *Pfizer Inc. v. Teva Pharm. USA, Inc.*, 555 F. App’x 961, 969–71, (Fed. Cir. 2014); *Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, 752 F.3d 967, 973. (Fed. Cir. 2014).

196. See *Tuning*, *supra* note 4, at 343. However, as mentioned *supra*, at note 140, he also said that the lead compound test treaded close to forbidden motivation rules, and that “this concern would be heightened if the rule becomes the foundation for a formalized hierarchy of corollaries, or if the rule is involved reflexively and woodenly to negate obviousness proofs irrespective of the factual context.” *Id.* at 345.

Otsuka

In *Otsuka Pharmaceutical Co., Ltd. v. Sandoz, Inc.*, the Federal Circuit tried to explain its continued use of its obviousness test for new pharmaceutical compounds in light of *KSR*. Otsuka had sued Sandoz and others for filing ANDA's to manufacture the generic equivalent of Otsuka's patented aripiprazole, an antipsychotic drug marketed under the name Abilify.¹⁹⁷ The district court concluded the patent was not obvious and enjoined the defendants' from manufacturing the generic equivalent.¹⁹⁸ The defendants appealed, and in 2012 the Federal Circuit affirmed.¹⁹⁹

The Federal Circuit said that the test for determining obviousness of a new chemical compound "ordinarily follows a two-part inquiry": (1) determining whether PHOSITA would have selected the prior art lead compounds and (2) "whether the prior art would have supplied [PHOSITA] with a reason or motivation to modify a lead compound to make the claimed compound with a reasonable expectation of success."²⁰⁰ The Federal Circuit placed this two-part test in the *Graham* standard of determining the differences between the claimed invention and the prior art.²⁰¹ Although it prefaced the test with the word "ordinarily," the Federal Circuit gave no indication of any alternative test to use, and in fact it used the pre-*KSR Lilly/Yamanouchi* test for new pharmaceutical compounds.

The Federal Circuit also said that identifying the suggestion for the lead compound from prior art was necessary, because "otherwise, the analysis would impermissibly rely upon *ex post* reasoning," and quoted *KSR* that "[a] fact-finder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning."²⁰² Yet the Supreme Court made that statement in the context of rejecting Teleflex's concern over *ex post* reasoning.²⁰³ The Court in *KSR* simply was warning against bias in using hindsight reasoning and was not warning against any hindsight analysis. Indeed, by expanding the amount of prior art to consider *ex post*, the Court increased in many cases the amount of hindsight analysis. § 103 mandates reasoning after the fact, or

197. *Otsuka*, 678 F.3d at 1283–84.

198. *Otsuka Pharm. Co., Ltd. V. Sandoz, Inc.*, No. 3:07-CV-01000 (MLC), 2010 WL 4596324, *37 (D.N.J. 2010).

199. *Otsuka*, 678 F.3d at 1283.

200. *Id.* at 1291–92.

201. *Id.* at 1290–91. *See supra* note 75 stating that the order of treatment of the *Graham* factors is not important.

202. *Id.* at 1292.

203. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 421 (2007). The Court said the Federal Circuit "drew the wrong conclusion from the risk of courts and patent examiners falling prey to hindsight bias. False rigid preventative rules that deny fact finders recourse to common sense, however, are neither necessary under our case law nor consistent with it." *Id.*

hindsight, to determine obviousness, as discussed in more detail below at IIB1.

Suggesting flexibility in its test, the Federal Circuit said, “[i]n keeping with the flexible nature of the obviousness inquiry, the reason or motivation for modifying the lead compound may come from any number of sources and need not necessarily be explicit in the prior art.”²⁰⁴ However, the Federal Circuit only seemed to be suggesting flexibility in interpreting prior art to determine if the steps of the obviousness test for new pharmaceutical compounds had been satisfied, not whether prior art identified the lead compound and the steps afterwards up to and including the invention.²⁰⁵ Indeed, the Federal Circuit rejected defendants’ argument that the lead compound part of the test should not apply.²⁰⁶

The Federal Circuit said that “mere structural similarity between a prior art compound and the claimed compound does not inform the lead compound selection,”²⁰⁷ because the properties of two similar structures could be different. Although structural similarity between compounds A and B would not always mean that the properties of compound B are similar to those of A, under *KSR* it could seem to be obvious to try to test the properties of compound B and possibly modify those properties and structure to try to improve the medical treatment that had been provided by A. If that research path led to success, even though the particular result was not known in advance, the improvement could be obvious under § 103, depending on the cost and time involved in the research.²⁰⁸

The Federal Circuit in *Otsuka* essentially ignored the teaching of *KSR* that using well-known research paths to improve the functioning of combinations of products can result in inventions that are obvious. In other words, the result of experiments that are obvious to try can be an invention that is obvious, even though prior art did not predict the result in advance before the completion of the experiments. The Federal Circuit in *Otsuka* did not satisfactorily distinguish *KSR*.

Eisai

204. *Otsuka*, 678 F.3d at 1292.

205. The Federal Circuit did say “[n]ew compounds may be created from theoretical considerations rather than from attempts to improve on prior art compounds. In this case, however, the parties’ arguments focus on selecting and modifying particular prior art compounds, designated as lead compounds.” *Id.* at 1291. That statement is difficult to understand, because subsequently the court said, “The inventor’s own path itself never leads to a conclusion of obviousness; that is hindsight. What matters is the path that the person of ordinary skill in the art would have followed, as evidenced by the pertinent prior art.” *Id.* at 1296.

206. 678 F.3d at 1291. Defendants asserted that “the lead compound analysis . . . ‘fall[s] into a rigid obviousness analysis precluded by *KSR*.” *Id.* at 1290.

207. 678 F.3d at 1292.

208. *See supra* notes 86–87, 115 and 147–48.

An earlier attempt by the Federal Circuit to distinguish *KSR* also failed. Eisai Co. Ltd. sued Dr. Reddy's Laboratories, Ltd. and others for infringement of Eisai's patent covering rabeprazole when Dr. Reddys filed an ANDA to manufacture generic rabeprazole.²⁰⁹ The district court concluded the patent claim was nonobvious, defendants appealed, and in 2008, the Federal Circuit affirmed.

The Federal Circuit described essentially the same test for new pharmaceutical compounds set forth in *Lilly* and *Yamanouchi* by stating first, "*post-KSR*, a prima facie case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound."²¹⁰ Second, the court said the challenger had to show "some motivation that would have led one of ordinary skill in the art to . . . modify a known compound (i.e. a lead compound) in a particular way to achieve the claimed compound."²¹¹ The court also referred to "the flexible nature of the obviousness inquiry,"²¹² without in fact showing any flexibility in whether or not the test had to apply, and then explained what it saw as three differences between *Eisai* and *KSR*.

First, the Federal Circuit said "*KSR* assumes a starting reference point or points in the art, prior to the time of invention, from which a skilled artisan might identify a problem and pursue potential solutions."²¹³ In fact, however, the Supreme Court in *KSR* did not assume a starting reference point, but considered at least six prior art references²¹⁴ and whether the invention was obvious regardless of the starting point.²¹⁵ Indeed, the Supreme Court observed that the "designers might have decided to design new pedals from scratch; but they also would have had reason to make pre-existing pedals work with the new engines."²¹⁶

209. *Eisai Co. Ltd. v. Dr. Reddy's Labs, Ltd.*, 533 F.3d 1353, 1356 (Fed. Cir. 2008). Rabeprazole is the active ingredient in Aciphex, marketed by Eisai to suppress gastric acid production. *Id.*

210. *Id.* at 1359.

211. *Id.* at 1357.

212. *Id.* at 1357(citing *KSR, Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007)). Professor Merges has observed, "In contrast to Kubin, other Federal Circuit decisions seem to adopt an extraordinarily narrow view of the Supreme Court's opinion [in *KSR*]. Though the very first sentence in the Supreme Court's legal analysis in *KSR* sets forth a seemingly clear rejection of the Federal Circuit's prior doctrine. . . , some circuit decisions assert that the TSM test is not at all dead and that the Supreme Court in *KSR* disapproved of only the 'rigid' applications of the test." Merges, *supra* note 44, at 676.

213. *Eisai*, 533 F.3d at 1359.

214. 550 U.S. at 408–09 (e.g., Asano, Redding, Smith, Rixon, the '068 patent and the '936 patent).

215. 550 U.S. at 425 ("Just as it was possible to begin with the objective to upgrade Asano to work with a computer-controlled throttle, so too was it possible to take an adjustable electronic pedal like Rixon and seek an improvement that would avoid the wire-chafing problem. Following similar steps to those just explained, a designer would learn from Smith to avoid sensor movement and would come, thereby, to Asano because Asano disclosed an adjustable pedal with a fixed pivot.").

216. *Id.* at 424. It also noted that "upgrading its own pre-existing model led *KSR* to design the pedal now accused of infringing the Engelgau patent." *Id.*

Second, the Federal Circuit said, “*KSR* presupposes that the record up to the time of invention would give some reasons, available within the knowledge of one of skill in the art, to make particular modifications to achieve the claimed compound.”²¹⁷ Yet the Supreme Court in *KSR* did not presuppose — and was not concerned about — the particular modifications in the claimed invention.²¹⁸ The Court instead looked at the reasons PHOSITA would have combined prior references to solve market demand for an improved product, not the exact invention claimed. On that point, the Court said that “it was obvious to a person of ordinary skill to combine Asano [one of the prior art patents] with a pivot-mounted pedal position sensor”²¹⁹ It added, “[t]here then existed a marketplace that created a strong incentive to convert mechanical pedals to electronic pedals, and the prior art taught a number of methods for achieving this advance.”²²⁰

KSR only required the challenger to show that prior art and PHOSITA’s common sense and creativity would have caused PHOSITA to take a path readily leading to the patent’s subject matter. In contrast, under *Eisai*, the challenger had to show that prior art²²¹ would have caused PHOSITA to (1) select the lead compound and (2) make the particular changes to the lead compound that resulted in the claimed invention. The Federal Circuit in *Eisai* held, “[t]he record . . . shows no discernible reason for a skilled artisan to begin with lansoprazole . . . the record contains no reasons a skilled artisan would have considered modification of lansoprazole by removing the lipophilicity-conferring fluorinated substituent as an

217. *Eisai*, 533 F.3d at 1359.

218. For instance, the Supreme Court did not address or indicate that prior art suggested the last element in claim 4 of the patent: “said apparatus (12) characterized by said electronic control (28) being responsive to said pivot (24) for providing a signal (32) that corresponds to pedal arm position as said pedal arm (14) pivots about said pivot axis (26) between rest and applied positions wherein the position of said pivot (24) remains constant while said pedal arm (14) moves in fore and aft directions with respect to said pivot (24).” *Teleflex, Inc. v. KSR Int’l Co.*, 119 F. App’x 282, 284 (Fed. Cir. 2005).

219. 550 U.S. at 424.

220. *Id.* Moreover, the Court observed “Well before Engelgau applied for his challenged patent, some inventors had obtained patents involving electronic pedal sensors for computer-controlled throttles.” *Id.* at 408–09.

221. See *supra* note 5 for a discussion of the content of prior art. At the time of the decision in *Eisai*, § 102(a) and (b) provided: “[a] person shall be entitled to a patent unless (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.” The categories in § 102(a) only referred to information from by others (since an inventor could not create any record of the invention before his/her invention), but § 102(b) included publications, uses and sales by the inventor more than one year before the patent application. Initially for purposes of § 103 the items in § 102(b) (which included patents of the inventor, publications by the inventor and the inventor’s public uses and sales) were not considered to be prior art for purposes, but that changed due to a series of Federal Circuit decisions. Also, prior to the AIA, § 102 was amended to include expressly as prior art certain categories of “secret” prior art — through the adoption of § 102(e) and (g). See PATENT LAW, *supra* note 5, at 284–93.

identifiable, predictable solution.”²²² *KSR* did not require such record and gave appropriate recognition in the obviousness analysis to known scientific research techniques.

Third, the Federal Circuit said, “*KSR* presumes that the record before the time of invention would supply some reasons for narrowing the prior art universe to a ‘finite number of identified, predictable solutions.’”²²³ The Federal Circuit also added while quoting another Federal Circuit decision, “easily traversed, small and finite number of alternatives . . . might support an inference of obviousness.”²²⁴ However, the Supreme Court in *KSR* did not refer to either “easily traversed” or “small.”²²⁵ Although the amount and ease of options to pursue would undoubtedly be relevant in determining whether a research path was obvious to try and the resulting product obvious,²²⁶ presumably that determination would be made by the factfinder through the eyes of PHOSITA, rather than the Federal Circuit.

This narrowing of “obvious to try” by the Federal Circuit may reflect continued resistance by the Federal Circuit to the rejection by the Supreme Court of the strict TSM test. Indeed for years prior to *KSR* the Federal Circuit had pursued its support of the TSM test against the contrasting position of the U.S. Patent and Trademark Office, which had followed a position similar to the Supreme Court in *KSR* before the Supreme Court’s decision in *KSR*.²²⁷

In addition, the Supreme Court has preferred to maintain general standards in applying patent statutes, whereas the Federal Circuit has generally preferred more detailed specific rules.²²⁸ This Supreme Court preference is consistent with Chief Justice Roberts’ comment in oral argument in

222. *Eisai*, 533 F.3d at 1358–59.

223. *Id.* at 1359 (citing 550 U.S. at 421).

224. *Id.* at 1359 (quoting *Ortho-McNeil Pharm., Inc. v. Mylan Labs, Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008)).

225. See Justin L. Krieger, *Effectively Traversing “Obvious to Try” Arguments in the Wake of KSR v. Teleflex*, ASPATORE, Mar., 2011, at *1, *2, 2011 WL 1120277 (“In interpreting *KSR*, the Federal Circuit . . . has adopted language slightly different from—some would say significantly narrower than—the Supreme Court when determining whether a finite number of identified, predictable solutions exist, and thus, whether an obvious to try rationale may be used in invalidating a claim for obviousness”).

226. See *supra* notes 86–87, 115 and 148 and accompanying text.

227. See, e.g., Arti K. Rai, *Essay: Patent Validity Across the Executive Branch: Ex Ante Foundations for Policy Development*, 61 DUKE J.L.J. 1237, 1247 (2012) (“For years, the PTO’s position on combining prior art to show nonobviousness was rebuffed by the Federal Circuit. Specifically, to demonstrate the obviousness of an applicant’s invention, many three-judge panels required PTO examiners to identify in the prior art a specific document that provided a ‘teaching, suggestion, or motivation’ (TSM) that had prompted the applicant to combine the prior art. Over a number of years, the PTO repeatedly argued that its examiners should not always have to point to documentary evidence indicating that particular prior art references should be combined.”)

228. See *supra* note 87 and accompanying text.

KSR that the Federal Circuit's obviousness test at the time complicated the obviousness inquiry rather than focusing on the statute.²²⁹

Consistent also with the Supreme Court's views on general standards, the absolute number of options should not be crucial to a determination of obviousness. For instance, as Professors Abramowicz and Duffy said, "[f]inding the right DNA sequence out of a trillion trillion trillion possibilities should be considered easy if standard, low-cost techniques can resolve the problem in a short time and there would be ample incentive to undertake the effort even without patents. Finding the right answer among a mere ten or twenty possibilities may be considered difficult if testing each possibility requires enormous expense, time, and effort."²³⁰

Even if the court's comments in *Eisai* factually distinguished *KSR* from *Eisai*, none provide a rationale for breaking the determination of the differences between prior art and the patent claim into multiple parts, and not considering the claim as a whole. The basic standard of *Graham*, confirmed in *KSR*, is that a court determines obviousness from the point of view of PHOSITA by comparing the "differences between the prior art and the claims at issue."²³¹ There is no suggestion in *KSR* that a court can only find obviousness if prior art teaches: (1) the selection of a lead compound or a few lead compounds based on structural similarity and properties; (2) the steps modifying the lead compound to create the next steps, and (3) a completed product, all without knowing what the patent claim. Not only is this stepped process inconsistent with *KSR*, but as discussed in part IV, it is inconsistent with § 103, which requires that PHOSITA consider the patent claim "as a whole." *Eisai*, in other words, did not provide a satisfactory rationale for departing from *KSR*.

Takeda

In *Takeda* in 2007, the Federal Circuit used its pre-*KSR* test for new pharmaceutical compounds and relied on *In re Deuel*, a decision that the Federal Circuit subsequently acknowledged *KSR* had discredited. Takeda marketed ACTOS®, with the active ingredient pioglitazone, to treat Type 2 diabetes, and sued Alphapharm and others for filing ANDAs to market generic pioglitazone.²³² The district court concluded the patent would not have been obvious.²³³

The Federal Circuit affirmed, repeating the two basic elements of the test for new pharmaceutical compounds set forth in *Lilly* and *Yamanouchi*

229. See *supra* note 14 and accompanying text.

230. *Inducement Standard*, *supra* note 3, at 1611.

231. *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 17 (1966).

232. *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1353–54 (Fed. Cir. 2007).

233. *Takeda Chem. Indus. v. Mylan Labs, Inc.*, 417 F. Supp. 2d 341, 344 (S.D.N.Y. 2006).

that prior art show: (1) “selection of compound b as lead compound,”²³⁴ and (2) identification of “some reason that would have led a chemist to modify a known compound in a particular manner.”²³⁵ On the first step of the test, the court concluded that PHOSITA would not have selected compound b, since “compound b was not identified as one of the three most favorable compounds,” even though it was identified in the prior art as lowering activity for TZD compounds.²³⁶ On the second part of the test, the court added that even if the preliminary showing had been made that prior art would have selected compound b as the lead compound, prior art “failed to show that there existed a reason, based on what was known at the time of the invention, to perform the chemical modifications necessary to achieve the claimed compounds.”²³⁷

In *Takeda*, the Federal Circuit did not use the word “flexible” or “generally” to describe the new pharmaceutical compounds test, but it did try to distinguish *Takeda* from *KSR*. The court said *KSR* did not mandate a finding of obviousness, because in *Takeda*, “Rather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation.”²³⁸ Although the Federal Circuit noted that compound b was the “closest prior art compound,” the court added compound b “exhibited negative properties that would have directed one of ordinary skill in the art away from that compound.”²³⁹

The Federal Circuit in *Takeda* relied on its earlier, pre-*KSR* decision, *In re Deuel*.²⁴⁰ In *Deuel*, the Federal Circuit held that structural similarities between compounds 1 and 2 could indicate a motivation or reason to modify compound 2, but added, “there must be adequate support in the prior art for the . . . claimed . . . change in structure, in order to complete the PTO’s *prima facie* case.”²⁴¹ Yet subsequently, in *In re Kubin*, the Federal Circuit recognized, “[i]nsofar as *Deuel* implies the obviousness inquiry cannot consider that the combination of the claim’s constituent elements was ‘obvious to try,’ the Supreme Court in *KSR* unambiguously discredited that

234. *Takeda*, 492 F.3d at 1360.

235. *Id.* at 1357. The court did not use either “flexible” or “generally” to describe the test, in contrast to *Otsuka and Eisai*.

236. *Id.* at 1358. The Federal Circuit noted, “In the 1990s, a class of drugs known as thiazolidinediones (“TZDs”) was introduced on the market as a treatment for Type 2 diabetes.” *Id.* at 1352.

237. *Id.* at 1363.

238. *Id.* at 1359.

239. *Takeda*, 492 F.3d at 1359.

240. *Id.* at 1356 (citing *In re Deuel*, 51 F.3d 1552, 1558 (Fed. Cir. 1995)).

241. *In re Deuel*, 51 F.3d. at 1558 (quoting *In re Grabiak*, 769 F.2d 729, 731-32 (Fed. Cir. 1985)).

holding. In fact, the Supreme Court expressly invoked *Deuel* as a source of the discredited ‘obvious to try’ doctrine.²⁴²

Takeda relied on the now discredited *In re Deuel* and reflects pre-KSR views on when a claim can be obvious. Whether or not structural similarity alone between chemicals can still establish prima facie obviousness,²⁴³ a structurally similar compound can be obvious to try. If success readily results from the further research, the resulting invention could be obvious under KSR and § 103, even though the particular product was not predicted at the start of the further research.²⁴⁴

4. Summary

As a result of KSR, an invention is obvious if prior art showed methods for reaching a resolution of market need that PHOSITA was likely to try and succeed at, even though there was no knowledge in advance of the particular resolution. *Pfizer*, *BMS*, *Otsuka*, *Eisai* and *Takeda* did not recognize this change in the obviousness standard, let alone the heightened standard for the skills of a PHOSITA, and essentially stuck to the pre-KSR test for new pharmaceutical compounds. They are inconsistent with the expanded view of obviousness set forth by the Supreme Court in KSR.

Although some of these cases refer to applying the test “flexibly,” they are really referring to applying the TSM test flexibly to determine if prior art showed the lead compound and each subsequent step up to the final compound, not whether the multi-part test for new pharmaceutical compounds was applicable. That multi-part test is inconsistent with the broadened standard for obviousness set forth in KSR, both because it requires a challenger to show that prior art identified (a) the likely lead compound, even though it was not part of the patent claim, and (b) each step in changing the lead compound up to and including the final invention. That test discounts the importance of advances in scientific methods making more improvements obvious, even though the particular improvements are not evident in advance.

The next section of this article shows that two factors may help explain the position of the Federal Circuit on the obviousness of new pharma-

242. *In re Kubin*, 561 F.3d 1351, 1358 (Fed. Cir. 2009). This article discusses *Kubin* in more detail *infra* notes 110–20.

243. *See supra* notes 150, 178 and 206.

244. In developing the invention, *Takeda* and Upjohn selected 50 compounds for further testing. *See Takeda Chem. Indus. v. Mylan Labs., Inc.*, 417 F. Supp. 2d 341, 356 (S.D.N.Y. 2006). *See also Structural Uncertainty*, *supra* note 12, at 423 (“the Federal Circuit in *Takeda*, a post-KSR case, squared the lead compound analysis with KSR’s directive to identify ‘a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.’ However, a closer look at KSR reveals the inconsistency of these two tests: KSR did not contain any rule concerning the motivation of the selection of the primary prior art references.”)

ceutical compounds. Those factors are (1) inappropriate resistance to hindsight analysis, and (2) not pursuing the increased importance of PHOSITA after *KSR*. Those factors, however, do not provide a justification for the Federal Circuit's test for new pharmaceutical compounds.

B. Stumbling Blocks to Implementation of KSR

1. Selective Resistance to Hindsight Analysis

§ 103 requires that the court determine on some date after the litigation commenced whether the claimed invention was obvious to PHOSITA at an earlier date before the litigation commenced.²⁴⁵ In other words, § 103 requires analysis by hindsight.²⁴⁶ One problem that can result from this timing of the obviousness determination is hindsight bias. Professor Mandel has argued that “once outcome information is known [i.e., what the invention is], . . . individuals consistently (and unconsciously) exaggerate what could have been anticipated in foresight and not only tend to view what occurred as having been inevitable, but also as having appeared relatively inevitable beforehand.”²⁴⁷ Another scholar has questioned the significance of the Mandel survey findings,²⁴⁸ but since its creation in 1982²⁴⁹ the Federal Circuit has expressed—and still expresses—great concern about hindsight bias.²⁵⁰

In 2012 the Federal Circuit said that “‘judicial hunches’ are encouraged by hindsight bias . . . ‘decision-makers unconsciously let knowledge of the invention bias their conclusion concerning whether the invention was obvious in the first instance.’”²⁵¹ In *Otsuka*, the Federal Circuit said, “[t]he

245. Either the date of the invention (pre-AIA) or the effective filing date of the patent application (post-AIA). See *supra* note 2.

246. *Nonobvious Problem*, *supra* note 5, at 383 (“This analysis is only possible ex post, when the evaluator knows what the invention as a whole is and can compare it to the prior art. The statutory analysis thus demands the use of a hindsight perspective.”)

247. Gregory Mandel, *Patently Non-Obvious II: Experimental Study on the Hindsight Issue Before the Supreme Court in KSR v. Teleflex*, 9 YALE J.L. & TECH. 1, 3 (2007). On the other hand, Professor Mandel also said that in spite of hindsight bias, “a number of factors may result in too many patents being issued or upheld against invalidity challenges,” such as “institutional pressures favoring patentability at the PTO,” the “presumption of validity that adheres to issued patents,” “potential jury and judge deference to experts” and general “problems in applying the non-obvious requirement.”

248. See, e.g., *Not So Obvious*, *supra* note 16, at 102 (“Professor Mandel’s work . . . we cannot tell if this difference [in outcome] is simply an artifact of the survey format, or whether it represents something likely to be present in real-world litigation. Even if the difference matches real-world experience, we also cannot tell whether this additional information leads to bias, in the sense of a deviation from the ideal, or merely a difference, in the sense of a deviation between the hindsight and foresight scenarios.”)

249. See *supra* note 11.

250. *Not So Obvious*, *supra* note 16, at 43–45 and 85 (referring to “[t]his paralyzing fear of hindsight” and stating that the Federal Circuit’s “jurisprudence also reflects a strong fear of hindsight”).

251. *Eurand, Inc. v. Mylan Pharms., Inc. (In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.)*, 676 F.3d 1063, 1079 (Fed. Cir. 2012) (quoting in part Gregory Mandel, *Patently*

inventor's own path itself never leads to a conclusion of obviousness; that is hindsight."²⁵² In *Pfizer*, the Federal Circuit said, "[a] patent challenger . . . must demonstrate the selection of a lead compound based on its 'promising useful properties,' not a hindsight-driven search for structurally similar compounds."²⁵³ Fear of hindsight bias has been a significant factor in the Federal Circuit's use of its obviousness test for new pharmaceutical compounds.

Even though hindsight bias can be a concern in cases,²⁵⁴ fear of hindsight bias should not inform the general rule of how a court determines obviousness for new pharmaceutical compounds. In an article on hindsight bias in general, Professor Rachlinski wrote, "courts have already done a remarkable job of adapting to the limitations of human judgment in hindsight . . . the courts have developed rules that take advantage of specific opportunities to avoid the bias."²⁵⁵ For instance, Professor Eisenberg has pointed out that the Supreme Court has taken such steps for obviousness determinations: "the palliative against the hindsight bias endorsed by the Supreme Court in *Graham v. John Deere* — consideration of secondary evidence — involves further use of ex post evidence. Although some forms of secondary evidence (e.g., failure of others, long-felt but unsolved need) may be observed ex ante, the most common form — commercial success — may only be observed ex post."²⁵⁶

Federal Circuit statements about avoiding hindsight have appeared incomplete or misleading.²⁵⁷ For instance, in *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.*, the Federal Circuit said, "[i]mportantly, the great challenge of the obviousness judgment is proceeding without any hint of hindsight."²⁵⁸ However, the Federal Circuit reversed the district court's finding of obviousness, concluding the invention was not obvious and there were "many secondary considerations that support nonobviousness," such as: (1) long-felt, unmet industry need, (2) unexpected results, (3) "considerable market acceptance" and (4) "commercial success."²⁵⁹ Clearly factors

Non-Obvious: Empirical Demonstration that the Hindsight Bias Renders Patent Decisions Irrational, 67 OHIO ST. L.J. 1391, 1393 (2006).

252. *Otsuka v. Sandoz*, 678 F.3d 1280, 1296. (Fed. Cir. 2012).

253. *Pfizer Inc. v. Teva Pharms. USA, Inc.*, 555 F. App'x 961, 970. (Fed. Cir. 2014).

254. Professor Eisenberg agrees hindsight bias "is a legitimate concern." *Nonobvious Problem*, *supra* note 5, at 382.

255. Jeffrey J. Rachlinski, *A Positive Psychological Theory of Judging in Hindsight*, 65 CHI. L. REV. 571, 574 (1998).

256. *Nonobvious Problem*, *supra* note 5, at 383.

257. *Not So Obvious*, *supra* note 16, at 91 ("Patent law's fear of hindsight is thus, at best, inconsistent. Patent law fears some types of hindsight but embraces others.")

258. *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.*, 655 F.3d 1364, 1375 (Fed. Cir. 2011).

259. *Id.* at 1376. Commercial success and long-felt, unmet need were secondary considerations the Supreme Court expressly mentioned in *Graham*. See *supra* note 10 and accompanying text. Courts

(3) and (4) involved using hindsight to judge obviousness. That does not mean factors (3) and (4) are inappropriate considerations (indeed the Supreme Court approved consideration of these factors in *Graham*), but the Federal Circuit has not explained why it believes some hindsight analysis is good and some is bad. Professor Eisenberg has said that “the selective use of hindsight only when it favors patentability at a minimum calls into question the meaning of the anti-hindsight shibboleth in (non)obviousness jurisprudence. Is the point to evaluate the invention at the time it was made, or is the point to support patentability by choosing the time frame that is most favorable to the inventor?”²⁶⁰

Professor Lunney and Mr. Johnson observed that the Federal Circuit’s “prohibition on hindsight seems focused on one particular type of hindsight—the use of the inventors’ own discovery against them. Yet this is not hindsight at all. An inventor’s own discovery does not arise after the date of invention, but simultaneously with it.”²⁶¹ However, in *Life Techs., Inc. v. Clontech Labs, Inc.* the Federal Circuit said in 2000, “[t]hat the inventors were ultimately successful is irrelevant to whether one of ordinary skill in the art, at the time the invention was made, would have reasonably expected success.”²⁶² The Federal Circuit concluded that the district court’s “finding to the contrary represents impermissible use of hindsight — using the inventors’ success as evidence that the success would have been expected.”²⁶³ Similarly in *Otsuka*²⁶⁴ the defendants relied “in large part on the inventors’ and Otsuka’s own development efforts in an attempt to prove that aripiprazole would have been obvious.”²⁶⁵ The Federal Circuit cited the last sentence of § 103(a) (“Patentability shall not be negated by the manner in which the invention was made”)²⁶⁶ and reversed the district court, concluding that the inventor’s path by itself “never leads to a conclusion of obviousness; that is hindsight.”²⁶⁷

sometime treat “unexpected results” as secondary considerations of nonobviousness and sometimes as part of the third *Graham* factor, the difference between prior art and the patent claim. See *supra* note 175.

260. *Nonobvious Problem*, *supra* note 5, at 379, n.11.

261. *Not So Obvious*, *supra* note 16, at 89.

262. *Life Techs., Inc. v. Clontech Lab., Inc.*, 224 F.3d 1320, 1326 (Fed. Cir. 2000).

263. *Id.*

264. *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280 (Fed. Cir. 2012),).

265. *Id.* at 1296. The defendant’s argument was that “Otsuka’s aripiprazole development involved a ‘short timeline’ and only ‘took a few months.’” *Id.* Otsuka was the assignee of the inventor. *Id.* at 1285.

266. The second sentence of Post AIA § 103 similarly states, “[p]atentability shall not be negated by the manner in which the invention was made.” The reason for the change is not apparent. See PATENT LAW, *supra* note 5, at 277, n.22.

267. *Otsuka*, 678 F.3d at 1296.

It is generally agreed that “Congress intended by the last sentence of § 103 to abolish the test it believed this Court announced in the controversial phrase ‘flash of creative genius,’ used in *Cuno Engineering Corp. v. Automatic Devices Corp.*”²⁶⁸ In other words, “an invention is no more obvious because it results from painstaking, long-running toil than from a ‘Eureka!’ moment,”²⁶⁹ but that does not mean the path the inventor took may not shed light on the obviousness or nonobviousness of the patent claim. Indeed, in 2002 in *Neupak, Inc. v. Ideal Manufacturing and Sales Corporation*,²⁷⁰ the Federal Circuit held, “the district court did not err by considering the inventors’ testimony in the course of reaching its decision. The inventors’ testimony was relevant to whether the inventions would have been obvious to a person of ordinary skill in the art”²⁷¹

Professor Lunney and Christian Johnson argue convincingly that it is difficult to see why a fact-finder should not in some cases consider the inventor’s own activities: “[i]f obviousness reflects a judgment as to whether an invention was substantial or trivial, difficult or easy, for a person having ordinary skill in the art, then whether the invention at issue was hard or easy for the patentee would seem relevant.”²⁷² They admitted that “the inferential chain is not foolproof. A fact-finder may mistakenly infer obviousness from the fact that it was easy for the patentee, when the ease was due to the patentee’s exceptional skill in the art. Or a fact-finder may mistakenly infer nonobviousness from the fact that it was hard for the patentee, when the difficulty was due to the patentee’s lack of skill in the art.”²⁷³ But they correctly point out that these difficulties are not different than the difficulties any fact-finder has in determining the credibility of a witness.²⁷⁴ Moreover, balancing against the fact that an inventor succeeded is that an inventor’s natural bias would be that the invention was not at all obvious.

As set forth in Part III.A.1., the district court in *BMS* considered in detail the actions of the inventors in developing their inventions, and the Federal Circuit affirmed the decision of the district court.²⁷⁵ As indicated above,²⁷⁶ sometimes the path of the inventor will support a claim of obvi-

268. *Graham*, 383 U.S. at 15, quoting in part from *Cuno Engineering Corp. v. Automatic Devices Corp.*, 314 U.S. 84, 90 (1942).

269. *PATENT LAW*, *supra* note 5, at 277.

270. *Neupak, Inc. v. Ideal Mfg. and Sales Corp.*, 41 F. App’x 435 (Fed. Cir. 2002). *Neupak* involved a patent for “a device used to fill containers, such as paint cans, with fluid.” *Id.* at 437.

271. *Id.* at 440.

272. *Not So Obvious*, *supra* note 16, at 50.

273. *Id.*

274. *Id.* at 51–52.

275. *See supra* notes 158–76 and accompanying text.

276. *See supra* notes 180–82 and accompanying text.

ousness, and sometimes the path of the inventor will support a conclusion that the invention was not obvious.

Although the Supreme Court acknowledged in *Graham* and *KSR* that courts should be aware of the risk of hindsight bias, in neither case did a fear of hindsight bias change the outcome or cause the Supreme Court to suggest that lower courts change the obviousness test to combat hindsight bias. For instance, in *KSR*, the Supreme Court dismissed the Federal Circuit's concern over hindsight bias,²⁷⁷ stating, "[t]he Court of Appeals, finally, drew the wrong conclusion from the risk of courts and patent examiners falling prey to hindsight bias. A fact-finder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning."²⁷⁸ Yet the Court added, "[r]igid preventative rules that deny fact-finders recourse to common sense, however, are neither necessary under our case law nor consistent with it."²⁷⁹

Trials on any subject over events that happened in the past always involve hindsight, and the judge or any jury must judge the credibility of witnesses, including evaluating any biases the witnesses may have. But that is no reason to abandon fact-finding responsibility or the application of the law to the facts based on all available information. Professor Underweiser pointed out that "the Federal Circuit's application of the TSM test discarded so much pertinent information as to badly distort the inquiry."²⁸⁰ Similarly, as mentioned in Part III.A.1. discussing *BMS*, the Federal Circuit's test for new pharmaceutical compounds effectively discards relevant information (*e.g.*, the inventor's path to invention and the structural similarity of the claimed invention to prior art as a whole) that distorts the obviousness inquiry.

Fear of hindsight bias is no reason to deprive the fact-finder of relevant evidence. Fear of hindsight bias does not justify the use of the Federal Circuit's obviousness test for new pharmaceutical compounds to look even

277. LAW OF PATENTS, *supra* note 27 at 393 Professor Nard said that the Court "viewed the hindsight rationale skeptically" and "did not elaborate a great deal on the hindsight issue." He argued, however, "KSR did not give the hindsight issue significant attention, or certainly the attention it deserves." *Id.*

278. *KSR*, 550 U.S. at 421. In the Federal Circuit's decision in *KSR*, the Federal Circuit had raised the risk of hindsight bias as the reason for the TSM test: "'Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references.' False Therefore, we have consistently held that a person of ordinary skill in the art must not only have had some motivation to combine the prior art teachings, but some motivation to combine the prior art teachings in the particular manner claimed." *Teleflex*, 119 F. App'x 282, 285–86 (Fed. Cir. 2005).

279. *KSR*, 550 U.S. at 421. Professor Miller concluded that as a result of *KSR*, "Hindsight dread has been demoted, and the PHOSITA reinvigorated." *Remixing*, *supra* note 17, at 256.

280. *Presumed Obvious*, *supra* note 12, at 265. See also *Two Cultures*, *supra*, note 183, at 38 ("[t]he TSM test truncates the nonobviousness inquiry").

further back in hindsight to the creation of a lead compound that is not part of the patent claim. Fear of hindsight bias is no reason for resisting the Supreme Court's rulings on "obvious to try" or on the mandate of § 103 to determine obviousness by comparing the invention as a whole, rather than in parts, to prior art.

2. Failure to Pursue the Importance of PHOSITA

Professor Dreyfuss said that "the level of ordinary skill in the art is the only part of the nonobviousness analysis that determines how large an advance is needed to merit patent protection."²⁸¹ If a PHOSITA at the date of the invention²⁸² deems the differences between the claimed invention and analogous prior art to have been obvious, then the claim is invalid. Generally the greater the differences between prior art and the invention, the less likely the invention will be found to be obvious. However, the greater the skill of a PHOSITA, the more likely the invention will be deemed to have been obvious.

Historically, a PHOSITA has not played much of a role. Before the decision in *KSR*, Professor Eisenberg criticized the Federal Circuit's then narrow approach to a PHOSITA. She said that courts consulted a PHOSITA on the scope, content and meaning of prior art, but "not on the ultimate question of whether the invention would have been obvious at the time it was made in light of the prior art."²⁸³ She pointed out that practitioners of a technology brought more skill to a problem than their educational credentials and that the limitation of the role of a PHOSITA excluded "from consideration the judgment, intuition and tacit knowledge of ordinary practitioners in the field that cannot be documented in the written record."²⁸⁴ This foreshadowed the Supreme Court's statements in *KSR* that a PHOSITA is not an automaton, that courts should take into account the creativity of a PHOSITA, and that advances in science, "once part of our shared knowledge, define a new threshold from which innovation starts once more."²⁸⁵

In very few Federal Circuit cases, however, has the issue of the precise skill of a PHOSITA been discussed in detail or been important,²⁸⁶ but

281. *Dreyfuss, supra* note 123, at 432.

282. Or, under the AIA, as of the effective filing date of the patent claim.

283. *To Whom, supra* note 102, at 888.

284. *Id.*

285. 550 U.S. at 418, 421 and 427. *See Mueller, supra* note 117, at 308, stating that as a result of *KSR*, "debate has already reframed around other issues, including (1) the level of ordinary skill in the art pertinent to a claimed inventionFalse"

286. CHISUM ON PATENTS has noted that "in *Graham, Calmar, and Adams* . . . and in the later cases of *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.* (1969), . . . *Dann v. Johnston* (1976), . . . and *Sakradia v. Ag Pro Inc.* (1976), . . . the Court analyzed the obviousness of the invention

in one case decided a few months after *KSR*, the skill of a PHOSITA was important. *Daiichi Sankyo Co., Ltd. v. Apotex, Inc.*²⁸⁷ involved a method of treating bacterial ear infections via topical administration of the antibiotic ofloxacin. The Federal Circuit set forth a non-exhaustive list of factors for a court to consider in determining the skill of a PHOSITA: “(1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in the field.”²⁸⁸ The Federal Circuit concluded that PHOSITA would be “a person engaged in developing pharmaceutical formulations and treatment methods for the ear or a specialist in ear treatments such as an otologist, otolaryngologist, or otorhinolaryngologist who also has training in pharmaceutical formulations,” not “a pediatrician or general practitioner” as found by the district court.²⁸⁹

The reference in the *Daiichi* list to “rapidity with which innovations are made” necessarily takes into account advances in technology. Although an argument has been made that the art for a PHOSITA should not include design, research and development arts,²⁹⁰ the Supreme Court rejected a similar argument in *KSR*. Specifically, the Court in *KSR* said, “The proper question [for the district court] to have asked was whether a pedal designer of ordinary skill, facing the wide range of needs created by developments in the field of endeavor, would have seen a benefit to upgrading Asano with a sensor.”²⁹¹ Also, the Federal Circuit considered the art in *In re Kubin* to be researchers: “the record shows that a researcher of ordinary skill in this art would have recognized that both Valiante and Mathew are indisputably focused on regulation of NK cells”²⁹² Similarly, Professor Mandel has written, “The ordinary creativity of a person working in a research laboratory, for instance, may often be greater than the ordinary creativity of a consumer who simply uses a product Consequently, the level of ingenuity necessary to satisfy the nonobviousness requirement may be greater in more sophisticated arts than in less sophisticated ones.”²⁹³

at issue without relying on any express finding as to the level of ordinary skill in the pertinent art.” 2 CHISUM ON PATENTS, *supra* n 2 at §5.03[4][a]. Therefore, it is perhaps not surprising that the Federal Circuit has not often discussed in detail the effect of PHOSITA on the obviousness determination.

287. 501 F.3d at 1254.

288. *Id.* at 1256.

289. *Id.* at 1256–57.

290. Jonathan J. Darrow, *The Neglected Dimension of Patent Law’s PHOSITA Standard*, 23 HARV. J.L. & TECH. 227, 249–54 (2009)

291. 550 U.S. at 424 (emphasis added).

292. 561 F.3d at 1351, 1357 (Fed. Cir. 2009)(emphasis added).

293. Gregory Mandel, *The Non-Obvious Problem: How the Indeterminate Nonobviousness Standard Produces Excessive Patent Grants*, 42 U.C. DAVIS L. REV. 57, 75 (2008) (emphasis added).

Advances in computer technology of course can make research paths more likely to succeed. In *BMS*,²⁹⁴ the district court found, “In the late 1980’s, a medicinal chemist would generally take one of three approaches to attempt to discover new drugs. The traditional approach—the easiest and probably the most common approach—was the modification of a known lead compound The second approach . . . involves random screening of compounds against an in vitro assay to find a lead compound The third approach . . . the most difficult, is known as the biological approach.”²⁹⁵ However, as a result of technological advances, the second approach became easier than before, and more than two-thirds of drug discovery now originate through “high throughput screening (HTS).”²⁹⁶ As a result of “these ultrahigh throughput screening approaches of the early part of the twenty-first century . . . it is possible to screen 100,000 compounds in day.”²⁹⁷

Judicial opinions and scholarship support the similar conclusion that whether or not a process is difficult to pursue and likely to lead to an obvious invention can vary significantly over time and circumstances. Professors Abramowicz and Duffy observed that in *Kubin*, the Federal Circuit “embraced the argument that, in determining the obviousness of DNA sequences coding for a particular protein, the courts must take into account ‘the ease and predictability’ of techniques for isolating those DNA sequences.”²⁹⁸ Specifically, in *Kubin* the Federal Circuit said, “substantial evidence supports the Board’s conclusion that [prior art] . . . reinforces the relative ease of deriving the claimed sequence following the teachings of the prior art.”²⁹⁹ Similarly, Professor Simon has said that “advances in search and processing technologies should free up time for innovation, reducing the costs of obtaining information and easing collaboration in many fields.”³⁰⁰

A related issue is how to determine a PHOSITA when, as is generally the case now, there are a team of inventors involved from many fields working on projects.³⁰¹ Professor Crouch has said, “[w]hen done well, teamwork can add tremendous value to the creative process and can also

294. 923 F. Supp. 2d 602 (D. Del. 2013)

295. *Id.* at 613.

296. RICHARD B. SILVERMAN & MARK W. HOLLADAY, *THE ORGANIC CHEMISTRY OF DRUG DESIGN AND DRUG ACTION* 24 (3d. ed. 2014)

297. *Id.*

298. *Inducement Standard*, *supra* note 3, at 1611. *See also* *In re Kubin*, 561 F.3d at 1357, 1360–61.

299. 561 F.3d at 1357.

300. *Implications*, *supra* note. 95, at 341.

301. *Id.* at 351–52 (“[I]n many fields now, the inventor is no longer an individual, but instead a ‘research entity’”).

provide a combined depth of knowledge beyond most individuals.”³⁰² He added that “person” in § 103 “certainly appl[ies] to teams of joint inventors.”³⁰³ So far the Federal Circuit does not seem expressly to have analyzed research teams in determining the skill of a PHOSITA, perhaps because counsel have not pursued that issue or so far the presence of a team would not have made a difference in the outcome of the obviousness determination.

Yet without taking into account the common presence today of research teams and rapid computer processing, the analysis of obviousness will be biased against a finding of obviousness when in fact the invention was the obvious result of commonplace research. Professor Duffy observed that the decision in *KSR* “seems to point courts toward more consideration of the facts of each case,”³⁰⁴ and that observation, considering more evidence, is certainly pertinent to the consideration of research teams and computer processing in the evaluation of a PHOSITA.

The Federal Circuit’s test for new pharmaceutical compounds limits the importance of a PHOSITA—and the evidence to consider—by saying that prior art must show the lead compound and each step from the lead compound to and including the invention. That test looks at some trees but disregards the forest. A PHOSITA may resolve problems differently than the Federal Circuit contemplates.³⁰⁵ Using computer processing and new scientific research methods, teams may be able to readily find answers to treating various diseases by starting down a path, reasonably knowing that the problems being investigated will be resolved, but without knowing the results in advance and without necessarily selecting a lead compound.

C. The Federal Circuit’s Test is Inconsistent with KSR

In *KSR*, by filling in gaps left by *Graham*, the Supreme Court expanded the meaning of what inventions are obvious. Professors Burk and Lemley said *KSR* showed that “some inventions may be obvious based upon the common knowledge in the art, even unwritten common knowledge,” and

302. Dennis Crouch, *THOSITA: Obvious to a Team Having Ordinary Skill in the Art*, PATENTLY-O, (Oct. 15, 2012) <http://patentlyo.com/patent/2012/10/the-number-of-inventors-per-patent-has-risen-fairly-steadily-for-the-past-40-years-today-most-patents-are-directed-toward-i.html>. Although he also pointed out that the last sentence of § 103 says “Patentability shall not be negated by the manner in which the invention was made,” but this simply means the path taken does not prevent patentability. It does not suggest the level of PHOSITA does not change with a team of inventors.

303. *Id.*

304. *Timing*, *supra* note 24, at 368.

305. *Presumed Obvious*, *supra* note 12, at 266 (“[i]t is the lack of focus on the substance of the invention or the true nature of the technology (through the eyes of the person of ordinary skill in the art . . .) [t]hat yields absurd results.”)

that “trying out obvious combinations from the prior art is likely to produce an unpatently obvious result.”³⁰⁶

The Federal Circuit’s test for new pharmaceutical compounds—which was adopted before, and maintained after, *KSR*—does not recognize this expansion. It requires lower courts to look for prior art that essentially predicts a lead compound and each step after the lead compound to the final product claimed (almost eliminating the difference between novelty and obviousness),³⁰⁷ even though *KSR* does not suggest such a test. Any flexibility referred to in post-*KSR* decisions by the Federal Circuit has referred to flexibility in determining what prior art revealed, not the applicability of the multi-part test for obviousness of new pharmaceutical compounds. Indeed, that test can make the determination of obviousness or nonobviousness more arbitrary by not considering other relevant evidence, such as how long an inventor worked on identifying the claimed compound or how little difference there is between the claimed compound and the closest prior art compound.³⁰⁸

The Federal Circuit’s test reflects a fear of hindsight bias not shared by the Supreme Court in *Graham* or *KSR* and not warranted by § 103, all three of which require hindsight analysis. The enhanced role of a PHOSITA under *KSR* generally has not been apparent since *KSR* in the obviousness test for new pharmaceutical compounds. In addition, there is no sound basis for applying a more difficult test for proving new pharmaceutical compounds obvious and an easier test for proving nucleic acid segments (such as in *Kubin*) and other products obvious.³⁰⁹

Even if the Supreme Court had not issued its decision in *KSR* and the Federal Circuit had not issued its decision in *Kubin*, however, the requirement in § 103 that a court consider the obviousness of an invention by considering the claim “as a whole”³¹⁰ would warrant eliminating the Federal Circuit’s test for new pharmaceutical compounds. This article discusses that point next.

306. *Patent Crisis*, *supra* note 46, at 151.

307. *Presumed Obvious*, *supra* note 12, at 258.

308. *See supra* notes 180–83 and 281 and accompanying text.

309. *See Structural Uncertainty*, *supra* note 23, at 423 (“[t]he statutory interpretation where obviousness means one thing in one situation, and another in a different context is questionable. The Supreme Court has previously warned against applying the same statutory text differently in different cases.”) (citing and quoting *U.S. v. Santos*, 553 U.S. 507, 522–23 (2008) (“[T]he meaning of words in a statute cannot change with the statute’s application. To hold otherwise, would render every statute a chameleon and would establish within our jurisprudence . . . the dangerous principle that judges can give the same statutory text different meanings in different cases.”) (citations and internal quotation marks omitted)).

310. Professors Bohannon and Hovenkamp note that “*KSR* required patent examiners to take a much more holistic look at the nonobviousness question.” *Creation*, *supra* note 45, at 108.

IV. THE FEDERAL CIRCUIT'S OBVIOUSNESS TEST FOR NEW PHARMACEUTICAL COMPOUNDS DISREGARDS THE TEXT OF § 103

The Federal Circuit's test for new pharmaceutical compounds is inconsistent with the text of § 103 (both pre and post AIA). First, § 103 mandates a comparison of prior art and the claim at issue "as a whole," whereas the Federal Circuit test splits up the invention into parts and never considers the parts as a whole in determining obviousness. Second, § 103 requires a comparison of prior art to the claim, whereas the Federal Circuit test starts with comparing prior art to a lead compound, which is not even part of the claim (since the invention will have modified any lead compound).

A. Considering the Invention as a Whole

Consistent with the text of § 103, in determining obviousness a court must consider the invention "as a whole." As mentioned above, in *Graham* the Court ruled, "If this difference [between the prior art and the invention] is such that the subject matter as a whole would have been obvious at the time to a person skilled in the art, then the subject matter cannot be patented."³¹¹

The requirement of considering a patent claim "as a whole" for purposes of obviousness is consistent Supreme Court cases analyzing whether a patent claim constitutes patentable subject matter under §101.³¹² In *Parker v. Flook*, the Court said that "a patent claim must be considered as a whole."³¹³ In *Diamond v. Diehr*, the Court said, "[i]t is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis."³¹⁴ In *Alice Corporation Pty. Ltd. v. CLS Bank Intn'l*, the Court said, "[b]ecause the approach we made explicit in *Mayo* considers all claim elements, both individuals and in combination, it is consistent with the general rule that patent claims 'must be considered as a whole.'"³¹⁵ In other words, a court can break a claim into elements, but it also must consider the patent claim "as a whole."

In considering prior art, a court must not simply consider the elements of prior art that suggest a combination of known elements. As the Supreme

311. 383 U.S. at 15 (emphasis added).

312. 35 U.S.C. § 101 (2012) provides, "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 therefor, subject to the conditions and requirements of this title."

313. 437 U.S. 584, 594 (1978).

314. 450 U.S. 175, 188 (1981).

315. 134 S.Ct. at 2355, n.3, referring to *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1305 (2012)).

Court concluded in *Adams*,³¹⁶ if prior art suggests a particular combination of elements will be harmful to resolving a problem (*i.e.*, it “teaches away” from the combination that is found in the invention), then considering prior art as a whole, a PHOSITA probably would not have combined the elements and the invention would not be obvious.³¹⁷ In *Dann v. Johnston*, the Supreme Court also looked at the prior art as a whole and the invention as a whole, a machine system for automatic record keeping of bank checks and deposits.³¹⁸ The Court said that obviousness was not a test “which turns on whether an invention is equivalent to some element in the prior art but rather whether the difference between the prior art and the subject matter in question ‘is a differen[ce] sufficient to render the claimed subject matter unobvious to one skilled in the applicable art.’”³¹⁹ The Court looked at the system as a whole and prior art as a whole.

KSR also involved Supreme Court consideration of prior art as a whole. In *KSR* the Court considered a number of different approaches, based on the totality of the prior art and not based on a single starting point for the invention. If a PHOSITA had looked at the Asano prior art reference (an adjustable pedal assembly with a fixed pivot point regardless of the adjustment of the pedal), she would have upgraded that pedal assembly by attaching an electronic sensor.³²⁰ If she had started with the Rixon reference (an adjustable pedal assembly with electronic sensor on the footpad, whose wires suffered from chafing), she would have through common sense moved the electronic sensor to a non-moving part of the pedal structure.³²¹ If she had started with the Smith reference (which taught that to prevent the wires connecting the sensor to the computer from chafing, the sensor should be placed on a fixed part of the pedal assembly), the most obvious non-moving point for the sensor would be the pivot point of the pedal assembly.³²² The Court did not simply consider the “closest” prior art reference, but considered prior art as a whole.³²³ The key in *KSR* was

316. See *supra* notes 58–62 and accompanying text.

317. In *Adams*, prior art suggested magnesium should not be used with water-activated batteries. Of course, in *Adams* the inventor had created such a combination (water-activated battery with magnesium electrode), but the invention was not obvious to PHOSITA before he tried the combination, because prior art taught away from that combination.

318. *Dann v. Johnston*, 425 U.S. 219, 219 (1976).

319. *Id.* at 228.

320. *KSR*, 550 U.S. at 408, 424.

321. *Id.* at 409, 425.

322. *Id.*

323. Looking at the whole picture, the Court said, “Just as it was possible to begin with the objective to upgrade Asano to work with a computer-controlled throttle, so too was it possible to take an adjustable electronic pedal like Rixon and seek an improvement that would avoid the wire-chafing problem. Following similar steps to those just explained, a designer would learn from Smith to avoid sensor movement and would come, thereby, to Asano because Asano disclosed an adjustable pedal with a fixed pivot.” *Id.* at 425.

whether all applicable factors would likely have caused a PHOSITA to take a path that readily³²⁴ led to the invention.

The Federal Circuit has also recognized that under § 103 a court or the PTO must consider the invention as a whole and the prior art as a whole, at least in cases not involving patent claims for new pharmaceutical compounds. For instance, in *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, the Federal Circuit affirmed the district court's conclusion that a patent for a device used to investigate the content of biological materials was obvious, emphasizing that "[§]103 specifically requires consideration of the claimed invention 'as a whole.'"³²⁵ The Federal Circuit explained, "[w]ithout this important requirement, an obviousness assessment might successfully break an invention into its component parts, then find a prior art reference corresponding to each component"³²⁶ The Federal Circuit concluded that to avoid hindsight bias, the court must consider the invention as a whole to prevent "using the invention as a roadmap to find its prior art components."³²⁷

In fact, the Federal Circuit – for inventions not involving new pharmaceutical compounds — has consistently stated that the courts must consider the whole invention and all applicable prior art. In *W.L.Gore Associates, Inc. v. Garlock, Inc.*, the then recently formed Federal Circuit reversed the district court's holding that the patent for stretching highly crystalline, unsintered teflon was invalid as obvious.³²⁸ The Federal Circuit said the district court had erred in "disregarding the unpredictability and unique nature of the unsintered PTFE to which the claimed inventions relate, . . . in considering claims in less than their entirety, . . . and in considering the references in less than their entirety, i.e., in disregarding disclosures in the references that diverge from and teach away from the invention at hand."³²⁹

324. How quickly the path would have led to the result is a legitimate question. See *supra*, notes 87-88, 116 and 148 and accompanying text. That question would appear to involve a question of fact for either the trial court or jury to determine, as part of the Graham factors determining the difference between the prior art and the patent claim in light of the skill of PHOSITA. *Supra* parts II.C.3-4.

325. *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 411 F.3d 1332, 1337 (Fed. Cir. 2005) (emphasis added).

326. *Id.* at 1337. It continued, "this improper method would discount the value of combining various existing features or principles in a new way to achieve a new result—often the essence of invention." *Id.*

327. *Id.* See also PATENT LAW, *supra* note 5 at 297 ("the question to be answered under 35 U.S.C. § 103 is not whether the differences [between the prior art and the claim] themselves would have been obvious to PHOSITA. Rather, § 103 asks whether the *subject matter as a whole* (i.e., the claimed invention as a whole) would have been obvious, in view of those differences plus the other factors required by the Graham analysis.") (emphasis in original).

328. 721 F.2d 1540 (Fed. Cir. 1983). The Federal Circuit explained that PTFE, polytetrafluorethylene, was known by the trademark TEFLON of E.I. du Pont de Nemours, Inc. *Id.* at 1544-45.

329. *Id.* at 1550 (emphasis added).

In *Ruiz v. A.B. Chance Co.*³³⁰, the Federal Circuit recognized that § 103 “specifically requires consideration of the claimed invention ‘as a whole.’”³³¹ The Federal Circuit explained, “[w]ithout this important requirement, an obviousness assessment might break an invention into its component parts (A + B + C), then find a prior art reference containing A, another containing B, and another containing C, and on that basis alone declare the invention obvious.”³³² The “as a whole” requirement in § 103 prohibits “using the invention as a roadmap to find its prior art components,” and allowing a challenger to follow the inventor’s path “would discount the value of combining various existing features or principles in a new way to achieve a new result—often the very definition of invention.”³³³

The Federal Circuit’s test for new pharmaceutical compounds does just what § 103 and *Princeton, Gore* and *Ruiz* rejected. The test breaks an invention into parts and requires the challenger, at each step, up to and including the invention, to show that prior art predicted each step perceived by the court, without putting the parts of the invention back together to compare to prior art. The test limits the path a PHOSITA might use to discover an invention, since a scientist or team of scientists may discover a new compound through a number of methods not involving a lead compound or modifications shown in advance by prior art. Alternatively that path may involve a large number of steps that are routinely carried out (as in *Kubin*) but are not identified in prior art, particularly in light of the explosion of computer processing capabilities.³³⁴

The fact that a new pharmaceutical compound may function differently than the elements put together to create the compound does not change the calculation. As mentioned above,³³⁵ all inventions are in one sense combinations of existing elements. Even with new pharmaceutical compositions, a new compound generally reflects an existing, very complex molecule, with certain substitutions at various parts of the molecule.³³⁶ The modifications may have changed the functioning of the new molecule, but

330. 357 F.3d 1270 (Fed. Cir. 2004). The patent involved a screw anchor system for supporting and stabilizing electrical transmission towers. *Id.* at 1272.

331. *Id.* at 1275.

332. *Id.*

333. *Id.*

334. See discussion of *Bristol-Myers Squibb supra* at Part III.A.1.

335. See *supra* note 73 and accompanying text.

336. For instance, in *Bristol-Myers Squibb*, the Federal Circuit said, “Entecavir is a modified version of the natural nucleoside 2'-deoxyguanosine (deoxyguanosine). Entecavir is structurally identical to deoxyguanosine except for one difference: it has a carbon-carbon double bond (also known as an exocyclic methylene group) at the 5' position of the carbocyclic ring where deoxyguanosine has an oxygen atom.” *Bristol-Myers Squibb*, 752 F.3d 967, 969 (2014).

that makes it even more important to consider the invention as a whole rather than separating an invention into parts and not considering the whole.

There certainly is no basis for not applying the requirement in § 103 of considering the claim as a whole to new pharmaceutical compounds but applying that requirement to other inventions.³³⁷

B. Considering the Claim

The special test for new pharmaceutical compounds, moreover, disregards the fact that “[i]t is a ‘bedrock principle’ of patent law that ‘the claims of a patent define the invention to which the patentee is entitled the right to exclude.’”³³⁸ Indeed, as far back as 1877, the Supreme Court said that the “formal claim” was “of primary importance, in the effort to ascertain precisely what it is that is patented.”³³⁹ In determining obviousness, § 103 requires the court to compare the differences in the prior art to the “claimed invention,” not to a particular embodiment of the invention, and certainly not to what might have been developed before the invention, such as a lead compound. For instance, in *Galderma Laboratories, L.P. v. Tolmar, Inc.*, the Federal Circuit pointed out that the obviousness requirement addresses whether the claim range, not a particular commercial embodiment of the claim, is obvious.³⁴⁰ It is the claim that is crucial in determining obviousness.

The Federal Circuit’s test for new pharmaceutical compounds, however, starts with the challenger having to show that a lead compound was identified in prior art, even though the lead compound is not part of the patent claim. There is no statutory basis for that test in § 103, at least without also considering the patent claim as a whole.

V. CONCLUSION

Although the Federal Circuit no longer pronounces the strict TSM test, the Federal Circuit’s obviousness test for new pharmaceutical compounds is a relative of the TSM test rejected by the Supreme Court in *KSR*. The

337. See *supra* note 127 (discussion of Kubin at Part.II.D and Pharmastem).

338. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc). See also *Merrill v. Yeomans*, 94 U.S. 568, 570 (1877) (“This distinct and formal claim is, therefore, of primary importance, in the effort to ascertain precisely what it is that is patented to the appellant in this case.”).

339. *Merrill*, 94 U.S. at 570.

340. *Galderma Labs. L.P. v. Tolmar, Inc.*, 737 F.3d 731, 737 (Fed. Cir. 2013) (“nothing in the statute or our case law requires Tolmar to prove obviousness by starting with a prior art commercial embodiment and then providing motivation to alter that commercial embodimentFalse [T]his is particularly true where, as here, the prior art teaches a range that encompasses both the prior art commercial embodiment and the claimed invention.”).

Federal Circuit's test for new pharmaceutical compounds is also difficult to understand, since it: (1) involves evaluating something (*e.g.*, a lead compound) that is not part of the patent claim; (2) splits predecessors of the patent claim into parts and does not consider the whole claim, whereas § 103 requires that courts consider the whole claim; and (3) is inconsistent with *KSR*. The test is also complicated and requires multiple steps not suggested in 103 or *KSR* and diverts attention from the text of § 103.³⁴¹

Regardless of whether it meets the definition of gobbledygook,³⁴² the Federal Circuit's test for the obviousness of new pharmaceutical compounds is a pre-*KSR* relic that is inconsistent with *KSR* and provides special, favored treatment for such compounds compared to other products. The test reflects selective resistance to hindsight analysis not shared by the Supreme Court and not required by § 103. It reduces the gatekeeping function of the obviousness requirement for one class of inventions, new pharmaceutical compounds, and lessens the discretion of district courts and juries to consider evidence unless that evidence fits within the parameters of the Federal Circuit's test.³⁴³

The Federal Circuit or, if an appropriate case reaches it, the Supreme Court should reject the Federal Circuit's test for new pharmaceutical compounds. Instead, the Federal Circuit should follow the general standards of § 103, *Graham* and *KSR* that provide a sound basis for determining obviousness and that the Federal Circuit uses for other products, consistent with the general gatekeeping function of patent law.

341. See *supra* note 14 and accompanying text for comments of Chief Justice Roberts during oral argument in *KSR*.

342. Meriam Webster's online dictionary defines gobbledygook as "speech or writing that is complicated and difficult to understand." See *supra* note 1. The Federal Circuit's test for new pharmaceutical compounds appears to meet this definition of gobbledygook.

343. See *Rai supra* note 182.