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# Journal of Intellectual Property Law

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Volume 13 | Issue 2

Article 4

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April 2006

## Access to the Safe Harbor: Bioterrorism, Influenza, and the Supreme Court's Interpretation of the Research Exemption From Patent Infringement

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### Recommended Citation

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## NOTES

# **ACCESS TO THE SAFE HARBOR: BIOTERRORISM, INFLUENZA, AND THE SUPREME COURT'S INTERPRETATION OF THE RESEARCH EXEMPTION FROM PATENT INFRINGEMENT**

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## I. INTRODUCTION

The global threats of infectious disease and bioterrorism are of great concern to the scientific community and the general public.<sup>1</sup> Although recent legislative and executive initiatives have attempted to address the risks posed by bioterrorism<sup>2</sup> and the outbreak of an infectious disease, such as an influenza pandemic,<sup>3</sup> the mere allocation of financial resources by the federal government represents only an initial step in promoting research endeavors directed at these formidable health issues. In fact, the exclusivity associated with patents and the underlying principles of intellectual property law present the greatest obstacles to innovative biomedical research.<sup>4</sup> The Supreme Court's decision in *Merck KGaA v. Integra LifeSciences I, Ltd.* represents the judiciary's most recent attempt to balance the property rights embodied in a patent against the availability of technology.<sup>5</sup> By providing legal access to technology, the *Merck KGaA* decision should encourage investment in research and development and thus expedite the discovery of novel drugs and therapeutics aimed at combating the threats of bioterrorism and the spread of infectious disease.

Pharmaceutical and biotechnology patents exemplify the competing notions of intellectual property law: the social benefits of providing economic incentives for biomedical discovery opposed by the social costs of limiting the dissemination of scientific knowledge.<sup>6</sup> The Patent Act provides pharmaceutical and biotechnology companies with the right to patent the fruits of their research and labor, which usually takes the form of innovative drugs.<sup>7</sup> Pharmaceutical patents grant a monopoly to the patent holder, preventing others from making, using, importing, or selling the patented invention in the United States.<sup>8</sup> Consequently, the patent provides its holder with exclusive access to the marketplace for a life-saving drug, allowing for the recovery of costs related to drug discovery.<sup>9</sup>

<sup>1</sup> Lawrence K. Altman, *What is the Next Plague?*, N.Y. TIMES, Nov. 11, 2003, at F8.

<sup>2</sup> William H. Frist, M.D., U.S. Senate Majority Leader, Lecture at the Nantucket Athenaeum: The Manhattan Project for the 21st Century (Aug. 3, 2005), available at [http://frist.senate.gov/index.cfm?FuseAction=Speeches.Detail&Speech\\_id=261](http://frist.senate.gov/index.cfm?FuseAction=Speeches.Detail&Speech_id=261).

<sup>3</sup> President George W. Bush, Address at the William Natcher Center of the National Institutes of Health (Nov. 1, 2005), available at <http://www.whitehouse.gov/news/releases/2005/11/20051101-1.html>.

<sup>4</sup> Norman G. Anderson & N. Leigh Anderson, *A Manhattan Project for Bioterrorism*, SCIENTIST, July 4, 2005, at 10.

<sup>5</sup> *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372 (2005).

<sup>6</sup> ROBERT P. MERGES ET AL., *INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE* 13 (3d ed. 2003).

<sup>7</sup> 35 U.S.C. § 101 (2000).

<sup>8</sup> See 35 U.S.C. § 154(a)(1) (2000).

<sup>9</sup> CONGRESSIONAL BUDGET OFFICE, *HOW INCREASED COMPETITION FROM GENERIC DRUGS*

In an effort to encourage drug development and to expedite the introduction of pharmaceuticals into the marketplace, Congress amended the patent laws through enactment of the Hatch-Waxman Act.<sup>10</sup> The Hatch-Waxman Act effectively insulated pharmaceutical research from patent infringement, providing that research utilizing a patented product is “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>11</sup> Section 202 of the Act, codified as 35 U.S.C. § 271(e)(1),<sup>12</sup> has become known as the safe harbor provision against patent infringement because it renders activities that would ordinarily constitute patent infringement non-infringing if performed for the purpose of gaining regulatory approval from the Food and Drug Administration (FDA) for a novel human or veterinary drug product, medical device, or food additive.<sup>13</sup>

Courts have struggled to define the scope of the safe harbor provision.<sup>14</sup> Recently, a unanimous Supreme Court in *Merck KGaA v. Integra LifeSciences I, Ltd.* broadly interpreted the safe harbor created by the research exemption of the Hatch-Waxman Act.<sup>15</sup> The Supreme Court, in evaluating the phrase “solely for uses reasonably related to” overruled the interpretation adopted by the Court of Appeals for the Federal Circuit<sup>16</sup> and determined that § 271(e)(1)’s research exemption extended to all uses of patented inventions when the research was conducted in a manner reasonably related to the submission of any information

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HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 33 (July 1998).

<sup>10</sup> H.R. REP. NO. 98-857(I), at 14, 15, 20 (1984), *reprinted in* 1984 U.S.C.A.N. 2647, 2648, 2653.

<sup>11</sup> Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, 1603.

<sup>12</sup> 35 U.S.C. § 271(e)(1) (2000). This section states:

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) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) 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 or veterinary biological products.

*Id.*

<sup>13</sup> *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990).

<sup>14</sup> *See* *Scripps Clinic & Research Found. v. Baxter Travenol Lab., Inc.*, 1988 WL 22602, 7 U.S.P.Q.2d (BNA) 1562, 1565 (D. Del. Mar. 9, 1988) (“The scope of section 271(e)(1) presents a question of law that has no clear answer.”).

<sup>15</sup> *See Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372 (2005).

<sup>16</sup> *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003), *rev’d*, 125 S. Ct. 2372 (2005).

required by the FDA's regulatory process.<sup>17</sup> Based on this interpretation, the research exemption applies equally to clinical trials as well as to preclinical research.<sup>18</sup> The Court justified this position as an investigational new drug application (IND) must be submitted to the FDA to gain authorization to conduct clinical trials,<sup>19</sup> and an IND must sufficiently describe preclinical data to gain such authorization.<sup>20</sup> Considering the trials and errors associated with biomedical research, the Supreme Court in *Merck KGaA* further construed the research exemption to embrace "experimentation on drugs that are not ultimately the subject of an FDA submission or [the] use of patented compounds in experiments that are not ultimately submitted to the FDA."<sup>21</sup> Accordingly, the Court held that Merck's use of Integra's patented invention was encompassed by the research exemption of § 271(e)(1) because Merck's preclinical biomedical research was designed to identify novel drug candidates, which could reasonably be the subject of an IND application to the FDA.<sup>22</sup>

By adopting a broad interpretation of the safe harbor, this Court distilled Congress' intent from the statutory text of the Hatch-Waxman Act<sup>23</sup> and its implicit preference for a policy favoring the availability of technology for the public's benefit as opposed to the patentee's interest in protecting property rights in the patent.<sup>24</sup> Application of the safe harbor to all uses of patented compounds reasonably related to the process of developing a drug in accordance with any federal law<sup>25</sup> is consistent with promoting drug development activities that could potentially benefit human health by accelerating the entry of novel, innovative drugs into the marketplace.<sup>26</sup> A broad safe harbor will permit biomedical researchers to immediately pursue a promising drug and perform the necessary experiments to gain regulatory approval so that the drug may reach patients as soon as possible upon expiration of the underlying patents.<sup>27</sup> Although the safe harbor restricts a patentee's right to exclude others from his patented invention,

<sup>17</sup> *Merck KGaA*, 125 S. Ct. at 2380.

<sup>18</sup> *Id.*

<sup>19</sup> 21 U.S.C.A. § 355(i) (West 2003).

<sup>20</sup> *Id.* § 355(i)(1)(A).

<sup>21</sup> *Merck KGaA*, 125 S. Ct. at 2382-83.

<sup>22</sup> *Id.* at 2383-84.

<sup>23</sup> *Id.* at 2380.

<sup>24</sup> *Id.* at 2383.

<sup>25</sup> *Id.*

<sup>26</sup> Brief of Petitioner for Writ of Certiorari to the United States Court of Appeals for the Federal Circuit at 12, *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372 (2005) (No. 03-1237), available at 2004 WL 406591; Brief of United States as Amicus Curiae Supporting Petitioner, *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372 (2005) (No. 03-1237), available at 2004 WL 2851214.

<sup>27</sup> Tony Mauro, *Justices Hand Drug Researchers Big Victory*, LEGAL TIMES, June 20, 2005, at 12.

the public welfare is benefited by early access to the patented invention, which will expedite the availability of novel pharmaceuticals.<sup>28</sup>

Interpretation of the safe harbor of § 271(e)(1) in a manner consistent with maximizing the benefit of the general welfare suggests that scientific knowledge can be considered a public good. Public goods, characterized by ideas and knowledge, are freely available to all and are not diminished by use.<sup>29</sup> Scientific knowledge is more appropriately viewed as an impure public good because intellectual property law regimes commonly restrict access; however, the broad interpretation of the safe harbor by the *Merck KGaA* Court curtails such restrictions, making available patented technology for developmental research reasonably related to securing regulatory approval.<sup>30</sup> Treatment of scientific knowledge as a public good is not a novel concept suggested by the *Merck KGaA* Court. Rather, numerous entities engaged in scientific research have realized the importance of moving scientific discovery into the public domain.<sup>31</sup> For instance, Celera Genomics, the biotechnology company credited with sequencing the human genome, has recently decided to place its database in the public domain.<sup>32</sup> The University of California, Berkeley has pioneered a “socially responsible licensing program” which provides technologies that promise exceptional benefit to the developing world, such as effective anti-malaria therapeutics, on a royalty-free basis.<sup>33</sup> Several other universities have adopted similar programs to transfer intellectual property rights to non-traditional pharmaceutical ventures in an effort to advance so-called “neglected disease” research.<sup>34</sup> Furthermore, a number of preclinical development projects have emerged,<sup>35</sup> particularly open-source initiatives designed to pool research resources to speed commercialization of pharmaceuticals, such as the Tropical Disease Initiative<sup>36</sup> and the Biological Innovation for Open Society.<sup>37</sup>

Although donation of intellectual property to the public domain through non-traditional pharmaceutical ventures, such as non-profit research organizations, represents a noble beginning to the dissemination of the public good that is

<sup>28</sup> Brief for the Petitioner, *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372 (2005) (No. 03-1237), available at 2004 WL 406591.

<sup>29</sup> Dana G. Dalrymple, *Scientific Knowledge as a Public Good*, SCIENTIST, June 20, 2005, at 10.

<sup>30</sup> *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372, 2380 (2005).

<sup>31</sup> Dalrymple, *supra* note 29, at 10.

<sup>32</sup> Andrew Pollack, *Celera to Quit Selling Genome Information*, N.Y. TIMES, Apr. 27, 2005, at C2.

<sup>33</sup> Bennett Daviss, *Malaria, Science, and Social Responsibility*, SCIENTIST, Mar. 28, 2005, at 42.

<sup>34</sup> Dave A. Chokshi, *Universities Should Foster Neglected Disease Work*, NATURE, May 12, 2005, at 143.

<sup>35</sup> *Id.*

<sup>36</sup> Tropical Disease Initiative, <http://www.tropicaldisease.org> (last visited Feb. 2, 2006).

<sup>37</sup> Biological Innovation for Open Society, <http://www.bios.net/daisy/bios/1093.html> (last visited Feb. 2, 2006).

scientific knowledge, the model is flawed. First, technology voluntarily placed in the public domain is usually not commercially viable, which generally means that the technology has little if any practical benefit.<sup>38</sup> Second, non-traditional pharmaceutical ventures offer no economic incentive for participation; these organizations rely solely upon a patent holder's donative intent.<sup>39</sup> Third, unlike academic and government entities, non-profit research organizations lack the resources to further develop patented technologies.<sup>40</sup>

Based on the shortcomings of relying solely upon a non-profit entity to propagate technological advancements aimed at expediting drug discovery for the public welfare, a logical alternative could involve a federal government-sponsored initiative aimed at eliminating many of the diseases and infectious agents that plague the human race. Unlike non-profit entities which are resource-poor, the federal government could initiate and direct an initiative aimed at the production of innovative pharmaceuticals by offering economic incentives to participants. The concept of a government-sponsored research initiative is not far-fetched. The Manhattan Project, which led to the development of the atomic bomb, is a classic example of the government's ability to harness traditional, basic, academic research for the development of a useful technology.<sup>41</sup> This government sponsored research initiative

had a clear central objective, a decisive test for success or failure, leadership by technically competent hands-on scientists, access to all discoverable intellectual property . . . budgets and facilities to match requirements, overwhelming dedication to projects and none to profit, an urgent time line, and a willingness and capability to change directions quickly as new information required it.<sup>42</sup>

The Manhattan Project represented a pure collaboration between academic and government research, as there was little influence from private industry.<sup>43</sup> Biotechnology and pharmaceutical researchers rarely utilize this research model today.<sup>44</sup>

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<sup>38</sup> Dalrymple, *supra* note 29, at 10; Pollack, *supra* note 32, at C2.

<sup>39</sup> Daviss, *supra* note 33, at 42.

<sup>40</sup> *Id.*

<sup>41</sup> Jed Scully, *The Virtual Professorship: Intellectual Property Ownership of Academic Work in a Digital Era*, 35 MCGEORGE L. REV. 227, 241 (2004).

<sup>42</sup> Anderson & Anderson, *supra* note 4, at 10.

<sup>43</sup> *Id.*

<sup>44</sup> *Id.*

United States Senate Majority Leader Bill Frist proposes a “Manhattan Project for the 21st Century” to combat infectious disease and bioterrorism.<sup>45</sup> Unlike its predecessor, the Manhattan Project for the twenty-first century will not create a destructive weapon but instead will defend against the destruction posed by infectious diseases and bioterrorism.<sup>46</sup> This proposal calls for an unprecedented collaboration between government, academia, and industry predicated by increases in support for basic research, biomedical education, and public health infrastructure to generate novel therapeutics and vaccines, which could be rapidly administered through vast distribution networks.<sup>47</sup> This bold initiative would require the detection, identification, and characterization of present and emerging infectious agents, the development of appropriate therapeutics, including vaccines, and the subsequent ability to timely manufacture, distribute, and administer such therapeutics.<sup>48</sup>

Along similar lines, President George W. Bush formulated the United States’ response to the increasing threat of an influenza pandemic in his plan entitled “Pandemic Influenza Preparations and Response.”<sup>49</sup> This plan provides for a tripartite approach to address the challenge of the evolving influenza virus, which includes increased surveillance measures, establishment of an emergency response plan, and development of novel vaccines and therapeutics.<sup>50</sup> Specifically, the President requested \$3.6 billion to accelerate the development of new influenza treatments and vaccines through increased collaborations among governmental, academic, and industrial biomedical research entities.<sup>51</sup>

One of the greatest obstacles facing an initiative that attempts to pool the research resources of government, academia, and private industry involves access to technology and intellectual property.<sup>52</sup> Prior to the Supreme Court’s ruling in *Merck KGaA*,<sup>53</sup> the only defense available to infringers performing biomedical research for the public good was the experimental use defense.<sup>54</sup> The experimental use defense states that use of a patented invention “for the mere purpose of philosophical experiment, or to ascertain the verity and exactness of

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<sup>45</sup> Frist, *supra* note 2.

<sup>46</sup> *Id.*

<sup>47</sup> *Id.*

<sup>48</sup> *Id.*

<sup>49</sup> Bush, *supra* note 3.

<sup>50</sup> *Id.*

<sup>51</sup> Press Release, Office of the Press Sec’y, Safeguarding America Against Pandemic Influenza (Nov. 1, 2005), available at <http://www.whitehouse.gov/news/releases/2005/11/20051101.html>.

<sup>52</sup> Anderson & Anderson, *supra* note 4, at 10.

<sup>53</sup> *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372 (2005).

<sup>54</sup> *Sawin v. Guild*, 21 F. Cas. 554 (C.C.D. Mass. 1813) (No. 12,391).



the specification” of the invention is not patent infringement.<sup>55</sup> The applicability of the experimental use defense appeared to turn on commercial intent.<sup>56</sup> As a result, the experimental use defense could not be utilized by profit-driven biotechnology companies performing research for a government initiative.

The experimental use defense would likely also be unavailable to academic research universities. The Federal Circuit excluded immunity for experimental use of unlicensed patented inventions that are used “in furtherance of the alleged infringer’s legitimate business.”<sup>57</sup> In *Madey v. Duke University*, the court characterized a university as a business designed to attract students, and Duke’s unlicensed use of a patented laser was seen as an effort toward recruiting students, as opposed to promoting education.<sup>58</sup>

Given the unavailability of the experimental use defense, the safe harbor created by the research exemption of the Hatch-Waxman Act could serve as a means to protect governmental, academic, and industrial scientists who perform research on patented inventions for the purposes of the Manhattan Project for the twenty-first century or the Pandemic Influenza Preparations and Response research initiatives.

This Note will examine the implications of the Supreme Court’s decision in *Merck KGaA* for the discovery and development of novel pharmaceuticals through a collaborative research initiative. Part II will analyze the legislative history and judicial interpretation of the safe harbor created by the research exemption of the Hatch-Waxman Act, emphasizing the balance between providing proper incentives to inventors and the public’s interest in benefiting from the technology. Part III will explore the recent decision by the Supreme Court to effectively broaden the safe harbor, and the impact this interpretation will have on drug discovery and collaborative research agreements aimed at advancing the public welfare.

## II. BACKGROUND

### A. THE PATENT DOCTRINE AND THE EXPERIMENTAL USE EXEMPTION

Article I of the United States Constitution states that, “Congress shall have Power . . . To promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective

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<sup>55</sup> *Id.* at 555.

<sup>56</sup> *See id.*

<sup>57</sup> *Madey v. Duke Univ.*, 307 F.3d 1351, 1362 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 958 (2003).

<sup>58</sup> *Id.* at 1362.

Writings and Discoveries.”<sup>59</sup> Based on these Constitutional provisions, Congress developed a patent protection system that encouraged invention by granting exclusive rights to practice the patented invention while simultaneously furthering the public welfare by disclosing and providing access to the inventions through published patents.<sup>60</sup> The exclusive rights imparted by the grant of a patent provide that anyone who “without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefore, infringes the patent.”<sup>61</sup> Patent exclusivity is granted for twenty years,<sup>62</sup> which is considered an adequate time to permit the recovery of investments in research and development thus providing an incentive to invent.<sup>63</sup>

Although patent exclusivity promotes incentive-based progress of the useful arts, technological progress may be stifled by patents that prevent subsequent inventors from building upon patented technology during the patent term.<sup>64</sup> Subsequent inventors could avoid patent infringement by entering into private licensing agreements with the patent holders that would allocate profits and balance incentives between the original inventor and subsequent user.<sup>65</sup> However, the transaction costs of such agreements are usually prohibitive. The coordination of multiple licenses, the difficulty in arranging mutually acceptable profit sharing regimes, and the possibility of anticompetitive refusals to license and collusive licensing practices all act to inhibit agreements between patent holders and subsequent inventors.<sup>66</sup>

Realizing that experimentation is the only means toward technological progress, the courts wrestled to balance the incentives for initial invention with the progress that ensues from the further development of existing patented technologies. In an attempt to alleviate the tension between these competing policy considerations, the courts created an experimental use exemption to patent infringement.<sup>67</sup> In *Whittemore v. Cutter*,<sup>68</sup> Justice Story originated the concept of

<sup>59</sup> U.S. CONST. art. I, § 8, cl. 8.

<sup>60</sup> Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017, 1023-24 (1989).

<sup>61</sup> 35 U.S.C. 271(a) (2000).

<sup>62</sup> 35 U.S.C. 154(a)(2) (2000).

<sup>63</sup> Katherine J. Strandburg, *What Does the Public Get? Experimental Use and the Patent Bargain*, 2004 WIS. L. REV. 81, 91.

<sup>64</sup> Roberto Mazzoleni & Richard P. Nelson, *The Benefits and Costs of Strong Patent Protection: A Contribution to the Current Debate*, 27 RES. POL'Y 273 (1998).

<sup>65</sup> Strandburg, *supra* note 63, at 92 (citing Nancy Gallini & Suzan Scotchmer, *Intellectual Property: What is the Best Incentive System?*, in 2 INNOVATION POL'Y AND THE ECON. 51, 69 (Adam B. Jaffe et al. eds., 2002)).

<sup>66</sup> Gallini & Scotchmer, *supra* note 65, at 65, 67-69, 71-72.

<sup>67</sup> See generally Richard E. Bee, *Experimental Use as an Act of Patent Infringement*, 39 J. PAT. OFF.

experimental use exemption in the alleged infringement of a machine that made playing cards by stating, "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>69</sup> Justice Story elaborated on the experimental use exemption in *Sawin v. Guild*,<sup>70</sup> which involved a machine for the cutting of brad nails, by stipulating that an infringing use must involve "an intent to use for profit, and not for the mere purpose of philosophical experiment, or to ascertain the verity and exactness of the specification."<sup>71</sup> Therefore, the test appeared to turn on commercial intent, and the experimental use doctrine created a dichotomy, which required classification of experiments as "for profit" or for "philosophical experiments."<sup>72</sup>

This dichotomy of the experimental use defense appears easy to apply: research conducted by commercial entities are ineligible to claim this defense, but basic, "academic," scientific research clearly falls under the scope of an experimental use. However, the rapid development of scientific research has fostered relationships between academic and commercial research.<sup>73</sup> These common relationships make it very difficult to delineate between the basic research embodied within academic inquiry and research conducted with some commercial expectation of future monetary gain.<sup>74</sup> For instance, the court in *Embrex, Inc. v. Service Engineering Corp.* involved a patent for vaccinating birds against disease by injecting vaccines into a specific region of the egg prior to hatching.<sup>75</sup> The patent holder alleged that university professors, who were attempting to work around the patent, infringed the patent.<sup>76</sup> Despite the fact that this basic research was conducted in an academic environment, the court determined that the common law defense of experimental use was inapplicable because the ultimate goal of the research was commercialization of an invention.<sup>77</sup>

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SOC'Y 357 (1957) (discussing the history of the U.S. common law experimental use exemption).

<sup>68</sup> *Whittemore v. Cutter*, 29 F. Cas. 1120 (C.C.D. Mass. 1813) (No. 17,600).

<sup>69</sup> *Id.* at 1121.

<sup>70</sup> *Sawin v. Guild*, 21 F. Cas. 554 (C.C.D. Mass 1813) (No. 12,391).

<sup>71</sup> *Id.* at 555.

<sup>72</sup> *Id.*; see also 3 WILLIAM C. ROBINSON, *THE LAW OF PATENTS FOR USEFUL INVENTIONS* § 898 (1890).

<sup>73</sup> Steve L. Bertha, *Intellectual Property Activities in U.S. Research Universities*, 36 IDEA 513 (1996).

<sup>74</sup> Gina C. Freschi, Comment, *Navigating the Research Exemption's Safe Harbor: Supreme Court to Clarify Scope—Implications for Stem Cell Research in California*, 21 SANTA CLARA COMPUTER & HIGH TECH. L.J. 855, 862 (2005).

<sup>75</sup> *Embrex, Inc. v. Serv. Eng'g Corp.*, 216 F.3d 1343 (Fed. Cir. 2000).

<sup>76</sup> *Id.* at 1346-47.

<sup>77</sup> *Id.* at 1349.

In a separate opinion, Judge Radar concluded that the Patent Act did not provide “room for . . . experimental use [as an] excuse[ ] for infringement.”<sup>78</sup>

Judge Radar’s suggestion was arguably adopted in *Madey v. Duke University*.<sup>79</sup> Madey invented and patented a free-electron laser and was subsequently recruited to Duke University to establish and direct a research laboratory that incorporated this patented technology.<sup>80</sup> Upon removal of Madey as laboratory director, Duke continued to use Madey’s patented laser technology in its teaching and research laboratories.<sup>81</sup> Madey sued for patent infringement, but Duke argued it was entitled to a defense of experimental use because it was a university conducting fundamental scientific research without a commercial intent.<sup>82</sup> The court rejected the profit versus philosophical inquiry dichotomy and instead examined whether the use was “in furtherance of the alleged infringer’s legitimate business.”<sup>83</sup> The court reasoned that the University’s legitimate business was the education and enlightenment of students and faculty, which serves to increase the status of the institution and to lure funding, students and faculty.<sup>84</sup>

If this reasoning is followed,<sup>85</sup> universities engaged in patent infringement will likely be treated as commercial entities. Therefore, universities will now be forced to enter into licensing agreements with patentees. This concept appears wholly consistent with the spirit of the Bayh-Dole Act of 1980, which permits U.S. universities to own and manage inventions discovered using federal funds.<sup>86</sup> Legal scholars and scientists consider the Bayh-Dole Act as the foundation for university technology transfer activities, resulting in increased licensing agreements between universities and the private sector.<sup>87</sup> Thus, if a university is granted intellectual property rights in its inventions, reciprocal recognition of the

<sup>78</sup> *Id.* at 1352.

<sup>79</sup> *Madey v. Duke Univ.*, 307 F.3d 1351, 1352 (Fed. Cir. 2002).

<sup>80</sup> *Id.*

<sup>81</sup> *Id.* at 1353.

<sup>82</sup> *Id.* at 1356.

<sup>83</sup> *Id.* at 1362 (holding that the manufacture and use of helicopter components for “[t]ests, demonstrations, and experiments . . . [which] are in keeping with the legitimate business” for which experimental use is not a defense) (citing *Pitcairn v. United States*, 547 F.2d 1106 (Ct. Cl. 1976)).

<sup>84</sup> *Id.*

<sup>85</sup> *Duke Univ. v. Madey*, 539 U.S. 958 (2003) (denying Duke University’s petition for certiorari).

<sup>86</sup> Bayh-Dole University and Small Business Patent Procedures Act, Pub. L. No. 96-517, 94 Stat. 3019 (1980) (codified as amended at 35 U.S.C. §§ 200-211 (2000)).

<sup>87</sup> Bertha, *supra* note 73, at 513; see John P. Walsh et al., *View from the Bench: Patents and Material Transfers*, 309 SCIENCE 2002-03 (Sept. 2005) (analyzing the burdens of technology transfer agreements in conducting research); see also Ted Agres, *I’ll See You in Court*, THE SCIENTIST, June 20, 2005, at 39 (acknowledging the legal challenges facing universities engaging in technology transfer); Ned T. Himmelrich & Jonathan M. Holda, *Technology Transfer Agreements: Don’t Be an Amateur*, 34 MD. B.J. 30 (2001) (discussing the legal issues underlying technology transfer agreements).

intellectual property rights of others only seems fair. Consequently, recent jurisprudence indicates that the common law experimental use defense is quite limited.

#### B. THE HATCH-WAXMAN ACT AND ITS SAFE HARBOR

The experimental use defense has been invoked in situations that extend beyond the context of experiments conducted for profit or for philosophical inquiry. In *Roche Products, Inc. v. Bolar Pharmaceuticals Co.*, the experimental use defense was raised to exempt pharmaceutical research activities performed to determine the “sufficiency of the machine to produce its described effects.”<sup>88</sup> Roche, the holder of a pharmaceutical patent for flurazepam hydrochloride, the active ingredient in the sleep aid “Dalmane,” sought to enjoin Bolar, a generic drug manufacturer, from taking the required regulatory steps, during the life of Roche’s patent, to bring a drug equivalent to the patented brand name drug to market.<sup>89</sup> Essentially, Bolar was performing bioequivalency experiments, by comparing the efficacy of their generic product to that of the patented drug, which is a prerequisite for FDA regulatory approval.<sup>90</sup> The purpose of the timing of the testing was to expedite marketing of the generic drug so that it would be available to the general public as soon as possible upon expiration of the patent term.<sup>91</sup> The court quickly dismissed the experimental use defense, as Bolar’s experimental use was solely for the furtherance of its legitimate business interests.<sup>92</sup> Although the court recognized that prohibition of such experimentation would effectively grant an extension of the drug’s patent term until such studies were completed, the court ignored this argument and categorically rejected an exemption for any experimental use that involved “definite, cognizable, and not insubstantial commercial purposes.”<sup>93</sup>

Following the *Roche* ruling, Congress enacted the Drug Price Competition and Patent Term Restoration Act, commonly referred to as the Hatch-Waxman Act.<sup>94</sup>

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<sup>88</sup> *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858, 862 (Fed. Cir. 1984), *superseded by statute*, Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 35 U.S.C. § 271(e)(1) (2000) (quoting *Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (No. 17,600)).

<sup>89</sup> *Roche*, 733 F.2d at 860.

<sup>90</sup> *Id.*

<sup>91</sup> *Id.*

<sup>92</sup> *Id.* at 863 (citing *Pitcairn v. United States*, 547 F.2d 1106 (Ct. Cl. 1976)).

<sup>93</sup> *Roche*, 732 F.2d at 863.

<sup>94</sup> Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified as amended at 35 U.S.C. § 271(e)(1) (2000)) (effectively overruling *Roche Prods., Inc. v. Bolar Pharm. Co.*). The Act was sponsored by Senator Orin Hatch and Congressman Henry Waxman. *Id.* See also Janice M. Mueller, No “*Dilettante Affair*”: Rethinking

The purpose of the Hatch-Waxman Act is two-fold: to make available lower-priced generic versions of drugs by establishing an abbreviated regulatory approval process for generic drugs<sup>95</sup> and to create new incentives to stimulate expenditures on research and development with the intention to “develop innovative and, ultimately, less costly treatment for diseases.”<sup>96</sup> The Act attempts to achieve these goals by striking a balance between the interests of generic and innovative drug manufacturers.<sup>97</sup>

First, the Act creates an abbreviated approval process for generic drugs, which, to the benefit of generic drug manufacturers, eliminates duplicative testing, such as safety and effectiveness testing, previously required for FDA approval of generic drugs.<sup>98</sup> This benefit to generic drug manufacturers is offset by a patent term restoration for innovative human and animal drugs, medical devices, and food and color additives, which are all subject to regulatory delays associated with pre-market government approval.<sup>99</sup>

Second, in order to temper the benefit of patent term restoration conferred to innovative drug manufacturers, Congress also attempted to prevent the de facto extension of an innovative drug’s patent term indirectly due to the regulatory delays encountered by generic drug manufacturers.<sup>100</sup> This de facto extension of the innovative drug’s patent term is created by the inability of the generic drug manufacturer to commence the necessary experimentation to gain FDA approval until the expiration of the innovative drug patent. Commencement of experimentation to gain regulatory compliance for a generic drug prior to expiration of the innovative drug’s patent term was considered an infringing use.<sup>101</sup> Therefore, the innovative drug patent holder retained a monopoly on the market beyond the expiration of the patent, which lasted until the generic manufacturer obtained FDA approval. Passage of section 202 of the Hatch-Waxman Act sought to eliminate de facto patent term extensions by establishing that “it shall not be an act of infringement to make, use, or sell a

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*the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 22-27 (2001) (reviewing the legislative and judicial developments resulting in the enactment of the Hatch-Waxman Act).

<sup>95</sup> H.R. REP. NO. 98-857(I), at 14 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647.

<sup>96</sup> *Id.* at 15, 20.

<sup>97</sup> CONGRESSIONAL BUDGET OFFICE, *supra* note 9, at 3.

<sup>98</sup> H.R. REP. NO. 98-857(I), at 14-15.

<sup>99</sup> *Id.* at 15. Patent term restoration extends the life of patents to compensate patent holders for marketing time lost while awaiting government approval. *Id.*

<sup>100</sup> *Id.* at 46.

<sup>101</sup> *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858 (Fed. Cir. 1984), *superseded by statute*, Drug Price Competition and Patent Restoration Term Restoration (Hatch-Waxman) Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 codified as amended at 35 U.S.C. § 271(e)(1) (2000), *as recognized in* *Abbott Labs. v. Zenith Labs.*, 934 F. Supp. 925, 930-31 (N.D. Ill. 1995).

patented invention solely for uses reasonably related to the development and submission of information under a federal law which regulates the approval of drugs.”<sup>102</sup> This clause has become known as a safe harbor from patent infringement.<sup>103</sup>

### C. JUDICIAL INTERPRETATION: THE SCOPE OF THE SAFE HARBOR

The existence of the safe harbor is largely attributable to two phrases: “patented invention” and “reasonably related.”<sup>104</sup> The interpretation of these phrases has greatly contributed to the controversy surrounding the scope of the safe harbor. For instance, the U.S. Supreme Court applied the safe harbor to patented inventions that include medical devices in *Eli Lilly & Co. v. Medtronic, Inc.*<sup>105</sup> The Court held that Medtronic’s use of Eli Lilly’s patented implantable cardiac defibrillator technology was not infringement because its use was related to obtaining FDA approval for a generic substitute, which was to be sold commercially upon expiration of the patent.<sup>106</sup> The Court evaluated the language of § 271(e)(1) in the context of the entire Hatch-Waxman Act, and reached the conclusion that the patent term restoration and the patent infringement provisions encompass “a single legislative package.”<sup>107</sup> Therefore, if a patented invention is eligible for the benefits of the patent term restoration aimed to compensate for delays at the beginning of the patent term, the invention must also be subject to the offset of the infringement exemption that is intended to alleviate the anticompetitive restriction at the end of the patent term.<sup>108</sup> Thus, the scope of § 271(e)(1) encompasses not only drugs, but also applies to medical devices.

After finding that the safe harbor is applicable to medical devices, the courts were next faced with defining the kinds of activities that may be “reasonably related” to FDA approval. In a similar medical device case involving an implantable defibrillator, the court in *Intermedics, Inc. v. Ventritex, Inc.* was required to evaluate whether activities, such as the manufacturing of the defibrillator, its sale to hospitals, and its demonstration at trade shows, were reasonably related to

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<sup>102</sup> H.R. REP. NO. 98-857(I), at 45 (codified as amended at 35 U.S.C. § 271(e)(1)(2000)). See 35 U.S.C. § 271(e)(1); *supra* text accompanying note 11.

<sup>103</sup> See, e.g., *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 864 (Fed. Cir. 2003), *rev’d*, 125 S. Ct. 2372 (2005).

<sup>104</sup> 35 U.S.C. § 271(e)(1).

<sup>105</sup> *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990).

<sup>106</sup> *Id.* at 666-74.

<sup>107</sup> *Id.* at 670 n.3.

<sup>108</sup> *Id.* at 672-73.

obtaining FDA approval.<sup>109</sup> The court held that all of these activities were reasonably related to clinical trials, which are necessary for FDA approval of the medical device.<sup>110</sup>

The court noted the congressional acknowledgment that parties seeking FDA approval will not always know what types of information or the quantity thereof are required to gain approval.<sup>111</sup> Based on this fluid standard, the court recognized Congress' justification for the phrase "reasonably related" and subsequently interpreted it to encompass "latitude in making judgments about the nature and extent of the otherwise infringing activities they would engage in as they sought to develop information to satisfy the FDA."<sup>112</sup> Consistent with this latitude, the court determined that the exemption should not be lost because some of the party's infringing uses fail to generate data of interest to the FDA or generated more data than was necessary to secure FDA approval.<sup>113</sup> The test forged by this court is whether it would have been objectively reasonable that the infringing use in question would contribute to the generation of the kinds of information that would likely be relevant in gaining FDA regulatory approval.<sup>114</sup>

In *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, a Massachusetts district court utilized the test set forth in *Intermedics*<sup>115</sup> to apply the safe harbor research exemption to preclinical drug discovery activities.<sup>116</sup> Amgen alleged that Hoechst infringed Amgen's patent for a recombinant form of erythropoietin (EPO), a hormone involved in the production of red blood cells. Hoechst used Amgen's patented EPO during their development and manufacture of a competing product, GA-EPO.<sup>117</sup> The court held that Hoechst's export and extensive use of the patented EPO were all activities encompassed by the patent infringement safe harbor created by § 271(e)(1).<sup>118</sup> This court adopted the objective test set forth in *Intermedics* emphasizing that an exempted use must be reasonably related to FDA approval, but need not be exclusively for the purpose of obtaining FDA approval.<sup>119</sup> Thus, an exempted use, such as preclinical functional analyses or clinical human trials, may be related to FDA approval, but could "be conducted

<sup>109</sup> *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269 (N.D. Cal. 1991).

<sup>110</sup> *Id.* at 1282-88.

<sup>111</sup> *Id.* at 1280.

<sup>112</sup> *Id.*

<sup>113</sup> *Id.*

<sup>114</sup> *Id.* at 1280-81.

<sup>115</sup> *Id.*

<sup>116</sup> *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104 (D. Mass. 1998).

<sup>117</sup> *Id.* at 106. Hoechst used the GA-EPO as a standard reference for studies on alternative manufacturing processes, purity and consistency testing, and for virus clearance experimentation.

*Id.*

<sup>118</sup> *Id.* at 109-12.

<sup>119</sup> *Id.* at 107-08.



for purposes other than, or in addition to, obtaining FDA approval . . . [because] ulterior motives or alternate purposes do not preclude application of the section 271(e)(1) exemption.”<sup>120</sup>

Following the *Amgen* decision, Rhone-Poulenc Rorer, Inc. brought suit against Bristol-Myers Squibb, Inc. for infringement upon a process patent for preparing the drug taxol,<sup>121</sup> an anti-cancer drug.<sup>122</sup> Bristol-Myers used patented chemical intermediates derived from the taxol synthesis, which were claimed in the Rhone-Poulenc patent, for the development of novel anti-cancer drugs that would replace taxol on the market.<sup>123</sup> Based on a detailed factual analysis and application of the *Intermedics* test, the court determined that it was objectively reasonable that Bristol-Myers believed that there was a “decent prospect” that experimentation with Rhone-Poulenc’s intermediates would generate information that was likely to be relevant to the FDA regulatory approval process.<sup>124</sup> Therefore, Bristol-Myers’s experimentation with Rhone-Poulenc’s patented intermediates were entitled to exemption under § 271(e)(1).<sup>125</sup> The court reasoned that although Bristol-Myers’s use of the patented intermediates in preliminary research may not generate data that could be directly submitted to the FDA, this use could be reasonably related to FDA regulatory approval providing the information was generated to determine if regulatory approval would be sought, or if the use relates to a preliminary research activity that could facilitate the generation of information that would be submitted to the FDA.<sup>126</sup> Furthermore, the exemption of § 271(e)(1) must apply to all activities reasonably related to a potential or actual FDA application, beginning with the initial synthesis of a pharmaceutical candidate.<sup>127</sup> If selection of a candidate drug or filing of an FDA application was a prerequisite for protection by the statutory exemption of § 271(e)(1), the exemption would never apply because the preliminary research and development necessary for FDA approval could never have been undertaken.<sup>128</sup>

<sup>120</sup> *Id.*

<sup>121</sup> *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833(RPP), 2001 WL 1512597 (S.D.N.Y. Nov. 28, 2001).

<sup>122</sup> *Id.* at \*4.

<sup>123</sup> *Id.*

<sup>124</sup> *Id.* at \*6 (quoting *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269, 1280 (N.D. Cal. 1991)).

<sup>125</sup> *Bristol-Myers Squibb Co.*, 2001 WL 1512597, at \*6.

<sup>126</sup> *Id.* at \*7. This is consistent with the legislative history of 35 U.S.C. § 271(e)(1) which states, “[a] party which develops such information, but decides not to submit an application for approval is protected as long as the development was done to determine whether or not an application for approval would be sought.” *Id.* at \*6.

<sup>127</sup> *Id.*

<sup>128</sup> *Id.*

Following the lead of the *Amgen* and the *Bristol-Myers Squibb* holdings, a Delaware district court also adopted the expansive view of the scope of the safe harbor in *Nexell Therapeutics, Inc. v. AmCell Corp.*<sup>129</sup> In developing magnetic-based cell separating technology for FDA approval, AmCell allegedly infringed Nexell's patented CD34 antibodies, which are used for isolation of stem cells from blood, by actively recruiting physicians to participate in clinical trials to evaluate the CD34-based cell-sorting technology.<sup>130</sup> Although AmCell's activities could be construed as a marketing endeavor, the court stated that these allegedly infringing activities were conducted in an effort to solicit physicians to participate in clinical trials aimed at gaining FDA regulatory approval.<sup>131</sup> Therefore, AmCell's research activities were reasonably related to obtaining FDA approval and fall within the scope of the research exemption of § 271(e)(1).<sup>132</sup>

Examination of the *Amgen*, *Bristol-Myers Squibb*, and *Nexell* cases indicates a judicial preference for a broad interpretation of the safe harbor for patent infringement. The courts have consistently adopted an expansive view of the research exemption, because to hold otherwise would be contrary to legislative intent by "chill[ing] parties from engaging in the very pre-approval testing that Congress sought to encourage."<sup>133</sup>

#### D. *MERCK KGAA V. INTEGRA LIFESCIENCES I, LTD.*

Integra LifeSciences and the Burnham Institute own five patents,<sup>134</sup> all of which are related to the fibronectin-derived RGD peptide, a tri-peptide sequence of the amino acids Arginine, Glycine, and Aspartic Acid (abbreviated in single letter notation R, G, D, respectively).<sup>135</sup> The RGD peptide promotes cell adhesion by interacting with integrin  $\alpha_v\beta_3$ .<sup>136</sup> Integrin-mediated cell adhesion plays a critical role in wound healing, biocompatibility of prosthetic devices, and angiogenesis—the process of blood vessel growth.<sup>137</sup>

<sup>129</sup> *Nexell Therapeutics, Inc. v. AmCell Corp.*, 199 F. Supp. 2d 197 (D. Del. 2002).

<sup>130</sup> *Id.* at 199.

<sup>131</sup> *Id.* at 204.

<sup>132</sup> *Id.*; see *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997) (holding that if an activity is reasonably related to gaining FDA approval, the underlying purposes or consequences of the activity are irrelevant to the applicability of the statutory exemption).

<sup>133</sup> *Nexell Therapeutics, Inc.*, 199 F. Supp. 2d at 204.

<sup>134</sup> *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372, 2377 (2005).

<sup>135</sup> U.S. Patent No. 5,695,997 (filed June 2, 1995) (issued Dec. 9, 1997); U.S. Patent No. 4,988,621 (filed Dec. 10, 1987) (issued Jan. 29, 1991); U.S. Patent No. 4,879,237 (filed May 24, 1985) (issued Nov. 7, 1989); U.S. Patent No. 4,792,525 (filed June 17, 1985) (issued Dec. 20, 1988); U.S. Patent No. 4,789,734 (filed Aug. 6, 1985) (issued Dec. 6, 1988).

<sup>136</sup> *Merck KGaA*, 125 S. Ct. at 2377.

<sup>137</sup> *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 863 (Fed. Cir. 2003), *rev'd*, 125 S.

Dr. David Cheresh, a scientist at the Scripps Research Institute (Scripps), discovered that blocking  $\alpha_v\beta_3$  integrin receptors inhibited angiogenesis.<sup>138</sup> Angiogenesis is a process integral to many diseases, such as solid tumor cancers, diabetic retinopathy, rheumatoid arthritis, psoriasis, and inflammatory bowel disease.<sup>139</sup> Dr. Cheresh demonstrated the tumor growth in chicken embryos could be reversed using either a monoclonal antibody that he developed himself or a patented cyclic RGD peptide (EMD 66203) provided by Integra.<sup>140</sup> Recognizing the importance of Cheresh's discovery, Merck provided funding for angiogenesis research conducted by Dr. Cheresh at Scripps<sup>141</sup> to finance the " 'necessary experiments to satisfy the biological bases and regulatory (FDA) requirements for the implementation of clinical trials' with EMD 66203 or a derivative thereof."<sup>142</sup>

Research performed at Scripps led to the identification of two derivatives of the RGD peptide EMD 66203: EMD 85189 and EMD 121974.<sup>143</sup> In a subsequent research agreement, Scripps agreed to initiate *in vitro*<sup>144</sup> and *in vivo*<sup>145</sup> studies of the RGD peptides necessary for an IND while Merck pledged an additional six million dollars towards this project and agreed to perform the toxicology tests necessary for FDA approval of clinical trials.<sup>146</sup>

Pursuant to the agreement, Dr. Cheresh directed experimentation " 'to evaluate the specificity, efficacy, and toxicity of EMD 66203, 85189, and 121974 for various diseases, to explain the mechanism by which these drug candidates work, and to determine which candidates were effective and safe enough to warrant testing in humans.' "<sup>147</sup> Specifically, these tests assayed the mechanism of action and pharmacokinetics of candidate drugs, including histopathology, toxicology, circulation, diffusion and half-life of the peptides in the

Ct. 2372 (2005).

<sup>138</sup> *Id.* at 863.

<sup>139</sup> *Id.*

<sup>140</sup> *Merck KGaA*, 125 S. Ct. at 2378.

<sup>141</sup> *Id.* at 2377.

<sup>142</sup> *Integra LifeSciences I, Ltd.*, 331 F.3d at 863.

<sup>143</sup> *Id.*

<sup>144</sup> *In vitro* literally means "in glass," but generally encompasses things outside the living body and in an artificial environment. MERRIAM WEBSTER'S COLLEGIATE DICTIONARY 659 (11th ed. 2003).

<sup>145</sup> *In vivo* literally means "in the living" and applies to things in the living body of an animal or plant. *Id.*

<sup>146</sup> *Merck KGaA*, 125 S. Ct. at 2378; see 21 C.F.R. § 312.23 (2005) (stating the requirements for an investigational new drug application).

<sup>147</sup> *Integra LifeSciences I, Ltd.*, 331 F.3d at 863 (quoting Brief for Defendant-Appellant Merck KGaA, Integra LifeSciences I, Ltd., 331 F.3d 860 (2003) (Nos. 02-1052, 02-1065), available at 2002 WL 32191414).

bloodstream.<sup>148</sup> In addition, experiments were also performed to evaluate the proper mode of administration of the peptides for optimum therapeutic effect.<sup>149</sup> Similar experiments were also performed on LM609, the monoclonal antibody developed by Dr. Cheresh that was also capable of inhibiting angiogenesis, and organic mimetics, which were thought to block  $\alpha_v\beta_3$  integrins in a similar manner to RGD peptides.<sup>150</sup> In regards to experimentation involving the monoclonal antibody or organic mimetics, the RGD peptides were used as a positive control, a measure for the efficacy of the experimental antibody or mimetics.<sup>151</sup> Based on the results of these experiments, Scripps determined that EMD 121974, a derivative of the Integra peptide, was the most promising angiogenesis inhibitor candidate for testing in humans.<sup>152</sup>

Upon learning of the Scripps-Merck agreement and believing that the angiogenesis research was a commercial project that infringed its patents, Integra offered Merck licenses to the RGD patents, which Merck declined.<sup>153</sup> Consequently, Integra, along with the Burnham Institute, filed a patent infringement suit against Merck, Scripps, and Dr. Cheresh in the Southern District of California.<sup>154</sup> Merck answered that its research performed in collaboration with Scripps and Dr. Cheresh fell under the safe harbor created by § 271(e)(1).<sup>155</sup>

The jury found that Scripps and Dr. Cheresh infringed Integra's patents and awarded Integra a reasonable royalty of fifteen million dollars.<sup>156</sup> Merck appealed the jury verdict of patent infringement to the Federal Circuit, which affirmed the district court's holding that the safe harbor of § 271(e)(1) did not apply because "the Scripps work sponsored by Merck was not clinical testing to supply

<sup>148</sup> *Id.*

<sup>149</sup> *Id.*

<sup>150</sup> *Merck KGaA*, 125 S. Ct. at 2378-79.

<sup>151</sup> *Id.* at 2379. Scripps licensed the patent for the LM609 monoclonal antibody to Ixsys, a California biotechnology company. *Id.* at 2379 n.4. Ixsys collaborated with Dr. Cheresh and Scripps to submit an investigational new drug application for a humanized version of the LM609 antibody, called Vitaxin. *Id.* This application included data collected from Dr. Cheresh's *in vitro* and *in vivo* experiments concerning the antibody's mechanism of action and efficacy as an inhibitor of angiogenesis. *Id.*

<sup>152</sup> *Id.* at 2378.

<sup>153</sup> *Integra LifeSciences I, Ltd.*, 331 F.3d at 863.

<sup>154</sup> *Id.* at 862.

<sup>155</sup> *Id.*

<sup>156</sup> *Id.* The Federal Circuit did not believe that the jury award of fifteen million dollars was supported by substantial evidence and held that the amount awarded seemed excessive when considering the scientific and marketing uncertainties of the technology involved. *Id.* at 871-72. On remand, the District Court reduced the damages award to approximately six million dollars. *Integra LifeSciences I, Ltd. v. Merck KGaA*, No. CV.96 CV 1307-B(AJB), 2004 WL 2284001, at \*11 (S.D. Cal. Sept. 7, 2004).

information to the FDA, but only general biomedical research to identify new pharmaceutical compounds.”<sup>157</sup>

The United States Supreme Court granted certiorari to review the construction of § 271(e)(1).<sup>158</sup> Through examination of the text of § 271(e)(1), the Court determined that the statute clearly provided a “wide berth for the use of patented drugs in activities related to the federal regulatory process.”<sup>159</sup> The Court held that § 271(e)(1)’s safe harbor from patent infringement encompassed all uses of patented inventions that are reasonably related to obtaining FDA approval, which necessarily includes preclinical studies.<sup>160</sup> The Court did not agree with the Federal Circuit’s limitation of the safe harbor to research conducted in clinical trials.<sup>161</sup> Since an IND must be filed with the FDA prior to the initiation of clinical trials, the IND represents a required regulatory step in gaining FDA approval.<sup>162</sup> Therefore, the Court concluded that research pertaining to preclinical studies should be included within the safe harbor of § 271(e)(1).<sup>163</sup> The Court also believed that § 271(e)(1) provided adequate space for the successes and failures of experimentation associated with drug development and associated regulatory approval.<sup>164</sup> Considering that scientific inquiry is a process of trial and error, the Court held that § 271(e)(1)’s safe harbor also extends to “experimentation on drugs that are not ultimately the subject of an FDA submission . . . [and to] use of patented compounds in experiments that are not ultimately submitted to the FDA.”<sup>165</sup> Provided that a drug developer has a reasonable basis for believing that research conducted on a patented compound could lead to an FDA submission, such uses should be exempted from patent infringement under the § 271(e)(1) regardless of whether the drug candidate is ever the subject of an FDA submission or the experimentation is ever included in an FDA application.<sup>166</sup> The Court justified the extension of the safe harbor to such research activities through the “reasonably related” requirement by deducing that the relationship between the experimental use of a patented compound and the submission of experimental

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<sup>157</sup> *Integra LifeSciences I, Ltd.*, 331 F.3d at 866.

<sup>158</sup> *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 823 (2005) (granting certiorari); *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372, 2380 (2005) (“We granted certiorari to review the Court of Appeals’ Construction of § 271(e)(1).”).

<sup>159</sup> *Merck KGaA*, 125 S. Ct. at 2380.

<sup>160</sup> *Id.*

<sup>161</sup> *Id.* (citing *Integra LifeSciences I, Ltd.*, 331 F.3d at 866).

<sup>162</sup> *Merck KGaA*, 125 S. Ct. at 2381.

<sup>163</sup> *Id.* at 2380-82.

<sup>164</sup> *Id.* at 2383.

<sup>165</sup> *Id.*

<sup>166</sup> *Id.*

data to the FDA does not become less reasonable or more attenuated because the data is omitted from an FDA application.<sup>167</sup>

### III. ANALYSIS

The Supreme Court's decision in *Merck KGaA v. Integra LifeSciences I, Ltd.* should facilitate investment in research and development of vaccines and therapeutics designed to combat the threats of bioterrorism and infectious disease, thus expediting drug discovery process by providing access to technology. The *Merck KGaA* decision represents the most recent judicial attempt to balance the property rights embodied in a patent against the availability of technology to promote the progress of science. In attempting to fulfill the congressional intent underlying the enactment of the Hatch-Waxman Act, the *Merck KGaA* decision adopted an approach to patent law that favors access to technology so as to stimulate innovative drug discovery. Considering that the common law experimental use defense is unavailable, the safe harbor created by the research exemption in the Hatch-Waxman Act, as interpreted by the Court in *Merck KGaA*, will have the net effect of expediting drug discovery by providing access to technology and will simultaneously foster research collaborations while driving competition. Although the Court's interpretation of § 271(e)(1)'s safe harbor will have ramifications on drug discovery, the perceived value of patents, and approaches to patent licensing, a balance will be maintained.

#### A. IMPLICATIONS OF THE SAFE HARBOR ON GOVERNMENT-SPONSORED RESEARCH COLLABORATIONS

Experimentation is the core of scientific inquiry. Effective and innovative scientific research requires broad access to patented technology and the freedom to use such technology to formulate and test hypotheses.<sup>168</sup> Critics of intellectual property law contend that patents, such as those involved in drug discovery, can stifle research and innovation.<sup>169</sup> Despite providing incentives for innovation, patent exclusivity can slow technological advancement by restricting the use of a patented invention.<sup>170</sup> The incentive of a monopoly chills maximal, and perhaps optimal, use of the technology for the development of novel drugs, which would

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<sup>167</sup> *Id.*

<sup>168</sup> Strandburg, *supra* note 63, at 82.

<sup>169</sup> Eric K. Steffe & Timothy J. Shea, Jr., *Drug Discovery Tools and the Clinical Research Exemption from Patent Infringement*, 22 BIOTECHNOLOGY L. REP. 369, 373 (2003).

<sup>170</sup> Strandburg, *supra* note 63, at 91.

be a benefit to society.<sup>171</sup> The stifling effect of patent exclusivity is compounded by the fact that the experimental use exemption is rarely available.<sup>172</sup> In fact, the decision by the Federal Circuit Court of Appeals in *Madey v. Duke University*,<sup>173</sup> which strictly limited the experimental use exemption, has been criticized for “undermin[ing] the balance between innovation and access that lies at the heart of the Patent Act.”<sup>174</sup> Similar to its holding in *Madey*, the Federal Circuit in *Integra LifeSciences I, Ltd. v. Merck KGaA* believed that the safe harbor from patent infringement should be narrowly construed,<sup>175</sup> further limiting access to patented technologies.

1. *Access to Technology.* In *Merck KGaA v. Integra LifeSciences I Ltd.*, the Supreme Court adopted a broad interpretation of the safe harbor from patent infringement as prescribed by § 271(e)(1), which is consistent with precedent from *Eli Lilly & Co. v. Medtronic, Inc.*<sup>176</sup> The Supreme Court held that § 271(e)(1)’s safe harbor “extend[ed] to all uses of patented inventions that are reasonably related to the development and submission of *any* information” to the FDA, which necessarily includes both preclinical and clinical research.<sup>177</sup> The Supreme Court’s broad interpretation of the safe harbor to extend to early research activities, such as preclinical studies, will promote innovative research aimed at combating bioterrorism and infectious disease by granting scientists increased freedom to operate.

Since preclinical research reasonably related to obtaining FDA approval will be considered exempt from patent infringement, researchers developing bioterrorism-related and infectious disease-related therapeutics and vaccines will have advanced access to use patented technologies prior to the expiration of the patent term. Increased access to patented technologies will necessarily expedite the evaluation and analysis of potential drug and vaccine candidates, achieving an integral goal of these broad-based research collaborations. Therefore, the availability of a broad safe harbor will putatively accelerate the drug and discovery process through government-sponsored initiatives, resulting in the development

<sup>171</sup> *Id.* at 123.

<sup>172</sup> *Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (No. 17,600); *Sawin v. Guild*, 21 F. Cas. 554, 555 (C.C.D. Mass. 1813) (No. 12,391); *Madey v. Duke Univ.*, 307 F.3d 1351, 1362-63 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 958 (2003).

<sup>173</sup> *Madey*, 307 F.3d at 1351.

<sup>174</sup> Tom Saunders, Case Comment, *Renting Space on the Shoulders of Giants: Madey and the Future of the Experimental Use Doctrine*, 113 YALE L.J. 261, 262 (2003).

<sup>175</sup> *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 866-68 (Fed. Cir. 2003), *rev’d*, 125 S. Ct. 2372 (2005).

<sup>176</sup> *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990) (adopting a similarly broad interpretation of the safe harbor).

<sup>177</sup> *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372, 2380 (2005).

of novel, safer, and more effective drugs targeting the threat of infectious disease and bioterrorism.<sup>178</sup>

2. *Impact on Licensing.* In its evaluation of damages, the Federal Circuit in *Integra LifeSciences* acknowledged the cumulative costs, both financial and transactional, of gaining access to the requisite number of patents, through licensing, to develop a drug.<sup>179</sup> However, the Supreme Court's express extension of the safe harbor from patent infringement to encompass both preclinical and clinical research<sup>180</sup> will likely have dramatic effects on licensing behaviors.

From the perspective of scientists collaborating in a government-based research initiative, the breadth of the safe harbor to include preclinical research activities will greatly reduce the costs associated with development of novel vaccines and pharmaceuticals. Successful vaccine and pharmaceutical research hinges on the ability to access existing patented technologies.<sup>181</sup> In the case of these government-sponsored research initiatives, almost every experiment performed is reasonably related to gaining FDA approval.<sup>182</sup> Therefore, a research entity participating in such a government-sponsored collaboration will necessarily avoid the high costs associated with acquiring numerous licenses to engage in drug and vaccine discovery. In addition, collaborative researchers will also avoid the phenomenon of the "anticommons,"<sup>183</sup> characterized by the occasional resistance of patentees who refuse to license their technologies, thereby completely obstructing research initiatives. The advantage of reduced transactional costs gained by researchers engaging in government-sponsored research initiatives is offset by two things. First, researchers lose the revenues they might derive from licensing their technology to research entities pursuing similar research goals.<sup>184</sup> Second, researchers are unable to thwart competitors' research by denying access to their patented technology.<sup>185</sup> However, this trade-off is of little consequence to participants in a government-based research initiative because the goal of such initiatives is scientific progress as opposed to successful competition in the marketplace. Therefore, a reduction in transaction

<sup>178</sup> See Brief for Eli Lilly & Co. et al. as Amici Curiae in Support of Petitioner, Merck KGaA v. Integra LifeSciences I, Ltd., 125 S. Ct. 2372 (2005) (No. 03-1237), available at 2005 WL 435888 (arguing that the Federal Circuit's narrow interpretation of the safe harbor from patent infringement would delay drug discovery).

<sup>179</sup> *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 870-72 (Fed. Cir. 2003).

<sup>180</sup> *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372, 2380 (2005).

<sup>181</sup> Kyla Dunn, *A Look at . . . Patents & Biotech*, WASH. POST, Oct. 1, 2000, at B3.

<sup>182</sup> Brief for Eli Lilly & Co. et al. as Amici Curiae in Support of Petitioner, Merck KGaA v. Integra LifeSciences I, Ltd., 125 S. Ct. 2372 (2005) (No. 03-1237), available at 2005 WL 435888.

<sup>183</sup> Walsh et al., *supra* note 87, at 2002.

<sup>184</sup> *Id.*

<sup>185</sup> *Id.*



costs should decrease the cost of drug discovery while simultaneously stimulating advancements in innovations by increasing access to technology.

Expansion of the safe harbor will also likely have a profound effect on the licensing behaviors of universities and research institutions, who will likely be major players in any government-sponsored research initiative. Collectively, U.S. universities, hospitals, and research institutions earned in excess of one billion dollars in licensing fees in fiscal year 2003.<sup>186</sup> Generation of this revenue is largely attributable to the Bayh-Dole Act of 1980, which allowed universities to retain title to discoveries made using federal funds.<sup>187</sup> Based on these figures, universities and research institutes stand to lose substantial revenues as a result of their decreasing ability to license their patented technology.

The majority of research universities and institutes operate on a non-profit basis.<sup>188</sup> Consistent with the underlying principles of a government-sponsored research initiative, the fundamental mission of research universities is the creation and dissemination of knowledge for the benefit of society, resulting in an emphasis on teaching, publishing, and furthering research performed at the university.<sup>189</sup> In addition to the monetary benefits of a successful technology transfer program, research universities also engage in licensing agreements to enhance the reputation of their institution. Although some commentators have asserted that "[u]niversities are sophisticated players in biomedical research,"<sup>190</sup> research universities inherently lack the resources to develop, manufacture, and eventually profit from innovative drug discovery. Rarely do university scientists engage in research that would require purchasing patent licenses.<sup>191</sup> First, academic research is usually basic research, aimed at answering scientific questions in an effort to generate knowledge, as opposed to the applied research performed by industrial entities, which is aimed at solving practical problems in hopes of

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<sup>186</sup> ASS'N OF UNIV. TECH. MANAGERS, UTM LICENSING SURVEY: FY 2003 (2004); Tao Huang, Note, *The Experimental Purpose Doctrine and Biomedical Research*, 11 MICH. TELECOMM. & TECH. L. REV. 97, 108-09 (2004), available at <http://www.mttlr.org/voleleven/huang.pdf>.

<sup>187</sup> 35 U.S.C. §§ 200-211 (2000); see Rebecca S. Eisenberg, *Patent Swords and Shields*, 299 SCIENCE 1018, 1018 (2003) ("[U]niversities have become players in the patent system in a way that could hardly have been imagined before the Bayh-Dole Act. Universities owned 1.1% of U.S. corporate-owned patents issued between 1969 and 1986; by 1999 that number had risen to 4.8%.").

<sup>188</sup> See *Madey v. Duke Univ.*, 307 F.3d 1351, 1362 (Fed. Cir. 2002), cert. denied, 539 U.S. 958 (2003); see generally Janice M. Mueller, *The Evanescent Experimental Use Exemption from United States Patent Infringement Liability: Implications for University and Nonprofit Research and Development*, 56 BAYLOR L. REV. 917 (2004).

<sup>189</sup> See, e.g., Bertha, *supra* note 73, at 525.

<sup>190</sup> Huang, *supra* note 186, at 109.

<sup>191</sup> See generally Bertha, *supra* note 73 (indicating that research universities are more inclined to grant licenses to industrial companies than to purchase similar licenses).

commercial gain.<sup>192</sup> Second, basic academic research usually has little prospect for economic gain.<sup>193</sup> Given the limitations of funding for university-based research, it would not be economically reasonable to purchase access to technology that would not pay for itself. Given their propensity to perform basic scientific research, research universities would not likely benefit as significantly as more sophisticated research entities that participate in a government-sponsored research initiative from an increase in access to the applied technology embodied in patents.

This conclusion operates under the assumption that research universities will continue to conduct basic scientific research. However, academic attitudes toward applied research may change following the Court's decision in *Merck KGaA*. Considering that the decision in *Merck KGaA* nearly eliminates the need to license technology, academic scientists and non-profit institutions may be economically induced to perform applied research, which by its nature has a greater chance of realizing an economic gain. Performance of applied research is certainly compatible with academic institutional philosophy of creating and disseminating knowledge for the benefit of society.<sup>194</sup> Academic researchers would have equal access to patented technologies, providing that they are used in a manner reasonably related with generating information for FDA approval. Furthermore, university-sponsored applied research would bolster the reputation of the university as an innovative center of learning with a firm commitment to serving the general public.

Assuming a continued absence of the resources necessary to manufacture and distribute pharmaceuticals, universities would still be required to interact and enter into agreements with private industry so that applied technologies could be manufactured and sold. It is unclear, however, when or how such agreements should be negotiated, considering the opportunity for free access following disclosure in the patent. Regardless, if academia switches to performing applied research, a shift in revenue-generating research activities would also likely occur, with universities and research institutions engaging in a reduced level of licensing agreements following disclosure of the patent and entering into more agreements prior to disclosure of the invention. This trend seemingly could slow the dissemination of scientific knowledge; however, reciprocal gains in efficiency would result as the agreements that are negotiated involve technology that is reasonably related to an FDA application as opposed to more primitive patented technology that has a tenuous possibility of development of an effective pharmaceutical.

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<sup>192</sup> Dalrymple, *supra* note 29, at 10.

<sup>193</sup> Bertha, *supra* note 73, at 515.

<sup>194</sup> *Id.* at 514.

3. *The Question of Research Tools.* One unanswered licensing question remaining after the *Merck KGaA* decision is whether § 271(e)(1)'s safe harbor extends to patents that involve research tools.<sup>195</sup> A research tool is "a product or method whose purpose is use in the conduct of research."<sup>196</sup> The Working Group on Research Tools at the National Institutes of Health (NIH) defines a research tool as "embrac[ing] the full range of resources that scientists use in the laboratory," including "cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry libraries, drugs and drug targets, clones and cloning tools (such as PCR), methods, laboratory equipment and machines, databases and computer software."<sup>197</sup> The controversy surrounding patented research tools is that the tool itself would not be the subject of an application to the FDA, but instead it is the technological progress resulting from use of the research tool that would be the subject of such an application.<sup>198</sup> Therefore, the case law does not clarify whether the safe harbor would extend to an indirect use of a patented technology in generating the information necessary for an FDA submission. This issue remains murky, as the Court expressly declined to resolve the issue in *Merck KGaA*.<sup>199</sup>

Considering that the *Merck KGaA* decision will decrease the incidence of licensing costs and simultaneously increase the access to patented technology, an efficient allocation of government resources should result. In the absence of burdensome licensing fees, participants in a collaborative, government-sponsored research initiative will be free to utilize their funding on the development of technology as opposed to first paying for access to the technology and then engaging in experimentation. The research, which is the essence of the research initiative, will serve as the primary expenditure for researchers attempting to remedy the ills of bioterrorism and infectious disease.

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<sup>195</sup> *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372, 2382 n.7 (2005).

<sup>196</sup> *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 878 (Fed. Cir. 2003) (Newman, J., dissenting).

<sup>197</sup> NATIONAL INSTITUTES OF HEALTH, REPORT OF THE NATIONAL INSTITUTES OF HEALTH (NIH) WORKING GROUP ON RESEARCH TOOLS (June 4, 1998), available at <http://www.nih.gov/news/researchtools/index.htm>; see also Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources: Final Notice, 64 Fed. Reg. 72,090, 72,092 n.1 (Dec. 23, 1999) (stating that research tools "embrace the full range of 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>198</sup> Strandburg, *supra* note 63, at 123.

<sup>199</sup> *Merck KGaA*, 125 S. Ct. at 2382 n.7.

## B. IMPLICATIONS OF THE SAFE HARBOR ON THE VALUATION OF PATENTS

Interpretation of § 271(e)(1)'s safe harbor in a manner that favors the societal benefits of accelerated drug discovery suggests that the Supreme Court's decision in *Merck KGaA* prefers access to technology over strong patent rights.<sup>200</sup> An expansion in the scope of the research exemption afforded by the safe harbor would logically result in a decrease in the perceived value of patents related to drug and vaccine development.<sup>201</sup> The safe harbor would effectively limit a patent holder's right of exclusivity. The inability of a patent holder to exclude others from using his invention denies the patent holder of the incentive offered in the form of a patent monopoly. If a patent can be readily infringed in the course of obtaining FDA regulatory approval, the economic incentives associated with exclusivity, namely the ability to recover costs, will be reduced.<sup>202</sup>

Reduction in the incentives associated with patents could arguably hinder drug research and development, as research entities may decide to channel capital away from drug research and development and into resources more likely to generate a return on their investment. However, patent valuation cannot be examined in a vacuum. Although an individual patent's right to exclusivity may be limited, the same is true for all patents whose use could be reasonably related to generating information for an FDA submission. Therefore, the right of exclusivity is equally extinguished from all drug-related patents. This loss of exclusivity is not uncompensated because what the patent holder loses in exclusivity, the patent holder gains in increased access to technology. This access to technology will almost certainly extend to patented technologies directly related to and in competition with the patent holder's patented technology. This trade-off will afford a patent holder the opportunity to utilize other existing patented technologies to build upon and improve the patent holder's patented technology.

This gain-loss rationale operates under the assumption of a tacit reciprocal agreement: one who gains, also loses. This rationale fails to consider the concept of the "free rider,"<sup>203</sup> who gains access to patented technology without contributing to the body of patented technology through a loss of exclusivity of his own. Two kinds of free riders likely exist: generic pharmaceutical developers and innovative drug developers. In the case of generic drug developers, the access to technology gained through the § 271(e)(1)'s safe harbor is limited by the

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<sup>200</sup> See *id.* at 2383-84 (protecting the use of patented compounds in preclinical studies).

<sup>201</sup> Freschi, *supra* note 74, at 893.

<sup>202</sup> Brief for Invitrogen Corp. et al. as Amici Curiae in Support of Respondents at 3-4, *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S. Ct. 2372 (2005) (No. 03-1237), available at 2005 WL 682093, at \*3-\*4.

<sup>203</sup> Strandburg, *supra* note 63, at 111.

patent itself. Although a generic drug developer may use technology reasonably related to the generation of information for FDA approval, once approval is acquired the generic drug developer is prevented from bringing the generic equivalent of the patented technology to market until the expiration of the patent term. Therefore, although generic developers gain access to the technology, they are unable to profit from such gains until expiration of the underlying technology's patent. Free riding, innovative drug developers are capable of patenting novel technology and entering the marketplace, pending FDA regulatory approval prior to expiration of the underlying patent. Once the patent is issued, however, others may now access that developer's technology provided the "reasonably related" standard is met.

A critical assumption regarding expansion of the safe harbor and its negative affects on the valuation of patents is that access to technology is synonymous with the practice of technology. Access to technology does not necessarily indicate that the technology can be practiced. Although the enablement requirement of the Patent Act compels the inventor to disclose how to make and use the invention,<sup>204</sup> an inherent difficulty exists in translating scientific discovery into written expression.<sup>205</sup> This difficulty is embodied by the doctrine of equivalents, which expands the scope of infringement beyond the literal language of the patent claims to compensate for the difficulty in articulating scientific phenomenon in words.<sup>206</sup> The enablement requirement also acknowledges the limitations of written expression, upholding a patent specification that requires some experimentation to enable the practice of the patented technology, provided that the amount of experimentation required is not "undue."<sup>207</sup> Since biomedical patents rarely facilitate the immediate practice of technology, expansion of the safe harbor to allow others to use patented technology actually provides an incentive to disclose the absolute minimum amount of information when applying for a patent in an effort to confuse the competition.

The perception of a decreased value of patents or an increased number of free riders as a result of a broad interpretation of the safe harbor from patent

<sup>204</sup> 35 U.S.C. § 112 (2000).

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

*Id.*

<sup>205</sup> Strandburg, *supra* note 63, at 102.

<sup>206</sup> See *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 731-32 (2002).

<sup>207</sup> *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (citing *Ex Parte Forman*, 1986 WL 83597, 230 U.S.P.Q. (BNA) 546, 547 (PTO Bd. Pat. App. & Int. 1986)).

infringement may result in a decrease in patented inventions. Unlike the alternative investment rationale offered above, innovative drug manufacturers may elect for an alternative form of intellectual property protection, namely trade secrets, in the absence of meaningful patent protection.<sup>208</sup> An increase in trade secrets would result in a reduction of public dissemination of research information, which would subsequently suppress innovation.

Since technology protected by trade secret is capable of gaining FDA approval,<sup>209</sup> an immediate solution to avoid the inhibition of innovation associated with trade secrets is not available. However, the transaction costs associated with utilizing and maintaining trade secret protection may be prohibitive.

Trade secret protection is not likely a viable means to protect the intellectual property of research entities engaged in a collaborative, government-sponsored research initiative. Conceptually, creation and maintenance of trade secrets are contrary to the spirit of the research initiative, which places the advancement and dissemination of scientific knowledge for the public good ahead of the private control and exploitation of technology. In addition, trade secret protection is likely impossible when considering the process for obtaining funding for government-sponsored research. Specifically, application and retention of government funding usually requires submission of a research proposal followed by subsequent progress reports, which are both readily available to the public.<sup>210</sup> Therefore, maintenance of a trade secret that involves data generated by government funding is not feasible.

<sup>208</sup> Steffe & Shea, *supra* note 169, at 374.

A trade secret is information, including a formula, pattern, compilation, program, device, method, technique, or process, that: (i) derives independent economic value, actual or potential, from not being generally known to, and not being readily ascertainable by proper means by, other persons who can obtain economic value from its disclosure or use, and (ii) is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

1 ROGER M. MILGRIM, MILGRIM ON TRADE SECRETS § 1.01[2] (2005) (quoting UNIFORM TRADE SECRETS ACT § 1 (1973)).

<sup>209</sup> 5 U.S.C. § 552(b)(4) (2000); Roberta Schugmann & Leslie Shaw, *The Application of Trade Secret Protection to Safety and Effectiveness Data of Patented Drugs*, 16 U.C. DAVIS L. REV. 463, 475 (1983); see Barry Meier, *F.D.A. Will Not Release Some Data on Heart Devices*, N.Y. TIMES, Aug. 6, 2005, at C3 (discussing FDA's refusal to release information on frequency and cause of heart device failure in response to Freedom of Information Act request, claiming such information exempted as "a corporate trade secret").

<sup>210</sup> Thomas O. McGarity, *Peer Review in Awarding Federal Grants in the Arts and Sciences*, 9 HIGH TECH. L.J. 1, 11 (1994); see, e.g., Computer Retrieval of Information on Scientific Projects, <http://crisp.cit.nih.gov>.

## IV. CONCLUSION

The Supreme Court's decision in *Merck KGaA v. Integra LifeSciences I, Ltd.* broadly interpreted § 271(e)(1)'s safe harbor from patent infringement to encompass the use of patented inventions that are reasonably related to obtaining FDA approval.<sup>211</sup> This interpretation is wholly consistent with the legislative intent of the Hatch-Waxman Act,<sup>212</sup> which attempted to stimulate the development of innovative treatments for diseases. The *Merck KGaA* decision will foster a research environment amenable to government-sponsored research initiatives, such as those proposed to combat the threats of bioterrorism and infectious disease. Through increased access to patented technology, government-sponsored research initiatives are poised to make great strides in the development of innovative vaccines and therapeutics aimed at protecting the general public from the global threats of bioterrorism and infectious disease.

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<sup>211</sup> *Merck KGaA v. Integra LifeScience I, Ltd.*, 125 S. Ct. 2732, 2782 (2005).

<sup>212</sup> *See* Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman) of 1984, Pub. L. No. 98-417, 1984 Stat. 1538.