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BY LAUREN B. WILLIS\*

## ***Merck KGaA v. Integra Lifesciences I, Ltd.*: How Broad Can You Go? The Supreme Court Makes Room for Preclinical Research in The Drug Price Competition and Patent Term Restoration Act's Safe Harbor Provision**

IN *MERCK KGAA v. INTEGRA LIFESCIENCES I, LTD.*,<sup>1</sup> THE United States Supreme Court considered whether preclinical research conducted using a patented peptide sequence was protected under the safe harbor provision of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch-Waxman Act (HWA).<sup>2</sup> The HWA, codified in part at 35 U.S.C. § 271(e)(1), provides:

*It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) . . . ) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs.*<sup>3</sup>

The Court held that the safe harbor provision should be broadly construed such that "§ 271(e)(1)'s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of *any* information under the [Food Drug and Cosmetic Act]" and therefore, preclinical research would fall within the protection of the statutory exemption.<sup>4</sup> Although Justice Scalia, writing for a unanimous Supreme Court, neglected to reconcile his interpretation with the legislative history of the HWA, the Court's broad interpreta-

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1. 545 U.S. 193 (2005).

2. Drug Price Competition and Patent Term Restoration Act of 1984, 15 U.S.C. §§ 68b-68c, 70b (1994); 21 U.S.C. §§ 301 note, 355, 360cc (1994); 28 U.S.C. § 2201(1994); 35 U.S.C. §§ 156, 271, 282 (1994).

3. 35 U.S.C. § 271(e)(1) (2006).

4. *Merck*, 545 U.S. at 202.

## MERCK KGAA v. INTEGRA LIFESCIENCES I, LTD.

tion of HWA's safe harbor provision protects innovation and promotes competition in the drug industry.<sup>5</sup> However, because of the ambiguity of the safe harbor provision, the uncertain boundaries of the safe harbor provision and the common law research exemption, and the questionable limits on the protection of research tools, the issues surrounding *Merck* will no doubt have to be addressed in the future by either the Food and Drug Administration (FDA), the courts, or the legislature. In the meantime, the Court's decision, though based on a broad reading of the statute, maintains a favorable interpretation of the HWA that is beneficial to both the drug industry and consumers.<sup>6</sup>

### I. THE CASE

Integra Lifesciences I, Ltd. (hereinafter "Integra") and the Burnham Institute own five patents related to a peptide sequence known as the "RGD peptide."<sup>7</sup> In 1988, Merck KGaA (hereinafter "Merck") began funding the work of Dr. David Cheresch at the Scripps Research Institute (hereinafter "Scripps"), providing him with a cyclic peptide for use in his research. In 1995, Merck accepted a three-year proposal from Dr. Cheresch and Scripps proposing that Dr. Cheresch develop his research using the RGD peptide in order to eventually submit an Investigational New Drug Application (IND) to the FDA. Integra filed a patent infringement suit against Merck, Scripps, and Dr. Cheresch in the United States District Court for the Southern District of California. In this complaint, Integra alleged that Merck had infringed upon Integra's RGD peptide patents by willfully supplying the peptides to Dr. Cheresch and Scripps and that Merck had likewise infringed the same patents by using the peptides in experiments.

The district court held that most of Merck's pre-1995 actions were protected by the common law research exemption,<sup>8</sup> but a question of fact remained as to whether Merck's post 1995 use of the RGD peptides was protected under the statutory safe harbor of the HWA.<sup>9</sup> The jury granted Integra damages of \$15 million

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5. See generally *id.* at 202–08 (analyzing the breadth of the statutory text).

6. See Alison Ladd, *Integra v. Merck: Effects on the Cost and Innovation of New Drug Products*, 13 J.L. & Pol'y 311, 311–14 (2005) (discussing the costs associated with researching and developing new drugs). In her article, Ladd notes that the Federal Circuit's decision in *Integra Lifescience I, Ltd. v. Merck KGaA* "effectively narrow[ed] the protection afforded to innovative drug manufacturers." *Id.* at 328–29. A broader safe harbor could provide greater incentives for drug manufacturers to innovate new products, thereby creating a more competitive market that could provide lower drug prices to consumers.

7. U.S. Patent No. 4,988,621 (issued Jan. 29, 1991); U.S. Patent No. 4,789,734 (issued Dec. 6, 1988); U.S. Patent No. 4,792,525 (issued Dec. 20, 1988); U.S. Patent No. 5,695,997 (issued Dec. 9, 1997); U.S. Patent No. 4,879,237 (issued Nov. 7, 1989).

8. *Integra Lifesciences I, Ltd. v. Merck KGaA*, No. 96CV1307–B(AJB), 2004 U.S. Dist. LEXIS 20725, at \*17 (S.D. Cal. Sept. 7, 2004). The United States District Court for the Southern District of California appears to have accepted the trial court's finding that some of Merck's activities with the RGD peptide were protected by the common law research exemption. See *id.* (noting that one "experiment played a role in drug development, and consequently was not exempted under the basic research exception").

9. *Merck*, 545 U.S. at 200–01.

after finding that Merck, Scripps, and Dr. Cheresch had failed to establish that their activities fell under the §271(e)(1) exemption for patent infringement.<sup>10</sup> After post-trial motions, the jury's damage award against Merck was affirmed in the district court and the suit against Dr. Cheresch and Scripps was dismissed.<sup>11</sup> On appeal by Merck, the United States Court of Appeals for the Federal Circuit affirmed in part, reversed in part, and remanded for further proceedings, holding that the denial of judgment as a matter of law to Merck should be affirmed, but the district court's refusal to modify the damages award should be reversed.<sup>12</sup> On remand, the district court reduced the damages award.<sup>13</sup> The United States Supreme Court granted certiorari to determine "whether uses of patented inventions in preclinical research, the results of which are not ultimately included in a submission to the [ ] FDA, are exempted from infringement by 35 U.S.C. §271(e)."<sup>14</sup>

## II. LEGAL BACKGROUND

Exemptions from patent infringement originated at common law around 1813 when courts began to recognize that laws governing patents should not extend to situations where a patented invention was being utilized solely to satisfy intellectual curiosity.<sup>15</sup> In 1984, the court in *Roche Products, Inc. v. Bolar Pharmaceutical Co., Inc.*<sup>16</sup> refused to extend this common law research exemption to allow generic drug manufacturers to utilize the patented inventions relating to a name-brand drug before the name-brand drug's patent had expired.<sup>17</sup> After *Roche*, the common law research exemption was narrowly construed, infrequently granted, and following the court's decision in *Madey v. Duke University*,<sup>18</sup> remained viable yet became, as a matter of function, obsolete.<sup>19</sup>

The *Roche* court's refusal to apply the common law research exemption, however, was most significant because it led to legislative action. Concerned with competition and the ability of generic drugs to enter the marketplace quickly, Congress responded to the *Roche* decision by passing the HWA,<sup>20</sup> which included a safe harbor provision exempting uses that would otherwise be infringing.<sup>21</sup> When district

10. *Id.* at 201.

11. *Id.*

12. *Id.*

13. *Id.* at n.5.

14. *Id.* at 195.

15. See *infra* Part II.A (discussing the origins of the common law research exemption).

16. 733 F.2d 858 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 856 (1984).

17. *Id.* at 863.

18. 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 958 (2003).

19. Kevin Sandstrom, Note, *How Much Do We Value Research and Development?: Broadening The Experimental Use Exemption to Patent Infringement In Light of Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003), 30 WM. MITCHELL L. REV. 1059, 1067 (2004).

20. Drug Price Competition and Patent Term Restoration Act of 1984, 15 U.S.C. §§ 68b-68c, 70b (1994);

21 U.S.C. §§ 301 note, 355, 360cc (1994); 28 U.S.C. § 2201(1994); 35 U.S.C. §§ 156, 271, 282 (1994).

21. See *supra* text accompanying notes 2-3 (quoting the HWA's safe harbor provision).

courts were faced with parties in patent infringement suits invoking the HWA safe harbor provision, they turned to legislative intent to interpret the statute.<sup>22</sup> In 1990, the interpretation of the HWA safe harbor was before the Supreme Court in *Eli Lilly & Co. v. Medtronic, Inc.*,<sup>23</sup> where the Court ignored legislative intent and instead broadly construed the HWA's safe harbor provision to include not only drugs, but medical devices.<sup>24</sup> Following this decision, the federal courts applied a broader interpretation of the safe harbor provision until the court in *Integra Lifesciences I, Ltd. v. Merck KGaA*,<sup>25</sup> adopted a narrower interpretation of the safe harbor provision.<sup>26</sup> Once again, the Supreme Court was faced with the challenge of addressing the scope of the HWA's safe harbor provision.<sup>27</sup>

#### A. The Origins of The Common Law Research Exemption

Before Congress enacted legislation granting patent exemptions, potentially infringing activities were protected by the common law research exemption.<sup>28</sup> This experimental use defense to liability for patent infringement originated in Supreme Court Justice Story's opinion in 1813's *Whittemore v. Cutter*.<sup>29</sup> Justice Story, seeking to justify jury instructions requiring the jury to find that a patent infringer intended to profit from the infringing use,<sup>30</sup> noted "it could never have been the intention of the legislature to punish a man who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects."<sup>31</sup> The exemption, as applied, meant that patented inventions could be used for research purposes, provided that their use was solely for intellectual or noncommercial reasons not hostile to the interests of the patent holder.<sup>32</sup> From Justice Story's statement, the

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22. See *infra* Part II.D (providing examples of district court decisions analyzing the HWA safe harbor provision).

23. 496 U.S. 661 (1990).

24. See *infra* Part II.E (analyzing the court's decision in *Eli Lilly*).

25. 331 F.3d 860 (Fed. Cir. 2003).

26. See *infra* Part II.F (tracing the analysis of the safe harbor provision after *Eli Lilly*).

27. See *infra* Part III (detailing the Court's analysis and holding regarding the breadth of the safe harbor provision).

28. See *Roche Products, Inc. v. Bolar Pharmaceutical Co., Inc.*, 733 F.2d 858, 862 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 856 (1984) (discussing the origins of the common law research exemption).

29. 29 F. Cas. 1120 (C.C.D. Mass. 1813) (No. 17,600).

30. *Roche*, 733 F.2d at 862.

31. *Whittemore*, 29 F. Cas. at 1121. Scholarly commentators differ on whether Justice Story "relied on the doctrine of *de minimis non curat lex* ('the law takes no account of trifles')" and intended the common law exemption to provide exceptions for *de minimis* infringing uses, or whether he relied on "the common law principle of *injuria absque damno* (wrong without damage)," that would recognize that a patent had been infringed, but it would be excused if a court could find the infringement had not caused cognizable harm. Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement For Biomedical Research Tools*, 76 WASH. L. REV. 1, at 20-21 (2001).

32. *Roche*, 733 F.2d at 862.

common law research exemption developed until it became a well-established part of patent law.<sup>33</sup>

*B. The Court in Roche Products Refused to Expand the Common Law Research Exemption, Resulting in the Passage of the Drug Price Competition and Patent Term Restoration Act*

In 1984, the United States Court of Appeals for the Federal Circuit in *Roche Products, Inc. v. Bolar Pharmaceutical Co., Inc.*<sup>34</sup> grappled with the common law research exemption. In *Roche*, a competitor used a patented ingredient to create a new generic equivalent of the patented name-brand drug and sought to obtain federal approval to market the generic equivalent when the name-brand drug's patent expired.<sup>35</sup> The court held that the competitor's use of a patented ingredient was not protected by the common law research exemption because the intended use of the patented ingredient was solely for business reasons.<sup>36</sup> Because the court's decision would restrict the speed at which generic drugs could enter the marketplace, a concerned Congress responded by ultimately overruling the decision with the Hatch-Waxman Amendments to the Food, Drug and Cosmetic Act,<sup>37</sup> also known as the Drug Price Competition and Patent Term Restoration Act of 1984.<sup>38</sup> Under the HWA, Congress provided an exception from the general rule that "whoever without authority makes, uses, offers to sell, or sells any patented invention . . . infringes the patent."<sup>39</sup> With the passage of the HWA, patent infringers conducting research for regulatory submission had another defense to liability besides the common law research exemption.

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33. See *Roche*, 733 F.2d at 862 (noting that the common law research exemption is well established); *Poppenhusen v. Falke*, 19 F. Cas. 1048, 1049 (C.C.S.D.N.Y. 1861) (No. 11,279) ("It has been held, and no doubt is now well settled, that an experiment with a patented article for the sole purpose of gratifying a philosophical taste, or curiosity, or for mere amusement, is not an infringement of the rights of the patentee."); *Byam v. Bullard*, 4 F. Cas. 934, 935 (C.C.D.Mass. 1852) (No. 2262) (citing Justice Story's opinion in *Whittemore*).

34. 733 F.2d 858 (Fed. Cir. 1984), cert. denied, 469 U.S. 856 (1984).

35. *Id.* at 860.

36. *Id.* at 863. The court refused to "construe the experimental use rule so broadly as to allow a violation of the patent laws in the guise of 'scientific inquiry,' when that inquiry has definite, cognizable, and not insubstantial commercial purposes." *Id.*

37. Ann K. Wooster, J.D., *Construction and Application of Hatch-Waxman Act*, Pub. L. No. 98-417, 98 STAT. 1585 (1984) (Codified As Amended at 21 U.S.C.A. § 355 and 35 U.S.C.A. § 271(E) (1994)), 180 A.L.R. Fed. 487 (2005).

38. See *Intermedics, Inc. v. Ventrix, Inc.*, 775 F.Supp. 1269, 1276 (N.D.Cal. 1991) *aff'd* 991 F.2d 808 (Fed. Cir. 1993) ("Congress enacted §271(e)(1) in 1984 in order to reverse the opinion of the United States Court of Appeals for the Federal Circuit in *Roche* . . . . The *Roche* court had ruled the experimental use exception was not broad enough to protect manufacturers of generic drugs while they were conducting the extensive field tests of their products that were necessary to generate the data that the FDA required before granting permission to market the drugs commercially.").

39. 35 U.S.C. § 271(a).

C. *The Roche and Madey Court Narrow The Common Law Research Exemption*

Although the court in *Roche* refused to apply the common law research exemption, the common law research exemption nevertheless survived the *Roche* decision and the subsequent passage of the HWA.<sup>40</sup> The *Roche* court stated in dicta that the common law research exemption should be narrowly construed<sup>41</sup> and, following *Roche*, the common law research exemption was narrowly interpreted and infrequently granted to infringing parties.<sup>42</sup>

The United States Court of Appeals for the Federal Circuit emphasized just how narrow courts should interpret the common law research exemption in *Madey v. Duke University*.<sup>43</sup> In *Madey*, a university professor sued Duke University, his former employer, for conducting research using his patented equipment. The University sought to invoke the common law research exemption as a defense to patent infringement. The court held, however, that the infringing use was outside of the common law research exemption because even though the University was operated not-for-profit, utilizing the equipment furthered the University's legitimate business objectives.<sup>44</sup> This holding effectively narrowed the common law research exemption beyond what the judges contemplated in dicta in *Roche*.<sup>45</sup>

D. *District Courts Look to Legislative Intent to Interpret the HWA*

After *Roche* and the passage of the HWA, courts were faced with the daunting task of applying a new statute that had no accompanying judicial precedent. Therefore, in order to interpret the HWA, courts looked to the legislative intent behind the

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40. See *Madey v. Duke Univ.*, 307 F.3d 1351, 1355 n.3 (Fed. Cir. 2002), cert. denied, 539 U.S. 958 (2003) (commenting on the effect of the HWA on the experimental use doctrine).

41. *Roche*, 733 F.2d at 863. The court not only stated that the common law research exemption ought to be narrowly construed, but noted that even using a small quantity of a patented invention would not be a "trifle in its economic effect" and therefore not a "dilettante affair such as Justice Story envisioned." *Id.*

42. Sandstrom, *supra* note 19, at 1065–68. See generally *Embrex Inc. v. Serv. Eng'g Corp.*, 216 F.3d 1343 (Fed. Cir. 2000) (interpreting the common law research exemption narrowly to hold that reverse engineering around a patented process constituted economically motivated patent infringement not protected by the common law research exemption).

43. 307 F.3d 1351, 1362 (2002).

44. *Id.* The court noted that although major research universities conduct research partly to satisfy intellectual curiosity, such research also has economic implications for the school. *Id.* Research attracts students and faculty to the school, bolsters the university's reputation, and also entices grants from private institutions or businesses. *Id.* This holding indicates that the common law research exemption does not necessarily immunize academic or non-profit institutions from patent infringement suits. See *id.* at 1361–62.

45. *Madey* took *Roche* a step further by holding that even seemingly academic or not-for-profit activities using a patented invention may have financial implications that would preclude the use from the protections of the common law research exemption. The *Roche* court only noted that the common law research exemption should be construed narrowly in dicta and did not have to rule on the scope of the common law research exemption because it was clear that the generic drug manufacturer's use of a patented invention was motivated by commercial gain.

safe harbor provision.<sup>46</sup> In *Scripps Clinic & Research Foundation v. Genentech, Inc.*,<sup>47</sup> the United States District Court for the Northern District of California narrowly construed 35 U.S.C. § 271(e)(1), holding that Genentech's uses of a patented protein were not protected under the safe harbor provision because the uses had multiple purposes which were not all solely related to meeting FDA requirements.<sup>48</sup> The court looked at comments made by the authors of the HWA<sup>49</sup> and declared: "the statute's meaning is clear: the use of a patented invention is protected so long as that use is solely for purposes reasonably related to meeting the reporting requirements of federal drug laws."<sup>50</sup>

The word "solely" was also the focus of a court's decision in *Scripps Clinic & Research Foundation v. Baxter Travenol Laboratories*.<sup>51</sup> In this case, the United States District Court for the District of Delaware discussed the "solely for the uses reasonably related to" language in order to determine whether foreign activities could be reasonably related to FDA approval of a drug.<sup>52</sup> The court decided that it should inquire further into the nature of Baxter's activities before reaching a decision because the legislative history of the HWA did not provide enough guidance on which activities could be "reasonably related" to FDA approval.<sup>53</sup> In both of these cases, the district courts favored a narrow interpretation of the HWA by noting the limiting effect of the word "solely" in the statutory language.<sup>54</sup>

#### E. Eli Lilly & Co.: The Supreme Court Broadens the Safe Harbor Provision

In 1990, the United States Supreme Court adopted a broader interpretation of the HWA when it addressed whether the safe harbor provision in 35 U.S.C. §271(e)(1) extended to medical devices.<sup>55</sup> In *Eli Lilly & Co. v. Medtronic, Inc.*,<sup>56</sup> Justice Scalia, writing for the majority, engaged in a textual analysis of 35 U.S.C. § 271(e)(1) in order to determine the scope of the terms "patented invention" and "a Federal law which regulates the manufacture, use, or sale of drugs."<sup>57</sup> In his majority opinion, Justice Scalia focused on the two distorting effects of the FDA's regulatory approval

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46. See Angela M. Davison, *Shrinking Waters in the Safe Harbor: Has Integra Lifesciences v. Merck Turned the Tide by Narrowing Available Exempted Infringing Uses?*, 59 FOOD & DRUG L.J. 79, at 83-84 (2004) (discussing district court cases analyzing the safe harbor provision).

47. 666 F. Supp. 1379 (N.D. Cal. 1987).

48. *Id.* at 1396.

49. See *id.* ("The comments of the authors of the House Report emphasize the narrowness of the exemption.").

50. *Id.*

51. 1988 U.S. Dist. LEXIS 1972 (D. Del. Jun. 21, 1988).

52. *Id.* at \*12-14.

53. *Id.* at \*14.

54. Davison, *supra* note 46, at 83-86 (noting the courts' focus on the word "solely" in the statutory language).

55. See *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990) (interpreting the HWA safe harbor provision).

56. *Id.*

57. *Id.* at 665-68. Justice Scalia stated the issue of the case as follows:



process that the HWA sought to remedy by looking at the language of the statute as a whole.<sup>58</sup> The Court held that the definition of "patented invention," as utilized in § 271(e)(1), should not just include drug-related inventions, but all inventions.<sup>59</sup> Additionally, the Court interpreted the statutory phrase "'a Federal law which regulates the manufacture, use, or sale of drugs'" by declaring that it does not only refer to legal provisions regulating drugs, but refers to any Act as a whole which has some provision that regulates drugs.<sup>60</sup> Under this interpretation, Medtronic Inc.'s testing and marketing of an implantable cardiac defibrillator, a medical device, was protected by the safe harbor provision from Eli Lilly & Co.'s patent infringement suit.<sup>61</sup> Justice Kennedy, joined by Justice White, dissented on the grounds that the Court should have looked at the ordinary usage of the words in the statute which did not include medical devices, but specifically discussed regulating drugs.<sup>62</sup> The Supreme Court had now effectively established a broad interpretation of the HWA; a feat that it accomplished without ever looking to the legislative intent of the statute.<sup>63</sup>

#### F. *The Federal Courts After Eli Lilly & Co. Expand the Safe Harbor Provision*

Before the United States Court of Appeals for the Federal Circuit's decision in *Integra Lifesciences I, Ltd. v. Merck KGaA*,<sup>64</sup> federal courts following *Eli Lilly* had consistently expanded the protections offered by the safe harbor provision of the

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[W]hether 35 U.S.C. § 271(e)(1) (1982 ed., Supp. V) renders activities that would otherwise constitute patent infringement noninfringing if they are undertaken for the purpose of developing and submitting to the Food and Drug Administration (FDA) information necessary to obtain marketing approval for a medical device under § 515 of the Federal Food, Drug, and Cosmetic Act (FDCA), 90 Stat. 552, 21 U.S.C. § 360e.

*Id.* at 663.

58. *Id.* at 669–73. The HWA sought to correct distortions both at the beginning and at the end of a patent's term. *Id.* at 669. The first distortion occurs when a patent holder cannot market the patented product because the product is going through the regulatory approval process, thereby causing the patent term to run without allowing the patent holder to gain financially. *Id.* Secondly, the patent term would be distorted if what would be infringing products were not allowed to begin the regulatory approval process until after a patent term expired. *Id.* at 670. Section 201 of the HWA sought to eliminate the first distortion by creating a patent-term extension for products "subject to lengthy regulatory delays . . . [that] could not be marketed prior to regulatory approval." *Id.* Section 202 of the HWA (codified in 35 U.S.C. § 271) sought to eliminate the second distortion by providing a safe harbor provision allowing exemptions for patent infringement. *Id.*

59. *Id.* at 665.

60. *Id.*

61. *Id.*

62. *Id.* at 682 (declaring that 35 U.S.C. § 271(e)(1) "refers only to the actual regulation of drugs and does not exempt the testing of a medical device from patent infringement").

63. See *id.* (Kennedy & White, JJ., dissenting) ("In this case, even if Congress could have clarified § 271(e)(1), the Court ascribes a most unusual meaning to the existing language. Numerous statutory provisions and court decisions, from a variety of jurisdictions, use words almost identical to those of § 271(e)(1), and they never mean what the Court says they mean here.").

64. 331 F.3d 860 (Fed. Cir. 2003).

HWA.<sup>65</sup> In 1991, the United States Court of Appeals for the Federal Circuit adopted the Supreme Court's reasoning in *Eli Lilly & Co.* in another medical device case, *Intermedics, Inc. v. Ventritex, Inc.*<sup>66</sup> In *Intermedics*, the Court of Appeals affirmed the United States District Court for the Northern District of California's holding that Ventrix's use of an implantable defibrillator (allegedly infringing Intermedics, Inc.'s patent) fell within the HWA's patent infringement exemption.<sup>67</sup> The lower court's decision focused its inquiry on an objective test: whether "*those acts of manufacture, use, or sale of a patented invention . . . would constitute acts of infringement but for [the] exemption.*"<sup>68</sup> If "it [would] have been reasonable, objectively, for a party in defendant's situation to believe that there was a decent prospect that the 'use' in question would contribute (relatively directly) to the generation of kinds of information that was likely to be relevant in the process by which the FDA would decide whether to approve the product," then the use would fall within the safe harbor provision.<sup>69</sup>

Although the court developed an objective test which focused on conduct rather than motive or the ultimate aim of the research, uncertainty still existed as to what constituted a use "reasonably related" to FDA approval of a drug or device. Once the United States Court of Appeals for the Federal Circuit engaged in a narrow interpretation of the HWA,<sup>70</sup> the United States Supreme Court exercised its jurisdictional authority to clarify how the safe harbor provision should be interpreted.<sup>71</sup>

### III. THE COURT'S REASONING

In *Merck v. Integra*, the United States Supreme Court vacated the judgment of the United States Court of Appeals for the Federal Circuit and remanded the case, holding that utilizing patented compounds in preclinical studies fell within the protection of the § 271(e)(1) safe harbor provision as long as one could reasonably expect the studies to produce information relevant to the FDA submission process for either a IND or New Drug Application (NDA).<sup>72</sup> Writing for an unanimous court, Justice Scalia held that the safe harbor provision of the HWA should be broadly construed such that "§ 271(e)(1)'s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development

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65. See generally *Allergan, Inc. v. Alcon Labs., Inc.* 324 F.3d 1332 (Fed. Cir. 2003); *Fitness Inc. v. TNWK Corp.*, 162 F.3d 1379 (Fed. Cir. 1998); *Intermedics, Inc. v. Ventrix, Inc.*, 775 F. Supp. 1269 (N.D. Cal. 1991).

66. 991 F.2d 808 (Fed. Cir. 1993).

67. See *Intermedics, Inc.*, 775 F.Supp. at 1289 (holding that Ventritex was protected by the infringement exemption).

68. *Id.* at 1277.

69. *Id.* at 1280.

70. See *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 872 (Fed. Cir. 2003) (holding that preclinical research was not "reasonably related" to FDA approval of a drug).

71. See *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005) (favoring a broad interpretation of the safe harbor provision).

72. *Id.* at 202 (quoting brief of the U.S. as *Amicus Curiae* at 23).

and submission of any information under the FDCA.<sup>73</sup> Rejecting the lower court's interpretation of the safe harbor provision, Justice Scalia refused to construe §271(e)(1) such that the statutory exemption would not protect preclinical research even if the research is ultimately never submitted to the FDA.<sup>74</sup> By looking at the statutory text and analyzing the FDA's drug approval process, Justice Scalia returned the analytical focus of the HWA to the broader reading originally adopted by the Court in *Eli Lilly & Co. v. Medtronic, Inc.*<sup>75</sup>

Analyzing the statutory text, Justice Scalia stated that "[t]here is simply no room in the statute for excluding certain information from the exemption on the basis of the phase of research in which it is developed or the particular submission in which it could be included."<sup>76</sup> In his analysis, Justice Scalia did not focus on the limiting term "solely" that is included in the safe harbor provision, but instead concentrated on the "reasonable relation" requirement in the statute.<sup>77</sup> Without discussing legislative intent, the Court instead noted what was absent from the statute, thereby determining that Congress did not specifically limit the safe harbor provision.<sup>78</sup>

The Court also looked to the Code of Federal Regulations to analyze the FDA's drug approval process in order to determine whether preclinical research could be "reasonably related" to FDA submission.<sup>79</sup> In doing so, the Court rejected arguments seeking to exclude the preclinical research from the safe harbor provision on the grounds that the research was not reasonably included in an FDA submission and not conducted following FDA's Good Laboratory Practice regulations.<sup>80</sup> By establishing that preclinical research data would be important to the FDA submission process even if it is never ultimately submitted, the Court held that preclinical research would be "reasonably related" to FDA submission and therefore, within the protections of the HWA safe harbor provision.<sup>81</sup> Because the court of appeals based its decision on "a construction of § 271(e)(1) that was not consistent with the text of that provision or the relevant jury instruction," the Court remanded the

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73. *Id.*

74. *Id.*

75. 496 U.S. 661, 669 (1990).

76. *Merck*, 545 U.S. at 202.

77. *Id.* at 206.

78. *Id.*

79. *See id.* at 204–05 (analyzing FDA's requirements for preclinical studies).

80. *See id.* at 204. In his analysis, Justice Scalia noted that preclinical studies could be within the scope of the exemption because FDA would have an interest in the information gathered during preclinical research. *See id.* at 203. The results of preclinical studies, including "a drug's efficacy, mechanisms of action, pharmacokinetics, and pharmacology," should be included in an IND and would also be used to assess the risk of a proposed clinical trial. *Id.* at 203–04. Additionally, the preclinical research scrutinized in this case would not be disqualified because it did not comport with the FDA's Good Laboratory Practice regulations because the regulations apply only to testing the safety of drugs; even if the research did not comport it is not automatically barred from submission in an IND. *Id.* at 204.

81. *Id.* at 206–07.

case so that the evidence could be reviewed under the broad interpretation of § 271(e)(1) adopted by the Supreme Court.<sup>82</sup>

#### IV. ANALYSIS

In *Merck KGaA v. Integra Lifesciences I, Ltd.*, the United States Supreme Court considered the breadth of the safe harbor provision of the Hatch-Waxman Act.<sup>83</sup> The Supreme Court broadly interpreted the safe harbor provision by holding that patented inventions could be used in preclinical research so long as the results garnered by their use would be reasonable to include in a FDA submission for an IND or NDA, regardless of whether the IND or NDA is actually ever submitted.<sup>84</sup> In so holding, the Court established that preclinical research on a patented drug may be exempt from patent infringement, but did not draw a clear line between infringing and non-infringing uses.<sup>85</sup>

Although the Court was not obligated to establish a test for determining a “reasonably related” use, the omission of such a formula leaves important questions unanswered. Even though the Court shifts the interpretation of the HWA safe harbor provision back to a broader reading that favors competition and innovation in the drug market, the Court’s decision does not indicate how far “upstream” the safe harbor provision may reach.<sup>86</sup> Without such a limitation, it is unclear to what extent the HWA’s safe harbor provision will affect or interact with the common law research exemption. Additionally, the Court’s decision could have implications for future decisions regarding the protections afforded to research tools. Because courts addressing the HWA have gone beyond the legislative intent of the statute, the uncertainty remaining after *Merck* may be better resolved through administrative, legislative, or additional judicial processes.

##### *A. Statutory Deconstruction: The Court Broadens the Reading of The Safe Harbor Exemption and Bypasses the Legislative Intent of the Act*

Even though the legislative history of the HWA indicates that the Act was intended to speed up the process of federal approval of generic drugs,<sup>87</sup> the Court’s opinion

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82. *Id.* at 208.

83. *Id.* at 195–96.

84. *See id.* at 206–07 (discussing the reasonable relationship standard of 35 U.S.C. § 271(e)(1)).

85. *See id.* at 205 (declaring that § 271(e)(1) doesn’t categorically exclude experiments or uses that don’t end up being submitted to the FDA, but does not necessarily “globally embrace all experimental activity that at some point, however, attenuated, may lead to an FDA approval process”).

86. *See* Brendan M. O’Malley, *Merck v. Integra and Its Aftermath: A Safe Harbor For the Commercial Use of Biotechnology Research Tools?*, 23 CARDOZO ARTS & ENT. L.J. 739, 740 (2006) (utilizing “upstream” and “downstream” references to generate a play on words in reference to the progress of research in relation to whether or not it would fall within the protection of HWA’s safe harbor provision).

87. *See* OFFICE OF THE FEDERAL REGISTER, NATIONAL ARCHIVES AND RECORDS ADMIN., PUBLIC PAPERS OF THE PRESIDENTS OF THE UNITED STATES, RONALD REAGAN 1362 (1987) (“The legislation will speed up the process of Federal approval of inexpensive generic versions of many brand name drugs, make the generic versions more widely available to consumers, and grant pharmaceutical firms added incentives to develop new

in *Merck* employed a broad reading to give § 271(e)(1) a "wide berth" in a patent infringement situation that did not involve a generic drug.<sup>88</sup> Although Justice Scalia explicitly rejects looking to legislative intent when engaging in statutory interpretation, the ambiguity of 35 U.S.C. § 271(e)(1) could be better resolved with some kind of legislative or administrative guidance.<sup>89</sup> Justice Scalia purported to decipher the relevant statutory sections, but he ultimately conceded in his opinion in *Eli Lilly* that "[n]o interpretation we have been able to imagine can transform § 271(e)(1) into an elegant piece of statutory draftsmanship."<sup>90</sup>

Although Justice Scalia in *Eli Lilly* admitted the safe harbor provision is not "plainly comprehensible in anyone's view,"<sup>91</sup> his opinion in *Merck* nevertheless sought to interpret it.<sup>92</sup> Because Justice Scalia believes "it is simply incompatible with democratic government, or indeed, even with fair government, to have the meaning of a law determined by what the lawgiver meant rather than by what the lawgiver promulgated," he ignored the legislative intent behind the statute.<sup>93</sup> Even though "[i]t is not the law that a statute can have no effects which are not explicitly mentioned in its legislative history,"<sup>94</sup> the HWA could benefit from some guidance to reconcile the apparent discrepancy between the language that designates safe harbor applicability to uses "solely" related to FDA submission with the Court-created application of the safe harbor provision to uses that are "reasonably related" to FDA submission.<sup>95</sup>

#### B. The Benefits of a Broader Safe Harbor Provision

Despite Justice Scalia's textualist approach, however, the ultimate holding in *Merck* still fosters the competition and innovation that the HWA originally intended to

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drugs . . . . The bill will promote medical breakthroughs and drug innovation by granting drug companies up to 5 more years of patent protection for new drugs. And this extension will help compensate for the years of patent life lost due to the time-consuming, but essential, testing required by the Food and Drug Administration."); see also H. Rep. No. 98-857 (1998) (detailing the legislative intent behind the HWA).

88. *Merck*, 545 U.S. at 202.

89. See Antonin Scalia, *Common-Law Courts in a Civil-Law System: The Role of United States Federal Courts in Interpreting the Constitution and Laws*, in *A MATTER OF INTERPRETATION: FEDERAL COURTS AND THE LAW: AN ESSAY 23* (Amy Gutman, ed., 1997) ("A text should not be construed strictly, and it should not be construed leniently; it should be construed reasonably, to contain all that it fairly means."). Although the Court in *Merck* established that preclinical research could constitute a use "reasonably related" to FDA submission, perhaps the FDA or even Congress may be in a better position to determine exactly where to draw the line between an infringing use and a use reasonably related to submission to the FDA. Establishing a hard line rule could inevitably involve technical or scientific analysis outside the expertise of the Court and better suited to agency or legislative discretion.

90. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 679 (1990).

91. *Id.* at 668.

92. *Merck*, 545 U.S. at 202-08.

93. Scalia, *supra* note 89, at 17.

94. *Eli Lilly*, 496 U.S. at 669 n.2 (quoting *Pittston Coal Group v. Sebben*, 488 U.S. 105, 115 (1988)); see also *Br. of the U.S. as Amicus Curiae* 14-15 (arguing that the lower court erred because the Supreme Court had determined that § 271(e)(1) is not limited to generic drugs).

95. See *supra* Part II.D (discussing district courts interpreting the HWA); see also *supra* note 89.

preserve.<sup>96</sup> By allowing preclinical trials to take advantage of the safe harbor provision, the Supreme Court gave drug researchers more leeway by recognizing that “scientific testing is a process of trial and error.”<sup>97</sup> A narrower interpretation of “uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs” would limit the ability of scientists to conduct tests using or involving patented drugs or devices, thereby stifling competition which could increase drug costs and hinder innovation.<sup>98</sup> By returning to the trend of focusing on any “reasonably related” use rather than on uses “solely” related to FDA submission,<sup>99</sup> the Court in *Merck* protected preclinical studies routinely submitted to the FDA under the Food Drug and Cosmetic Act as part of INDs, and even extended protection to studies that produce information that is never submitted to the FDA.

### *C. The Implications of a Broader Safe Harbor Provision for the Common Law Research Exemption*

Although there is a general consensus that the common law research exemption is still viable after the passage of the HWA,<sup>100</sup> it remains to be seen how or whether these defenses to patent infringement will interact. Even though the common law research exemption was not before the Supreme Court in *Merck*, Justices O'Connor and Kennedy nevertheless demonstrated their interest in the relation between the common law research exemption and the safe harbor provision when they questioned Merck's and Integra's counsel during oral argument.<sup>101</sup> The attorney for Merck urged the court to not address the common law research exemption because, on appeal, Merck in its pleadings did not rely on the common law research exemption as a defense to patent infringement.<sup>102</sup> The trial court, however, did hold that some of Merck's uses of the RGD peptide were protected by the common law research exemption and, pursuant to this finding, subsequent court decisions focused solely on Dr. Cheresh's research activity related to drug discovery.<sup>103</sup>

96. See *supra* note 87.

97. *Merck*, 545 U.S. at 206.

98. See Ladd, *supra* note 6 at 336–37.

99. *Merck*, 545 U.S. at 207–08.

100. Mueller, *supra* note 31, at 31–32.

101. See *Merck KGaA v. Integra Lifesciences I. Ltd.*, et al., 24 BIOTECHNOLOGY L. REP. 659 at 660, 664, 668 (Oct. 2005) (questioning the application of the common law research exemption to the *Merck* case).

102. See *id.* at 660 (urging the court to not address issues not properly presented).

103. See *Merck*, 545 U.S. at 198 (noting that the lower court held that some of Merck's actions were protected by the common law research exemption); see also *Integra Lifesciences I, Ltd. v. Merck KGaA*, No. 96CV1307-B(AJB), 2004 U.S. Dist. LEXIS 20725, at \*17 (D. Cal. Sept. 7, 2004) (stating that “any experiments conducted by Dr. Cheresh prior to 1995, with the exception of one chick embryo pharmacokinetic experiment in August 1994, were held to not infringe Telios' RGD Patents under the common law research exception”); *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 872–77 (Fed. Cir. 2003) (Newman, J., dissenting) (discussing the common law research exemption in relation to Merck's activities).

While the common law research exemption relies on the intent behind utilizing a patented invention, the HWA's safe harbor provision involves an objective analysis of whether the use of a patented invention could be reasonably related to the submission of information under a federal law which regulates drugs. The creations of these two defenses to patent infringement were also spurred by different circumstances. The common law research exemption developed to protect non-economic intellectual endeavors, whereas the HWA was passed because of the successful lobbying tactics of generic drug manufacturers.<sup>104</sup>

Based on the narrow interpretation of the common law research exemption adopted in *Madey*, it would seem that the common law research exemption and the HWA's safe harbor provision are mutually exclusive during the drug discovery process. The Court of Appeals for the Federal Circuit recognized this when it refused to apply the common law research exemption to Merck's activities for the reason that the peptides were clearly being utilized for commercial purposes.<sup>105</sup> In research situations involving drugs, common law research exemptions are probably very rare because there is usually a commercial motive for infringing a patent.<sup>106</sup> Because the common law research exemption is rarely utilized in these situations, it is questionable to what extent the common law remains as a fall back exemption during drug research for unique non-commercial situations that would otherwise be infringing uses.<sup>107</sup>

*D. The Court's Interpretation of the Safe Harbor Provision in Merck Bolsters the Court's Holding in Eli Lilly & Co. that the HWA Safe Harbor Extends Beyond Protection of Research for Generic Drugs*

By holding that the HWA's safe harbor provision extends to protect preclinical research or other uses of a patented invention reasonably related to gathering data for FDA submission in *Merck*, the Supreme Court also bolstered its holding in *Eli Lilly & Co.* that the HWA safe harbor provision should not be interpreted as protecting generic drugs exclusively.<sup>108</sup> The Court in *Merck* recognized that if the safe harbor provision was interpreted not to protect research that uses patented compounds unless that research is subsequently submitted to the FDA, then that would essentially limit the safe harbor provision to only protect research conducted dur-

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104. Mueller, *supra* note 31, at 26–27.

105. See George Fox, *Integra v. Merck: Limiting the Scope of the § 271(E)(1) Exception to Patent Infringement*, 19 BERKELEY TECH. L.J. 193, 214–15 (2004).

106. See Phillip B.C. Jones, *Navigating the Hatch-Waxman Act's Safe Harbor*, 57 FOOD & DRUG L.J. 475, 476 (2002) (noting the rare application of the common law research exemption).

107. See Mueller, *supra* note 31, at 25–26 (claiming that the HWA supports a broader interpretation of the common law research exemption).

108. See generally *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990) (holding that the HWA safe harbor provision may be extended to medical devices).

ing the development of a generic drug.<sup>109</sup> Although the legislative intent of the HWA illustrates that the Act was drafted specifically to provide patent exemptions for generic drug researchers, the Court's interpretation of the safe harbor in *Merck* indicates that, as in *Eli Lilly & Co.*, the statute may be read more broadly than the original legislative intent.

*E. The Implications of Merck on the Protections Afforded to Research Tools*

Justice Scalia declined to address the issue of whether research tools would fall under the statutory exemption for patent infringement because the issue was not before the Court in *Merck*.<sup>110</sup> A research tool is research that is conducted using the patented invention to develop other products as opposed to researching the patented invention itself.<sup>111</sup> Specifically, the National Institutes of Health define "research tools" or "unique research resources" as "tools that scientists use in the laboratory, including cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones and cloning tools (such as PCR), methods, laboratory equipment and machines."<sup>112</sup> Because the peptides utilized at Scripps were not research tools (Merck was advocating a study of the patented peptides themselves), the Court did not have to address the issue.<sup>113</sup>

Nevertheless, whether research tools fall within the § 271(e)(1) exemption is an important question that will have to be addressed at some juncture. If research tools could be exempt from patent infringement under § 271(e)(1), patent holders could be deprived of the value of their patents.<sup>114</sup> This would both encourage research (because research could be conducted with patented research tools without fear of infringement) and discourage research (because scientists would have no motivation to patent research tools knowing that the value of their patent would be diminished), creating a "tragedy of the anticommons."<sup>115</sup> Because research tools are broadly and vaguely defined, a decision regarding whether patented research tools

109. *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 207 (2005). The Court recognized that "[o]ne can know at the outset that a particular compound will be the subject of an eventual application to the FDA only if the active ingredient in the drug being tested is identical to that in a drug that has already been approved." *Id.*

110. See *id.* at 205 n.7 ("We therefore need not—and do not—express a view about whether, or to what extent, § 271(e)(1) exempts from infringement the use of 'research tools' in the development of information for the regulatory process.").

111. Jian Xiao, *Carving Out a Biotechnology Research Tool Exception to the Safe Harbor Provision of 35 U.S.C. § 271(E)(1)*, 12 TEX. INTELL. PROP. L.J. 23, 63 (Fall 2003).

112. Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, 64 Fed. Reg. 72090–01 (Dec. 23, 1999); see also *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 872 n.4 (Fed. Cir. 2003).

113. See *Merck*, 545 U.S. at 205 n.7. But see *Integra*, 331 F.3d at 877–88 (Newman, J., dissenting) (noting that "[u]se of an existing tool in one's research is quite different from study of the tool itself").

114. See Xiao, *supra* note 111, at 55–56 (stating why Congress did not intend to exempt biotechnology research tools).

115. See *id.* at 60 (noting that the increase in research tool patents may inhibit the pace of research).



fall within the protections of the safe harbor provision needs to be given special attention because it could have serious implications for many different industries.

#### V. CONCLUSION

The Supreme Court in *Merck* engaged in a broad reading of the Hatch-Waxman Act in order to protect preclinical research of patented drugs or devices from patent infringement suits, thereby promoting innovation and supporting the trial and error process of drug development. After *Eli Lilly & Co.*, case law indicated a trend of broadly construing § 271(e)(1) to extend protections beyond generic drugs, and the decision in *Merck* is consistent with this trend. Even though the legislative intent of the statute does not assist in this interpretation, the Court is not bound by legislative intent alone, but could benefit from legislative or administrative guidance regarding how far "upstream" the safe harbor provision may actually go to protect uses of patented inventions.

Although the common law research exemption was not an issue in the *Merck* decision, in the future the courts or the legislature will undoubtedly have to resolve how the common law research exemption relates to 35 U.S.C. § 271(e)(1). Likewise, the Court was not faced with deciding how much protection should be afforded to research tools, yet the *Merck* Court's interpretation of § 271(e)(1) could influence and impact the already uncertain and delicate balance between infringing and non-infringing uses of patented research tools. Without a judicable standard for the limits of § 271(e)(1) and a functional definition of research tools, future courts could be resigned to adjudicating patent infringement claims on a case by case basis, shaping the boundaries via the common law.

For now, the decision in *Merck* will guide future interpretations of the HWA's safe harbor provision and will give researchers more breathing room in conducting research on patented drugs or devices. However, because the Court in *Merck* utilized a broad reading of the HWA, but did not draw a finite line between infringing and non-infringing uses, in the future, courts may have to decide exactly how broad the HWA's safe harbor provision should extend and establish exactly where 35 U.S.C. § 271(e)(1) fits in the drug discovery process.