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## A NEW FORMULA FOR ANALYZING FORMULATION-PATENT OBVIOUSNESS\*

### I. INTRODUCTION

The generic drug industry, which is estimated to save American consumers \$10 billion a year,<sup>1</sup> owes much of its current market success to Congress's enactment of the Hatch-Waxman Act in 1984.<sup>2</sup> The Hatch-Waxman Act sought to achieve a delicate balance, one where Americans could obtain unprecedented access to low-cost prescription medicine without somehow undermining the incentive of brand name drug manufacturers to invest large sums of money toward developing new and better drugs.<sup>3</sup> To achieve this balance, the Act allows regulatory approval for generic drugs without costly clinical trials,<sup>4</sup> and enhances patent protections for brand name drug companies by prohibiting generic competition for five years after newly developed drugs are approved.<sup>5</sup>

A recent United States Supreme Court decision could upset this delicate balance. In *KSR International Co. v. Teleflex Inc.*,<sup>6</sup> the Supreme Court criticized the Federal Circuit's use of "rigid and mandatory formulas" in determining the obviousness of a patent.<sup>7</sup> The Supreme Court mandated, instead, an "expansive and flexible approach."<sup>8</sup> Commentators have had different views on *KSR*'s impact on the pharmaceutical industry. Some have concluded that *KSR* makes it easier to establish a prima facie case of obviousness for pharmaceutical patents and that the effect is substantial.<sup>9</sup> Others think that *KSR* affects only a limited category of pharmaceutical patents and that

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1. Michael Hiltzik, *Biotech Bonanza Lurks in Healthcare Reform Bills*, L.A. TIMES, Dec. 17, 2009, <http://articles.latimes.com/2009/dec/17/business/la-fi-hiltzik17-2009dec17>.

2. Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 15, 21, 35, and 42 U.S.C. (2006)).

3. See David Bickart, *The Hatch-Waxman Act*, in PHARMACEUTICAL AND BIOTECH PATENT LAW 205, 212-214 (2008) (providing overview of Hatch-Waxman Act).

4. 21 U.S.C. § 355(j) (2006).

5. *Id.* § 355(c)(3)(E)(ii), (j)(5)(F)(ii).

6. 550 U.S. 398 (2007).

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

8. *Id.* at 415.

9. See Scott D. Locke & William D. Schmidt, *Protecting Pharmaceutical Inventions in a KSR World*, 50 IDEA 1, 24 (2009) (concluding that pharmaceutical patents are likely to face more obviousness rejections and challenges); Janice M. Mueller, *Chemicals, Combinations, and "Common Sense": How the Supreme Court's KSR Decision Is Changing Federal Circuit Obviousness Determinations in Pharmaceutical and Biotechnology Cases*, 35 N. KY. L. REV. 281, 282 (2008) (stating that *KSR*'s long-term impact in chemical arts will be "significant and pervasive").

innovator companies can adopt various tactics to minimize *KSR*'s impact.<sup>10</sup> Many nevertheless agree, though, that the *KSR* decision may have shifted the balance between innovator and generic drug companies by (1) reducing the patentability of certain discoveries made during the late-stage development of a drug and thereby (2) removing some patent protection barriers that generics must overcome before entering the market.<sup>11</sup>

This Comment discusses *KSR*'s impact on a particular type of pharmaceutical patent—formulation patents—and proposes a new formula to qualitatively determine formulation-patent obviousness. Part II.A of this Comment describes the pharmaceutical industry's reliance on the patent system. Part II.B briefly introduces the history of patent-obviousness analysis and the *KSR* case. Part II.C discusses several post-*KSR* cases involving formulation-patent obviousness. In these cases, generic drug companies challenged the formulation patents of brand name drugs as obvious. Based on the *KSR* principles, Part III.A identifies three factors that should be considered for the obviousness analysis of a combination patent. Part III.B briefly addresses the current inadequacies of lower courts' obviousness analyses of formulation patents. Part III.C then proposes a new formula for determining the obviousness of formulation patents, applies the new formula to the post-*KSR* cases, and discusses the benefits that the proposed formula would provide.

## II. OVERVIEW

### A. *The Patent System and Pharmaceutical Industry*

Innovator pharmaceutical companies rely on patent protection for their brand name drugs in order to recoup their large research investments and continue the search for new drugs.<sup>12</sup> It typically takes an innovator company ten to fifteen years of research and development to commercially launch a new drug.<sup>13</sup> The success rate is so low that only one in every 5,000 to 10,000 compounds initially tested will eventually make it to the market.<sup>14</sup> Thus, the average cost, therefore, for introducing a new drug is enormous—around \$800 million.<sup>15</sup> When a patent is issued, the patentee obtains twenty years of market exclusivity, calculated from the time when the patent application was filed.<sup>16</sup> Pharmaceutical companies, however, usually enjoy a much shorter patent

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10. See Diane Christine Renbarger, Note, *Putting the Brakes on Drugs: The Impact of KSR v. Teleflex on Pharmaceutical Patenting Strategies*, 42 GA. L. REV. 905, 939 (2008) (stating that *KSR* will impact close cases for certain combination patents in pharmaceutical industry).

11. Christopher M. Jackson, Comment, *The War on Drugs: How KSR v. Teleflex and Merck v. Integra Continue the Erosion of Pharmaceutical Patent Protection*, 36 CAP. U. L. REV. 1029, 1061 (2008); Renbarger, *supra* note 10, at 906–07.

12. Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503, 508 (2009).

13. Jackson, *supra* note 11, at 1030.

14. *Id.*

15. Roin, *supra* note 12, at 510.

16. 35 U.S.C. § 154(a)(2) (2006).

exclusivity period for new drugs because they are not allowed to actually market a drug until all of the regulatory requirements are satisfied.<sup>17</sup>

In addition to patenting the new chemical compounds discovered during the initial phases of research, innovator pharmaceutical companies also seek to patent other inventions made during the development of a drug.<sup>18</sup> In particular, formulation patents are frequently sought to extend a new drug's market exclusivity. Drug companies, for example, can patent different versions or aspects of a drug, such as an extended release version, a liquid version of a known pill form, or a new dosage.<sup>19</sup> In "staggering the dates of these [formulation] patents, patent protection for versions of a drug lasts longer than any single patent."<sup>20</sup>

Formulation studies are a critical step for drug development, and they ensure that a drug substance—i.e., an active pharmaceutical ingredient ("API")—will be administered "at a therapeutic concentration to a particular site of action for a specified period of time."<sup>21</sup> For instance, formulation scientists investigate controlled release, bio-availability improvement, and different modes of administration such as capsules, tablets, gel, and transdermal.<sup>22</sup> Unlike chemical-compound patents that usually claim a new API, formulation patents typically apply a known formulation technology to an already-patented API.<sup>23</sup> Therefore, formulation patents can be categorized as combination patents,<sup>24</sup> which are more susceptible to validity challenges.<sup>25</sup>

While patent-based market exclusivity for brand name drugs allows innovator pharmaceutical companies to generally enjoy a relatively high margin of profit.<sup>26</sup> generic companies are able to compete with innovator companies by producing and distributing drugs with expired or invalidated API patents.<sup>27</sup> Without huge investments on research and development work, generic companies can offer generic drugs at much

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17. See Jackson, *supra* note 11, at 1030 (stating that effective time of pharmaceutical patent is just 11.5 years).

18. JOHN R. THOMAS, PHARMACEUTICAL PATENT LAW 38–46 (2005) (describing types of pharmaceutical patent claims, including drug substances, formulations, chemical intermediates, isomers, salts, combination therapies, methods of using, and methods of making).

19. Renbarger, *supra* note 10, at 925–26; see also Michael Enzo Furrow, *Pharmaceutical Patent Life-Cycle Management After KSR v. Teleflex*, 63 FOOD & DRUG L.J. 275, 298–300 (2008) (describing pharmaceutical companies' strategies to prolong effective market life of brand name drugs).

20. Renbarger, *supra* note 10, at 926.

21. Dewey H. Barich et al., *Physicochemical Properties, Formulation, and Drug Delivery*, in DRUG DELIVERY: PRINCIPLES AND APPLICATIONS 57, 58 (Binghe Wang et al. eds., 2005).

22. See THOMAS, *supra* note 18, at 39 (discussing subject matters that formulation patents can cover).

23. Furrow, *supra* note 19, at 294–95.

24. See BLACK'S LAW DICTIONARY 1235 (9th ed. 2009) (defining combination patent as "patent granted for an invention that unites existing components in a novel and nonobvious way").

25. See Furrow, *supra* note 19, at 289 (stating that patents on drug substances, methods of making, and methods of using are not controversial as to patentability, while there is more validity with challenges to patentability of salts, enantiomers, formulations, polymorphs, and combinations).

26. See Rick Newman, *Why Health Insurers Make Lousy Villains*, U.S. NEWS & WORLD REP. (Aug. 25, 2009), <http://www.usnews.com/money/blogs/flowchart/2009/08/25/why-health-insurers-make-lousy-villains.html> (comparing pharmaceutical companies' profit margin, 16.4%, with that of other industries).

27. Furrow, *supra* note 19, at 284.

lower prices compared with those of brand name drugs.<sup>28</sup> Today, the generic drug industry, which accounts for about seventy percent of all prescriptions dispensed in the United States,<sup>29</sup> owes its success largely to the enactment of the Hatch-Waxman Act in 1984.<sup>30</sup>

Before the expiration of a brand name drug's patent, others are precluded from making or using the drug without the patent owner's permission.<sup>31</sup> The Hatch-Waxman Act, however, provides a safe harbor from patent infringement by allowing a would-be generic company to conduct experiments "reasonably related to the development and submission of information" to the Food and Drug Administration (FDA).<sup>32</sup> Thus, generic companies can make and use a patented drug to conduct experiments before the drug's patent expiration, and accordingly, the time between a patent's expiration and the generic entry into the market can be minimized.<sup>33</sup> In addition, generic companies are not required to conduct time-consuming tests to demonstrate a generic drug's safety and efficacy. Instead, companies can simply file an Abbreviated New Drug Application (ANDA) that certifies the generic drug as bioequivalent to the corresponding brand name drug.<sup>34</sup> Furthermore, the first generic company to file the ANDA with a Paragraph IV certification claiming the brand name drug's patent to be invalid, or that generic production will not infringe upon the brand name drug's patent, will get a 180-day exclusivity period for marketing its generic version of that drug.<sup>35</sup> During the 180-day exclusivity period, the first filer can enjoy a significant economic profit as the sole competitor to the innovator drug company.<sup>36</sup>

The Hatch-Waxman Act has helped, therefore, to foster the development of generic drugs—and thereby save consumers a significant amount of money.<sup>37</sup> In particular, the 180-day exclusivity period has provided a strong incentive for generic companies to be the first one to challenge the validity of a brand name drug's patents.<sup>38</sup>

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28. See Naomi Wax, Editorial, *Generic Drugs: Are They Really Identical to the Brand Names?* PRESS OF ATLANTIC CITY, Dec. 24, 2007, at A9 (comparing average price of \$102 to fill brand name drug with average price of \$29 for generic drug).

29. Marilyn Alva, *Generic Drugs' New Frontier*, INVESTOR'S BUS. DAILY, Nov. 9, 2009.

30. Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended in scattered sections of 15, 21, 35, and 42 U.S.C.).

31. 35 U.S.C. § 271(a) (2006).

32. *Id.* § 271(e)(1).

33. Jackson, *supra* note 11, at 1041.

34. 21 U.S.C. § 355(j) (2006).

35. *Id.* § 355(j)(5)(B)(iv).

36. See Bickart, *supra* note 3, at 271 (stating that "first ANDA applicant . . . is rewarded with a 180-day head-start over competing generic versions of the same product"); Michael A. Carrier, *Unsettling Drug Patent Settlements: A Framework for Presumptive Illegality*, 108 MICH. L. REV. 37, 46-47 (2009) (explaining benefits and reduced costs for generic companies that successfully file an ANDA and obtain 180-day exclusivity period).

37. The first generic entrant can charge a price for its generic drug five to twenty-five percent lower than that of the corresponding brand name drug, while the entrance of a second generic lowers the price to about half of the brand price. Carrier, *supra* note 36, at 50; see also Hiltzik, *supra* note 1 (stating that generic drugs save Americans \$10 billion a year).

38. Bickart, *supra* note 3, at 271-72.

In the context of ANDA filings, many formulation patents are the targets of generic companies because they are perceived as more vulnerable to patentability challenges.<sup>39</sup>

*B. History of Patent-Obviousness Analysis*

1. Basics of the Obviousness Analysis

To qualify for patent protection, an invention must meet three statutory requirements: utility,<sup>40</sup> novelty,<sup>41</sup> and non-obviousness.<sup>42</sup> Both the utility and novelty requirements were set forth in the Patent Act of 1793,<sup>43</sup> while the non-obviousness requirement was not codified until Congress revised the Patent Act in 1952 with the addition of section 103.<sup>44</sup> Section 103(a), which is based upon an 1850 Supreme Court decision,<sup>45</sup> denies an invention's patentability

if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.<sup>46</sup>

In *Graham v. John Deere Co. of Kansas City*,<sup>47</sup> the Supreme Court interpreted section 103 of the Patent Act of 1952 for the first time, and established a framework for determining obviousness.<sup>48</sup> This framework still controls the patent-obviousness analysis today. First, the factfinder must determine the scope and content of the prior art.<sup>49</sup> Second, the factfinder must ascertain the differences between the prior art and the patent claim at issue.<sup>50</sup> Third, the factfinder must resolve the skill level of a person having ordinary skill in the art ("PHOSITA").<sup>51</sup> Against this background, the factfinder determines whether the claimed invention would have been obvious to a PHOSITA at the time of the invention.<sup>52</sup> To guard against hindsight bias in the obviousness determination, the Court also set out secondary considerations such as "commercial success, long felt but unsolved needs, [and] failure of others," as circumstantial

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39. See, e.g., *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1078 (Fed. Cir. 2008) (stating that generic drug company Apotex challenged drug formulation patent in its ANDA application); *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1352 (Fed. Cir. 2007) (same).

40. 35 U.S.C. § 101 (2006).

41. *Id.* § 102.

42. *Id.* § 103.

43. Patent Act of 1793, ch.11, 1 Stat. 318–19.

44. Patent Act of 1952, Pub. L. No. 82-593, 66 Stat. 792, 798 (codified as amended in scattered sections of 35 U.S.C.).

45. *Hotchkiss v. Greenwood*, 52 U.S. (11 How.) 248, 267 (1850) (holding that new and useful innovation must be beyond "the work of the skilful mechanic").

46. 35 U.S.C. § 103(a).

47. 383 U.S. 1 (1966).

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

49. *Id.* Prior art refers to "[k]nowledge that is publicly known, used by others, or available on the date of invention to a person of ordinary skill in an art, including what would be obvious from that knowledge." BLACK'S LAW DICTIONARY 126 (9th Ed. 2009).

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

51. *Id.*

52. *Id.*

evidence of non-obviousness.<sup>53</sup> The Court acknowledged, however, the difficulty in applying the non-obviousness test, and analogized the case-by-case factual inquiry to that of negligence cases.<sup>54</sup>

After applying the framework to the facts, the Court in *Graham* found that the patent at issue was obvious.<sup>55</sup> The patent at issue in *Graham* claimed a particular spring-hinge-shank combination, which was clamped to a plow frame.<sup>56</sup> This device rendered the plow capable of withstanding the shock of obstructions in the soil, and thereby helped prevent the plow's shanks from breaking.<sup>57</sup> In analyzing the obviousness of the patent, the Court first addressed Graham's prior patent, which shared similar elements except that (1) the latter had a bolted connection and (2) the positions of the shank and the hinge plate were reversed.<sup>58</sup> Second, the Court considered another prior art reference, the Glencoe clamp device, which had all of the elements of the patent at issue and had an identical mechanical operation for the shank and hinge plate.<sup>59</sup> While the Court concluded that the distinction between Graham's prior patent and the patent at issue would have been sufficient to support a non-obviousness finding, it noted that the Glencoe device served "exactly the same function" and the mere reverse position of the shank "present[ed] no operative mechanical distinctions."<sup>60</sup> Therefore, Graham's patent at issue was found obvious.

## 2. The TSM Test

Since the obviousness determination under the *Graham* framework entails a broad post-hoc analysis that creates a risk of hindsight bias,<sup>61</sup> the Court of Appeals for the Federal Circuit has employed the teaching, suggestion, or motivation ("TSM") test. The test, which seeks to standardize and formalize the obviousness analysis, is applied when the patent at issue is based on a combination of elements found in the prior art.<sup>62</sup> The TSM test requires a factfinder to establish why a PHOSITA would find the invention to be obvious, and thus entails consideration of two *Graham* factors: (1) the scope and content of the prior art and (2) the skill level of a PHOSITA.<sup>63</sup> In applying

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53. *Id.* at 17–18, 35–36 (stating such secondary considerations may "serve to 'guard against slipping into use of hindsight'" (quoting *Monroe Auto Equip. Co. v. Heckethorn Mfg. & Supply Co.*, 332 F.2d 406, 412 (6th Cir. 1964))).

54. *Id.* at 18.

55. *Id.* at 25–26.

56. *Id.* at 19–20.

57. *Id.* at 20–21.

58. *Id.* at 22.

59. *Id.* at 26.

60. *Id.*

61. *See, e.g.*, Rebecca S. Eisenberg, *Pharma's Nonobvious Problem*, 12 LEWIS & CLARK L. REV. 375, 383 (2008) (stating that obviousness inquiry under § 103(a) can only be possible ex post).

62. *E.g.*, *In re Kahn*, 441 F.3d 977, 987–88 (Fed. Cir. 2006); *In re Bergel*, 292 F.2d 955, 956–57 (C.C.P.A. 1961) (establishing requirement of demonstrating teaching, suggestion, or motivation to combine known elements in order to prove obviousness). The *Kahn* court also observed that "[m]ost inventions arise from a combination of old elements and each element may often be found in the prior art." 441 F.3d at 986.

63. *Kahn*, 441 F.3d at 986.

the test, the factfinder “must provide some rationale, articulation, or reasoned basis” for a determination of obviousness,<sup>64</sup> as mere conclusory statements will not suffice.<sup>65</sup>

While designed to “enable predictability in law,”<sup>66</sup> the Federal Circuit has applied the TSM test in a somewhat contradictory manner. In some cases, the Federal Circuit has applied the TSM test quite flexibly. For instance, in *In re Kahn*<sup>67</sup> the court stated that a teaching, suggestion, or motivation to combine the prior art elements “does not have to be found explicitly in the prior art.”<sup>68</sup> According to *Kahn*, the TSM test asks whether a PHOSITA, “possessed with the understandings and knowledge reflected in the prior art, and motivated by the general problem facing the inventor,” would have made the claimed invention at issue.<sup>69</sup> In other cases, however, the Federal Circuit has required that a factfinder adequately document in the evidentiary record the teaching, suggestion, or motivation to reach an obviousness conclusion.<sup>70</sup> Under this approach, when such documentary evidence does not exist, the TSM test will find a patent to be nonobvious even if the invention would otherwise have been obvious to one with ordinary skill in the art.<sup>71</sup>

### 3. KSR’s Expansive and Flexible Approach

While recognizing that the Federal Circuit employed the TSM test correctly in some cases,<sup>72</sup> the Supreme Court has rejected the Federal Circuit’s rigid application of the TSM test. In *KSR International Co. v. Teleflex Inc.*,<sup>73</sup> the Court mandated an “expansive and flexible approach” when determining the obviousness question.<sup>74</sup> The case involved Teleflex’s patent infringement claims against KSR, where the patent at issue covered an automobile pedal assembly with an electronic sensor.<sup>75</sup> After applying the *Graham* framework and the TSM test, the district court granted summary judgment in favor of KSR, holding that the patent was an obvious combination of prior art

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64. *Id.* at 987.

65. *Id.* at 988.

66. The TSM test was “intended to provide some protections against hindsight bias, and to enable predictability in the law.” Furrow, *supra* note 19, at 302.

67. 441 F.3d 977 (Fed. Cir. 2006).

68. *Kahn*, 441 F.3d at 987. Knowledge of a PHOSITA, prior art teaching, and the nature of the problem to be solved can be considered as a whole to determine whether there is an implicit teaching, suggestion, or motivation. *Id.* at 987–88 (quoting *In re Kotzab*, 217 F.3d 1365, 1370 (Fed. Cir. 2000)).

69. *Id.* at 988.

70. See *In re Lee*, 277 F.3d 1338, 1342–43 (Fed. Cir. 2002) (concluding that obviousness holding requires specific findings in evidentiary record of suggestion, teaching, or motivation to combine prior art references); *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1125 (Fed. Cir. 2000) (“This showing [of TSM] must be clear and particular, and broad conclusory statements about the teaching of multiple references, standing alone, are not ‘evidence.’”).

71. See Eisenberg, *supra* note 61, at 385 (“[T]he Federal Circuit’s approach has sometimes seemed as a practical matter to require documentary evidence of a sort that simply may not exist, even for the most obvious inventions.”).

72. See *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 419 (2007) (acknowledging that Federal Circuit applied TSM test correctly in many cases).

73. 550 U.S. 398 (2007).

74. *KSR*, 550 U.S. at 415.

75. *Id.* at 405–06.

elements.<sup>76</sup> The Federal Circuit vacated the district court ruling and remanded the case for further findings on “the specific understanding or principle” that would have motivated one skilled in the art to combine the prior art elements.<sup>77</sup>

After granting certiorari to hear the case, the Supreme Court criticized the Federal Circuit’s rigid approach, applied a more flexible standard, and held that the patent in dispute was obvious.<sup>78</sup> While recognizing that the TSM test provides “helpful insight,” the Supreme Court indicated that a court need not find “precise teachings directed to the specific subject matter” at issue.<sup>79</sup> Instead, the court can determine whether there was a “reason to combine” known elements, based on design incentives, market demand, or common sense.<sup>80</sup> Further, the combination of known elements according to their “established functions” is likely to be obvious when “it does no more than yield predictable results.”<sup>81</sup>

As a result of the Supreme Court’s decision in *KSR*, the Patent and Trademark Office (PTO) adopted new rules for the patent-obviousness analysis.<sup>82</sup> The PTO listed the following seven “[e]xemplary rationales that may support a conclusion of obviousness,”:

(A) Combining prior art elements according to known methods to yield predictable results;

(B) Simple substitution of one known element for another to obtain predictable results;

(C) Use of known technique to improve similar devices (methods, or products) in the same way;

(D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;

(E) “Obvious to try”—choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;

(F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;

(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.<sup>83</sup>

Based on these guidelines, some commentators have speculated that the PTO may reject more claims on obviousness grounds and issue fewer patents.<sup>84</sup> If true, the

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76. See *Teleflex, Inc. v. KSR Int’l Co.*, 119 F. App’x 282, 290 (Fed. Cir. 2005) (describing district court ruling).

77. *Teleflex*, 119 F. App’x at 288 (quoting *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000)).

78. *KSR*, 550 U.S. at 427–28.

79. *Id.* at 418.

80. *Id.*

81. *Id.* at 416, 418.

82. U.S. PATENT & TRADEMARK OFFICE, MANUAL OF PATENT EXAMINING PROCEDURE § 2143 (rev. 8th ed. 2010), available at [http://www.uspto.gov/web/offices/pac/mpep/mpep\\_e8r6\\_2100.pdf](http://www.uspto.gov/web/offices/pac/mpep/mpep_e8r6_2100.pdf).

83. *Id.*



patents that do get issued will be less vulnerable to obviousness challenges. Others, however, have argued the *KSR* decision will have only a limited effect because, as one observer put it, “the Supreme Court did little to constrain the Federal Circuit beyond admonishing the Federal Circuit not to apply rigid rules.”<sup>85</sup> As such, the Federal Circuit still has a “plenary review power” to “reshape obviousness doctrine over the years.”<sup>86</sup>

### C. *Post-KSR Cases Involving the Obviousness Analysis on Formulation Patents*

The impact of the *KSR* decision on pharmaceutical patents could vary depending on the type of patent at issue.<sup>87</sup> For patents claiming a new chemical compound, it is difficult to prove obviousness based on structural similarity to prior art compounds,<sup>88</sup> as a small change in the structure of a compound can result in significant changes in its properties.<sup>89</sup> A patent owner, therefore, can rebut the alleged prima facie obviousness based on the evidence of unexpected properties.<sup>90</sup> In contrast, *KSR*'s impact on formulation patents could be much more significant because most formulation patents simply entail further processing of patented drug substances.<sup>91</sup> The following sections discuss Federal Circuit and district court cases that have addressed the obviousness analysis for formulation patents in the wake of the Supreme Court's grant of certiorari in *KSR*.

#### 1. Cases Finding Formulation Patents Obvious

The cases in this section involve validity challenges by generic drug companies to the patents of three brand name drugs: Pfizer's Norvasc, Bayer's Yasmin, and Purdue Pharma's Ultram ER. In these cases, the generic companies were successful in showing that the formulation patents covering the salt form, particle size and pill form, or extended release were obvious under 35 U.S.C. § 103(a).

##### a. *Pfizer, Inc. v. Apotex, Inc.*

While *KSR* was pending before the Supreme Court, the Federal Circuit overruled the district court's decision in *Pfizer, Inc. v. Apotex, Inc.*,<sup>92</sup> and found as obvious the

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84. See D. Christopher Ohly et al., *It Is Not So Obvious: The Impact of KSR on Patent Prosecution, Licensing, and Litigation*, 36 AIPLA Q.J. 267, 287 (2008) (stating that higher rates of patent application rejection on obviousness grounds might be expected).

85. Rebecca S. Eisenberg, Commentary, *The Supreme Court and the Federal Circuit: Visitation and Custody of Patent Law*, 106 MICH. L. REV. FIRST IMPRESSIONS 28, 32 (2007), <http://www.michiganlawreview.org/assets/fi/106/eisenberg.pdf>.

86. *Id.*

87. See Furrow, *supra* note 19, at 310–18 (assessing *KSR*'s impact on various pharmaceutical patents).

88. See *id.* at 310 (noting recent compound obviousness arguments have relied “heavily upon factual considerations”).

89. Eisenberg, *supra* note 61, at 378.

90. *Id.*

91. See Renbarger, *supra* note 10, at 939 (arguing that *KSR* will make it more difficult to obtain formulation patents).

92. 480 F.3d 1348 (Fed. Cir. 2007).

formulation patent on a salt form.<sup>93</sup> The case involved Apotex's challenge to the validity of Pfizer's patent, which claimed the besylate salt of amlodipine, a chemical compound used to treat hypertension and angina.<sup>94</sup> One primary prior art reference, Pfizer's previous patent, claimed amlodipine and its maleate salt.<sup>95</sup> Another prior art article by Berge listed fifty-three FDA-approved and commercially marketed anions, including besylate salt, for making pharmaceutically acceptable salts.<sup>96</sup> The difference, therefore, between the claimed invention and the prior art was the substitution of the maleate salt with the besylate salt.

The Federal Circuit began its analysis, as per *Graham*, by ascertaining the scope of the prior art and the difference between the prior art and the claimed invention.<sup>97</sup> Next, the court set out a requirement for obviousness analyses in cases where "all claim limitations are found in a number of prior art references."<sup>98</sup> In such cases, the challenger of the patent must show that a PHOSITA would have been motivated to combine the prior art elements and that "the skilled artisan would have had a reasonable expectation of success in doing so."<sup>99</sup>

In assessing whether Apotex could make this showing, the Federal Circuit found that there was a reason to combine the prior art elements and try the other salts listed in the Berge article.<sup>100</sup> The record indicated that Pfizer was trying to solve the problems associated with the maleate salt: (1) chemical instability and (2) stickiness during the tablet-making process.<sup>101</sup> A PHOSITA would study other FDA-approved salts to solve these problems.<sup>102</sup> In addition, other prior art references indicated that the besylate salts of other drugs possessed excellent pharmaceutical properties.<sup>103</sup>

Next, the court concluded that a PHOSITA would have had a reasonable expectation of success for the besylate salt of amlodipine.<sup>104</sup> Although admitting that the formation and properties of any particular salt are "unpredictable" at the time of invention, the court stated that "the expectation of success need only be reasonable, not absolute."<sup>105</sup> The record showed that the inventor first chose to try seven other salts, including besylate, with the expectation that some might deliver the desirable results.<sup>106</sup> The court also indicated that Pfizer's previous patent provided "a strong suggestion that any and all pharmaceutically-acceptable anions . . . would work."<sup>107</sup>

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93. *Pfizer*, 480 F.3d at 1372.

94. *Id.* at 1352–53. Amlodipine besylate is "an acid addition salt form of amlodipine, formed from the reaction of amlodipine, a weak base, and benzene sulphonic acid." *Id.* at 1353.

95. *Id.* at 1353.

96. *Id.* at 1355. Besylate is also commonly referred to as benzene sulphonate. *Id.* at 1353 n.1.

97. *Id.* at 1360–61.

98. *Id.* at 1361.

99. *Id.*

100. *Id.* at 1364.

101. *Id.* at 1353–54.

102. *Id.* at 1362–63.

103. *Id.* at 1363.

104. *Id.* at 1365.

105. *Id.* at 1364.

106. *Id.*

107. *Id.* at 1365.

The court then found that it would have been not only “obvious to try,” but also obvious to make the amlodipine besylate.<sup>108</sup> While acknowledging “some degree of unpredictability of salt formation,” the court stated that the only parameter to be varied was “the anion with which to make the amlodipine . . . salt.”<sup>109</sup> The court concluded that on “the *particularized facts of this case*,” Pfizer performed “routine testing”<sup>110</sup> that derived “from the ‘normal desire of scientists or artisans to improve upon what is already generally known.’”<sup>111</sup>

Finally, the Federal Circuit evaluated the secondary considerations and rejected the argument that the superior properties of the amlodipine besylate salt amounted to “unexpected results.”<sup>112</sup> Pfizer’s discovery of the besylate salt was nothing more than “routine optimization that would have been obvious to one of ordinary skill in the art.”<sup>113</sup>

*b. Bayer Schering Pharma AG v. Barr Laboratories, Inc.*

In *Bayer Schering Pharma AG v. Barr Laboratories, Inc.*,<sup>114</sup> the Federal Circuit affirmed a district court’s holding that Bayer’s formulation patent for the unmodified “normal pill” of drospirenone was obvious.<sup>115</sup> Drospirenone, the active ingredient for Yasmin, was known to be suitable for making an oral contraceptive.<sup>116</sup> It was also known in the prior art that drospirenone is not stable under acidic conditions, such as in the human stomach.<sup>117</sup> Further, drospirenone is poorly water soluble, making its bioavailability low and reducing its desirability as a drug.<sup>118</sup>

To increase the dissolution rate of drospirenone and thus enhance its bioavailability, Bayer chose to micronize<sup>119</sup> the drug substance. Micronization of drospirenone, however, can reduce its bioavailability by increasing its isomerization in the acidic stomach environment.<sup>120</sup> For five years, therefore, Bayer scientists had used an enteric-coating formulation of drospirenone in their studies because they believed

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108. *Id.* at 1366.

109. *Id.* “[T]he mere possibility that some salts may not form” does not mean that “those that do are necessarily nonobvious.” *Id.*

110. *Id.* at 1367 (emphasis original).

111. *Id.* at 1368 (quoting *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003)).

112. *Id.* at 1369–72.

113. *Id.* at 1371.

114. 575 F.3d 1341 (Fed. Cir. 2009).

115. *Bayer*, 575 F.3d at 1350.

116. *Id.* at 1343.

117. *Id.* Drospirenone isomerizes under acidic conditions; “that is, the acid catalyzes a reaction that rearranges drospirenone’s molecular structure while its molecular composition remains constant.” *Id.*

118. *Id.* Bioavailability is measured by “the amount of the active drug absorbed into the bloodstream and available to act on the body.” *Id.*

119. *Id.* Micronization is a technique to reduce a drug’s particle size and increase its overall surface area, thus increasing its dissolution rate. *Id.* Generally, an increase in the dissolution rate will correspond to an increase in bioavailability. *Id.* at 1343–44.

120. *Id.* at 1344.

the enteric coating was necessary to prevent the drug's isomerization in the stomach.<sup>121</sup> In a later study, however, Bayer discovered that a normal pill and the enteric-coated pill offered the same bioavailability.<sup>122</sup> The patent at issue thus claimed the normal-pill formulation of micronized drospirenone.<sup>123</sup>

In its analysis, the Federal Circuit began with the Supreme Court's "obvious to try" standard from *KSR* and identified two exceptions to this criterion.<sup>124</sup> The court described these exceptions as "when the inventor would have had to try all possibilities in a field unreduced by direction of the prior art," and "where vague prior art does not guide an inventor toward a particular solution."<sup>125</sup>

The Federal Circuit agreed with the district court's conclusion that micronizing drospirenone was taught in the prior art and "using a normal pill would have been obvious to try."<sup>126</sup> Although one prior art article by Nickisch disclosed that drospirenone isomerizes when exposed to acid in vitro,<sup>127</sup> another prior art textbook indicated that in vitro tests did not necessarily correspond to a drug's properties in the stomach, unless the in vitro tests could be related to in vivo results.<sup>128</sup> After finding that a "person of ordinary skill would not accept in vitro testing as valid without a correlation to in vivo tests,"<sup>129</sup> the district court concluded that a PHOSITA "would have seen [micronization] as a viable option" despite the vitro results in the Nickisch article.<sup>130</sup>

Next, the Federal Circuit found that there was a sufficient reason to prepare a normal pill of drospirenone, thus avoiding the enteric coating. While recognizing the necessity of an enteric coating to formulate acid-sensitive drugs, the prior art textbook identified the disadvantages that an enteric coating would cause, such as lower and more variable bioavailability.<sup>131</sup> In addition, a closely related compound, spirorenone, was known in the prior art, and a PHOSITA would have believed that drospirenone and spirorenone would behave similarly.<sup>132</sup> Moreover, three prior art articles by a Bayer scientist indicated that spirorenone is absorbed in vivo before it isomerizes.<sup>133</sup> Thus, the court found that a PHOSITA would have had an incentive to try the normal-pill

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121. *Id.* at 1345. For a normal pill, the drug is immediately released into the stomach. *Id.* at 1344. An enteric coating can protect "the drug from stomach acid, and only releases the drug when it has passed into the less acidic duodenum and small intestine." *Id.*

122. *Id.*

123. *Id.*

124. *Id.* at 1347. The *Bayer* court, in noting the *KSR* standard, stated that "an invention may be found obvious if it would have been obvious to a [PHOSITA] to try" under certain circumstances. *Id.*

125. *Id.*

126. *Id.* at 1348.

127. *Id.* at 1345. "In vitro" means outside of a living body and in an artificial environment. WEBSTER'S THIRD NEW INTERNATIONAL DICTIONARY 1190 (1981).

128. *Bayer*, 575 F.3d at 1346. "In vivo" means in a living body. WEBSTER'S THIRD NEW INTERNATIONAL DICTIONARY 1190 (1981).

129. *Bayer*, 575 F.3d at 1348.

130. *Id.*

131. *Id.* at 1349.

132. *Id.*

133. *Id.* at 1344, 1349.

formulation because “drospirenone, like spirorenone, may absorb in vivo, but isomerize in vitro.”<sup>134</sup>

In reaching its determination, the Federal Circuit emphasized that a PHOSITA only needed to choose between two known options: micronized drospirenone in a normal pill, or micronized drospirenone in an enteric-coated pill.<sup>135</sup> The court stated that the prior art offered “identified, predictable solutions,” and the selection of micronized drospirenone in a normal pill was obvious to try.<sup>136</sup> Accordingly, the court found Bayer’s invention obvious.<sup>137</sup>

c. *Purdue Pharma Products L.P. v. Par Pharmaceutical, Inc.*

More recently, in *Purdue Pharma Products L.P. v. Par Pharmaceutical, Inc.*,<sup>138</sup> a district court held that the patents at issue, an oral and extended-release formulation for tramadol hydrochloride, were obvious.<sup>139</sup> Tramadol is a weak pain-relieving compound used to treat moderate to severe pain.<sup>140</sup>

After discussing the *Graham* framework and the *KSR* decision, the court started its factual analysis by establishing the scope and content of the prior art.<sup>141</sup> One prior art reference, the Oshlack patent, described controlled-release oral dosage formulations, specifically providing examples for morphine, hydromorphone, and acetaminophen.<sup>142</sup> The Oshlack patent also broadly claimed that the formulations could be applied to fourteen similar pain relieving compounds, including tramadol.<sup>143</sup> The court analogized the facts to those of *Pfizer*,<sup>144</sup> and concluded that the instant case had a stronger showing of obviousness due to the fact that the Oshlack patent disclosed a shorter list of active ingredients to test without any indication that tramadol would be disfavored.<sup>145</sup>

Next, the court rejected Purdue’s claim that the prior art taught away from selecting tramadol, and instead found that the characteristics of tramadol disclosed in the prior art would make it “more beneficial” as a pain reliever.<sup>146</sup> Prior art articles, for example, indicated that tramadol’s lack of side effects, good water solubility, long half-life, and high bioavailability, would actually “encourage a person of ordinary skill in the art to select tramadol as an active ingredient in a controlled-release formulation.”<sup>147</sup>

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134. *Id.* at 1349.

135. *Id.* at 1350.

136. *Id.*

137. *Id.*

138. 642 F. Supp. 2d 329 (D. Del. 2009).

139. *Purdue*, 642 F. Supp. 2d at 334, 374.

140. *Id.* at 334.

141. *Id.* at 368–69.

142. *Id.* at 350.

143. *Id.*

144. See *supra* Part II.C.1.a for a discussion of the *Pfizer* case.

145. *Purdue*, 642 F. Supp. 2d at 369–70. In *Pfizer*, the prior art provided fifty-three FDA-approved salts that a PHOSITA could try and it also disclosed that the besylate salt at issue had a frequency of use of 0.25%. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1355 (Fed. Cir. 2007).

146. *Purdue*, 642 F. Supp. 2d at 370–71.

147. *Id.* at 370.

Although the Oshlack patent did not disclose the proper dissolution rates claimed in the patent at issue for once-a-day dosing, the court stated that developing a once-a-day formulation of tramadol “would have been obvious to one of skill in the art.”<sup>148</sup> One prior art patent, for instance, disclosed examples of controlled-release formulations of morphine, a similar compound to tramadol, with the desired dissolution rates.<sup>149</sup> Another prior art article taught how to achieve proper dissolution rates using a particular system.<sup>150</sup> Although the number of options for achieving such a once-a-day formulation seemed to be large, the court concluded that the potential options were “relatively ‘easily traversed.’”<sup>151</sup> The court asserted that “there existed a ‘resoundingly’ reasonable expectation of success” in combining the known elements to deliver the claimed invention, partly because of the “self-confessed expectation of success that the inventors had” before beginning their research work.<sup>152</sup>

Finally, after concluding that Purdue’s controlled-release formulation was invalid on obviousness grounds in light of the prior art, the court stated that “secondary considerations . . . do not rebut a clear showing of invalidity.”<sup>153</sup>

## 2. Cases Finding Formulation Patents Not Obvious

In contrast to the previously discussed cases, the courts in the following opinions found that the formulation patents at issue were not obvious. The brand name drugs involved in the cases are: AstraZeneca’s Prilosec, Sanofi’s Plavix, Depomed’s Glucophage XR, and Ortho McNeil’s Ortho Tri-Cyclen Lo.

### a. In re Omeprazole Patent Litigation

In *In re Omeprazole Patent Litigation*,<sup>154</sup> the Federal Circuit affirmed a district court decision finding that AstraZeneca’s two formulation patents for Prilosec, a drug treating acid-reflux, were not obvious.<sup>155</sup> Omeprazole, the API for Prilosec, is not stable in acidic media, such as the gastric juices in the stomach.<sup>156</sup> To solve the drug stability problem, the patents at issue used an inert subcoating between an acidic enteric coating and the drug core.<sup>157</sup> The claimed invention not only avoided negative interaction between the enteric coating and the drug core, but also provided sufficient gastric-acid resistance to prevent the acid-labile API from degrading in the stomach, thus allowing the drug substance to be released in the small intestine.<sup>158</sup>

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148. *Id.* at 372.

149. *Id.*

150. *Id.* at 372–73.

151. *Id.* at 373 (quoting *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008)).

152. *Id.* (quoting *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009)).

153. *Id.*

154. 536 F.3d 1361 (Fed. Cir. 2008).

155. *Omeprazole Patent Litig.*, 536 F.3d at 1381.

156. *Id.* at 1364–65.

157. *Id.* at 1365.

158. *Id.*

One prior art reference, a European patent application, described a tablet containing omeprazole magnesium salt with an enteric coating.<sup>159</sup> The Federal Circuit found that the European application did not suggest any negative interaction between the enteric coating and the drug core, nor did it disclose any sort of subcoating.<sup>160</sup> With sufficient evidence pointing to the contrary conclusion, the court gave little weight to Apotex's expert testimony that a PHOSITA would have recognized the possibility that an acidic enteric coating could negatively interact with the omeprazole magnesium salt.<sup>161</sup>

Next, the court reasoned that even if a PHOSITA had recognized the negative interaction, it would not have been obvious to try a water-soluble subcoating to solve the problem because there were multiple options available.<sup>162</sup> Finally, the court rejected Apotex's argument of "reasonable expectation of success" based on the *KSR* decision, and emphasized that a PHOSITA would not have any reason to combine the known subcoating element with elements disclosed in the European application.<sup>163</sup> Therefore, the Federal Circuit affirmed the district court's conclusion of non-obviousness.<sup>164</sup>

*b. Sanofi-Synthelabo v. Apotex, Inc.*

In *Sanofi-Synthelabo v. Apotex, Inc.*,<sup>165</sup> the patent at issue involved the API for Sanofi's heart-disease drug Plavix, the bisulfate of clopidogrel.<sup>166</sup> The Federal Circuit affirmed the district court's holding that separating the enantiomer<sup>167</sup> clopidogrel from a known mixture of two enantiomers and preparing clopidogrel as a bisulfate salt were not obvious.<sup>168</sup> The mixture of the two enantiomers was known in the prior art, and Apotex argued that the general knowledge that enantiomers may be separated and may possess favorable biological properties would be "suffic[ient] to render the separation obvious."<sup>169</sup>

The Federal Circuit indicated, however, that a PHOSITA could not predict the biological properties of an enantiomer without separating and testing it.<sup>170</sup> Expert witnesses for both sides agreed that the activity and toxicity of a particular enantiomer would likely be positively correlated.<sup>171</sup> Witnesses also stated that for compounds like clopidogrel, "whose biological activity is delivered through metabolism within the body," the possibility of the enantiomer being converted back to the mixture in the

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159. *Id.* at 1379.

160. *Id.*

161. *Id.* at 1380.

162. *Id.*

163. *Id.* at 1381.

164. *Id.*

165. 550 F.3d 1075 (Fed. Cir. 2008).

166. *Sanofi-Synthelabo*, 550 F.3d at 1077.

167. "Enantiomers . . . have the same chemical formula and the same chemical structure, but differ in their orientation in three-dimensional space." *Id.* at 1080. In other words, enantiomers are "mirror images of each other." *Id.*

168. *Id.* at 1090.

169. *Id.* at 1086.

170. *Id.* at 1087.

171. *Id.*

acidic stomach environment would probably deter a PHOSITA from separating the mixture.<sup>172</sup> For these reasons, the court concluded that a PHOSITA “would not reasonably have predicted” that separated enantiomer would have the bioactivity without the toxicity.<sup>173</sup>

The Federal Circuit agreed with the district court’s finding that the separation of the mixture of two enantiomers was not “a simple or routine procedure and that success in separation . . . was unpredictable.”<sup>174</sup> There were at least ten techniques available to separate enantiomers at the time of the invention, and experimentation with various conditions was required to determine which technique might be successful.<sup>175</sup> With respect to the bisulfate salt, the district court distinguished the instant case from *Pfizer*,<sup>176</sup> and indicated that “the prior art taught away from [using] sulfuric acid with an enantiomer.”<sup>177</sup>

Because of “the wide range of possible outcomes and the relative unlikelihood that the resulting compound” would exhibit superior biological properties, the district court found that Sanofi’s formulation patent on clopidogrel bisulfate was not obvious.<sup>178</sup> Describing the obviousness analysis as fact dependent in each case, the Federal Circuit agreed with the district court that “the result of this separation of enantiomers was unpredictable” and that the principles of *KSR* did not alter the conclusion.<sup>179</sup>

c. *Depomed, Inc. v. Ivax Corp.*

In *Depomed, Inc. v. Ivax Corp.*,<sup>180</sup> the district court held that Depomed’s two patents for the controlled-release formulation of a highly soluble drug, metformin hydrochloride, were not obvious.<sup>181</sup> Depomed’s patents at issue claimed an oral drug tablet formulation—which utilizes a polymeric matrix to incorporate the drug.<sup>182</sup> The matrix swells in the presence of gastric fluid and the swelling keeps the drug tablet in the stomach for a longer period of time.<sup>183</sup> The swelling also helps to slow down the drug’s rate of diffusion out of the tablet.<sup>184</sup> Thus, the invention “promotes drug delivery to the upper [gastrointestinal] tract” and “helps avoid transient overdosing” by extending drug delivery.<sup>185</sup> There was little doubt that one skilled in the art would have recognized the benefits of such a controlled-release formulation.<sup>186</sup>

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172. *Id.*

173. *Id.*

174. *Id.* at 1088.

175. *Id.* at 1087.

176. See *supra* Part II.C.1.a for a discussion of the *Pfizer* case.

177. *Sanofi-Synthelabo*, 550 F.3d at 1089.

178. *Id.*

179. *Id.* at 1090.

180. 532 F. Supp. 2d 1170 (N.D. Cal. 2007).

181. *Depomed*, 532 F. Supp. 2d at 1185.

182. *Id.* at 1174.

183. *Id.*

184. *Id.*

185. *Id.*

186. *Id.* at 1184.



The district court started the obviousness analysis by identifying relevant prior art references.<sup>187</sup> One prior art reference, Depomed's prior patent, disclosed formulations for controlled-release and gastric-retentive dosage forms using cellulose-based polymers.<sup>188</sup> The prior patent involved a dissolution-controlled release system and was primarily useful for low solubility drugs.<sup>189</sup> Another prior art reference, a technical publication by Dow, described the use of a polymer, hydroxypropylmethylcellulose ("HPMC"), in controlled-release drug formulations.<sup>190</sup> The Dow reference taught the use of the HPMC polymer for both soluble and insoluble drugs, where the former were released by diffusion and erosion and the latter by erosion only.<sup>191</sup>

Ivax argued that a PHOSITA would have a reason to combine the gastric-retentive formulation in Depomed's prior patent and the polymers for the highly soluble drug in the Dow reference.<sup>192</sup> The district court, however, noted that the question, under *KSR*, was whether "one of skill in the art would have had a reasonable expectation of success in combining" the two prior art references.<sup>193</sup>

The court concluded that there was no reasonable expectation of success because the prior art taught away from the claimed invention at issue.<sup>194</sup> First, Depomed's prior patent explicitly taught away from using its formulation for "unmodified, soluble drugs."<sup>195</sup> Second, the Dow reference explained that its specific drug formulation controlled delivery by both diffusion and erosion, thus teaching away from the claimed formulation that controlled drug delivery through swelling and remaining substantially intact until the drug was released.<sup>196</sup> Lastly, while the prior patent disclosed Dow's HPMC polymer, it suggested that the polymer was not useful for controlled release of unmodified soluble drugs.<sup>197</sup> Therefore, the court found that Ivax failed to prove the patents at issue were obvious in light of Depomed's prior patent and the Dow reference.<sup>198</sup>

*d. Ortho-McNeil Pharmaceutical, Inc. v. Barr Laboratories, Inc.*

As with *Depomed*, the district court in *Ortho-McNeil Pharmaceutical, Inc. v. Barr Laboratories, Inc.*,<sup>199</sup> held that Ortho's formulation patent was not obvious.<sup>200</sup> The case, a preliminary injunction proceeding, involved an invention that claimed a low dosage (twenty-five micrograms) of ethinyl estradiol ("EE") for use in the oral

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187. *Id.* at 1183.

188. *Id.*

189. *Id.*

190. *Id.* at 1184.

191. *Id.*

192. *Id.* at 1185.

193. *Id.* at 1184.

194. *Id.* at 1185.

195. *Id.*

196. *Id.*

197. *Id.*

198. *Id.*

199. No. 03-4678, 2009 WL 2182665 (D.N.J. July 22, 2009).

200. *Ortho-McNeil*, 2009 WL 2182665, at \*8.

contraceptive Ortho Tri-Cyclen Lo (“TCL”).<sup>201</sup> Prior art patents had disclosed a range of twenty to fifty micrograms of EE.<sup>202</sup>

The court indicated that when a claimed invention falls within a range disclosed in the prior art, the invention is presumed to be obvious.<sup>203</sup> The patentee can rebut this presumption, however, by showing: “[t]hat the prior art taught away from the claimed invention; or . . . that there are new and unexpected results relative to the prior art.”<sup>204</sup> In the case, one prior art article surveyed various contraceptive methods, concluding that oral contraceptives containing twenty micrograms of estrogen had higher rates of undesirable side effects than those containing thirty or thirty-five micrograms of estrogen.<sup>205</sup> The court gave the article significant weight due to its impartial scientific nature, and determined that the art at the time of the invention taught away from low dosages.<sup>206</sup> The court also found the article served as evidence that the cycle-control characteristics related to the lower EE dosage in the contested patent were an unexpected result.<sup>207</sup>

Although Barr argued that Ortho’s reduction of the EE dosage was “the obvious use of a known technique to modify a known device,” the court was not convinced.<sup>208</sup> The court found that applying *KSR*’s principles to the evidence would support the non-obviousness of Ortho’s patent because the claimed formulation—using twenty-five micrograms of EE—led to an unexpected result and achieved a side-effect profile similar to the formulation using a higher EE dose.<sup>209</sup>

The court also gave significant weight to the fact that Ortho overcame an obviousness rejection during the patent prosecution where all of the relevant references were before the PTO.<sup>210</sup> While the court gave the evidence of TCL’s commercial success little weight because Ortho’s prior patent prohibited any competition, the overall evidence supported the fact that Ortho was likely to succeed in rebutting the presumption of obviousness.<sup>211</sup>

In summary, in all of the formulation patent cases discussed above, the courts usually cited the *Graham* framework and addressed *KSR*’s principles, without dwelling on the TSM test. While all courts conducted a factual inquiry to determine whether the formulation patent on the brand name drug was obvious, there was no systematic approach that courts adopted in their obviousness analysis. Some courts emphasized the number of options that a PHOSITA could try at the time of the invention,<sup>212</sup> while

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201. Ethinyl estradiol is a type of estrogen that can be used in a contraceptive. *Id.* at \*5.

202. *Id.* at \*4.

203. *Id.* at \*5 (quoting *Iron Grip Barbell Co. v. USA Sports, Inc.*, 392 F.3d 1317, 1322 (Fed. Cir. 2004)).

204. *Id.* (quoting *Iron Grip*, 392 F.3d at 1322).

205. *Id.*

206. *Id.*

207. *Id.*

208. *Id.* at \*6.

209. *Id.* at \*6–7.

210. *Id.* at \*8.

211. *Id.* at \*9.

212. See, e.g., *Bayer Schering Pharma AG v. Barr Labs., Inc.*, 575 F.3d 1341, 1350 (Fed. Cir. 2009) (explaining that prior art identified two predictable solutions); *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1087 (Fed. Cir. 2008) (identifying the number of techniques that existed for separating enantiomers);

others focused on whether the prior art taught away from the claimed invention at issue.<sup>213</sup> The result is a lack of uniformity and predictability in current formulation-patent case outcomes.

### III. DISCUSSION

As interpreted by the Supreme Court in *Graham v. John Deere Co. of Kansas City*,<sup>214</sup> Congress added section 103 to the Patent Act to promote “uniformity and definiteness” in patent-obviousness determinations.<sup>215</sup> Congress intended that § 103 would “have a stabilizing effect and minimize great departures which ha[d] appeared in some cases.”<sup>216</sup> To effectuate these purposes, the Court set forth the *Graham* framework to apply the statutory language of § 103.<sup>217</sup>

Following *Graham*, Federal Circuit developed the teaching, suggestion, or motivation (“TSM”) test to further standardize the obviousness analysis.<sup>218</sup> The Federal Circuit’s rigid application of the TSM test, however, has recently drawn criticism from the Supreme Court. In *KSR International Co. v. Teleflex Inc.*,<sup>219</sup> the Court mandated an “expansive and flexible” approach to obviousness analysis,<sup>220</sup> but failed to provide a clearly defined test to guide lower courts. As a result, the Federal Circuit and district courts, while mostly shunning the TSM test, have been unable to carry out the case-by-case obviousness analysis with a uniform approach.<sup>221</sup>

Based on the principles set forth in *KSR*, this Comment proposes that the following three factors should be considered for obviousness analyses of combination patents: (1) whether there was a reason to combine the known elements in the prior art;<sup>222</sup> (2) whether there was a reasonable expectation of success from the perspective of a person having ordinary skill in the art (“PHOSITA”) at the time of the invention;<sup>223</sup> and (3) whether any secondary considerations support the non-obviousness of the claimed invention.<sup>224</sup> Further, this Comment explains how these

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Pfizer, Inc. v. Apotex, Inc., 480 F.3d 1348, 1363 (Fed. Cir. 2007) (explaining that of fifty-three FDA-approved anions that existed, most were rarely used and PHOSITA would have chosen benzene sulphonate).

213. See, e.g., *Ortho-McNeil*, 2009 WL 2182665, at \*5 (emphasizing that prior art taught away from using lower EE doses); *Depomed, Inc. v. Ivax Corp.*, 532 F. Supp. 2d 1170, 1185 (N.D. Cal. 2007) (explaining that prior art taught away from using patent’s formulation for particular drugs).

214. 383 U.S. 1 (1966).

215. *Graham*, 383 U.S. at 15 (quoting S. REP. NO. 82-1979, at 6 (1952); H.R. REP. NO. 82-1923, at 7 (1952)).

216. *Id.* (quoting S. REP. NO. 82-1979, at 6; H.R. REP. NO. 82-1923, at 7) (internal quotation marks omitted).

217. *Id.* at 17–18.

218. See *supra* Part II.B.2 for a discussion of the TSM test.

219. 550 U.S. 398 (2007).

220. *KSR*, 550 U.S. at 415. See *supra* Part II.B.3 for a discussion of *KSR*.

221. See *supra* Part II.C for a discussion of multiple cases that, taken together, demonstrate a lack of uniformity in the post-*KSR* obviousness analysis.

222. See *KSR*, 550 U.S. at 418 (discussing whether PHOSITA would be inclined to combine elements).

223. See *id.* at 416–17, 419 (explaining that design is non-obvious when its elements work together in manner that is unexpected from PHOSITA’s perspective).

224. See *id.* at 415 (stating that courts may consider instructive secondary factors).

three factors are derived from *KSR* and why they are also consistent with *Graham*. Finally, this Comment sets out a new formula encompassing the three factors to provide a uniform and definite approach for patent-obviousness analysis. It concludes by applying the formula to the post-*KSR* cases discussed in Part II.C above.

A. *Three Factors for Determining Obviousness of Combination Patents*

It is well recognized that the obviousness analysis entails “a broad inquiry.”<sup>225</sup> In fact, the Supreme Court indicated that the difficulties of obviousness determinations are similar to those of negligence analyses.<sup>226</sup> The reasonableness test used in negligence cases requires a fact-finder to evaluate all relevant factors. The famous Hand formula includes three factors in an algebraic formula:  $B < P * L$ , where B is the burden on a defendant to prevent the harm, P is the probability of the harm, and L is the magnitude of the harm.<sup>227</sup> The obviousness analysis should similarly require a balanced consideration of all relevant factors.

Under the *Graham* framework, a factfinder must determine “the scope and content of the prior art,” the “difference[] between the prior art and the [patent] claim[] at issue,” and the skill level of a PHOSITA.<sup>228</sup> In addition, a factfinder must take into account any relevant secondary considerations.<sup>229</sup>

In *KSR*, the Supreme Court reiterated that “a patent based on the combination of elements found in the prior art” should be granted with caution; and stated that an obvious combination patent would deprive the public of what is already in the public domain.<sup>230</sup> The Court set out one criterion for a combination patent’s obviousness: there must be “an apparent reason to combine the known elements in the fashion claimed by the patent at issue.”<sup>231</sup> The Court rejected the Federal Circuit’s requirement of “precise teachings directed to the specific subject matter,”<sup>232</sup> and allowed a factfinder to determine whether an “apparent reason to combine” existed by considering market forces, design incentives, or even common sense.<sup>233</sup>

The Court also stated a second criterion for a combination patent’s obviousness: the combination must “yield[] no more than one would expect from such an arrangement.”<sup>234</sup> In deciding this question, a factfinder should ask “whether the improvement is more than the predictable use of prior art elements according to their established functions.”<sup>235</sup>

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225. *Id.*

226. *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 18 (1966).

227. *United States v. Carroll Towing Co.*, 159 F.2d 169, 173 (2d Cir. 1947).

228. *Graham*, 383 U.S. at 17. See *supra* notes 48–54 and accompanying text for a discussion of the *Graham* framework.

229. *Graham*, 383 U.S. at 17–18. The Federal Circuit also recognizes that secondary considerations “must . . . be considered en route to a determination of obviousness.” *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983).

230. *KSR*, 550 U.S. at 415–16, 418.

231. *Id.* at 418.

232. *Id.*

233. *Id.* at 417, 421.

234. *Id.* at 417.

235. *Id.*

In light of *KSR*, therefore, the following three factors should be considered to determine the obviousness of a combination patent: (1) whether there was a reason to combine the prior art elements; (2) whether there was a reasonable expectation of success from the perspective of a PHOSITA at the time of the invention; and (3) whether there are any relevant secondary considerations. These three *KSR* factors are consistent with the *Graham* framework; the third factor being identical to that in *Graham*.<sup>236</sup> To decide the first two factors, one must ascertain the scope and content of the prior art, and the difference between the prior art and the claimed invention. Additionally, the first two factors should be decided from the perspective of a person of ordinary skill in the art, which in turn will require a preliminary determination of the skill level of a PHOSITA.<sup>237</sup>

*B. Lower Courts Have Failed to Conduct a Balanced Analysis of All Three KSR Factors in Formulation-Patent Cases*

Drug formulation patents are considered combination patents and, as a consequence, are more susceptible to validity challenges.<sup>238</sup> A well-balanced consideration of all three *KSR* factors, therefore, is required when determining a drug formulation patent's obviousness. To ensure that such patents are given proper protection under the Patent Act and that innovator companies are properly incentivized to invest in formulation research and development, a court must conduct a fair and balanced obviousness analysis in formulation patent cases.

In some post-*KSR* lower court cases, however, the three factors have not always been considered to determine the obviousness of formulation patents. For instance, in *Bayer Schering Pharma AG v. Barr Laboratories, Inc.*,<sup>239</sup> the Federal Circuit did not specifically determine whether there was a reason for Bayer to combine the micronized drospirenone with the normal pill formulation, but merely affirmed the district court finding that micronization was taught and the normal pill formulation was obvious to try.<sup>240</sup> Indicating that using a normal pill was a "viable" possibility, the court failed to address how reasonable the expectation of success was.<sup>241</sup> Similarly, in *Purdue Pharma Products L.P. v. Par Pharmaceutical, Inc.*,<sup>242</sup> the court did not explicitly consider whether there was any reason to combine prior art elements, although the facts

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236. See *supra* notes 48–54 and accompanying text for a discussion of the *Graham* framework.

237. 35 U.S.C. §103(a) (2006) (requiring that question of obviousness be resolved from perspective of PHOSITA).

238. See *supra* notes 18–25 and accompanying text for a discussion of drug formulation patents. See *supra* Part II.C for a discussion of cases where generic companies have challenged drug formulation patents on obviousness grounds.

239. 575 F.3d 1341 (Fed. Cir. 2009). See *supra* Part II.C.1.b for a discussion of *Bayer*.

240. *Bayer*, 575 F.3d at 1348.

241. *Id.* at 1349.

242. 642 F. Supp. 2d 329 (D. Del. 2009). See *supra* Part II.C.1.c for a discussion of *Purdue*.

indicated that there might be such a reason.<sup>243</sup> In addition, secondary considerations were not even mentioned by the courts in several cases.<sup>244</sup>

In other cases, courts focused on a certain factor (or factors) and gave less weight to others. For example, in *Bayer*, even if the court had found that there was a reason to combine micronization and the normal-pill formulation, the reasonable expectation of success was low.<sup>245</sup> Indeed, the prior art article revealing in vitro test results cast doubt on such a combination.<sup>246</sup> Furthermore, the prediction based on a similar compound, spirorenone, was at best tenuous, as experts had indicated that a small change in a compound's structure might lead to major differences in its properties.<sup>247</sup> In *Purdue*, the district court merely made the conclusory statement that there was a "resoundingly" reasonable expectation of success" without providing any convincing evidence.<sup>248</sup>

Post-*KSR* cases, therefore, do not appear to follow a uniform and definite approach for determining obviousness of formulation patents.<sup>249</sup> As a result, some otherwise valid formulation patents may lose to obviousness challenges and thus not enjoy the patent protection they deserve.

### C. A New Formula for Determining Obviousness of Formulation Patents

#### 1. Proposal of a New Formula

To ensure that a factfinder considers and gives proper weight to all three *KSR* factors in making obviousness determinations, this Comment proposes a new formula to qualitatively calculate a patent's obviousness:  $R * E - S$ , where R is the reason to combine the prior art elements, E is the reasonable expectation of success at the time of the invention, and S is the sum total of secondary considerations.

Under the formula, the value of R is defined as zero when there was no reason to combine the prior art elements. When evidence demonstrates a reason to combine, the value of R increases accordingly. Likewise, the value of E is defined as zero when there was no reasonable expectation of success, and increases to the extent that evidence demonstrates a reasonable expectation. Lastly, the value of S will increase to the extent that secondary considerations apply. For example, if the patent at issue has achieved commercial success or has met long felt but unsolved needs, the value of S would be large. If there is no such secondary evidence, the value of S would be zero.

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243. *Purdue*, 642 F. Supp. 2d at 370.

244. E.g., *Bayer*, 575 F.3d at 1341; *In re Omeprazole Patent Litig.*, 536 F.3d 1361 (Fed. Cir. 2008); *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075 (Fed. Cir. 2008); *Depomed, Inc. v. Ivax Corp.*, 532 F. Supp. 2d 1170 (N.D. Cal. 2007).

245. *Bayer*, 575 F.3d at 1348.

246. *Id.*

247. *Id.* at 1349–50. See *supra* notes 88–90 and accompanying text for a discussion of the relationship between chemical structure and property.

248. *Purdue*, 642 F. Supp. 2d at 373 (quoting *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009)).

249. See *supra* Part II.C for a discussion of cases involving challenges to formulation patents on obviousness grounds.

By applying this formula, a factfinder will be required to consider all three factors at the same time and determine the obviousness of a patent based on the outcome of the equation. If  $R * E - S > 0$ , the patent is obvious. The larger the outcome of the equation, the more convincing any conclusion of obviousness would be. On the other hand, if  $R * E - S \leq 0$ , the patent is not obvious. The formula uses a product of R and E to reflect the interdependent relationship between these two factors. The absence of either factor will render the patent non-obvious. When both factors are present, the factor S functions as a guard against hindsight bias.

This new formula is fully compliant with the *KSR* decision, and provides a flexible and balanced approach for the patent-obviousness analysis. After ascertaining the relevant facts under the *Graham* framework, a factfinder would apply the formula to the facts, assign values to each factor, and arrive at a qualitative conclusion based on the outcome of the equation.

In determining R (a reason to combine), the factfinder could consider market forces, design incentives, knowledge of a PHOSITA, or common sense.<sup>250</sup> A prior art element can come from either the same or a different field as the invention at issue.<sup>251</sup> The fewer options a PHOSITA can choose to solve the problem, the more likely there is a reason to combine.<sup>252</sup> In determining E (a reasonable expectation of success), the factfinder should look to the “established functions” of prior art elements.<sup>253</sup> The predictability, however, does not have to be absolute.<sup>254</sup> Any prior art that teaches away will make the factor E close to zero. As for S (secondary considerations), the factfinder can look at “commercial success, long felt but unsolved needs, failure of others, etc.”<sup>255</sup> If either R or E is determined to be zero, the absence of secondary considerations will not render the patent at issue obvious.

One might argue that the new formula seems to force a factfinder to adopt the type of formalistic and rigid approach expressly prohibited by *KSR*. The rigidity, however, is mitigated by the broad scope of each factor and the balanced approach inherent in the formula. Compared to the Federal Circuit’s TSM test,<sup>256</sup> the new formula provides a broader and more balanced approach. The TSM essentially inquires into only one factor: whether there is a reason—that is, teaching, suggestion, or motivation—to combine the prior art elements. The new formula adds to this by incorporating R, which was expanded by the *KSR* decision to include market force, design incentive, and common sense.<sup>257</sup> The formula also requires a factfinder to evaluate all three *KSR* factors simultaneously in determining the obviousness of the patent at issue.

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250. See *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 417–419 (2007) (indicating possible reasons to combine known elements).

251. *KSR*, 550 U.S. at 417.

252. See *id.* at 421 (stating that “a finite number of identified, predictable solutions” would make a “good reason” for PHOSITA to combine known elements).

253. *Id.* at 417.

254. *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007).

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

256. See *supra* Part II.B.2 for a discussion of the TSM test.

257. See *supra* Part II.B.3 for a discussion of *KSR*’s expansive and flexible approach.

## 2. Application of the New Formula

A key benefit of the formula is the fact that it can be used in the obviousness analysis of all forms of combination patents. It will be particularly helpful in guiding the obviousness analysis of formulation patents, where a fair and balanced determination is warranted to preserve innovator drug companies' incentive to conduct research and development. This is critical, because without adequate patent protection, pharmaceutical companies would be reluctant to invest in formulation studies for new drugs, and consequently, consumers would lose the benefits that drugs with unique formulations can provide.<sup>258</sup> After the *KSR* decision, some courts may be more inclined to hold formulation patents invalid on obviousness grounds, thus shifting the delicate balance between innovator and generic drug companies in favor of the latter.<sup>259</sup> Application of the new formula will help limit the extent of this shift and thereby ensure that innovator drug companies continue to have adequate incentives and resources to develop new and better drugs, which, ultimately, will benefit generic drug companies and the public in the long term.

### a. $R^*E - S$ Applied: Consistent Outcomes

In *In re Omeprazole Patent Litigation*,<sup>260</sup> the court found that the prior art did not suggest any negative interaction between the enteric coating and the drug core.<sup>261</sup> There was no reason for a PHOSITA, therefore, to change the prior art formulation. Thus, in applying the  $R^*E - S$  formula,  $R$  would be zero. In addition, because there were multiple alternative options to solve the problem, the reasonable expectation of success was not high.<sup>262</sup> Thus, the value of  $E$  would be low. The court did not mention any secondary considerations, but—because  $R$  is zero—the overall outcome of the equation,  $R^*E - S$ , would not be greater than zero. Therefore, the formulation patent at issue was non-obvious.

Applying the formula to *Sanofi-Synthelabo v. Apotex, Inc.*<sup>263</sup> is similarly straightforward. The factor  $E$  should be zero because: (1) a PHOSITA could not predict biological properties of an enantiomer without separating and testing it,<sup>264</sup> (2) separating the mixture of two enantiomers was not predictable at the time of the invention,<sup>265</sup> and (3) the prior art taught away from making a bisulfate salt with an enantiomer.<sup>266</sup> In addition, a PHOSITA would be discouraged from separating the mixture due to the possibility of the separated enantiomer being converted back to the

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258. An extended-release dosage, for example, can avoid the problems that can result from frequent dosing and thereby increase patient compliance. Barich, *supra* note 21, at 66–67.

259. See *supra* notes 9–11 and accompanying text for a discussion of *KSR*'s potential impact on the balance between innovator and generic drug companies.

260. 536 F.3d 1361 (Fed. Cir. 2008).

261. *Omeprazole Patent Litig.*, 536 F.3d at 1380–81.

262. *Id.*

263. 550 F.3d 1075 (Fed. Cir. 2008).

264. *Sanofi-Synthelabo*, 550 F.3d at 1087.

265. *Id.* at 1087–88.

266. *Id.* at 1089.



mixture in the stomach.<sup>267</sup> Therefore, even without considering the factor S, the outcome of the  $R^*E - S$  equation is equal to zero, and the formulation patent at issue is not obvious.

The obviousness determination in two recent district court cases can be carried out using the new formula as well. In *Depomed, Inc. v. Ivax Corp.*,<sup>268</sup> E should be zero because the prior art taught away from using the formulation technique on any soluble drug, which the patent at issue covered.<sup>269</sup> Likewise, in *Ortho-McNeil Pharmaceutical, Inc., v. Barr Laboratories, Inc.*,<sup>270</sup> the unexpected result of the claimed invention<sup>271</sup> would result in E having a value of zero. Therefore, the application of the new formula would find the formulation patents in both cases non-obvious.

While the proposed new formula gives consistent results for cases where courts held the formulation patents to be non-obvious, it also provides consistent results with some of the cases where formulation patents were held obvious. For example, in *Pfizer, Inc. v. Apotex, Inc.*,<sup>272</sup> strong evidence supported that there was a reason to combine the amlodipine with the besylate salt.<sup>273</sup> Thus, R would be relatively large. In addition, there was evidence that the besylate salt would have given a PHOSITA a reasonable expectation of success,<sup>274</sup> so E would be well above zero. Although the superior performance of the besylate salt vis-à-vis the maleate salt would tend to support a finding that the results were unexpected,<sup>275</sup> this would not be enough to cause the  $R^*E - S$  formula to be less than or equal to zero.<sup>276</sup> Therefore, Pfizer's formulation patent on the besylate salt would likely be deemed obvious.

*b. R\*E - S Applied: Altered Outcomes*

In some cases, however, courts could have benefited from conducting a more thorough obviousness analysis in accord with the proposed formula. In *Bayer*, for instance, the court might have reached a different conclusion if it had used the proposed formula. First, no strong evidence supported a reason to combine micronization with normal-pill formulation.<sup>277</sup> While there might have been business reasons to simplify the manufacturing process by using a normal pill, the standard practice at the time of the invention was to use an enteric coating for acid-sensitive drugs.<sup>278</sup> In addition, the in vitro test results would have led a PHOSITA to believe that

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267. *Id.* at 1087.

268. 532 F. Supp. 2d 1170 (N.D. Cal. 2007).

269. *See Depomed*, 532 F. Supp. 2d at 1184 (stating that both Depomed's prior patent and Dow's reference taught away from claimed invention).

270. No. 03-4678, 2009 WL 2182665 (D.N.J. July 22, 2009).

271. *Ortho-McNeil*, 2009 WL 2182665, at \*5.

272. 480 F.3d 1348 (Fed. Cir. 2007).

273. *Pfizer*, 480 F.3d at 1361-64.

274. *Id.* at 1364-65.

275. *Id.* at 1371.

276. *See id.* at 1372 (holding that "secondary consideration does not overcome the strong showing of obviousness").

277. *Bayer Schering Pharma AG v. Barr Labs., Inc.*, 575 F.3d 1341, 1350-51 (Fed. Cir. 2009) (Newman, J., dissenting).

278. *Id.* at 1344 (majority opinion).

the drug substance in a normal pill would not be stable in the stomach.<sup>279</sup> Further, while the well known inconsistency between in vitro and in vivo tests did not rule out the possibility of success for the claimed combination, it by no means provided a strong reason for such a combination.<sup>280</sup> Thus, R would not have been large in *Bayer*.

E would not necessarily have been large in *Bayer* either. The court relied heavily on the fact that there were only two known options available to solve the problem: a normal pill, or an enteric-coated pill.<sup>281</sup> While acknowledging the known disadvantages of an enteric coating, the prior art textbook indicated that it was necessary to use the enteric coating for an acid-sensitive drug, such as drospirenone.<sup>282</sup> Thus, the prior art taught away from using micronized drospirenone in a normal pill. The prior art reference on the stability of a similar compound offered possible, but not convincing, evidence for an expectation of success.<sup>283</sup> In the end, the analysis is a factual determination, but a factfinder could have concluded that the expectation of success in this case was not high.

Finally, the court failed to address any secondary considerations in *Bayer*. The court indicated that Bayer scientists had used the enteric-coating formulation in their research for five years until they discovered that the normal-pill formulation provided the same bioavailability.<sup>284</sup> This evidence supports that the invention met “long felt but unsolved needs.”<sup>285</sup> The claimed combination also offered the unexpected result that a normal pill of micronized drospirenone did not cause the drug to isomerize in the stomach.<sup>286</sup> Thus, there were significant secondary considerations favoring non-obviousness in this case. Overall, therefore, the outcome of the R\*E – S formula is likely less than zero, and Bayer’s formulation patent would have been non-obvious.

Likewise, application of the new formula in *Purdue* would have revealed the deficiency in the court’s obviousness analysis. While there was probably strong evidence for a reason to combine tramadol with the controlled release formulation,<sup>287</sup> the court did not fully analyze whether there was a reasonable expectation of success. Despite acknowledging that there were a significant number of options to create a formulation with desirable dissolution rates, it concluded that the optimization process would have been “routine experimentation.”<sup>288</sup> The court also failed to determine the

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279. *Id.* at 1344–45.

280. *Id.* at 1349–50.

281. *Id.* at 1350.

282. *Id.* at 1349.

283. The district court found five similarities between spirorenone and drospirenone, but drospirenone isomerizes faster and it is more soluble than spirorenone, which would lead to faster isomerization in the stomach. *Id.*

284. *Id.* at 1345.

285. See *Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 17–18 (1966) (stating that “long felt but unsolved needs” are a secondary consideration for obviousness analysis).

286. See *Bayer*, 575 F.3d at 1349 (noting that, contrary to Bayer’s claimed invention, the prior art taught “that drospirenone isomerizes when exposed to acid”).

287. A prior art reference described the controlled release formulation for other similar pain relieving drugs. *Purdue Pharma Prods. L.P. v. Par Pharm., Inc.*, 642 F. Supp. 2d 329, 370 (D. Del. 2009). Moreover, tramadol possessed beneficial characteristics for such a formulation. *Id.* at 370–71.

288. *Id.* at 373.

reasonable expectation from a PHOSITA's perspective, instead relying solely on the inventor's expectation.<sup>289</sup> Thus, the evidence in the record would not have supported a high value for E.

Lastly, the *Purdue* court did not give secondary considerations their proper weight. The court only briefly discussed the competitor's imitation and the commercial success of the drug, and merely provided the conclusory statement that "secondary considerations . . . do not rebut a clear showing of invalidity" due to obviousness.<sup>290</sup> A factfinder might thus have been able to find that S was above zero in the case. The outcome of the R\*E – S formula, therefore, would not have been necessarily greater than zero. Accordingly, the obviousness determination in *Purdue*, failed to fully evaluate the relevant facts.

As demonstrated above, applying the proposed formula leads to the same conclusion which some courts have reached without using the formula, while leading to contrary conclusions in others. Overall, a key benefit of the formula is that it requires courts to consider all three *KSR* factors when determining the obviousness of formulation patents, thereby ensuring a fair and balanced analysis. This, in turn, will help provide the deserved protection for formulation patents and help prevent the balance from being shifted in favor of generic drug companies.

#### IV. CONCLUSION

To maintain the balance between innovator and generic drug companies, courts must give adequate patent protection for brand name drugs. The recent Supreme Court case, *KSR International Co. v. Teleflex Inc.*,<sup>291</sup> has been perceived as lowering the burden for invalidating patents on obviousness grounds. Moreover, some courts have interpreted *KSR* in a manner whereby they only consider a limited number of the factors for determining the obviousness of formulation patents. As a result, some otherwise valid drug formulation patents are at risk of being deemed invalid.

Following *KSR*'s teaching, this Comment identifies three factors for determining the obviousness of a combination patent: namely, (1) whether there was a reason to combine the known elements in the prior art; (2) whether there was a reasonable expectation of success from the perspective of a person having ordinary skill in the art at the time of the invention; and (3) whether there are any secondary considerations that support non-obviousness of the claimed invention.<sup>292</sup> Further, a new formula is proposed to qualitatively calculate a patent's obviousness: R\*E – S.<sup>293</sup> By balancing all of the relevant considerations suggested by the Court in a clear and predictable manner, the proposed formula will help effectuate Congress's interest in ensuring "uniformity and definiteness"<sup>294</sup> in patent law enforcement.

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289. *Id.*

290. *Id.*

291. 550 U.S. 398 (2007).

292. See *supra* Part III.A for a discussion of these three factors.

293. See *supra* Part III.C for an explanation and application of the proposed new formula.

294. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 15 (quoting S. REP. NO. 82-1979, at 6 (1952); H.R. REP. NO. 82-1923, at 7 (1952)).

