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Ruth E. Freeburg

University at Buffalo School of Law (Student)

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COMMENTS

No Safe Harbor and No Experimental Use: Is It Time for Compulsory Licensing of Biotech Tools?

RUTH E. FREEBURG†

INTRODUCTION

The Biotech Century—A Biotech Revolution—not just the excited hyperbole of a hopeful venture capitalist or a few impressionable investors—these are fitting phrases describing a phenomenon that has exploded into the world’s spotlight.¹ Biotechnology, though existing in limited form

† J.D. Candidate, State University of New York at Buffalo Law School, 2005; B.S., Niagara University, 2001.

1. See, e.g., RICHARD W. OLIVER, *THE COMING BIOTECH AGE: THE BUSINESS OF BIO-MATERIALS* 70-72 (1999) (noting the 2006 projected dollar amount and GDP for biotech products in the United States); JEREMY RIFKIN, *THE BIOTECH CENTURY: HARNESSING THE GENE AND REMAKING THE WORLD* 15 (1998) (noting that the more than 1,300 biotech companies in the United States with over 100,000 employees “has occurred in only the first decade of a technological . . . revolution that will likely span several centuries.”). Though Mr. Rifkin denies personally that he is opposed to technological advancement, *id.* at 227-237, others find him an opponent of the biotech industry noting his notorious patent application for a 50% human-animal chimeric in 1997. The patent was denied. See also ROBERT PATRICK MERGES & JOHN FITZGERALD DUFFY, *PATENT LAW AND POLICY: CASES AND MATERIALS* 130-31 (3d ed. 2002); Rochelle K. Seide & Carmella L. Stephens, *Ethical Issues and Application of Patent Laws in Biotechnology*, in *WHO OWNS LIFE?*, at 59, 67 (David Magnus et al. eds., 2002).

for thousands of years,² has been poised to leave the practice arena and enter center stage since Watson and Crick unlocked the storehouse of DNA in 1953.³ The Information Age made its entrance at nearly the same time, making possible many of the advancements in biotechnology, but it now moves backstage behind the coming biotech revolution.⁴ *Biotech*—an abbreviation chosen for a role in the phenomenon along with *biologics*, *bioethics*, *bioinformatics*, *biomedicine*, *bioeconomics* and many more—takes a prominent position in the development of innovative medical research.⁵ As one author notes, “[M]edical discovery [used to be] based mainly on observation and serendipity. The discovery of penicillin is a classic example.”⁶ Yes, Alexander Fleming’s finding of antibiotics may have been serendipitous, but the road to this century’s new drugs is far more likely to be meticulously and carefully planned.⁷ Not accidental or fortuitous, the development of Gleevec is a prime example.⁸ This drug has been hailed as a great breakthrough in cancer therapy, receiving perhaps the fastest Food and Drug Administration (FDA) approval ever, due to astounding results in its early clinical trials.⁹

2. See, e.g., OLIVER, *supra* note 1, at 118-19.

3. See, e.g., LESLIE ALAN HORVITZ, EUREKA! SCIENTIFIC BREAKTHROUGHS THAT CHANGED THE WORLD 198-206 (2002).

4. See OLIVER, *supra* note 1, at 7-11. See also RIFKIN, *supra* note 1, at 9 (noting the computer’s role in managing genetic information); Jim Hopkins, *Venture Capital Flows into Biotech*, USA TODAY, Jan. 26, 2004, at 2B (noting increased interest in biotech for development of drugs and biologics while computer investment falls).

5. See, e.g., OLIVER, *supra* note 1, at 115-23; GEORGE WOLFF, THE BIOTECH INVESTOR’S BIBLE 9 (2001).

6. TOM ABATE, THE BIOTECH INVESTOR: HOW TO PROFIT FROM THE COMING BOOM IN BIOTECHNOLOGY 97 (2003).

7. *Id.* at 97-98.

8. See, e.g., GERALD WEISSMANN, THE YEAR OF THE GENOME: A DIARY OF THE BIOLOGICAL REVOLUTION 34-38 (2002). The impetus in the creation of new drugs is to target the defect without affecting the other cells in the body. Gleevec is an example of one of the new “target” drugs.

9. WEISSMANN, *supra* note 8, at 34 (quoting Tommy Thompson, Secretary of Health and Human Services, in May of 2001, announcing FDA approval of Gleevec as a “medical breakthrough[] that is outstanding”). See also Michelle Healy, *Leukemia Drug Glivec Clears Cancer in Trial*, USA TODAY, Dec. 5, 2000, at 9D; *Talk of the Nation: Targeted Cancer Drugs* (Nat’l Pub. Radio broadcast, June 1, 2001), at <http://www.npr.org/templates/story/story.php?storyId=>

Gleevec's development was carefully initiated and painstakingly planned after decades of cellular research and advancement involving deliberate attention first, to normal mechanisms of cell growth and then, to detailed minutia of the mechanisms behind cellular abnormalities.¹⁰

Biotechnology is truly at the forefront of today's medical research. Genetically engineered biologics¹¹ are used to treat heart disease, cancer, AIDS, strokes, kidney and liver disease, diabetes, anemia, cystic fibrosis, and autoimmune diseases like multiple sclerosis and lupus, while other uses include vaccines and disease screening.¹² Not only the end-product biologics themselves, but biotech tools are also major players in this new revolution.¹³ The tools include innu-

1123743 (last visited Mar. 14, 2005). Gleevec has also had good success in some other cancers besides chronic myelogenous leukemia. See Kathleen Fackelman, *Leukemia Drug Gets Rave Review*, USA TODAY, Feb. 27, 2002, at D8.

10. Gleevec (imatinib mesylate), marketed as *Glivec* abroad and known as STI-571 in early research trials, is a tyrosine kinase inhibitor at the cellular level—preventing components from receiving the *signals* leading to continued production of malignant cells, rather allowing for a “natural death” of the unnatural cells. See, e.g., Alan O. Perantoni, *Cancer-Associated Genes*, in THE BIOLOGICAL BASIS OF CANCER 133-61 (1998) (discussing tyrosine kinase inhibitors, cell signaling and cell death). Far from being a quick *discovery*, Gleevec is the result of a culmination of biotech research of the past half-century with the cause of the particular leukemia discovered in 1960, Robert G. McKinnell, *Cancer Genetics*, *id.*, at 121-23, and research continuing across continents and in multiple laboratories. See, e.g., Philipp le Coutre et al., *In Vivo Eradication of Human BCR/ABL-Positive Leukemia Cells with an ABL Kinase Inhibitor*, 91 J. NAT'L CANCER INST. 163 (1999) (conducting research in Italy); Michael W. N. Deininger et al., *The Tyrosine Kinase Inhibitor CGP57148B Selectively Inhibits the Growth of BCR-ABL-Positive Cells*, 90 BLOOD 3691 (1997) (conducting research in the United Kingdom); Bernd Kasper et al., *Favorable Therapeutic Index of a p210(BCR-ABL)-Specific Tyrosine Kinase Inhibitor*, 44 CANCER CHEMOTHERAPY PHARMACOLOGY 433 (1999) (conducting research in Germany); Shingo Dan et al., *Selective Induction of Apoptosis in Philadelphia Chromosome-Positive Chronic Myelogenous Leukemia Cells by an Inhibitor of BCR-ABL Tyrosine Kinase*, CGP 57148, 5 CELL DEATH AND DIFFERENTIAL 710 (1998) (conducting research in Japan).

11. The FDA categorizes *biologics* as medical products such as vaccines, blood derivatives, tests for genetics, cells, tissues, and biological modifiers for treating cancer, arthritis and other diseases. The first Biologics Control Act was passed in 1902 as the result of a tragedy involving a diphtheria vaccine tainted with tetanus. See the FDA website, at <http://www.fda.gov> (last visited Mar. 14, 2005).

12. See, e.g., RIFKIN, *supra* note 1, at 22-23.

13. See, e.g., ABATE, *supra* note 6, at 58-68, 97-98 (describing a variety of tools produced by different biotech companies); CYNTHIA ROBBINS-ROTH, PH.D.,

merable products and processes used in scientific laboratories including cell lines, monoclonal antibodies, reagents, animal models, growth factors, gene sequences, microarrays, DNA libraries, clones, cloning tools (such as polymerase chain reaction or PCR), and screening methods, as well as laboratory equipment and machines.¹⁴ At each step of the development of a new treatment or medical discovery, biotech tools are not just props in the background but essential elements without which the task is not just formidable, but impossible.¹⁵

Dr. David Cheresch was involved in precisely this sort of innovative research when he found that blocking particular receptors or *doors* on the surface of cells would inhibit the production of new blood vessels.¹⁶ Angiogenesis is the technical name for the growth of these vessels, and it is a vital element in the spread of tumors and malignancy.¹⁷ The pharmaceutical giant, Merck, realizing the importance of this discovery, hired Dr. Cheresch and his employer, Scripps Foundation, to research potential drug candidates by finding those that inhibit angiogenesis.¹⁸ In his research Dr. Cheresch used a very short sequence from a human protein that is known to bind to these particular cell receptors or doors, thereby causing cell adhesion and promoting blood vessel growth.¹⁹ Dr. Cheresch tested various potential drug candidates to see which ones prevented the short peptide from binding to the receptors.²⁰ If a candidate prevented

FROM ALCHEMY TO IPO: THE BUSINESS OF BIOTECHNOLOGY 118 (2000) ("The key to discovery is using the emerging new tools of molecular biology, cell biology, assay development, combinatorial chemistry, and high-throughput screening to probe the inner workings of cells and decipher just what is causing disease."). See also *infra* note 182 and accompanying text.

14. See National Institutes of Health (NIH) Report of the Working Group on Research Tools (June 4, 1998), available at <http://www.nih.gov/news/researchtools/index.htm> (last visited Feb. 7, 2005).

15. See ROBBINS-ROTH, *supra* note 13, at 12.

16. *Integra Lifesciences I, Ltd. v. Merck KgaA*, 331 F.3d 860, 863 (Fed. Cir. 2003) (Newman, J., dissenting), cert granted, 125 S. Ct. 823 (2005); see *infra* note 397.

17. *Id.* See also Robert G. McKinnell, *Metastasis*, in THE BIOLOGICAL BASIS OF CANCER, *supra* note 10, at 50, 67-68.

18. *Integra*, 331 F.3d at 862-63, 874.

19. *Id.* at 863.

20. *Id.*

the binding, it could potentially prevent new blood vessel growth, thereby starving an existing tumor and preventing the spread of new tumors.²¹ Dr. Charesch found a number of possibilities and after running numerous tests including toxicology and administration routes, one drug candidate in particular was chosen for clinical development.²² The potential drug candidate's path would, however, take a different route.

Integra Lifesciences owns the patent to the short peptide of only three amino acids that was used by Dr. Charesch for screening.²³ Integra is a biotech company whose business has primarily involved the development of prosthetics such as materials for blood vessel grafts and agents used in regeneration of human tissue.²⁴ The patent applications filed by Integra for the peptide make no mention of its use as a screening tool.²⁵ Rather, the patent applications list utilitarian possibilities such as wound healing following surgery or assisting with cell adhesion to flasks when growing cultures for research.²⁶ To this date the peptide has apparently not been developed for any of the uses described by Integra in the patent applications.²⁷

Upon learning of Dr. Charesch's research, Integra notified Merck of potential infringing activity and then sued Merck when licensing negotiations failed.²⁸ Merck's defense claimed safe harbor through the Hatch-Waxman Act, passed by Congress expressly for the purpose of exempting

21. *Id.*

22. *Id.* at 863, 874.

23. *Id.* at 862.

24. See Integra Lifesciences's webpage, at <http://www.integra-ls.com> (last visited Feb. 16, 2005).

25. 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. 4,879,237 (issued Nov. 7, 1989); U.S. Patent No. 4,988,621 (issued Jan. 29, 1991); U.S. Patent No. 5,695,997 (issued Dec. 9, 1997), available at <http://www.uspto.gov/> (last visited Feb. 8, 2005).

26. *Id.*

27. See *supra* note 24.

28. *Integra*, 331 F.3d at 863.

drugs, that are seeking FDA approval, from infringement.²⁹ However, the Court of Appeals for the Federal Circuit (CAFC)³⁰ ruled in June of 2003 that Merck was guilty of patent infringement.³¹ Though the safe harbor provision of Hatch-Waxman had been expanded by the courts to include, not just the drugs under FDA regulation but also biotech tools used to develop these drugs, the CAFC called a halt to this upstream protection of biotech tools in its *Integra* decision.³² Ironically, if Merck had been farther along in development of its cancer drug, safe harbor might have been available for its use of the peptide as a biotech tool for screening potential drugs.³³

There is another judicial decision from the summer of 2003 affecting the future availability of research tools. In June, the Supreme Court denied a writ of certiorari in *Madey v. Duke*, letting the prior CAFC ruling stand that had found Duke University guilty of patent infringement for its laboratory use of laser equipment.³⁴ Duke University claimed an experimental use defense for its operation of the research tool patented by one of Duke's former professors.³⁵ The court refused to apply an experimental use exemption for patent infringement, continuing to construe this common law provision very narrowly.³⁶

The courts' expansion of Hatch-Waxman's safe harbor provision prior to *Integra* is evidence of a recognized need

29. Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. §§ 301, 355, 360cc (2003); 28 U.S.C. § 2201 (1993); 35 U.S.C. §§ 156, 271, 282 (2003)) (hereinafter Hatch-Waxman).

30. In 1982 Congress created the new Court of Appeals for the Federal Circuit with one of its primary functions being to hear all patent appeals from the federal district courts (previously the Court of Customs and Patents Appeals).

31. *Integra*, 331 F. 3d at 872.

32. Though the dissent in *Integra* objects to calling the infringed peptide a "research tool," others define biotech tools as any type of product used by scientists in the laboratory. *Integra*, 331 F.3d at 872, 878. See also *supra* note 14 and accompanying text.

33. *Integra*, 331 F.3d at 877.

34. *Madey v. Duke Univ.*, 307 F. 3d 1351 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 958 (2003).

35. *Id.* at 1353, 1355.

36. *Id.* See also *infra* text accompanying notes 246-69.

for an exemption from patent infringement for biotech tools.³⁷ The *Integra* decision shuts down that passage into a safe harbor while *Madey* ensures that no other gate will be opened in its place.³⁸ With the impact of biotech tools felt in all areas of medical research, these two judicial decisions are key to the future development of therapies, drugs, and biologics for Americans. Medical research needs to develop unimpeded by licensing disagreements, competitors' blocking patents,³⁹ or judicial decisions bound by a presumption of patent validity.⁴⁰ The American public cannot be assured that the best in medical research and innovation will be available under the system currently in place. Is it time for compulsory licensing of biotech tools?

I. BACKGROUND

A. Constitutional Basis

The Constitution's Framers felt strongly enough about the benefit to the public of patent protection that provision for these limited monopolies was included in the Constitution. Congress has the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries."⁴¹ Thomas Jefferson was instrumental in passage of the first U.S. Patent Act of 1790, and was included, as Secretary of State, in the first body to administer patents.⁴² Jefferson believed that limited monopolies were necessary to see continued progress in inven-

37. See *infra* text accompanying notes 127-205.

38. *Integra*, 331 F.3d at 872; *Madey*, 307 F. 3d at 1364.

39. Blocking patents refers to an improvement on a patented invention that requires licensing to practice because otherwise it infringes upon the original invention. See Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. R. 839, 860-62 (1990).

40. See *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy*, FTC Rep., Exec. Summ., at 8 (Oct. 2003) (recommending that challenges of a patent's validity should be proved by a lesser standard than is presently used).

41. U.S. CONST. art. I, § 8, cl. 8.

42. ROBERT P. MERGES ET AL., *INTELLECTUAL PROPERTY IN THE NEW TECHNOLOGICAL AGE* 109 (3d ed. 2003).

tions that would eventually benefit the public, though he was initially not a proponent of a monopolistic system for patents.⁴³ In a 1966 patent case the Supreme Court notes, "Jefferson, like other Americans, had an instinctive aversion to monopolies. It was a monopoly on tea that sparked the Revolution and Jefferson certainly did not favor an equivalent form of monopoly under the new government."⁴⁴ This grant of an "exclusive Right" (monopoly) was for the specific purpose of encouraging invention and was specifically noted "for limited Times" only.⁴⁵

B. Philosophy

It is clear from Jefferson's writings that the key component in granting patent monopolies was to benefit the public, an economic/utilitarian philosophy of patent law as opposed to a *reward for labor* (also called *sweat of the brow*) or a *natural rights* theory, prominent in the European philosophy of patent law.⁴⁶ In every recent decade the Supreme Court has emphasized that the purpose behind intellectual property law in the United States is to benefit the public. In the important 1966 case, *Graham v. Deere*, the Court stresses this intent in speaking of the 1793 Patent Act author, Thomas Jefferson. Justice Clark notes, "He [Jefferson] rejected a natural-rights theory in intellectual property rights and clearly recognized the social and economic rationale of the patent system. The patent monopoly was not designed to secure to the inventor his natural right in his discoveries."⁴⁷ In 1974 the Court states, "The patent laws promote . . . progress . . . [to] have a positive effect on society through the introduction of new products and processes of manufacture into the economy [with] better lives for our citizens."⁴⁸ In its consequential 1984

43. See *Graham v. Deere*, 383 U.S. 1, 7-8 (1966) (citing V WRITINGS OF THOMAS JEFFERSON (Ford, ed 1985, and Washington, ed)).

44. *Id.* at 7.

45. U.S.CONST. art. I, § 8, cl. 8.

46. MERGES ET AL, *supra* note 42, at 2-5, 10-11. See also CRAIG JOYCE ET AL., COPYRIGHT LAW 56-65 (6th ed. 2003) (discussing differences in continental and U.S. intellectual property philosophies).

47. *Graham*, 383 U.S. at 8-9.

48. *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 480 (1974).

decision, *Sony v. Universal Studios*, the Court reiterates, "The monopoly privileges that Congress may authorize are neither unlimited nor primarily designed to provide a special private benefit. Rather, the limited grant is a means by which an important public purpose may be achieved."⁴⁹ And, yet again in 1991 Justice O'Connor writes, "The primary objective of [intellectual property law] is not to reward the labor . . . but 'to promote the Progress of Science and useful Arts.'"⁵⁰

Patent rights in the United States do not exist because of a recognized innate right of an inventor to monopolize his invention.⁵¹ The economic reward produced through limited monopolies is provided as an incentive for the ultimate benefit to the public from advancement in the designated fields.⁵² The Framers recognized this principle, and the Supreme Court continues to uphold this philosophy in its rulings.⁵³ The Legislature has accepted its role, carving out exceptions that place additional limitations on the rights created by the Patent Act when necessitated by public interest.⁵⁴

C. *Evolution of the Patent System*

In 1836 the patent system was revised to include a formal administrative system for examination of patent applications by professionals, in order to determine validity.⁵⁵

49. *Sony Corp. of America v. Universal City Studios, Inc.*, 464 U.S. 416, 429 (1984).

50. *Feist Publ'ns Inc. v. Rural Tel. Serv. Co.*, 499 U.S. 340, 349 (1991)(quoting U.S. CONST. art. I, § 8, cl. 8).

51. See *supra* text accompanying notes 46-50.

52. See *supra* notes 41-45 and accompanying text.

53. See *supra* text accompanying notes 46-50. See also ARTHUR R. MILLER & MICHAEL H. DAVIS, *INTELLECTUAL PROPERTY: PATENTS, TRADEMARKS, AND COPYRIGHT IN A NUTSHELL* 16-17 (3d ed. 2000) (discussing the bargain or contract theory of patent law where rewards are offered as an incentive as opposed to the "natural rights" theory).

54. See *infra* text accompanying notes 360-62, 367-73.

55. *MERGES ET AL.*, *supra* note 42, at 109. Under the system originally established in 1790, the "examining" group was comprised of the Secretary of State (Jefferson), the Secretary of the Department of War, and the Attorney General. In the 1793 Patent Act this was changed to a registration system until the 1836 revision reverted back to examination. See also *MERGES & DUFFY*,

This system continues today through the Patent and Trademark Office (PTO). In 1952 a major codification of U.S. Patent Law was completed, bringing the system into the modern era of patent procedure as known today.⁵⁶ This was the last major revision of U.S. Patent Law until compliance with the revised General Agreement on Tariffs and Trade required some significant changes in 1994.⁵⁷ The U.S. patent term was changed from seventeen years at issuance of the patent, to twenty years from the date of filing the application with the PTO.⁵⁸ The changes were greater, however, in developing countries as these signatories of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), in becoming members of the newly formed World Trade Organization, were now required to allow patenting of pharmaceuticals.⁵⁹

supra note 1, at 8-9; John F. Duffy, *Harmony and Diversity in Global Patent Law*, 17 BERKELEY TECH. L. J. 685, 714 (2002).

56. MERGES & DUFFY, *supra* note 1, at 10. The 1952 revision was the last and third (following 1793 and 1836) major revision of Patent Law in the United States. The present Patent Act is codified in 35 U.S.C. §§ 101-132 (2002).

57. General Agreement on Tariffs and Trade, Oct. 30, 1947, 61 Stat. A-11, T.I.A.S. 1700, 55 U.N.T.S. 194, revised by Final Act Embodying the Results of the Uruguay Round of Multilateral Trade Negotiations, Apr. 15, 1994, LEGAL INSTRUMENTS – RESULTS OF THE URUGUAY ROUND vol. 1 (1994), 33 I.L.M. 1125 (1994).

58. Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, LEGAL INSTRUMENTS – RESULTS OF THE URUGUAY ROUND vol. 31, 33 I.L.M. 81, 96 (1994) (hereinafter TRIPS Agreement). Since the average time from application filing to issuance is close to three years, the extension may not be that significant. Prior to the revision of 1836 a patent term in the United States was for 14 years, the period of two terms of an apprenticeship in the Old World trade system. In 1836 a 7 year renewable term was added for a total of 21 years. The 17 year term existing until 1994 was the result of an 1861 legislative compromise. See MERGES ET AL., *supra* note 42, at 114 n.26.

59. See TRIPS Agreement, *supra* note 58, art. 27 (requiring patents to be available for inventions “in all fields of technology”); MERGES & DUFFY, *supra* note 1 at 57. See also generally Duffy, *supra* note 55; Dora Kripapuri, Comment, *Reasoned Compulsory Licensing: Applying U.S. Antitrust’s “Rule of Reason” to TRIP’s Compulsory Licensing Provision*, 36 NEW ENG. L. REV. 669 (2002). See also *infra* notes 344-47, 374-81 and accompanying text.

D. Patent 101

The Patent Act states that a patent may be procured for “any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof.”⁶⁰ This provides four basic categories of patentable inventions plus a blanket provision for an *improvement* on any of the four—process, machine, manufacture, or composition. The improvement provision highlights one problem with the lack of an infringement defense for experimental use in U.S. Patent Law. Unless a patent term has expired, how can an improvement be created without infringing on the unimproved, patented invention?⁶¹ Without either safe harbor or an experimental use exception, unless a license is secured from the patent holder, it is unlikely that improvements can be made.⁶² This is not without significance for technological inventions, particularly in the area of medical research.⁶³

Patentable subject matter has been expanded through the years to include natural substances and life forms.⁶⁴ In

60. 35 U.S.C. § 101 (1952).

61. In Europe, a patent right for *first users* exists to allow a defense for infringement for a first inventor by a second who files a patent on the invention. In 1999 Congress amended the Patent Law to include a “prior user right” defense for infringement of a “method of doing or conducting business.” 35 U.S.C. § 273 (1999). This amendment came one year after the CAFC ruling in *State Street* allowing patenting of a computer business method. *State St. Bank & Trust Co v. Signature Fin. Group, Inc.*, 149 F.3d 1368 (Fed. Cir. 1998). However, if there’s a *first user* under U.S. Patent Law, the invention should not be patentable since the second user is not the original inventor. 35 U.S.C. § 111 (2002). (Only an original inventor can apply for a patent in the United States though assignments of rights are frequently made, for example, to the inventor’s employer. In Europe a patent is granted to the first to file, rather than the first to invent.) It should be noted that the U.S. “prior user right” may not be in compliance with the TRIPS Agreement since article 27, though not prohibiting a prior user defense, does require that a defense be applicable to all fields. See MERGES & DUFFY, *supra* note 1, at 173.

62. See Merges & Nelson, *supra* note 39, at 861-62.

63. See *id.*

64. See *Parke-Davis & Co. v. H. K. Mulford & Co.*, 196 F. 496 (2d Cir. 1912) (ruling that a purified substance from a living creature, adrenaline, is patentable); *Diamond v. Chakrabarty*, 447 U.S. 303 (1980) (holding that a living organism, genetically engineered bacteria, can be patented). Interestingly, though the European Patent Convention prohibits the patenting of plant or animal “varieties,” a patent was eventually granted for the

general, however, patents are not granted for laws of nature, physical phenomena, or abstract ideas.⁶⁵ Patents must also meet requirements related to novelty (created by the applicant and not in public use for more than one year from the date of filing), usefulness (no perpetual motion machines, but just about anything else goes),⁶⁶ and nonobviousness (lots of leeway here as well).⁶⁷ In addition, the application to the PTO must include a written description and the best mode of practicing the invention so that someone “skilled in the art” will be enabled to reproduce and practice the invention.⁶⁸ The description and enablement requirements are key in providing for the public’s ability to utilize the technology when the patent term is expired. Supreme Court Justice Story succinctly ties this requirement to the philosophy behind U.S. Patent Law in an 1813 circuit case:

Harvard/Onco-Mouse; however, the Canadian Supreme Court reversed the Canadian Federal Court of Appeal and denied patentability of “transgenic animals” including the Harvard/Onco-Mouse. *Harvard College v. Canada* (2002) 4 S.C.R. 45. For a discussion of the European Patent Office decision, see MERGES & DUFFY, *supra* note 1, at 129-30.

65. *See Diamond*, 447 U.S. at 309.

66. 35 U.S.C. §§ 102-103 (2004). In earlier cases dealing with medical research patents, the courts required a definite utility. *See, e.g., Brenner v. Manson*, 383 U.S. 519 (1966) (ruling that a process for making a known steroid was unpatentable for lack of known utility though a closely related steroid had shown tumor-inhibiting effects in mice). With the advent of the human genome project, the PTO published guidelines allowing patents on unknown gene sequences and other *potential* research tools of DNA. Utility Examination Guidelines, 60 Fed. Reg. 36,263 (July 14, 1995). With an avalanche of patent applications for expressed sequence tags (small portions of DNA that might be used as probes) the PTO published new guidelines requiring “substantial” utility. Revised Interim Utility Guidelines, 64 Fed. Reg. 71,440 (Dec. 21, 1999), *amended after public comment* by Utility Examination Guidelines, 66 Fed. Reg. 1092 (Jan. 5, 2001).

67. There is a lot of discontent with the granting of “frivolous” patents—particularly, though not solely, evident in some of the patents related to computers (Amazon’s *One-Click*, for example). Most of this can be traced to leeway in respect to the nonobviousness requirement for patentability. *See* James Gleick, *Patently Absurd*, N.Y. TIMES MAGAZINE, Mar. 12, 2000, at 44. Timothy J. Muris, FTC Chairman, recently remarked on the necessity of narrowing the nonobviousness standard for patents. Timothy J. Muris, Remarks at the N.Y. State Bar Antitrust Div. Ann. Meeting (January 29, 2004), *available at* <http://www.nysba.org> (last visited Mar. 28, 2005). *See also supra* note 40.

68. 35 U.S.C. § 112 (1975).

[T]he monopoly is granted upon the express condition, that the party shall make a full and explicit disclosure, so as to enable the public, at the expiration of his patent, to make and use the invention or improvement in as ample and beneficial a manner as the patentee himself. If . . . this cannot be done, it is defrauding the public of all the consideration, upon which the monopoly is granted.⁶⁹

II. WAS THERE EXPERIMENTAL USE BEFORE HATCH-WAXMAN?

A. *Early Cases*

Unlike *fair use*—its closest counterpart in U.S. Copyright Law⁷⁰—Patent Law had no statutory exemption for an experimental use defense before Hatch-Waxman. The same case used by Justice Story to advocate the necessity of an enabling disclosure, is credited as the source for the common law experimental use exception to patent infringement.⁷¹ In *Whittemore v. Cutter*, Justice Story remanded for a new trial and noted, “[I]t could never have been the intention of the legislature to punish a man, who constructed such a machine merely for philosophical experiments”⁷²

This doctrine of experimental use as a defense for patent infringement was upheld in court dicta of the nineteenth century and was expounded in a well-respected treatise on patent law,⁷³ though it was not found sufficient in the scattered cases claiming its use. The district judge in an 1861 case, *Poppenhusen v. Falke*, declined to find the defense applicable but declared, “It has been . . . now well settled, that an experiment with a patented article for the

69. *Whittemore v. Cutter*, 29 F. Cas. 1120, 1122 (C.C.D. Mass. 1813).

70. 17 U.S.C. § 107 (1992). See also *infra* notes 356-59 and accompanying text.

71. See *Whittemore*, 29 F. Cas. at 1121. See also *supra* text accompanying notes 68-69.

72. *Whittemore*, 29 F. Cas. at 1121. See also *Sawin v. Guild*, 21 F.Cas. 554, 555 (1813) (referring to *Whittemore*).

73. 3 WILLIAM C. ROBINSON, THE LAW OF PATENTS FOR USEFUL INVENTIONS § 898 (1890).

sole purpose of gratifying a philosophical taste, or curiosity, or for mere amusement, is not an infringement."⁷⁴

In the twentieth century, the Court of Claims considered the experimental use defense in a number of cases, and though each case confirms the existence of an experimental use defense,⁷⁵ only *Pitcairn v. United States* sufficiently states the law under which the exemption should be applied.⁷⁶ *Pitcairn* involves the experimental use of helicopters manufactured for the United States by the plaintiffs. Licensed agreements between Plaintiffs and the United States existed, but the government wanted to exclude payment for the period during which the helicopters were being "tested."⁷⁷ The court states:

Tests, demonstrations, and experiments of such nature are intended uses of the infringing aircraft manufactured for the defendant and are in keeping with the legitimate business of the using agency. Experimental use is [therefore] not a defense in the present litigation.⁷⁸

The court reasoned that the testing and evaluation were part of the defendant's normal course of business and, therefore, not to be deemed experimental.⁷⁹ Compensation would need to be paid by the government. An experimental use defense continued to be confirmed by the courts, but only narrowly construed.⁸⁰

74. *Poppenhusen v. Falke*, 19 F.Cas. 1048, 1049 (C.C. S.D.N.Y. 1861).

75. See *Pitcairn v. United States*, 547 F.2d 1106 (U.S.C.C. 1976); *Douglas v. United States*, 510 F.2d 364 (U.S.C.C. 1974); *Chesterfield v. United States*, 159 F. Supp. 371 (U.S.C.C. 1958); *Ordnance Eng'g Corp. v. United States*, 84 Ct. Cl. 1 (1936). These cases, all binding precedent on the present-day Court of Appeals for the Federal Circuit, involve litigation against the United States. See also *Roche Products, Inc. v. Bolar Pharm. Co.*, 733 F.2d 858, 863 (Fed. Cir. 1984).

76. *Pitcairn*, 547 F.2d at 1124-26. See also *Roche*, 733 F.2d at 863.

77. *Pitcairn*, 547 F.2d at 1125.

78. *Id.* at 1125-26.

79. *Id.* at 1124-26.

80. *Id.*

B. Roche v. Bolar

In 1984, Roche Products sued Bolar Pharmaceuticals for infringement of a patented ingredient in Roche's sleeping pill.⁸¹ The CAFC refused to expand the experimental use doctrine to exempt Bolar's use of the component though it involved FDA testing.⁸² Bolar's infringement did not apply to the judicially created exceptions of "amusement, to satisfy idle curiosity, or for strictly philosophical inquiry," but was admittedly for uses related to business and profit.⁸³ Bolar argued, "[E]ven if no *established* doctrine exists [to] escape liability for patent infringement, public policy requires that [the court] create a new exception"⁸⁴

Bolar's rationale for a new exception was based on the increased length of time required to complete FDA testing with the passage of the Drug Amendments of 1962.⁸⁵ When the Federal Food, Drug, and Cosmetic Act (FDCA) was passed in 1938, it required the filing of a New Drug Application (NDA) with the FDA, including information on safety. If no notification came from the FDA to the pioneer company within sixty days, marketing could begin.⁸⁶ With the amendments to the Act in 1962, an NDA required not only safety data but proof of efficacy as well, and the FDA would affirmatively approve the application before marketing could begin.⁸⁷ The court in *Roche* noted that seven to ten years was the average time from application by the

81. Roche, 733 F.2d 858.

82. *Id.* at 867.

83. *Id.* at 863 (quoting from *Poppenhusen v. Falke*, 19 F.Cas. 1048, 1049 (C.C. S.D.N.Y. 1861)).

84. *Id.*

85. Drug Amendments of 1962, 76 Stat. 780 (codified as amended at 21 U.S.C. § 355 (2003)).

86. Fed. Food, Drug, and Cosmetic Act, 52 Stat. 1040 (1938) (current version at 21 U.S.C. §§ 301-393 (2004)). Congress had previously passed legislation regulating food processing, including an act in 1906, but the 1938 statute greatly expanded FDA authority. FDCA passage resulted because of a public health disaster with the death of some 100 people taking an adulterated drug product. See the story at the FDA website, at <http://www.fda.gov/oc/history/historyoffda/section2.htm> (last visited Mar. 23, 2005).

87. See *supra* note 85.

pharmaceutical company to FDA approval.⁸⁸ Therefore, once a pioneer drug finally received FDA approval, a patent term of seven years (rather than seventeen) might be all that remained until expiration. However, the companies gained another *de facto* monopoly of two or more years when their patent expired because it took the generic manufacturers this long to complete their own FDA approval.⁸⁹ Bolar contended that it was not intended, with passage of the FDCA, that an increased duration of the monopoly be given to the pioneer companies; rather the court should allow experimental use for the generic drug's testing during the pioneer drug's patent term "so that the public can enjoy the benefits of competition as soon as possible, consistent with the need to encourage invention."⁹⁰ The court responded negatively to Bolar's suggestion and "decline[d] the opportunity . . . to engage in legislative activity proper only for the Congress."⁹¹ Congress accepted this responsibility, and the passage of Hatch-Waxman followed.⁹²

III. HATCH-WAXMAN PROVIDES A NEEDED SAFE HARBOR

A. *Congress Acts*

In 1984 the U.S. Patent Law and the Federal Food, Drug, and Cosmetic Act were amended, addressing a serious need for cheaper and more readily available generic drugs to a graying population.⁹³ At the same time, passage

88. *Roche*, 733 F.2d at 864.

89. *Id.*

90. *Id.*

91. *Id.* at 863-64.

92. Hatch-Waxman, *supra* note 29. The Hatch-Waxman Act is sometimes called the Bolar Amendment (particularly overseas) after the case that was a catalyst to its passage. Legislation was before Congress regarding faster and more efficient means to market generic drugs at the time of the court's ruling in *Roche*. See *Roche*, 733 F.2d at 865.

93. Hatch Waxman, *supra* note 29. See also J. Grana, *The Aged in America*, in 1 (2) HEALTH AFFAIRS 103 (Spring 1982) (listing increasing percentage of aged population); Alex Kucherov & Abigail Trafford, *Coming: New Kinds of Drugs that Could Save Your Life*, U.S NEWS & WORLD REPORT, Oct. 5, 1981, at 55 (addressing the pressure on the FDA for faster drug approval, as well as

of this Hatch-Waxman Act pacified pharmaceutical companies holding the patent monopolies on name-brand drugs.⁹⁴ Hatch-Waxman was designed to allow the generic companies to utilize the prior testing and data that had been completed by the name-brand (pioneer) companies. These pioneer companies were then given an extension on their patent term to compensate for the time taken in obtaining the data and clinical testing results.⁹⁵

To accomplish these goals, the new legislation addressed “two unintended distortions of the . . . patent term produced by the requirement that certain products must receive premarket regulatory approval.”⁹⁶ As the court had noted in *Roche*, at one end of the patent term, a “distortion” kept drug companies from reaping any profit for their research and development costs since valuable patent time was used while waiting for FDA approval.⁹⁷ In the other “distortion” after the expiration of the patent term, a *de facto* monopoly was enjoyed by the pioneer company on its drug while the generic company complied with requirements for its own FDA approval.⁹⁸ The patent extension portion of Hatch-Waxman, 35 U.S.C. § 156, dealt with the first “distortion” by giving an extension of the patent term to the pioneer company, making up for the lack of profit during its approval process.⁹⁹ The other portion of the amendment, 35 U.S.C. § 271 (e)(1), addressed the second “distortion” of the *de facto* monopolies.¹⁰⁰ The generic company is exempted from infringement of the pioneer drug and able to begin the approval process before

reporting on new drugs); Mark Sherman, *9.3% Increase Reported in Costs for Health Care*, BUFFALO NEWS, Jan. 9, 2004, at A4 (charting the increases in health costs of the past three decades).

94. See generally Sheila R. Shulman et al., *Patent Term Restoration: The Impact of the Waxman-Hatch Act on New Drugs and Biologics Approved 1984-1995*, 2 (4) J.BIOLAW & BUS 63 (1999).

95. *Id.* at 64.

96. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 669 (1990).

97. *Id.* at 669-70. See also *Roche*, 733 F.2d at 864.

98. *Eli Lilly*, 496 U.S. at 669-71.

99. *Id.*

100. See text accompanying *infra* note 113 for 35 U.S.C. § 271(e)(1). 35 U.S.C. § 271(e)(2) creates the act of *artificial infringement* through the filing of an ANDA for a generic drug; 35 U.S.C. § 271 (e)(4) prescribes the remedies for an act of infringement created in (2). See also 21 U.S.C. § 355 (2000).

the pioneer patent term is expired.¹⁰¹ In addition, the generic company actually uses the original data submitted by the pioneer company, needing only studies showing bioequivalence to the pioneer drug.¹⁰² The generic product is on the market *immediately* upon expiration of the pioneer drug's patent term, and the public is benefited by the lower prices of generic brands that did not incur the same expenses of research and development as the pioneer drugs.¹⁰³

A generic company desiring to utilize the data provided to the FDA by the pioneer company, files an Abbreviated New Drug Application (ANDA) including the evidence of bioequivalence.¹⁰⁴ The ANDA filing must also include certification in regard to the status of all patents related to the original pioneer company's drug.¹⁰⁵ The four possible options in regard to this certification are: (1) "that such patent information has not been filed," (2) "that such patent has expired," (3) "the date on which such patent will expire," or (4) "that such patent is invalid (and, therefore, the generic drug will not be infringing)."¹⁰⁶ Upon notice of a Paragraph IV certification, that the generic drug will *not* be infringing the pioneer's patent because the patent is invalid, the pioneer company must be notified and then has a limited time to file an infringement suit against the generic company. (Under the first three paragraph certifications, no infringement is filed as the generic company is exempted, and marketing will not begin until the pioneer patent's expiration.)

B. *Litigation Follows Hatch-Waxman's Passage*

Inevitably, litigation followed the passage of Hatch-Waxman as, in some cases, the makers of generic drugs may have felt that they had little to lose in respect to filing

101. See Shulman, *supra* note 94, at 63.

102. *Id.*

103. See *id.*

104. *Id.*

105. *Id.* at 64.

106. 21 U.S.C. §§ 355(b)(2)(A), 355 (j)(2)(A)(vii) (2000).

a Paragraph IV certification.¹⁰⁷ The court might rule in their favor by declaring the pioneer patent invalid, and then the generic brand (minus the research and development costs) could be placed on the market much sooner. Abuses were also inevitable as pioneer companies made minor variations in a drug component (dose, size, or color) to obtain a new patent and renew their monopoly on the market.¹⁰⁸

Pioneer and generic companies also made deals to keep the cheaper brand off the market, which resulted in the filing of anti-trust suits against some large pharmaceutical entities.¹⁰⁹ Hatch-Waxman was amended to close some of these loopholes,¹¹⁰ and special intellectual property guidelines by the Federal Trade Commission (FTC) developed in direct response to some of the anti-competitive license agreements between generic and pioneer drug companies.¹¹¹

107. See, e.g., *Ben Venue Lab., Inc. v. Novartis Pharm. Corp.*, 10 F. Supp. 2d 446 (1998).

108. See FTC Rep., *supra* note 40, ch. 3, at 12-13; *Health Registration Data Exclusivity, Biomedical Research, and Restrictions on the Introduction of Generic Drugs: Hearing Before the Subcomm. on Labor, Health and Human Services and Education and Related Agencies, Comm. on Appropriations, U.S. Senate* (1997) (statement of James P. Love, Consumer Project on Technology), at <http://www.cptech.org/pharm/senhregd.html> (last visited Feb. 16, 2005). See also Gardiner Harris, *Research Company Receives 2 Patents, Could Delay Generic Forms of Prilosec*, WALL ST. J., July 20, 2001, at B5; Sheryl Gay Stolberg & Jeff Gerth, *How Companies Stall Generics and Keep Themselves Healthy*, N.Y. TIMES, July 23, 2000, at 1; *infra* notes 368-70 and accompanying text.

109. See *infra* notes 368-70 and accompanying text.

110. Hatch-Waxman was amended in the Medicare Prescription Drug, Improvement, and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2448-63 (amending 21 U.S.C. § 355 (2003)). *But see* Sarah M. Yoho, Comment, *Reformation of the Hatch-Waxman Act, an Unnecessary Resolution*, 27 NOVA L. REV. 527 (2003); Congressman Henry Waxman, Address at the Center for Business Intelligence's Generic Drug Conference (Nov. 29, 2001) (noting that though consumers had paid for abuses of Hatch-Waxman with higher drug prices, amendments might further disrupt the balance necessary to maintain availability of generics with pioneer research), summary at <http://lists.essential.org/pipermail/ip-health/2001-December/002534.html> (last visited Mar. 24, 2005).

111. Antitrust Guidelines for the Licensing of Intellectual Property (April 6, 1995), reprinted in 4 TRADE REG. REP. (CCH) 13, 132 (1995).

Litigation resulted not only from the infringement created by the filing of an ANDA under § 271(e)(2), the Act's conditions for establishing an "artificial infringement" with one of four possible certifications, but litigation also arose as a result of the safe harbor provision of § 271(e)(1).¹¹² This section of Hatch-Waxman states:

It shall not be an act of infringement to make, use, offer to sell, or sell . . . 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.¹¹³

Not surprisingly, the language of § 271(e)(1) has come under scrutiny in litigation.¹¹⁴ The courts have particularly analyzed the phrases "solely for uses reasonably related to the development" and "under a Federal law."¹¹⁵ Early after Hatch-Waxman's passage, "solely for uses" was interpreted narrowly, allowing exemption only for activities directly involved in seeking FDA approval.¹¹⁶ Later the emphasis moved from "solely for uses" to "reasonably related."¹¹⁷ In its 1997 *Abtox* decision, the CAFC interpreted the language of the statute ("solely for uses reasonably related to") to mean that the "uses" of the infringing behavior needed only be "reasonably related to" FDA approval, not "solely related to" FDA approval.¹¹⁸ Hatch-Waxman would expand, giving safe harbor from patent infringement for trade shows, demonstrations, and recruitment since these activities could be "reasonably related" to development for eventual FDA approval.¹¹⁹

112. See *supra* text accompanying notes 105-07.

113. 35 U.S.C. § 271(e)(1) (2003).

114. See, e.g., *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 670-71 (1990).

115. *Id.* at 666-69.

116. See, e.g., *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379 (N.D. Cal. 1987).

117. See *supra* text accompanying note 113.

118. *Abtox, Inc. v. Exitron Corp.*, 122 F. 3d 1019, 1030 (Fed. Cir. 1997).

119. *Id.*

In addition to broadening the boundaries of allowed *activities* under Hatch-Waxman's safe harbor, the courts would expand the eligibility of *products* given an exemption. The phrase "under a Federal Act" would be interpreted to include, not just drugs and devices under the lengthy FDA approval process, but any product developed under federal guidelines.¹²⁰

Besides the language of the Act, the intent of Congress would be pertinent in the courts' interpretation of Hatch-Waxman's safe harbor. Hatch-Waxman was initially perceived to have provided only for those patented inventions that were affected by both sections of the Act—both the regulatory FDA process that extended into the initial patent term (before marketing could begin) and the possibility of *de facto* monopolies at the end of the term (before generic companies could complete FDA approval).¹²¹ The courts, however, would eliminate this qualification, as devices *not* affected by the lengthy FDA approval process would also be granted safe harbor.¹²² Even biotech tools eventually made successful attempts to navigate into safe harbor.¹²³

What was the reason for the enlarged boundaries and scope of Hatch-Waxman? With the courts' narrow interpretation of the experimental use exception,¹²⁴ Hatch-Waxman provided the only safe harbor for the rapidly changing biotech field, and companies sought its protection well upstream from the FDA approval process.¹²⁵ Expanded interpretation of Hatch-Waxman's safe harbor filled a chasm, particularly noticeable in U.S. Patent Law where—unlike the rest of the industrialized world—no patent exemption exists for medical-related research.¹²⁶

120. *Id.*

121. *See, e.g.,* Scripps Clinic & Research Found. v. Genentech, Inc., 666 F.Supp. 1379 (N.D. Cal. 1987).

122. *See infra* text accompanying notes 148-52.

123. *See infra* text accompanying notes 178-205.

124. *See supra* text accompanying notes 70-92.

125. *See infra* text accompanying notes 178-205.

126. *See* Thiru Balasubramaniam & Andrew Goldman, *Selected Compulsory Licensing, Governmental Use, and Patent Exceptions Provisions in Various Countries*, at <http://www.cptech.org/ip/health/cl/examples2.html> (last visited Feb. 8, 2005). *See also infra* text accompanying notes 374-77.

IV. SAFE HARBOR EXPANDED

A. *An Early Case*

The courts did not initially use Hatch Waxman's safe harbor to fill the need for an exemption for biotech tools. An example of the courts' initial reluctance to expand the exemption of § 271(e)(1) is demonstrated in the 1987 district court decision, *Scripps Clinic & Research Foundation v. Genentech*.¹²⁷ The court refused to grant safe harbor to Genentech for its infringement of the purified Factor VIII:C owned by Scripps.¹²⁸ The patents owned by Scripps included the purified form of *human* Factor VIII:C, a necessary clotting agent in human blood.¹²⁹ There was an obvious advantage and public need to produce a *recombinant* form of Factor VIII:C that could be used to treat hemophilia without the danger of transmitting HIV and other viruses.¹³⁰ The broad claims allowed in Scripps Clinic's patents is an example of a recurring problem in the biotech field whereby early biotech inventions are granted broad patents that prevent further development in the field.¹³¹

Not only was the scope of Scripps's Factor VIII:C broad, but the subject, a component of human blood, would not have been considered patentable subject matter prior to an earlier decision.¹³² In *Parke-Davis*, Judge Learned Hand ruled that a purified form of *natural* adrenaline could be the subject of a patent.¹³³ In nineteenth century decisions, the courts, including the Supreme Court, had consistently ruled that products of nature were non-patentable, but

127. *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F.Supp. 1379 (N.D. Cal. 1987).

128. *Id.*

129. *Id.*

130. *See infra* notes 291-94 and accompanying text.

131. *See generally* FTC Rep. *supra* note 40; Merges & Nelson, *supra* note 39.

132. *Parke-Davis & Co. v. H.K. Mulford & Co.*, 189 F. 95 (C.C.N.Y. 1911), *aff'd in part, rev'd in part* by 196 F. 496 (2d Cir. 1912).

133. *Id.* Previously, only the *process* of purifying natural components had been patented.

Judge Hand found precedent in two cases (including one sustaining a patent for aspirin) to support his ruling.¹³⁴ The PTO and courts have followed Hand's decision—human components are patentable. With the explosion of biotechnology on the scene in the mid-twentieth century—one of the biotech advances was the development of recombinant forms of DNA, allowing for the production of Factor VIII:C.¹³⁵

The *Genentech* court narrowly interpreted Hatch-Waxman's phrase, "solely for," to mean only activities involved in FDA approval, not just "reasonably related to FDA testing."¹³⁶ The court insisted that Genentech's commercial purpose and actions "clearly lie beyond the protection of § 271(e)(1)" as evidenced both by the statutory language and by the intent of Congress.¹³⁷ Interestingly, the district court not only found infringement of claims relating to the purity of Factor VIII:C that the recombinant form literally infringed, but also found infringement in a claim that related to the "product of a process."¹³⁸ The recombinant form was not produced without *first* using a purified form to obtain the necessary sequence, and the process by which this was initially determined was also patented by Scripps.¹³⁹ This was, by a broad definition, a research tool in that the component (*purified* Factor VIII:C) was first infringed to make *recombinant* Factor VIII:C (which then infringed another claim of the patent—the actual product).¹⁴⁰

In this decision, the court ruled that infringement had occurred, but refused to enjoin Genentech from continuing with development because of the importance of recombinant

134. *Id.* at 103. The *Kuehmsted* case cited by Hand refers to a patent for acetylsalicylic acid (aspirin)—the *natural* form originating from the bark of the willow tree. *Kuehmsted v. Farbenfabriken of Elberfeld Co.*, 179 F. 701 (7th Cir. 1910). See also MERGES & DUFFY, *supra* note 1, at 101-04 (discussing the law before and after *Parke-Davis*).

135. See *infra* notes 292-94.

136. *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379, 1396 (N.D. Cal. 1987).

137. *Id.*

138. *Id.* at 1387-88.

139. *Id.* at 1388.

140. See *supra* text accompanying note 14.

forms in treating hemophilia.¹⁴¹ On appeal in 1991 the CAFC remanded to the district court for consideration of the validity of the Scripps patent; the case, however, was settled before the district court reached a decision on remand.¹⁴² It is noteworthy that the importance of the discovery for the public was recognized and, in essence, an exception was made by the district court early in the period following passage of Hatch-Waxman by not imposing an injunction.¹⁴³ Though not comfortable in expanding Hatch-Waxman's safe harbor, on appeal the CAFC also recommended an unusual defense, recognizing the obvious benefit to the public for the recombinant form.¹⁴⁴

B. Supreme Court and CAFC Expansion

It would take expansion of the safe harbor by higher courts before actual biotech tools were openly granted an exemption under § 271(e)(1), the safe harbor provision of Hatch-Waxman. With a broadening of the Act's scope by a 1990 Supreme Court decision, district courts and the CAFC soon followed. In *Eli Lilly v. Medtronic*, the Court faced the issue of whether medical devices would be included in the non-infringement exemption.¹⁴⁵ Since the lengthy FDA approval process addressed by the portion of Hatch-Waxman providing an extension in patent term also affects Class III medical devices, the Court determined that the safe harbor of § 271(e)(1) should also be applied.¹⁴⁶ Otherwise, a patentee could receive the benefit of patent term extension without being disadvantaged by the infringement exemption given to competitors (§ 271(e)(1)). Justice Scalia, writing the majority opinion, noted that "under Federal

141. *Scripps Clinic*, 666 F. Supp. at 1401.

142. *See Genentech, Inc. v. Scripps Clinic & Research Found.*, 927 F.2d 1565 (Fed. Cir. 1991) (remanding the case to trial for consideration of patent validity). *See also* MERGES & DUFFY, *supra* note 1, at 997.

143. *Scripps Clinic*, 666 F. Supp. at 1401.

144. *See Genentech v. Scripps*, 927 F.2d 1565 (Fed. Cir. 1991). *See also* text accompanying *infra* notes 312-23.

145. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 670-71 (1990).

146. *Compare* 35 U.S.C. § 156 (2002), *with* Fed. Food, Drug & Cosmetic Act § 515 (codified as amended at 21 U.S.C. § 355) (2003) (governing premarket approval of new drugs), *and* 21 U.S.C. § 360 (governing premarket approval of medical devices) (2004). *See also Lilly*, 496 U.S. at 667.

law" denotes the entire scheme of the FDA's regulation duties, not just drugs.¹⁴⁷

In 1993 and 1997, the CAFC ensured the continued expansion of the exemption by granting safe harbor to all medical devices, not just Class III devices.¹⁴⁸ A cardiac defibrillator had been the Class III device at issue in the Court's expansion of Hatch-Waxman in *Lilly*.¹⁴⁹ Now Class I and II medical devices would also receive the benefit of an infringement defense before competitors' patents had expired, even though no lengthy FDA approval process is needed for Class I and II devices such as sterilizers and sanitary gloves.¹⁵⁰ In the *Abtox v. Exitron* decision, as well as earlier in *Chartex v. M.D. Personal Products*, the CAFC ruled that the Supreme Court's "broader holding" in *Lilly* was *not* dependent on the relationship between the patent term extension (§ 156 for pioneers) with the exemption for infringement related to FDA approval (§ 271 for generics). Rather the "entire statutory scheme of [Hatch-Waxman]" was to be considered.¹⁵¹ The court states, "In other words, the Supreme Court commands that statutory symmetry is preferable but not required."¹⁵²

Influenced by these rulings, a district court vacated its original 1991 decision that had not allowed a safe harbor for infringement of a non-Class III medical device.¹⁵³ It was no longer necessary for both portions of Hatch-Waxman, one giving the generic company an early start at the end of the pioneer's patent term and one supplying the pioneer company a patent extension, to be relevant for safe harbor

147. *Lilly*, 496 U.S. at 666-67.

148. Medical devices under classification by the FDA fall into one of three classes based on the element of risk involved to the public with the device's use. Only Class III devices (the highest risk) are under the same lengthy FDA approval process as prescription drugs. See FDA website, *supra* note 11.

149. *Lilly*, 496 U.S. at 661.

150. *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997); *Chartex Int'l v. MD. Personal Products Corp.*, 5 F.3d 1505 (Fed. Cir. 1993) (unpublished table decision).

151. *Abtox*, 122 F.3d at 1028.

152. *Id.* at 1029.

153. *Baxter Diagnostics, Inc. v. AVL Scientific Corp.*, 954 F. Supp. 199 (C.D. Cal. 1996).

to be granted.¹⁵⁴

In 1993 the CAFC ruled in *Intermedics v. Ventritex* that all of the infringing activities of Ventritex could be "reasonably related" to obtaining FDA approval for its implantable cardiac defibrillator, including the data from its foreign sales and its U.S. trade shows even though premarket approval had not yet been obtained from the FDA.¹⁵⁵ The court notes that the Supreme Court in *Lilly* rejected the argument that an infringer should not be able to develop potential markets if engaged in infringing activities "reasonably related" to FDA approval.¹⁵⁶ The *Intermedics* decision also specifically refutes that the intention of Congress was to limit the safe harbor to clinical trials shortly before an original patent's expiration.¹⁵⁷ The court states, "Congress specifically rejected an amendment to the Act that would have permitted testing only during the last year of any patent term."¹⁵⁸ Later in its 1997 *Abtox* decision, the CAFC interpreted the language of the statute ("solely for uses reasonably related to") to mean that the "uses" of the infringing behavior needed only be "reasonably related to" FDA approval, not "solely related to" FDA approval.¹⁵⁹

C. The District Courts Follow

District court decisions generally followed the expansion of the CAFC and the Supreme Court, though in 1996 the U.S. District Court for Massachusetts declined to extend the safe harbor exemption in *Biogen v. Schering*.¹⁶⁰ The court distinguished its opinion by noting that Biogen had shipped actual samples of interferon-beta overseas in preparation for marketing and ruled that such large-scale

154. See *supra* text accompanying notes 145-47.

155. *Intermedics, Inc. v. Ventritex Co., Inc.*, 991 F.2d 808 (Fed. Cir. 1993) (unpublished table opinion), *cert denied*, 513 U.S. 876 (1994).

156. Though a careful reading of *Lilly* failed to substantiate this claim other than that the Appeal Court's note on economic loss was quoted by the Court.

157. *Intermedics*, 991 F. Supp. at 810.

158. *Id.*

159. *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019, 1028 (Fed. Cir. 1997).

160. *Biogen, Inc. v. Schering AG*, 954 F. Supp. 391 (D. Mass. 1996).

production and market preparation removed it from the safe harbor exemption.¹⁶¹

In 1998, however, this same Massachusetts district court followed the higher courts' lead with a broad interpretation of Hatch-Waxman's safe harbor in *Amgen v. Hoechst*.¹⁶² The opinion stated, "[The statute's] phrase 'solely for uses reasonably related' is not equivalent to the phrase 'use is solely for purposes reasonably related.'"¹⁶³ Amgen held a patent on recombinant erythropoietin (EPO) and claimed Hoechst's activities were far more extensive than those necessary for FDA approval considering the length of the patent term remaining on Amgen's EPO patent.¹⁶⁴ In this decision the court followed the higher courts' broad interpretations and examined whether any possible infringing activities might "bear reasonable prospects of yielding information that might be relevant in the FDA approval process."¹⁶⁵ If so, the conduct would come under the safe harbor provision. Hoechst's infringement of recombinant erythropoietin is ruled exempt.¹⁶⁶

A further expansion of the § 271(e)(1) exemption was applied in 2002 when the U.S. District Court for Delaware ruled that an infringer could continue to sell a product *after* FDA approval was received.¹⁶⁷ In *Wesley Jessen v. Bausch & Lomb*, the court allowed Bausch & Lomb to continue in the safe harbor though Jessen's patent on an extended-wear contact lens had not yet expired. Bausch & Lomb claimed that the safe harbor exemption was still necessary since the FDA had requested follow-up data.¹⁶⁸ The court followed

161. *Id.* at 396-97.

162. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104 (D. Mass. 1998).

163. *Id.* at 107.

164. *Id.* Erythropoietin is the hormone that stimulates red blood cell production.

165. *Id.* at 108.

166. *Id.*

167. *Wesley Jessen Corp. v. Bausch & Lomb, Inc.*, 235 F. Supp. 2d 370 (D. Del. 2002).

168. *Id.* at 372

the broad interpretation of the Act and granted a safe harbor to Bausch & Lomb's infringing use.¹⁶⁹

One of the only district court cases not following the expansive rulings of the higher courts is an earlier decision by the U.S. District Court for the Western District of Wisconsin, in its 1999 *Infigen v. Advanced Cell Technology* (ACT) ruling.¹⁷⁰ The court rejected ACT's claimed safe harbor exemption for the use of Infigen's patented process of activating unfertilized bovine eggs.¹⁷¹ The court's opinion, however, may misread the ruling of *Lilly*.¹⁷² Judge Crabb asserts that symmetry between the safe harbor for infringement in § 271(e)(1) and the pioneer patent term extension of § 156 is required for the exemption.¹⁷³ The opinion further notes, "Defendants have cited no cases that support their reading of § 271(e)(1) as applying [to a product not] identified in § 156," and goes on to state, "My own research shows no [such] cases."¹⁷⁴ This is not the best reading of the earlier CAFC *Abtox* ruling that Judge Crabb cites,¹⁷⁵ nor does it recognize the broad holding of *Lilly*.¹⁷⁶ Considering these discrepancies, *Infigen* may not be the best decision to cite for a judicial example of a refusal to expand Hatch-Waxman's safe harbor to research tools.¹⁷⁷

The interpretation of Hatch-Waxman by the higher courts had evolved from granting an exemption only for a

169. *Id.* at 375.

170. *Infigen, Inc. v. Advanced Cell Tech. Inc.*, 65 F. Supp. 2d 967 (W.D. Wisc. 1999).

171. The patent at issue is a process for fertilizing bovine eggs to produce embryos without the addition of sperm—in essence, the potential of cloning cows.

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

173. *Infigen*, 65 F. Supp. 2d at 980.

174. *Id.*

175. *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997).

176. *Compare Infigen*, 65 F. Supp. 2d at 980 (noting that Defendant's products, though under potential FDA regulation, are *not* subject to premarket approval), *with Abtox*, 122 F.3d at 1029 (noting that the Supreme Court's "broader holding" in *Lilly* allows for devices not under rigid FDA premarket approval). *See also Lilly*, 496 U.S. at 666-67 (emphasizing the entire scheme of "by Federal law" for the Hatch-Waxman exemption).

177. *See Bristol-Myers Squibb Co., v. Rhone-Poulenc Rorer, Inc.*, 2001 WL 1512597 (S.D.N.Y.) at 5 (stating that the *Infigen* court misread the *Abtox* case).

drug undergoing FDA approval, to the provision of safe harbor for almost any product or activity that could claim to be upstream from FDA approval. The gate was opening for biotech tools to navigate into a safe harbor exemption.

D. *Biotech Tools Granted Safe Harbor*

In 2001, a district court upheld an exemption for the infringement of patented taxane derivatives being used in the development of potential taxol analogues.¹⁷⁸ Taxol, a drug used for breast cancer and other malignancies, was originally derived from natural sources.¹⁷⁹ Synthetic versions have since been developed with taxane derivatives being the *intermediates* obtained before the final synthetic form.¹⁸⁰ Though not strictly *biotech tools* under all definitions, patented derivatives are similar to research tools that block further patents unless licenses are obtained.¹⁸¹ With this new exemption for infringement of the patented derivatives, safe harbor was granted for a product that was not itself the subject of FDA approval. Research tools would be next in line to utilize the exemption.¹⁸²

Another 2001 case, *Nexell v. Amcell*, illustrates both the search for a safe harbor and some of the problems that occur with licensing of biotech tools.¹⁸³ FDA approval was pending for Amcell's stem cell separator, and safe harbor

178. Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., 2001 WL 1512597 (S.D.N.Y.), *aff'd by other grounds*, 326 F.3d 1226 (Fed. Cir. 2003). On appeal to the CAFC, Rhone-Poulenc's taxol patents were invalidated due to nondisclosure to the Patent and Trademark Office.

179. See Mike Miller, *Taxanes and Platinum Drugs in Cancer Treatment*, 2 (12) BENCHMARKS, Dec. 30, 2002, at 2, Nat'l Cancer Inst., available at <http://www.cancer.gov/newscenter/benchmarks> (last visited Mar. 29, 2005). Taxol's original source was from the Pacific Northwest yew tree. See the story of its discovery at Nat'l Res. Canada, at http://www.pfc.forestry.ca/ecology/yew/taxol_e.html (last visited Mar. 29, 2005).

180. Taxanes can also now be classified and used as treatment drugs in themselves. See Miller, *supra* note 179.

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

182. See Brian D. Coggio & F. Dominic Cerrito, *The Safe Harbor Provision of the Hatch-Waxman Act: Present Scope, New Possibilities, and International Considerations*, 57 FOOD & DRUG L.J. 161, 169 (2002).

183. *Nexell Therapeutics, Inc. v. Amcell Corp.*, 143 F. Supp. 2d 407 (D. Del. 2001), *amended by* 199 F. Supp. 2d 197 (D. Del. 2002).

was claimed for the use of Nexell's patented monoclonal antibody, a biotech tool necessary for utilization of the stem cell device.¹⁸⁴ The stem cell separator is used with stem cell transplants for numerous diseases and conditions including leukemia, lymphoma, breast cancer, and lupus.¹⁸⁵ In an autologous stem cell transplant the patient's own stem cells (undifferentiated cells that have the potential of becoming red blood cells, white blood cells or platelets) can be selected by the separator (undifferentiated stem cells are believed to be free of malignancy) and these *good* stem cells replaced back in the patient after treating the marrow to destroy the malignant cells.¹⁸⁶ The separator has the job of selecting or separating the good stem cells and does so with the assistance of the monoclonal antibodies that *stick to* the desired stem cells. Nexell had acquired the rights to these particular antibodies and granted a license to Amcell for their use in Amcell's stem cell separator.¹⁸⁷ Nexell and Amcell were in competition with each other; Nexell had its own stem cell separator that was already FDA approved and, due to a different means of selection, was not being infringed by Amcell's separator.¹⁸⁸ Nexell claimed that Amcell's activities of physician/hospital recruitment, as well as promotional trade shows and publications, were uses beyond those necessary for FDA approval.¹⁸⁹ Its monoclonal antibodies, Nexell asserted, *were* being infringed.¹⁹⁰ The district court's initial decision focused on the activities for approval of the cell separator and took the unusual course of deferring to the FDA for a decision on whether the activities were "reasonably related" to FDA approval (though it

184. *Id.* See also *infra* notes 300-04 and accompanying text.

185. See, e.g., Federico Silvestri et al., *Positive Selection of CD34+ Cells: A Short Review of the Immunoabsorption Methods Currently Available for Experimental and Clinical Use*, 2 J. OF HEMATOTHERAPY 473 (1993).

186. *Id.*

187. Nexell holds the license for the patented monoclonal antibodies from Becton Dickinson who purchased the rights from Johns Hopkins University where they were *invented* by a researcher/physician.

188. *Nexell*, 143 F. Supp. 2d at 408-09.

189. *Id.* at 414-16.

190. *Id.*

was the monoclonal antibodies at issue for infringement, not the stem cell separator).¹⁹¹

It is worth noting that these same antibodies had been the subject of previous litigation in the same court with the same judge.¹⁹² In this prior case a biotech company was litigated out of business by Nexell's predecessors—Baxter Healthcare, Becton-Dickinson, and Johns Hopkins University.¹⁹³ Though CellPro's stem cell separator had passed FDA approval and been used by 5000 patients in 300 institutions, the start-up biotech company was found guilty of infringement of the monoclonal antibodies patented by Johns Hopkins.¹⁹⁴ CellPro had negotiated with its competitor, Baxter/Johns Hopkins, regarding licensing of the antibodies but felt that the licensing fee was too high considering CellPro's advanced competitive position in stem cell technology.¹⁹⁵ In addition, CellPro decided that their own monoclonal antibodies were not infringing given that in the biotech arena it was understood the two sets of antibodies were distinct from each other.¹⁹⁶ This reasoning would be fatal as Judge McKelvie overturned the first jury's verdict, which was in CellPro's favor, and ordered a new trial.¹⁹⁷

191. *Id.* at 423.

192. *Johns Hopkins Univ. v. CellPro*, 931 F. Supp. 303 (D. Del. 1996), 978 F. Supp. 184 (D. Del. 1997), *aff'd in part, vacated in part* by 152 F.3d 1342 (Fed. Cir. 1998).

193. *Id.* See also Tyrone Beason, *Suit-Ravaged CellPro Declares Bankruptcy*, SEATTLE TIMES, Sept. 29, 1998, at C1.

194. See Avital Bar-Shalom & Robert Cook-Deegan, *Patents and Innovation in Cancer Therapeutics: Lessons from CellPro* in 80 (4) MILLBANK Q. 637, 652-53 (Dec. 2002).

195. RICK MURDOCK & DAVID FISHER, PATIENT NUMBER ONE 48-52, 252 (2000).

196. See Bar-Shalom & Cook-Deegan, *supra* note 194, at 657 (suggesting the scope of Johns Hopkins's patents was too broad). See also generally Merges & Nelson, *supra* note 39 (discussing the problem with broad patents granted in pioneer areas of biotechnology).

197. Judge McKelvie overturned and granted a new trial on the basis of a new ruling by the Supreme Court, *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996), finding claim construction in patents to be a matter of law. The first trial's jury had found that Johns Hopkins's claims were not infringed by CellPro; Judge McKelvie ordered a second trial and said that there was infringement. See MURDOCK & FISHER, *supra* note 195, at 268-69.

Judge McKelvie's unusual deferral to the FDA in the first *Nexell* decision may have been influenced by the enormous negative publicity that surrounded his 1997 *CellPro* ruling, including his punitive judgment that sent *CellPro* into bankruptcy.¹⁹⁸ In the original 2002 *Nexell* decision, Judge McKelvie granted summary judgment to Amcell, but this decision would then need "clarification" when *Nexell* queried the FDA as to which of Amcell's activities could be deemed exempted by Hatch-Waxman.¹⁹⁹ The FDA declined the responsibility for determining which prior activities might be "reasonably related" to potential FDA approval.²⁰⁰ The amended decision states that Amcell's activities related to FDA trials are exempt under Hatch-Waxman's safe harbor,²⁰¹ but those activities not related to FDA trials can be litigated in respect to licensing violations.²⁰² Which activities are *not* related to FDA approval is not clarified.²⁰³ The court tries to evade the question on research tools by equating the stem cell separator *with* the monoclonal antibodies as one invention, a medical device exempt under Hatch-Waxman.²⁰⁴ Nonetheless Judge McKelvie's opinion has been interpreted to expand the Act's provision to include research tools, and it does grant safe

198. See, e.g., Bill Richards, *Cancer Fighters: How a Corporate Feud Doomed Human Trials of Promising Therapy*, Wall St. J., Aug. 6, 1999, at A1; see also Beason, *supra* note 193; MURDOCK & FISHER, *supra* note 195, at 259-60.

199. *Nexell Therapeutics, Inc. v. Amcell Corp.*, 143 F. Supp. 2d 407 (D. Del. 2001), amended by 199 F. Supp. 2d 197, 201 (D. Del. 2002). See also text accompanying *supra* note 191.

200. *Nexell*, 199 F. Supp. at 205.

201. *Id.*

202. *Nexell*, 199 F. Supp. at 207. The opinion does not deal with the licensing issue. *Nexell* claimed that Amcell violated the license for use of the monoclonal antibodies since the agreement expressly excluded "research dedicated to a therapeutic in vivo use" and though Amcell might be using the patented antibodies only for in vitro (test tube) use, the "research [is] dedicated to in vivo [in the body] use" and should therefore be excluded. Judge McKelvie states that the licensing issue is yet to be resolved though it appears to be key to the entire issue. *Id.* at 206.

203. *Id.*

204. *Id.* at 206. The opinion calls the separator an "allegedly infringing device" but it is the monoclonal antibodies that are infringed, not the medical device seeking FDA approval.

harbor to a patented biotech tool, the monoclonal antibodies.²⁰⁵

E. *Integra v. Merck*

The tide of expansion was stemmed in 2003 when the CAFC declined to extend safe harbor to a research tool in *Integra v. Merck*.²⁰⁶ The court reexamines the issues of congressional intent and statutory language, forming different opinions from those reached in prior decisions.²⁰⁷ For example, the court emphasizes that the House Committee proposing the Hatch-Waxman Act intended that the infringement upon a patent holder's rights would be "*de minimis*" rather than "substantial."²⁰⁸ The court also examines the language of the statute and, though conceding that the term "reasonably" allows for some experiments outside of those needed for FDA approval, states, "The exemption . . . does not endorse an interpretation of § 271(e)(1) that would encompass drug development activities far beyond those necessary to acquire information for FDA approval . . ." ²⁰⁹ The court, therefore, refuses to extend the "reach of the reasonable relationship test" to biotech tools like the short protein peptide patented by *Integra*.²¹⁰ *Merck*, though discovering a valuable use for the peptide sequence in identifying potential cancer drugs, is not exempt from infringement.²¹¹

This establishes a definite break in the trend of expansion that started with the Supreme Court in *Lilly* (need not be a generic *drug*) to the CAFC's decisions in *Intermedics*

205. See William L. Warren et al., *Experimental Uses and Research Tool Licensing Alternatives*, presented at the Biotechnology Georgia ICLE (April 2003), available at http://www.sablaw.com/files/tbl_s47Details%5CfileUpload265%5C2552%5CExperimentalUsesResearchToolLicensing.pdf (last visited Feb. 18, 2005). See also generally Coggio & Cerrito, *supra* note 182.

206. *Integra Lifesciences I, LTD. v. Merck KgaA*, 331 F.3d 860 (Fed. Cir. 2003), *cert granted*, 125 S. Ct. 823 (2005). See also text accompanying *supra* notes 16-33. Will the Supreme Court seal the hole in the dike temporarily plugged by the CAFC, or open the floodgates? See *infra* note 397.

207. *Id.*

208. *Id.* at 865 (quoting from H.R.Rep. No. 857, at 8).

209. *Id.* at 867. See also *supra* text accompanying notes 155-59.

210. *Id.* at 866. See also *supra* text accompanying notes 155-59.

211. *Integra*, 331 F.3d at 872. See *supra* text accompanying notes 16-22.

(activities need only be *reasonably related* to potential FDA approval) and *Abtox* (*any* patented product under FDA regulation can be exempt), and continued on through a district court's opinion in *Nexell* (research tools *not* seeking FDA approval can be exempted).²¹²

The courts have come full circle back to the decision in the early case discussed, *Genentech*.²¹³ In that case, Genentech had already produced recombinant Factor VIII:C, infringing Scripps's patent of the purified form.²¹⁴ The district court, though ruling against an exemption for Genentech under Hatch-Waxman's safe harbor, refused to grant an injunction because of the potentially enormous benefit for the treatment of hemophilia with a recombinant form rather than with Factor VIII extracted from human blood.²¹⁵ On appeal, the CAFC then found a potential way to get around Scripps's broad pioneer patent. Now, in *Integra*, the CAFC refuses to extend the safe harbor provision to Merck's activities, but also remands for reconsideration of the high royalties assessed by the lower court for Merck's use of the peptide.²¹⁶ Still the court opines that to offer exemption for the downstream development of potential drugs "would effectively vitiate the exclusive rights of patentees owning biotechnology tool patents."²¹⁷ Justice Newman offers a spirited dissent in *Integra*, bemoaning the demise of the common law experimental exemption and distinguishing between research "tools" and the peptide "composition" at issue.²¹⁸

212. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 669-71 (1990); *Intermedics, Inc. v. Ventritex Co., Inc.*, 991 F. 2d 808 (Fed. Cir. 1993); *Abtox, Inc. v. Exitron Corp.*, 122 F. 3d 1019 (Fed. Cir. 1997); *Nexell Therapeutics, Inc. v. Amcell Corp.*, 143 F. Supp. 2d 407 (Del. 2001), *amended by* 199 F.Supp.2d 197 (Del. 2002).

213. *See supra* text accompanying notes 127-42.

214. *Scripps Clinic & Research Found. V. Genentech, Inc.*, 666 F. Supp. 1379, 1388 (N.D. Cal. 1987). *See also supra* text accompanying notes 127-42.

215. *Id.* at 1404. *See also supra* text accompanying notes 127-42.

216. *Integra*, 331 F.3d at 872. *Integra* was originally awarded \$15,000,000 in damages and fees, but the CAFC remanded for a smaller award.

217. *Id.* at 867.

218. *Id.* at 878.

Royalties without punitive damages are really a *de facto* compulsory license.²¹⁹ Unlike the ruling in *CellPro* where total damages of \$15.6 million were upheld, the CAFC in *Integra* reversed the lower court's \$15 million fees and damage award against Merck, and remanded for consideration of a more reasonable award.²²⁰ It is the courts deciding which biotech tools are exempt, which infringers will be the benefactors of *de facto* compulsory licensing, and which biotech companies will stay in business. A better solution is needed.

V. IS THERE EXPERIMENTAL USE AFTER HATCH-WAXMAN?

A. Roche and Pre-Madey

With an experimental use defense effectively cut off from the medical research field after *Roche*, it was a natural outcome for companies to test the judicial waters around Hatch-Waxman's safe harbor. Few examples exist of an experimental use defense being claimed in the two decades following passage of Hatch-Waxman, prior to *Madey v. Duke*.

In one of the handful of cases, the defense tries to get the court to broaden the criteria for the experimental use exemption.²²¹ In 1990 the defendant's attorney in *Deuterium Corp. v. United States* argued for the establishment of a defense of experimental use, with criteria that are reserved by the PTO and courts in determining whether a *first party's* use is experimental.²²² An inventor's own, first party, use of his invention prior to patent application bars the right to a patent if the invention has been in public use for over one year, unless that use is for the perfecting of the invention.²²³ In that case the inventor's own use is experi-

219. See *Atlas Powder Co. v. Ireco Chems.*, 773 F.2d 1230, 1233 (Fed. Cir. 1985) (noting that when injunctions are not granted "infringers could become compulsory licensees").

220. *Integra*, 331 F.3d at 872. See also MURDOCK & FISHER, *supra* note 195, at 246.

221. *Deuterium Corp. v. United States*, 19 Cl.Ct. 624 (1990).

222. *Id.* at 632.

223. See MERGES & DUFFY, *supra* note 1, at 558-59, 575-82.

mental and does *not* prevent a patent from being granted.²²⁴ The *Deuterium* court found the first party experimental use criteria inapplicable to the common law experimental use defense for third party infringement.²²⁵

Interestingly, the *Deuterium* court did not emphasize a commercial purpose in its rejection of the defense, as did the CAFC in *Roche*; rather the court cited precedent and ruled that if the infringing use was related to the regular business conducted by a company, it could not be experimental.²²⁶ This is the same emphasis and precedent followed by the CAFC in *Madey*. The experimental use defense was not rejected because Duke University's use of the laser gun had been proven to be a commercial venture, but rather because research tools were part of Duke University's regular business.²²⁷

Research tools were not the issue in *Deuterium*, but rather the issue was government licensing of patented items—typical of many of the pre-Hatch-Waxman experimental use cases. In a 1998 district court case, research tools *are* the issue.²²⁸ In *Giese v. Pierce Chemical Co.*, the patents cover a method for detection of cancer cells.²²⁹ The defendants are charged with contributory infringement because the kits they sell, containing chemical reagents, will be utilized by purchasers using the patented method.²³⁰ The defendants correctly assert that there can be no contributory infringement without direct infringement.²³¹ Since many of the purchasers of the kits are universities conducting research that is exempt from infringement under experimental use—with no direct infringement by these universities, there is no contributory infringement, maintains *Pierce*.²³² The district court states, "*Roche* established a restrictive definition of the traditional common law doc-

224. *Id.* at 586-91.

225. *Deuterium*, 19 Cl.Ct. at 632.

226. *Id.* at 631-32.

227. *Madey v. Duke Univ.*, 307 F.3d 1351, 1361-62 (Fed. Cir. 2002).

228. *Giese v. Pierce Chem. Co.*, 29 F. Supp. 2d 33 (D. Mass. 1998).

229. *Id.* at 34.

230. *Id.*

231. *Id.* at 35.

232. *Id.*

trine, but in no way eliminated it.”²³³ The court does not evaluate whether the research conducted by purchasers of the kits qualifies as experimental use, noting that there is no agreement on what proportion of the kits were sold to academic researchers.²³⁴ The implication of the court’s dicta is that the use of the kits by university researchers is exempt from infringement though no determination is possible for a summary judgment on this claim.²³⁵

In 2000 the CAFC upheld a lower court’s ruling in *Embrex, Inc. v. Service Engineering Corp.* (SEC) that found tests performed by defendants’ scientists, attempting to design around the method patent licensed by Embrex, were not defensible as experimental use.²³⁶ To *design around* a claim from a patented invention is not illegal; it is a common means in industry for developing competitive technology and products.²³⁷ In many cases, particularly when a technology is not the pioneer in a field, the PTO rejects broad patent claims that would prevent designing around by competitors.²³⁸ Embrex was the exclusive licensee of a government-patented technology for inoculating birds from disease while still in the egg.²³⁹ The patented claim for the inoculation method was not so broad as to cover injection anywhere into the egg; rather the vaccine was to be injected into either the amnion or the yolk sac.²⁴⁰ The *design around* by SEC attempted to inoculate into a different part of the egg that would not infringe the patented method. SEC was not successful, accidentally hitting an area of egg claimed in

233. *Id.* at 36.

234. *Id.* at 35.

235. *Id.* at 37.

236. *Embrex, Inc. v. Serv. Eng’g Corp.*, 216 F.3d 1343, 1352 (Fed. Cir. 2000).

237. See FTC Rep., *supra* note 40, ch. 3, at 10 (noting the rise in innovation by designing around patents). See also *‘Designing Around’ Valid U.S. Patents*, a course offered by Patent Resources Group, April 2005. Course syllabus, at <http://www.patentresources.com> (last visited March 5, 2005).

238. There is no mention of prosecutorial history estoppel (PHE) in the case, but it would be interesting to know whether the original application to the PTO had tried to claim injection into any area of the egg, with that claim being rejected by the PTO as too broad (with a more narrow claim of injection only into the amnion or yolk sac then allowed). Since literal infringement occurred, PHE is not specifically applicable.

239. *Embrex*, 216 F.3d at 1346.

240. *Id.*

Embrex's patent.²⁴¹ It is important to note that it was not SEC's unsuccessful attempt to produce and sell injection machines that was found to be infringing.²⁴² The infringement was in hitting the area of the egg claimed in the patent application and, though it was an accidental infringement while experimenting, no defense was available.²⁴³

Since SEC had a commercial motive for attempting to design around the inoculation method, the court did not need to apply the *Pitcairn* standard, also used by the district court in *Deuterium*, that disallowed an experimental use defense if the activity was part of an entity's normal business.²⁴⁴ The *Embrex* court instead cites a commercial motive and notes the *Roche* opinion which would not "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."²⁴⁵

B. *Madey v. Duke*

In 2002 a district court decision in *Madey v. Duke University* was overturned as the CAFC denied the school an experimental use exemption for a patent used under a federal research grant.²⁴⁶ In June of 2003 the Supreme Court denied certiorari; the CAFC decision against Duke University, for its use of the patented free electron laser technology, stands.²⁴⁷

241. *Id.* at 1347.

242. *Id.* at 1352.

243. *Id.* at 1353. Interestingly, a concurring opinion in *Embrex* argues that since the Supreme Court has removed the issue of *intent* from patent infringement, no experimental use exemption exists. See *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 36 (1997) (stating that proof of intent is unnecessary to determine literal infringement).

244. See *supra* text accompanying note 226.

245. *Embrex, Inc. v. Serv. Eng'g Corp.*, 216 F.3d 1343, 1349 (Fed. Cir. 2000) (quoting *Roche Prods. Inc. v. Bolar Pharm. Co.*, 733 F.2d 858, 863 (Fed. Cir. 1984)).

246. *Madey v. Duke Univ.*, 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 958 (2003).

247. *Id.*

John Madey, the research professor holding the patents on the highly regarded laser technology, was removed as director of the Free Electron Laser Laboratory at Duke University, resulting in his resignation from the university in 1998.²⁴⁸ Duke continued to operate some of the equipment in the lab that had been originally developed by Madey while he was a professor at Stanford University in the 1980s.²⁴⁹ Madey sued Duke for infringement and though the district court decision held for the university, on appeal to the CAFC, Duke's contention of experimental use was rejected.²⁵⁰

The CAFC agreed with Madey that the district court had applied too broad a standard in respect to the experimental use doctrine on one patent at issue while affirming the lower court's ruling in respect to nonuse by Duke on another of Madey's patents.²⁵¹ The district court had rejected Madey's claim that part of Duke's business was "developing possible commercial applications," but the CAFC notes that commercial intent is only one type of conduct "immunize[d]" from an experimental use exception.²⁵² "The correct focus," states the court, "should not be on the non-profit status of Duke but on the legitimate business Duke is involved in."²⁵³

The precedent relied on in *Madey*, as well as that cited earlier by the *Deuterium* court, is found in the *Pitcairn* ruling—it is not an exempted use if the experiments are conducted as part of the normal course of business.²⁵⁴ The *Madey* opinion is consistent with the narrow interpretation of experimental use found in *Roche* and *Embrex*, but is the

248. *Id.* at 1352-53.

249. *Id.* at 1352.

250. *Madey v. Duke Univ.*, 266 F. Supp. 2d 420 (M.D.N.C. 2001), *aff'd in part and rev'd in part*, 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 958 (2003).

251. *Madey*, 307 F.3d at 1361.

252. *Id.*

253. *Id.* at 1362.

254. *Id.* See *Deuterium Corp. v. United States*, 19 Cl.Ct. 624, 631 (1990); *Pitcairn v. United States*, 547 F.2d 1106, 1125-26 (Ct. Cl. 1976). See also generally Tom Saunders, Note, *Renting Space on the Shoulders of Giants: Madey and the Future of the Experimental Use Doctrine*, 113 YALE L. J. 261 (2003).

reliance that these decisions place on *Pitcairn* for experimental use law really applicable?²⁵⁵ In *Pitcairn* the rejection of experimental use if the activities “are in keeping with the legitimate business of the using agency” had little to do with finding a definitive explanation of experimental use and everything to do with making sure that a licensee received due compensation.²⁵⁶ The suit had been in litigation for over twenty years; it involved helicopters and parts worth \$639 million that had been produced for the U.S. government from 1946-64, with the United States planning on compensation of only \$532,279.²⁵⁷ The government’s excuse for such a low reimbursement for the patented products? A number of the helicopters, for part of the time, were only being tested—it was experimental use.²⁵⁸

This was a taking, not an experimental use defense for infringement, and the court rightly determined that compensation was owed, though it is unfortunate that the special circumstance of governmental mandatory licensing should be confused with a private party’s patent infringement.²⁵⁹ When the government uses a patented invention, it is considered a taking of property in the eminent domain.²⁶⁰ Patents *are* called intellectual *property*, and therein lies part of the problem.²⁶¹

255. See *Pitcairn*, 547 F.2d at 1106.

256. *Id.* at 1125-26.

257. *Id.* at 1111.

258. *Id.* at 1124-25.

259. *Id.* at 1114-15. See also KENNETH L. PORT ET AL., LICENSING INTELLECTUAL PROPERTY IN THE DIGITAL AGE 197 (1999).

260. See *Pitcairn*, 547 F.2d at 1114.

261. The term *property* was not used in respect to patents until the 1950’s in Europe with the combination of two bureaus—one for Industrial Property and one for Literary and Artistic Works. In English *intellectual property* was first used with the 1967 creation of the World Intellectual Property Organization. See George Koumantos, *Reflections on the Concept of Intellectual Property*, reprinted in GRAEME B. DINWOODIE ET AL., INTERNATIONAL AND COMPARATIVE PATENT LAW 5 (2002). See also *supra* note 46 and accompanying text. But see 35 U.S.C. § 261 (1982) (giving patents the attributes of property).

C. *Is an Invention Property?*

The U.S. Framers, unlike their European counterparts, considered it somewhat differently.²⁶² Thomas Jefferson stated it succinctly,

He who receives an idea from me, receives instruction himself without lessening mine; as he who lites his taper at mine, receives light without darkening me. That ideas should freely spread from one to another over the globe, for the . . . improvement of his condition, seems to have been . . . designed by nature . . . incapable of confinement or exclusive appropriation. Inventions then cannot, in nature, be a subject of property.²⁶³

Lawrence Lessig reminds his readers of the difference in intellectual property in Europe where the philosophical basis is the moral right of the inventor.²⁶⁴ He recognizes the distinctions of *real* versus *intellectual* property and philosophizes, "With ordinary property, the law must both create an incentive to produce and protect the right of possession; with intellectual property, the law need only create the incentive to produce."²⁶⁵ The question in respect to experimental use needs to be based, not on the moral or natural right of the original inventor, not on a *sweat of the brow* doctrine, but rather on what produces the greatest benefit to the public.²⁶⁶

Therefore, the *Madey* court's emphasis on the *Pitcairin* ruling pertaining to the relationship of the business, rather than the commercial motive used to decide *Roche* and *Embrex*, is misplaced. *Pitcairin*, with its primary motivation being to prevent a taking without compensation, implies a *natural right* to property or *reward for labor*, prominent in European patent laws.²⁶⁷ It is not the

262. *Id.*

263. THOMAS JEFFERSON: WRITINGS 1291-92 (Merrill D. Peterson ed., The Library of America 1984).

264. LAWRENCE LESSIG, CODE AND OTHER LAWS OF CYBERSPACE 134 (1999).

265. *Id.* at 133.

266. *Feist Publ., Inc. v. Rural Tel. Serv. Co.*, 499 U.S. 340 (1991) (finding throughout that a *sweat of the brow* theory is not the basis for U.S. intellectual property law). See also *supra* notes 45-54 and accompanying text.

267. See *supra* note 261.

economic/utilitarian basis consistent with the purpose and philosophy underlying U.S. Patent Law.²⁶⁸ (Ironically, might *moral right* or *sweat of the brow* be the *real* motivation behind the *Madey* decision? It was John Madey's laser equipment that he brought with him when first employed by Duke University. Even the Solicitor General's brief to the Supreme Court calls *Madey* primarily an employment dispute.²⁶⁹)

The *Madey* ruling has been widely criticized by institutions and adjudicators alike.²⁷⁰ Justice Newman makes use of her dissent in the *Integra* decision to vent dissatisfaction with the "sweeping dictum" in *Madey*, as well as the *Integra* ruling.²⁷¹ She links together Hatch-Waxman's safe harbor and the common law experimental use exemption noting, "[T]he statutory immunity of [Hatch-Waxman's safe harbor] takes effect wherever the research exemption ends."²⁷²

The necessity for a research exemption is reiterated in a brief filed with the request for certiorari in *Madey v. Duke*.²⁷³ The Consumer Project on Technology and Public Knowledge opens its brief with a warning, "If patent law too strongly favors incentives for initial invention, it discourages sequential invention."²⁷⁴ An opposite opinion is offered by the Solicitor General's brief arguing, "When the public is permitted to engage in the unlicensed use of patented inventions without incurring liability for infringement, even with respect to 'experimental' uses that may offer other scientific benefits, the incentives provided by the patent laws are diminished and the nature of the patent 'bargain'

268. See *supra* note 46 and accompanying text.

269. See Mary Ann Liebert, *Certiorari Denied in Madey v. Duke*, 22 (5) BIOTECHNOLOGY L. REP. 485, 486-87 (2003) (quoting from Br. of Amicus Curiae Solicitor General in support of Madey for writ of cert. by Duke University to the Supreme Court). *Madey v. Duke*, 539 U.S. 958 (2003).

270. See, e.g., Saunders, *supra* note 254, at 262.

271. *Integra Lifesciences I, Ltd. v. Merck KgaA*, 331 F.3d 860, 878 n. 10 (Fed. Cir. 2003) (Newman, J., dissenting), *cert granted*, 125 S. Ct. 823 (2005).

272. *Id.* at 876.

273. Br. of Amicus Curiae of the Consumer Project on Tech. & Pub. Knowledge in supp. of pet'r, Duke University, for writ of cert. to the Supreme Court. *Duke v. Madey*, 539 U.S. 958 (2003) (No. 002-1007), at 3.

274. *Id.*

altered.”²⁷⁵ What both briefs have in common is the understanding that patent law is based on a bargain theory of reward as an incentive for the public’s benefit.²⁷⁶

VI. WHAT’S THE PROBLEM?

A. *Broad Infringement Exemptions Denied, but Broad Patents Allowed*

The elimination of Hatch-Waxman’s safe harbor for research tools in *Integra* and the denial of an experimental use exception for a research tool in *Madey*, effectively negate the possibility of patented biotech tools being exempted from infringement without licensing from patent holders.

Though a broad interpretation of the infringement exemptions is denied to biotech tools, the broad pioneer patent that stifles improvement, innovation, and competition for twenty years is still available and being readily granted to biotech tools.²⁷⁷ Companies that have been awarded broad pioneer patents in research tools, described by the Supreme Court as “a patent covering a function never before performed, a wholly novel device [so] as to mark a distinct step in the progress of the art,” have the superior bargaining position in any licensing transaction.²⁷⁸ The theory behind the granting of broad patent rights for the first to develop a new technology is that the first inventor has both the incentive and head start to facilitate further innovation, thereby benefiting the public.²⁷⁹ In reality, biotech research is more about a race than

275. See Liebert, *supra* note 269, at 485 (quoting from Br. of Amicus Curiae Solicitor General in support of Madey for writ of cert. by Duke University to the Supreme Court). *Madey v. Duke*, 539 U.S. 958 (2003).

276. See JOYCE, *supra* note 46.

277. See FTC Rep., *supra* note 40, Exec. Summ., at 7 (“[Q]uestionable patents can introduce new kinds of licensing difficulties, such as royalties stacked one on top of another, and can increase uncertainty . . . complicating business planning.”); *id.*, ch. 3, at 23-24 (discussing the possibility of an anticommons effect with biotech patents); *infra* note 309. See also generally Merges & Nelson, *supra* note 39.

278. *Westinghouse v. Boyden Power Brake Co.*, 170 U.S. 537, 561-62 (1898).

279. See, e.g., Bar-Shalom & Cook-Deegan, *supra* note 194, at 663.

invention, and broad patents mean only that no further research can stem from that patented discovery without permission. The PTO maintains that these strict patent rules prevent the attachment of "free riders" and keep the system intact in respect to reward as an incentive for research, with a resulting benefit to the public. The reality is that no one running in a race is a "free rider."²⁸⁰

Consider this scenario—Corporate Behemoth A holds the patent on a biotech tool that Behemoth B would like to license for a promising search of new biologics to treat leukemia. Behemoth A already markets a leukemia treatment and plans on using the patented biotech tool on other developments, or perhaps on no research at all. Is this illegal? Not at all—though patent misuse can be claimed as a defense by an infringer, the courts have upheld the rights of companies to block or simply hold on to patented technology.²⁸¹ The public loses.

This is not the only scenario possible with large corporate entities. Behemoth A could agree to negotiate a license with Behemoth B but demand a royalty rate and/or upfront payments that are simply too high or unreasonable. With a high risk that new research will not result in the development of a commercially viable product,²⁸² Behemoth

280. See, *id.* at 657 (noting that *CellPro* was not a "free-rider"). See also HALL, *infra* note 338.

281. Patent misuse is an equitable defense for an accused patent infringer, and is a means of limiting patent anticompetitive practices that do not rise to the level of antitrust violations. See *Mallinckrodt, Inc. v. Medipart, Inc.*, 976 F.2d 700 (Fed. Cir. 1992). *But see In re Indep. Serv. Org. Antitrust Litig. v. Xerox Corp.*, 203 F.3d 1322 (Fed. Cir. 2000) (upholding a patent holder's right to refuse to license or sell patented parts); *B. Braun Medical, Inc. v. Abbott Lab.*, 124 F.3d 1419 (Fed. Cir. 1997); *Continental Paper Bag Co. v. Eastern Paper Bag Co.*, 210 U.S. 405 (1908).

282. See, *e.g.*, ROBBINS-ROTH, *supra* note 13, at 112, 123 (noting that it can take 15 years and \$500 million from discovery of a new potential drug to marketing, or of 5000 compounds that are involved in preclinical testing, only five will go to human testing and only one of those will be marketed, though the time can be considerably less for a biologic). *But see James Love, Call for More Reliable Costs Data on Clinical Trials*, in MARKETLETTER 24-25 (Jan. 13, 1997) (noting discrepancies in pharmaceutical reporting of research & development costs), available at <http://www.cptech.org/pharm/marketletter.html> (last visited Feb. 17, 2005); Ralph Nader & James Love, *Federally Funded Pharmaceutical Inventions*, Test. before the Special Comm. on the Aging, February 24, 1993 (noting that much of the research for new drug development is partially funded

B's board may reject the offer and forget the leukemia drug. The public loses.

In yet another scenario, Behemoth B rejects the inflated licensing offer of Behemoth A, but decides to infringe and do the research anyway. In the past this might have been a better risk than paying an excessive fee for a license that ends up producing no new product or development. Before *Integra*, Behemoth B might have been granted safe harbor from infringement. After *Integra*, it may be only the companies close in time to commercialization and FDA approval of a product that are favored with a safe harbor exemption.²⁸³ (Keep in mind that Behemoth A and B are not the only possible players in these analogies to real-life situations.²⁸⁴ Corporate Shrimp A can also make unreasonable demands, or choose to grant an exclusive license to Behemoth A who allows the patented biotech tool to sit idle. Or, Shrimp B and Behemoth C may have already combined resources, blocking Behemoth B's development in a particular field.²⁸⁵)

The *Integra* ruling appears to result in decreased innovation, but could it actually have a positive effect by motivating larger companies to obtain licenses?²⁸⁶ Not necessarily—companies may still find it less risky to infringe,

by public monies), available at <http://www.cptech.org/pharm/pryor.htm> (last visited Feb. 17, 2005). See also *infra* notes 348-55 and accompanying text.

283. *Integra Lifesciences I, Ltd. v. Merck KgaA*, 331 F.3d 860 (Fed. Cir. 2003), cert granted, 125 S. Ct. 823 (2005). See also *infra* note 397.

284. See ABATE, *supra* note 6, at 112-13 (characterizing the market for biotech tools as "a chaotic arena" with "too many small companies"); OLIVER, *supra* note 1, at 201 (describing the alliances formed between small biotech startups and large pharmaceuticals); BERNICE SCHACTER, ISSUES AND DILEMMAS OF BIOTECHNOLOGY 94 (1999) (reporting of \$1.3 billion investment deals of biotech companies with large pharmaceuticals in 1996 and more recently at least 76 alliances with almost exclusively large pharmaceuticals and biotechs). See also Jon F. Merz, *Discoveries: Are There Limits on What May Be Patented?*, in WHO OWNS LIFE?, *supra* note 1, at 99, 102-11 (discussing a particular grievous patent licensing case).

285. See, e.g., ABATE, *supra* note 6, at 45. See also FTC Rep., *supra* note 40, ch. 3, at 17 (noting that biotech companies frequently partner with pharmaceutical companies for commercialization of a product). But see *id.* at 23-25 (discussing that blocking or royalty stacking is a possibility).

286. See Nicholas Groombridge & Sheryl Calabro, *Integra Lifesciences v. Merck – Good for Research or Just Good for Research Tool Patent Owners?*, 22 (5) BIOTECHNOLOGY L. REP. 462 (2003); Charles Raubicheck et al., *Integra v. Merck: A Mixed Bag for Research Tool Patents*, in 21 NATURE BIOTECHNOLOGY 1099-1101 (2003).

particularly if the *Integra* ruling means biotech tool patent holders will expect higher licensing fees. Also, an infringement does not necessarily mean that punitive damages will be imposed by the court.²⁸⁷ If the discovery is important enough, court-imposed royalties may be no more than a licensing fee, and there is a chance that the court will grant safe harbor or find the original patent invalid.²⁸⁸ Injunctions are also less likely to occur if the infringing invention or activity is close to producing a marketed product.²⁸⁹

B. *Biotech Tools Are Crucial*

Biotech tools are absolutely crucial to medical research, and patents on these tools need not deter sequential innovation if they are reasonably and accessibly licensed.²⁹⁰ The story of the revolutionizing technique that resulted in genetic engineering is a case in point.²⁹¹ In 1973 two scientists inserted a gene for a particular mammalian protein into a bacterial host cell, with the bacteria then acting as a mass production factory for that specific protein.²⁹² The scientists patented the technology on the advice of their university employer, but the licensing has been available to all.²⁹³ The result is the genetic expression of recombinant proteins including the interferons, human growth hormone,

287. See text accompanying *supra* note 220.

288. See text accompanying *supra* notes 219-21.

289. See generally Warren, *supra* note 205.

290. See, e.g., FTC Report, *supra* note 285.

291. Stanley N. Cohen et al., *Construction of Biologically Functional Bacterial Plasmids In Vitro*, 70 PROC. NAT'L ACAD. SCI. 3240 (1973).

292. See, e.g., RIFKIN, *supra* note 1, at 11-12 (calling the Cohen-Boyer technique a "feat . . . rival[ing] the importance of harnessing of fire" and "the most dramatic technological tool to date in the growing biotechnological arsenal"). It is interesting to note, however, that simultaneous development can be considered evidence of *obviousness*, MERGES & DUFFY, *supra* note 1, at 747, in which case the Cohen-Boyer technique would be unpatentable since others were gene splicing at the same time. See, e.g., LISA YOUNT, BIOTECHNOLOGY AND GENETIC ENGINEERING 6-7 (2000) (noting the first genetic engineering experiments in the laboratory of Paul Berg at Stanford University).

293. See, e.g. YOUNT, *supra* note 292, at 18-19 (noting that Herbert Boyer would later co-found Genentech, the first company to produce recombinant insulin and the first biotech company to be publicly owned). See ROBBINS-ROTH, *supra* note 13, at 13-28 (detailing the events leading to the start of Genentech). See also text accompanying *supra* notes 127-44.

Factor VIII:C, EPO, insulin, vaccines, and so on as the list continues to grow.²⁹⁴

Polymerase chain reaction (PCR) is another biotech tool that has changed the lives of all within the past two decades.²⁹⁵ Miniscule amounts of DNA—from a microscopic fiber, a human hair, or semen—can now be reproduced in quantities vast enough for identification.²⁹⁶ The resulting value to the science of forensics is widely known, but the discovery has been no less important to biotech and medical research in the mapping of the human genome, for example, and in the diagnosis of numerous diseases and conditions.²⁹⁷ PCR was invented in 1983 and already in wide use in academia when Roche acquired the license to the technology for \$300 million in 1991.²⁹⁸ Although Roche did not block basic research, the potential to block was there and may only have been thwarted by intense lobbying from the research community.²⁹⁹

Also crucial to the twentieth century's advances in medicine, and also widely available to scientific researchers, has been the innovating discovery of monoclonal antibodies.³⁰⁰ Monoclonal antibody technology was developed in 1975 by two scientists who would be awarded the Nobel

294. See RIFKIN, *supra* note 12 and accompanying text. The story of *recombinant human growth hormone* is another fascinating example, as a form of Mad Cow Disease was found to have affected some humans given *animal growth hormone*; a moratorium was declared until the recombinant human form was developed. See National Institute of Neurological Disorders and Stroke website, at http://www.ninds.nih.gov/disorders/cjd/detail_cjd.htm (noting the story of Creutzfeldt-Jakob Disease or Mad Cow developed from growth hormone) (last visited Mar. 14, 2005).

295. See YOUNT, *supra* note 292, at 26-27.

296. *Id.*

297. See, e.g., SCHACTER, *supra* note 284, at 84; Weissmann, *supra* note 8, at 141-42.

298. See Suzanne T. Michel, Comment, *The Experimental Use Exception to Infringement Applied to Federally Funded Inventions*, 7 HIGH TECH. L.J. 369, 387-88 (1992).

299. *Id.*

300. See e.g., STEPHEN S. HALL, A COMMOTION IN THE BLOOD: LIFE, DEATH, AND THE IMMUNE SYSTEM 397-98 (1997) (calling the development of monoclonals "breathtaking," "stunn[ing]" and "promis[ing] a revolution in human diagnostics and therapy").

prize for their work.³⁰¹ Kohler and Milstein discovered that by injecting a mouse with an antigen for a particular antibody, cells from the mouse's spleen could then be fused with malignant cells for a mass production of the exact antibody desired.³⁰² The uses of monoclonal antibodies for medical diagnosis, research, and treatment are myriad. Their availability has not, however, been dependent upon the generosity of the patent holder or a licensee as was the case with genetic engineering and PCR, respectively.³⁰³ The production of these specific antibodies, credited along with the invention of recombinant DNA as the two most important "pathbreaking" innovations in the biotech revolution, was widely available because the technology was never patented.³⁰⁴

In contrast to the availability of genetic engineering, PCR, and monoclonal antibodies, the story behind the patenting of the screening test for two genes linked to breast cancer is not as successful in respect to public access and affordability.³⁰⁵ The biotech company holding the patent enforced its rights against researchers and charged an exorbitant price for the screening technology, though the genes were first identified by part of a coordinate group of researchers from academia and the National Institute of Health (NIH).³⁰⁶

301. *Id.*

302. *Id.*

303. *See, e.g.,* Merges & Nelson, *supra* note 39, at 905-06.

304. *Id.* However, the validity of a broad patent for a method of producing monoclonal antibodies has been upheld by the CAFC, *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (1986), in spite of the wide-spread contention in the industry that the Hybritech patented method was *obvious* since it was a common method used to produce *polyclonal* antibodies. *See* MERGES & DUFFY, *supra* note 1, at 745-47. *See also* ROBBINS-ROTH, *supra* note 13, at 49-52 (detailing the beginning of Hybritech as a biotech company).

305. *See* Donna M. Gitter, *International Conflicts over Patenting Human DNA Sequences in the United States and the European Union: An Argument for Compulsory Licensing and a Fair-Use Exemption*, 76 N.Y.U. L. REV. 1623, 1650-51 (2001) (noting that Myriad Genetics, patent holder of the screening test also holds a patent on the genes themselves, BRCA1 and BRCA2). *See also* Ari Berkowitz & Daniel J. Kevles, *Patenting Human Genes: The Advent of Ethics in the Political Economy of Patent Law, in WHO OWNS LIFE?*, *supra* note 1, at 75, 89-90.

306. *See* Gitter, *supra* note 305, at 1650-51 (noting that Myriad Genetics eventually, under pressure, agreed to provide NIH-funded researchers access to

Adequate examples exist to give evidence that research and development is not hindered when a patent's scope is narrow, or research innovation is shared.³⁰⁷ Quite to the contrary, competition is healthy; it is the anti-competitive monopoly that requires particular scrutiny and occasional modification to prevent anemic economies.³⁰⁸ The potential problem is explained by the "anticommons" effect described by authors Michael A. Heller and Rebecca S. Eisenberg.³⁰⁹ "People often overuse resources they own in common because they have no incentive to conserve," say Heller and Eisenberg.³¹⁰ In "anticommons" a lack of resources is also at risk due to scarcity "when too many owners hold rights in previous discoveries that constitute obstacles to future research."³¹¹ Biotech tools, if not already, have the potential of becoming "anticommons." The expansion of Hatch-Waxman's exemption illustrates a search by the medical research community to find a safe harbor for its use of biotech tools and prevent the problem of an "anticommons" shortage.

VII. WHAT'S THE SOLUTION?

A. A Patent Defense

A suggestion to the problem of sequential technology being prevented by patent exclusion is given by Robert

the screening tests at about one-half of the public's cost). *See also supra* note 282.

307. *See* Merges & Nelson, *supra* note 39, at 868-76 (criticizing the "prospect theory" of monopolistic efficiency and noting, "The real problem is not controlling overfishing, but preventing *underfishing* after exclusive rights have been granted.").

308. *See, e.g.*, FTC Rep., *supra* note 40, Exec. Summ., at 1 ("Competition . . . is the organizing principle for most of the U.S. economy. [It] works best to achieve optimum prices, quantity, and quality of goods and services for consumers.") *See also* Merges & Nelson, *supra* note 39, at 874-75 ("In our own research, we have not found a single case where the holder of a broad patent used it effectively through tailored licensing to coordinate the [research and development] of others.")

309. Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, in *SCIENCE* 698 (1998).

310. *Id.*

311. *Id.*

Merges.³¹² He suggests allowing a judicial solution through the application of the reverse doctrine of equivalents. This is the defense that the CAFC suggested for Genentech's recombinant Factor VIII:C, the blood clotting agent infringing on Scripps's patent.³¹³ Merges's thesis, dealing with broad pioneer patents and improved inventions that are blocked, recognizes a problem particularly in the biotech field.³¹⁴ He notes, "Courts have seen that if a socially beneficial transaction is to take place between the pioneer and the improver, they must intervene (or at least pose the threat of intervention)."³¹⁵ His recommendation is for the reverse doctrine of equivalents to be applied. The courts have previously upheld a patent's validity even if the claims of the patent are not literally infringed. This is called the doctrine of equivalents in U.S. Patent Law.³¹⁶ The Supreme Court applied a different doctrine in an 1898 case involving Westinghouse air brakes on trains.³¹⁷ Though the claims of the pioneer patent *were* literally infringed by the new innovation, the improved brakes were considered so much more beneficial that the court looked for a fair solution and applied a *reverse doctrine of equivalents*.³¹⁸

A reverse doctrine of equivalents has never been applied by the CAFC though the defense was claimed in at least four cases in recent decades.³¹⁹ Even Merges admits, "[T]he chances that a court will apply the doctrine are very small."³²⁰ Yet, he finds, "The primary argument against compulsory licensing is that it allows courts, not the parties themselves, to set the terms of exchange."³²¹ At the same time, Merges states that the reverse equivalents rule is to be preferred because "it can be implemented by courts with

312. Robert Merges, *Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents*, 62 TENN. L. REV. 75 (1994).

313. See text accompanying *supra* notes 141-44.

314. See Merges, *supra* note 312, at 93.

315. *Id.* at 79.

316. See MERGES & DUFFY, *supra* note 1, at 915, 938.

317. *Westinghouse v. Boyden Power Brake Co.*, 170 U.S. 537 (1898).

318. *Id.* at 572.

319. See Merges, *supra* note 312, at 93 n.79.

320. *Id.* at 95.

321. *Id.* at 99.

no legislative enactment.”³²² (It is interesting that Merges does not tout the common objection that compulsory licensing reduces the incentive to invent.³²³)

B. A Patent Problem

Implementation by the courts is precisely the problem. It is the courts deciding whether Genentech will be granted safe harbor, be required to just pay royalties, or face penalties and an injunction.³²⁴ It is the courts deciding whether Merck’s use of a patented peptide to discover a new cancer drug has sufficiently advanced to grant it safe harbor, or will royalties be imposed?³²⁵ And, if so, will there also be a penalty and injunction?³²⁶ Bristol Myers was apparently far enough along to get a safe harbor exemption for its use of the patented taxol intermediates,³²⁷ and Amcell was allowed to continue its commercial activities with patented

322. *Id.* at 105 n.102.

323. *See, e.g.*, Joseph A. Yosick, Note, *Compulsory Patent Licensing for Efficient Use of Inventions*, U. ILL. L. REV. 1275 (2001).

Compulsory licensing has been opposed on the grounds that it would diminish the purpose of the patent system by reducing inventors’ incentive to develop new technologies and encouraging inventors to keep inventions secret. The possibility of a compulsory license would reduce the value of the patent; therefore, inventors would be less likely to invest money to develop a new invention because the return on investment would be smaller. Inventors would be more likely to keep the invention secret, if feasible, rather than patent it, to avoid the possibility of a license being granted. These two results would defeat the main purposes of the patent system: to promote innovation and to encourage disclosure of inventions.

Id. at 1291-92.

324. *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379 (N.D. Cal. 1987). *See also* text accompanying *supra* notes 213-15.

325. *Integra Lifesciences I, LTD. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003), *cert granted*, 125 S. Ct. 823 (2005). *See also* text accompanying *supra* notes 216-20.

326. *See* text accompanying *supra* notes 216-20.

327. *Bristol-Myers Squibb Co., v. Rhone-Poulenc Rorer, Inc.*, No. 95-8833, 2001 WL 1512597 (S.D.N.Y. Nov. 28, 2001). *See also* text accompanying *supra* note 178.

antibodies.³²⁸ Embrex, however, infringed when it tried to design around,³²⁹ and Duke's use of a research tool cannot be exempted because it is part of Duke's business to do research.³³⁰

Not only in respect to Hatch-Waxman's safe harbor and common law experimental use, but in numerous other patent validity cases the courts determine whether biotech tools will be used to the maximum potential for the public's benefit. Hybritech's patent on a procedure for using monoclonal antibodies is ruled by the courts to be *nonobvious* so the patent is valid,³³¹ but the Sibia Neurosciences patent on a screening method for detecting possible new drugs is *obvious*, and the patent is invalid.³³² The CAFC reversed itself and ruled that Enzo Biochem's patent of a DNA probe, allowing the diagnosis of gonorrhea to be distinguished from meningitis, is valid *without* a complete sequence of the DNA,³³³ but Eli Lilly's insulin patent and Amgen's EPO patent are invalid because the DNA sequences are missing.³³⁴ The University of Rochester's pioneer patent, allowing painkillers to be produced without gastrointestinal

328. *Nexell Therapeutics, Inc. v. Amcell Corp.*, 143 F. Supp. 2d 407 (Del. 2001), *amended by* 199 F. Supp. 2d 197 (Del. 2002). *See also* text accompanying *supra* notes 199-203.

329. *Embrex, Inc. v. Serv. Eng'g Corp.*, 216 F.3d 1343, 1353 (Fed. Cir. 2000). *See also* text accompanying *supra* notes 236-43.

330. *Madey v. Duke Univ.*, 307 F.3d 1351 (Fed. Cir. 2002). *See also* text accompanying *supra* notes 250-53.

331. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986). *See also supra* notes 67 and 304, and accompanying text.

332. *Sibia Neurosciences, Inc. v. Cadus Pharm. Corp.*, 225 F.3d 1349 (Fed. Cir. 2000). Sibia's patent was on a method for rapidly screening reactions to the signal transduction pathway in cells—an important means of identifying potential drug candidates. The CAFC reversed the district court's ruling of patent validity. *See also* Parentoni, *supra* note 10 (discussing the signal transduction pathway in cells).

333. *Enzo Biochem, Inc. v. Gen-Probe Incorp.*, 285 F.3d 1013 (Fed. Cir. 2002) *vacated en banc*, 323 F.3d 956. *See also generally* John C. Stolpa, Note, *Toward Aligning the Law with Biology? The Federal Circuit's About Face in Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 4 MINN. INTELL. PROP. REV. 339 (2003).

334. *Regents of Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997) (ruling that “[a]n adequate written description of a DNA [sequence] requires a precise definition”); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991) (ruling that analogues of EPO claimed could not be so numerous as to require undue experimentation to obtain).

side effects, is ruled *too broad* by the court,³³⁵ but Johns Hopkins University's pioneer patent on a stem cell monoclonal antibody is *not* too broad.³³⁶

Court decisions in respect to biotech tools are frequently fraught with subjectivity and often inconsistent. There is no reason to believe that application of the reverse doctrine of equivalents by the courts would be the exception, creating objectivity and consistency. Nor would applying the reverse doctrine of equivalents provide any incentive to the patent holder of biotech research tools.³³⁷ It is not in the public's best interest to eliminate the reward altogether, just be sure that it is spread around to all involved in the chase.³³⁸ Research and development in biotechnology is a conjoined effort. The reverse doctrine of equivalents is not the solution.

C. New Legislation—*Experimental Use Defense*

The key to finding a solution may be found in an amicus brief filed with the Supreme Court regarding *Madey v. Duke*.³³⁹ The Solicitor General states that the policy issues "may be better suited for legislative rather than judi-

335. *Univ. of Rochester v. G.D.Searle & Co., Inc.*, 249 F. Supp. 2d 216 (W.D.N.Y. 2003), *aff'd*, 358 F.3d 916 (Fed. Cir. 2004). *See also infra* note 355 and accompanying text.

336. *Johns Hopkins University v. CellPro*, 931 F. Supp. 303 (D. Del. 1996), 978 F. Supp. 184 (D. Del. 1997), *aff'd in part, vacated in part* by 152 F.3d 1342 (Fed. Cir. 1998). *See also text* accompanying *supra* notes 192-97.

337. *See* FTC Rep., *supra* note 40, ch. 3, at 20, 22 (stressing the importance to the biotech industry to have viable patents on biotech tools in order to raise capital for research and development).

338. *See text* accompanying *supra* notes 279-80. The *race* analogy is used frequently in medical research involving biotechnology. Stephen Hall, in describing the cloning of interferon, states, "Science has always had its competitive . . . interludes [with] occasionally cutthroat races [in] an era marked by rivalries between academic laboratories and biotechnology companies, and sometimes even within laboratories and within companies." HALL, *supra* note 300, at 181. *See also* Merges & Nelson, *supra* note 39, at 870. For an interesting discussion of the "chase" of DNA sequencing with a reward for the "capture," in the mode of *Pierson v. Post*, 3 Cai. R. 175, (N.Y. Sup. Ct. 1805), *see* MERGES & DUFFY, *supra* note 1, at 858-59. *But see Enzo*, 323 F.2d at 969-70 (ruling that the *chase* is sufficient for reward without *capture*).

339. *Madey v. Duke Univ.*, 266 F. Supp. 2d 420 (M.D.N.C. 2001), *aff'd in part and rev'd in part*, 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 958 (2003).

cial consideration.”³⁴⁰ The 1984 Hatch-Waxman Act was just such a legislative response following the court’s refusal to grant an experimental use exception in *Roche v. Bolar*.³⁴¹ A clamor for reform, as after the *Roche* decision, can again be heard following *Integra* and *Madey*.³⁴² As was also true with Hatch-Waxman’s passage, it is the underlying policy concerns that need to be addressed, not just a reversal of one court decision.³⁴³ Congress can be urged to bring about change, but it needs to be the correct change—change benefiting the public. Unfortunately not all pressure on legislature is beneficial to the public in regard to biotechnology.³⁴⁴

Legislation regarding an experimental use defense for patented research would face a particular problem under TRIPS.³⁴⁵ A broad experimental use exception in the United States could result in developing countries returning to their pre-TRIPS practice of not allowing patents on pharmaceuticals.³⁴⁶ Other countries could return to experimental use exceptions for pharmaceuticals, allowing generic drugs to be sold before international companies’ patents had expired—the very thing the United States lobbied to exclude in TRIPS by requiring a clause that no field could be exempt from patentability.³⁴⁷

There is another problem in regard to legislation granting an experimental use exemption from infringement. Universities are tied to commercial entities. Pharma-

340. See Liebert, *supra* note 269.

341. See text accompanying *supra* notes 81-92.

342. See Groombridge & Calabro, *supra* note 286, at 468 (noting that *Integra* is a clear “change of direction” and that “preclinical research work must now be considered outside the scope of [safe harbor]”); Jeffrey L. Fox, *U.S. Courts Narrow Patent Exemptions*, 21 (8) *NATURE BIOTECHNOLOGY* 834 (2003) (quoting David Korn, senior vice president of the Assoc. of Amer. Medical Colleges—“[T]he two rulings . . . raise policy concerns for both industry and academic institutions.”); Saunders, *supra* note 254, at 262 (“[T]he *Madey* court erred . . . [I]t also undermines the balance between innovation and access that lies at the heart of the Patent Act.”).

343. See text accompanying *supra* notes 91-94.

344. See, e.g., SHELFON KRIMSKY, *SCIENCE IN THE PRIVATE INTEREST: HAS THE LURE OF PROFITS CORRUPTED BIOMEDICAL RESEARCH?* 103-04 (2003) (noting conflicts of interest in government agencies).

345. See *supra* notes 57-59 and accompanying text.

346. See *supra* note 59 and accompanying text.

347. See TRIPS Agreement, *supra* note 59.

ceutical, healthcare, and biotech companies collaborate with universities by building laboratories, conducting research, and obtaining licenses to the patents obtained.³⁴⁸ As one author notes, "Companies are increasingly looking to research universities as sources for new technologies, and are competing with each other to gain preferential access to university labs, especially in biotechnology."³⁴⁹ In 1982 Washington University in St. Louis started the trend when a major company committed \$50 million for biotech research.³⁵⁰ Stanford University has recouped millions of dollars just from its recombinant DNA license.³⁵¹ In 1999 Columbia University received \$20 million in royalties on just one glaucoma drug.³⁵² An oncologist/professor at the Oregon Health Sciences University collaborates with an international pharmaceutical company to produce one of the biggest leukemia breakthrough drugs ever.³⁵³ Even small

348. See generally KRIMSKY, *supra* note 344 (writing of the entanglement of university research with commercial interests); Joshua A. Newberg & Richard L. Dunn, *Keeping Secrets in the Campus Lab: Law, Values and Rules of Engagement for Industry-University R&D Partnerships*, 39 AM. BUS. L.J. 187 (2002).

349. PORT, *supra* note 259, at 139.

350. See *id.* This climate of university/business partnerships began with passage of the Bayh-Dole Act in 1980. Congress approved the legislation to promote research and development by encouraging universities to patent inventions and license them to businesses. Bayh-Dole was originally designed to aid small businesses and to allow the government to purchase drugs, developed with government aid, more cheaply. The government has not taken advantage of the provision, and the bill was amended long ago to allow large companies to become partners with universities through licensing of patented inventions. Patent and Trademark Law Amendments Act of 1980, Pub. L. No. 96-517, 94 Stat. 3015 (codified as amended at 35 U.S.C. §§ 200-212 (2002)). See also, e.g., Bar-Shalom & Cook-Deegan, *supra* note 194, at 637; Robert Lee Hotz, *Falling From Grace: Science and the Pursuit of Profit*, in WHO OWNS LIFE?, *supra* note 1, at 175, 180 ("By 1994, 90 percent of companies involved in the life sciences had developed formal ties with academic researchers, and 92 percent of university-based researchers in the life sciences reported they received some form of support from companies."); KRIMSKY, *supra* note 344, at 30-31 (detailing some of the other congressional acts that have fostered relationships between university research and industry besides Bayh-Dole).

351. See Newberg & Dunn, *supra* note 348, at 201 n.48.

352. Jeff Gerth & Sheryl Gay Stolberg, *Drug Makers Reap Profits on Tax-Backed Research*, N.Y. TIMES, Apr. 23, 2000, at A1.

353. See Oregon Health & Sciences University, News Release, *Brian Druker Receives \$7.5 Million Leukemia Grant* (Aug. 3, 2000), available at

schools are seeking to cash in on the monies available through partnerships with big business, with nearly every campus sporting an Office of Technology Transfer.³⁵⁴ The University of Rochester's recent lawsuit highlights the size of royalties and license fees available, as the school believes it forfeited billions of dollars from the district court's ruling of patent invalidity.³⁵⁵

A more convincing argument for legislation of an experimental use exemption in patent law lies in the comparison with its closest counterpart in copyright law, the fair use exemption.³⁵⁶ In 1976 Congress adopted major revisions to the Copyright Act, among them making statutory the common law exemption of fair use.³⁵⁷ The courts have interpreted this fair use exemption to allow infringement of copyrighted elements in a computer system in order to get at functional (unprotected by copyright) elements.³⁵⁸ How can biotech research be less important?³⁵⁹

<http://www.ohsu.edu/news/archive/2000/080300druker.html> (last visited Mar. 14, 2005). See also *supra* text accompanying notes 8-10.

354. See KRIMSKY, *supra* note 344, at 165-66 (estimating 1,000 university-industry research centers were established in over 200 universities just in the first decade after the Bayh-Dole Act's passage).

355. See Andrew Pollack, *Battling Searle, University Gets Broad Patent for New Painkiller*, N.Y. TIMES, Apr. 12, 2000, at C1. The interesting sidenote to this story is that the patent ruled invalid was for cox-2 inhibitors—better known by the brand names of which *Vioxx* is now infamous. Although Rochester's lawsuit was with the manufacturer of *Celebrex*, the invalid patent covered all cox-2 inhibitors. Merck withdrew *Vioxx* from the market in September of 2004; *Celebrex* and others continue to be sold, though an apparent increased risk of cardiac events exists for all. See Mary Duenwald, *For Pain Management, Doctors Prescribe Caution*, N.Y. TIMES, FEB. 20, 2005, at 11. See also *supra* note 335 and accompanying text.

356. A fair use exemption from infringement in copyright has been expanded by the courts from limited photocopying for educational use, to allowing some copying of protected elements in computer object codes. 17 U.S.C. § 107 (1992). See also *infra* note 358.

357. The 1976 revisions replaced the prior Copyright Act of 1909. Copyright Act, Pub. L. No. 94-553, 90 Stat. 2541 (1976) (codified as amended at 17 U.S.C. §§ 101-803 (2003)).

358. See, e.g., *Sega Enters. Ltd. v. Accolade, Inc.*, 977 F.2d 1510, 1514 (9th Cir. 1993).

359. In 1990 an amendment to the Patent Act failed to pass that would have provided a broad experimental use exception. Patent Competitiveness and Technological Innovation Act, H.R. 5598, 101st Cong. §402 (1990). Justice Newman mentions the fair use of copyright in her *Integra* dissent. *Integra*

Congress has tinkered with patent law on a number of occasions in recent decades.³⁶⁰ Besides the 1984 Hatch-Waxman Act, legislation was passed in 1997 that provides another exemption for patent infringement liability.³⁶¹ A claim of infringement had been filed against a physician for using a patented incision technique during eye surgery; Congress reacted with an amendment to U.S. Patent Law.³⁶² Legislators addressed a need to limit the scope on patent infringement involving critical medical procedures. Biotech research is no less important; the importance is just less apparent.

Congress and the courts clearly recognize that sometimes, for the benefit of the public, changes are necessary in intellectual property law. The Constitution states that patent monopolies are limited, and the purpose is always to benefit the public.³⁶³ Legislation providing for an experimental use exemption for research may not, however, be the best solution when universities are so closely intertwined with commercial enterprises.³⁶⁴ In addition, the small start-up biotech companies that have taken an increased financial risk in development of biotech tools,³⁶⁵ are insistent that patents are an essential element in attracting investment capital.³⁶⁶ A legislated experimental use exemption has the potential of drying up necessary funding, because it does not allow the biotech tool inventor (start-up

Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860, 876 (Fed. Cir. 2003) (Newman, J., dissenting), *cert. granted*, 125 S. Ct. 823 (2005).

360. The Clean Air Act, 42 U.S.C. § 7608 (1977), the Atomic Energy Act, 42 U.S.C. § 2183(c) (1992), and the Plant Variety Protection Act, 7 U.S.C. § 2404 (1994), all have provisions for compulsory licensing of patents.

361. The Omnibus Consolidated Appropriations Act of 1997, Pub. L. No. 104-208, 110 Stat. 3009 (1996) (codified as amended at 35 U.S.C. § 287 (1999)).

362. *Id.* See also Bradley J. Meier, *The New Patent Infringement Liability Exception for Medical Procedures*, 23 J. LEGIS. 265 (1997).

363. See *supra* text accompanying notes 41-45.

364. See *supra* notes 348-55 and accompanying text. But see generally Michel, *supra* note 298; Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1 (2001).

365. See WOLFF, *supra* note 5, at 16 ("No other industrial group spends anything near [the] proportion of total revenues on research [as biotech], not even the major pharmaceutical companies").

366. See FTC Rep., *supra* note 40, ch. 3, at 1.

company) to be rewarded with a patent that has monetary value. It is not the best answer to the problem of availability of biotech research tools. There is a different solution that is reasonable, equitable, and acceptable.

D. *New Legislation—Compulsory Licensing*

Compulsory licensing is a solution that is reasonable, equitable, and acceptable to the American public. Compulsory licensing of biotech tools will ensure that medical research is unimpeded by blocking tactics, licensing inequities, and inconsistent court decisions.

Compulsory licensing is not a new concept in the United States.³⁶⁷ Required licensing may be imposed by the courts or by the FTC to prevent anticompetitive practices.³⁶⁸ Specific instances of pharmaceutical companies trying to circumvent the requirements of the Hatch-Waxman Act have resulted in severe penalties.³⁶⁹ As a result of some of these cases, guidelines for licensing related to intellectual property endeavors were published by the

367. The Hart Bill of 1993 and Affordable Prescription Drugs Act were unsuccessful in passing compulsory licensing related to health care costs. H.R. 1708, 107th Cong. (2001). The anthrax scare in 2001 led to talk of compulsory licensing of Cipro before the manufacturer lowered the cost. Public Health Emergency Medicines Act, H.R. 3235, 107th Cong. (2001). See, e.g., Colleen Chien, *Cheap Drugs at What Price to Innovation: Does the Compulsory Licensing of Pharmaceuticals Hurt Innovation?*, 18 BERKELEY TECH. L.J. 853, 867-68 (2003). In a 1945 case the Ninth Circuit suggested that compulsory licensing could be required of a patent that produced Vitamin D in foods by ultraviolet radiation. *Vitamin Technologists, Inc. v. Wis. Alumni Research Found.*, 146 F.2d 941, 945-46 (9th Cir. 1945).

368. See *In re Intel Corp.*, F.T.C. Order No. 9288 (Aug. 3, 1999); *United States v. Glaxo Group Ltd.*, 410 U.S. 52 (1973). See also James Love & Michael Palmedo, *Examples of Intellectual Property in the United States, Ch. III: Compulsory Licensing as Remedy to Anticompetitive Practices*, Consumer Project on Technology (2001), available at <http://cptech.org/ip/health/cl/us-at.html> (last visited Feb. 17, 2005).

369. Bristol-Myers, for example, paid fines of \$670 million for filing new frivolous patents to prevent generic brands from entering the market and for paying rival generic-brand companies to keep the cheaper drug off the market. See John R. Wilke, *Bristol-Myers Settles Charges of Patent-Law Abuse*, WALL ST. J., Mar. 10, 2003, at A5. Abbott Laboratories is another company receiving an administration order against it for negotiating to keep a generic brand drug off the market. *In re Abbott Labs.*, F.T.C. Order No. C-3945 (May 22, 2000). See also *supra* note 108.

FTC and Department of Justice.³⁷⁰ Licensing of patented products can also be required if needed by the military or other government agencies.³⁷¹ In addition, a provision in the Bayh-Dole Act allows the government to “march-in,” requiring licensing to a third-party in certain circumstances.³⁷² Incredibly, compulsory licensing exists under U.S. Copyright Law in respect to public performance of recorded music.³⁷³ Is this benefit to the public more important than the availability of biotech tools?

The importance of compulsory licensing for research is recognized outside of the United States. Required licensing for medical research is allowed in nearly the entire developed world.³⁷⁴ European countries with provisions for compulsory licensing in their patent laws include Denmark, France, Italy, Germany, Spain, Sweden, and Switzerland.³⁷⁵ The United Kingdom and Japan allow compulsory licensing

370. See *supra* note 111 and accompanying text.

371. The government’s *taking* of a patented invention was conceived with military needs in mind. See 28 U.S.C. § 1498 (2001). See also *supra* notes 256-60 and accompanying text.

372. Why isn’t this enough to require licensing of biotech tools? Even if university research was involved in some way with the development of a biotech tool, most university-industry agreements are private and accountability to the public is lacking. See generally KRIMSKY, *supra* note 344; Bar-Shalom & Cook-Deegan, *supra* note 194, at 651-54 (doubting whether the Bayh-Dole “march-in” rights will ever be used); Barbara M. McGarey & Annette C. Levey, *Patents, Products, and Public Health: An Analysis of the CellPro March-In Petition*, 14 BERKELEY TECH. L.J. 1095. See also Nat’l Inst. of Health, Determination in the Case of Petition of CellPro, Inc. (Aug. 1997), available at <http://www.nih.gov/news/pr/archives/index.htm>. (last visited Feb. 17, 2005). After Judge McKelvie’s initial ruling, CellPro petitioned the NIH to require Baxter (holder of Johns Hopkins’s government-funded patents) to license CellPro’s use of the Johns Hopkins monoclonal antibodies, but the “march-in” request was denied. See *supra* text accompanying notes 192-97.

373. Copyright Law establishes six statutory compulsory licenses that include, besides cable and satellite transmissions, the use of some copyrighted works by noncommercial broadcasters, the reproduction of nondramatic musical works, and the performance of digitalized sound recording transmissions. 17 U.S.C. §§ 111, 114, 115, 118, 119, 122 (2002).

374. See *supra* note 126.

375. See Balasubramaniam & Goldman, *supra* note 126. Besides medicine, food, and medical research, the most common compulsory licensing provisions are allowed for nonuse and blocking patents. See, e.g., Kurt M. Saunders, *Patent Nonuse and the Role of Public Interest as a Deterrent to Technology Suppression*, 15 HARV. J.L. & TECH. 389, 438-39 (2002).

if a patented invention is not being used.³⁷⁶ Canada, pressured to abolish its compulsory licensing of pharmaceuticals under TRIPS, still allows a compulsory license for nonuse of a patented invention.³⁷⁷ TRIPS, Articles 30 and 31, though somewhat vaguely written, make provision for countries to allow compulsory licensing.³⁷⁸ Article 31 includes a list of possible circumstances including nonuse, national emergency, governmental use, and anti-competitive practices.³⁷⁹ Yet another condition allows required licensing where one invention "cannot be exploited without infringing another patent."³⁸⁰ On this basis compulsory licensing of biotech tools is in compliance with TRIPS.³⁸¹

A common objection to compulsory licensing is that it reduces the incentive to invent, but at least one study on the results of required licensing under FTC rulings found no evidence of economic harm to the system or loss of research and development.³⁸² In some cases, just the existence of a compulsory licensing statute has been sufficient to see licenses negotiated voluntarily.³⁸³ Another common objection to any type of compulsory licensing is that it has a negative effect on competition. On the contrary, in the case of biotech tools compulsory licensing should increase competition in the downstream development of inventions. (Remember, patents *are* monopolies!) As noted by Heller

376. See Yosick, *supra* note 323, at 1289-90.

377. See, e.g., Kripapuri, *supra* note 59, at 686-87.

378. Article 30 allows for "limited exceptions to the exclusive rights conferred by a patent," and Article 31 lists the requirements for such "other use of the subject matter of a patent without the authorization of the right holder." TRIPS Agreement, *supra* note 58, arts. 30, 31.

379. TRIPS Agreement, *supra* note 58, art. 31.

380. *Id.*

381. See, e.g., Saunders, *supra* note 375, at 437-39. *But see* Gitter, *supra* note 305, at 1683 (taking the view that TRIPS would need modification for required licensing of patented DNA sequences).

382. See Chien, *supra* note 367, at 873.

383. Provision by pharmaceutical companies of a cheaper supply of AIDS drugs in Africa may have been a direct result of the threat of emergency compulsory licensing allowed by TRIPS, as pressure was brought upon drug companies by both government and stockholders. See Donald G. McNeil, *Bush Keeps Clinton Policy on Poor Lands' Need for AIDS Drugs*, N.Y. TIMES, Feb. 22, 2001, at A9. The threat of lawsuits, by AIDS-drug patent holders upon generic makers sending drugs to Africa, was dropped.

and Eisenberg, “[A]n unintended and paradoxical consequence of biomedical privatization [is that the] proliferation of intellectual property rights upstream may be stifling life-saving innovations downstream.”³⁸⁴

A more compelling and probably a more honest objection to compulsory licensing is the *slippery slope* argument. Require licensing of biotech tools, and what’s next? What about agricultural and environmental concerns? Aren’t they important too? And though small biotech firms may not object, it is the fear of plunging down a slippery slope that would have large pharmaceutical companies vociferously lobbying against any such compulsory licensing of biotech tools. The answer to this objection lies not only in the vital importance of biotech, but also in the speed with which changes occur in this unique industry. A 2003 Report by the Federal Trade Commission notes, “[T]he pace of innovation in the biotechnology industry is so rapid that by the time a court determines the question of patent validity, the research or product opportunity has passed.”³⁸⁵ Another observer of the biotech industry has calculated the result of all patent approvals since 1977 and found biotech patents increased *sevenfold* in twenty years while all patent approvals in the same time period increased by only 60 percent.³⁸⁶ This economist has analyzed the number of biotech patent approvals and used this figure as a basis for calculating accumulation of knowledge.³⁸⁷ He states, “Commercial biotechnology knowledge has been increasing exponentially in recent years [T]he rate of daily doubling [of biotech knowledge] could be reached in 2005.”³⁸⁸ There clearly *is* a difference in biotech that needs addressing.

384. Heller & Eisenberg, *supra* note 309, at 698.

385. FTC Rep., *supra* note 40, ch. 3, at 21. It is interesting, and noteworthy, first that the FTC is involving itself with patent issues, and then that the FTC Report’s conclusion lies in recommendations to change PTO procedures rather than mention of compulsory licensing. *See id.*, Exec. Summ., at 1-16. The report lists some panelist remarks, however, that indicate biotech patents in the PTO *do* receive higher scrutiny by the PTO, but other panelists listed problems with biotech patents in particular. *Id.*, ch. 3, at 20-21.

386. OLIVER, *supra* note 1, at 56. *See also* WOLFF, *supra* note 5, at 14-17, 45.

387. OLIVER, *supra* note 1, at 56-69.

388. *Id.* at 58-59.

E. Implementation of Compulsory Licensing

How might compulsory licensing of biotech tools work? One suggestion is to wait and determine the size of the royalty or fee after the commercial value of the downstream invention has been determined.³⁸⁹ Reach-through royalties, where licenses can continue to collect fees on downstream inventions, has been suggested as a means of risk sharing and reducing upfront costs.³⁹⁰ This could create a problem of royalty stacking and is probably not a good suggestion unless the end product actually *contains* the research tool.³⁹¹

If no license fee is initially provided for use of the biotech tool, there is no immediate incentive to the biotech tool inventor. Rather, reward the inventor with an upfront fee, allowing the biotech tool's scope to determine the amount. A pioneer biotech tool with a broad scope should actually receive a lesser fee since more licensees will be utilizing it. A biotech tool with fewer applications may command a higher initial fee, though options could be made available allowing the licensee a time period to decide the value of the tool to its research. The biotech tool inventor still receives the incentive to continue through the option fee, and the market will dictate whether the reward is high enough to act as an incentive for further development.³⁹² Some limited royalty arrangements could still be included (as when the biotech tool is actually a component *in* the downstream invention), with the actual monetary percents

389. See Gitter, *supra* note 305, at 1679.

390. See FTC Rep., *supra* note 40, ch. 3, at 26-27 (recommending reach through royalties as a possibility). *But see* Heller & Eisenberg, *supra* note 309, at 699 (noting that reach through licensing increases the possibility of "anticommons").

391. With a recent CAFC affirmation in *Bayer v. Housey*, finding no infringement on patented cell-based assays performed abroad, with the drugs identified by those assays then imported into the United States, pharmaceutical companies are unlikely to risk licensing an assay that requires reach-through royalties. They can simply import into the United States the information on the drug candidate and then generate the data that is "reasonably related" to FDA approval under Hatch-Waxman's safe harbor. *Bayer Ag v. Housey Pharm., Inc.*, 169 F. Supp. 2d 328 (D. Del. 2001), *aff'd*, 340 F.3d 1367 (Fed. Cir. 2003).

392. See PORT, *supra* note 259, at 162-63, 209-219 (discussing valuation for the purpose of computing royalties in licensing).

dictated by the particular field of use in which the tool is eventually commercialized.³⁹³

Compliance with TRIPS would require that the compulsory license be non-exclusive.³⁹⁴ Cross-licensing could be possible (with a lesser initial fee, for example) and non-blocking agreements required.³⁹⁵ It is not being suggested that implementation of compulsory licensing of biotech tools would be easy. Valuation, monitoring, and enforcement are all issues that would need to be addressed—if not by the parties negotiating themselves, then in arbitration with third parties from within the industry.³⁹⁶ The issues, however, are the same ones that must now be dealt with in voluntary licensing.

CONCLUSION

In 1984 the passage of Hatch-Waxman addressed a particular problem related to a population phenomenon—the need for cheaper drugs for a rapidly graying population. A similar response is needed today—not to provide generic drugs for the older generation, but to ensure that medical advancement continues unimpeded for the future generation. The courts' expansion of Hatch-Waxman's safe harbor provision up to the *Integra* decision is evidence of a void existing in U.S. Patent Law regarding accessibility of patented biotech tools.³⁹⁷ At the same time the courts have con-

393. *Id.*

394. TRIPS Agreement, *supra* note 58, art. 31(d) ("such use shall be non-exclusive"). Biotech companies may prefer non-exclusive licensing, though at present only about one-half of the licensing agreements are non-exclusive. See FTC Rep., *supra* note 40, ch. 3, at 28 (noting that exclusive licensing commits the biotech company to a product that may never be developed).

395. See PORT, *supra* note 259, at 402-03. See also Antitrust Guidelines for the Licensing of Intellectual Property, *supra* note 111; FTC Rep., *supra* note 40, ch. 3, at 26-29 (discussing licensing for biotech tools).

396. See PORT, *supra* note 259, at 433-38 (discussing present alternative dispute resolution mechanisms available for licensing disputes).

397. At the time of this publication, the Supreme Court has granted certiorari in the *Integra* decision. *Merck KGaA v. Integra Lifesciences I, Ltd.*, 125 S.Ct. 823 (2005). Reversing the CAFC ruling would expand Hatch-Waxman but would probably be seen as a weakening of patent law. Remanding for possible consideration of experimental use seems unlikely after *Madey*, and remanding for patent validity would also be problematic. Congress needs to consider compulsory licensing of biotech tools, regardless of the Supreme

tinued to apply the experimental use defense with a strict adherence to the rights of the patent holder as found in *Madey v. Duke*.

Legislating an experimental use exemption is not the best response to this problem. It is not necessary that biotech tools be freely available, only that they be reasonably and readily available. Compulsory licensing provides biotech companies with the incentive to produce research tools. Compulsory licensing allows Hatch-Waxman's safe harbor to be used for its intended purpose. Compulsory licensing does not require exceeding the narrow boundaries of common law experimental use. Compulsory licensing guarantees that the public will receive the intended benefit that is the basis for U.S. Patent Law.

Is it time for compulsory licensing of biotech tools? Yes.