MERCK V. INTEGRA AND ITS AFTERMATH: A SAFE HARBOR FOR THE COMMERCIAL USE OF BIOTECHNOLOGY RESEARCH TOOLS?

I. INTRODUCTION

One of the biggest challenges currently facing the U.S. patent system as it relates to the biotechnology and pharmaceutical industries is that of balancing the diverse interests of research tool patentees, drug discovery researchers, and the general public. While biotech and pharmaceutical research toolmakers strive to maximize revenue by licensing their patented inventions, drug companies have a countervailing interest in acquiring and using research tools without paying unreasonable license fees and incurring high licensing-related transaction costs.[1] Finally, the public at large has a more complicated and usually unarticulated interest in a patent system that balances the interests of research tool patentees and drug discovery companies in a way that ensures continued development and availability of new drugs and vaccines.

The current news media abound with reports of the worldwide spread of a deadly H5N1[2] strain of avian influenza ("bird flu") virus.[3] The H5N1 strain has so far crossed the species barrier into humans at relatively low levels,[4] but experts warn that adaptation of the avian virus to human hosts could result in the worst flu pandemic since 1918, when approximately 2-5% of the world's human population was killed by an influenza virus strain that likely jumped directly from birds to humans.[5] Influenza viruses mutate

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[1] For a discussion of the economic and transactional problems associated with patent licensing, see Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 6-8 (2001).

[2] Influenza virus subtypes are generally identified by their variable surface proteins, hemagglutinin ("HA") and neuraminidase ("NA"). There are sixteen different HA subtypes and nine different NA subtypes. Hence, an H5N1 virus has hemagglutinin subtype 5 and neuraminidase subtype 1. For a general discussion of bird flu and influenza viruses in general, *see* CTRS. FOR DISEASE CONTROL AND PREVENTION, KEY FACTS ABOUT AVIAN INFLUENZA (BIRD FLU) AND AVIAN INFLUENZA A (HN51) VIRUS (2005), http://www.cdc.gov/flu/avian/gen-info/facts.htm.

[3] A recent search of Google News using the phrase "bird flu" as a search term yielded 50,000 hits (http://news.google.com/news?hl=en&ned=us&ie=UTF-8&q=bird+flu&btnG=Search+News), while a search using "H5N1" returned 20,100 hits (http://news.google.com/news?hl=en&ned=us&q=h5n1&btnG=search+News) (last visited Nov. 28, 2005).

[4] As of Nov. 9, 2005, the World Health Organization put the number of recorded cases of human infection with H5N1 avian influenza virus ("bird flu") at 125, with sixty-four resulting in death, a death rate of 51%. *See* WORLD HEALTH ORGANIZATION, CUMULATIVE NUMBER OF CONFIRMED HUMAN CASES OF AVIAN INFLUENZA A/(H5N1) (2005), http://www.who.int/csr/disease/avian_influenza/country/cases_table_2005_11_09/en/index.html.

[5] The 1918 strain was recently "resurrected," and was found to kill both bird embryos

quickly, necessitating ongoing vaccine development to keep potential pandemics in check on a yearly basis.[6] No currently available vaccines are effective for immunizing humans against H5N1 flu.[7]

I will use a hypothetical drawn from the bird flu example to frame a discussion of recent developments in the case law concerning the safe harbor defense to patent infringement, by considering what might happen if vaccine development depended on the licensing of multiple research tools, and a vaccine developer decided to make unlicensed use of the tools in question.[8] The hypothetical assumes the existence of a vaccine developer, VaxDev, and a research toolmaker, ResTool. One of ResTool's patented inventions allows researchers (normally after purchasing an expensive license) to synthesize avian influenza virus in laboratory cell culture[9] as an upstream[10] step in the process of vaccine development. A second ResTool patent concerns an equally costly product that allows VaxDev researchers downstream in the development process to detect antibodies against the H5N1 virus in blood samples drawn from vaccinated patients participating in clinical trials. Both research tools, which I will refer to respectively as the "preclinical research tool" and the

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and mice; such cross-species tropism is unusual. The 1918 strain was also found to bear substantial genetic similarity to avian flu viruses. Jocelyn Kaiser, *Resurrected Influenza Virus Yields Secrets of Deadly 1918 Pandemic*, 310 SCIENCE 29 (Oct. 7, 2005). For a general discussion of the 1918 flu epidemic, *see* WIKIPEDIA, SPANISH FLU, http://en.wikipedia.org/wiki/1918_flu (last visited Dec. 8, 2005).

6 *See* U. S. DEP'T OF HEALTH & HUMAN SERVS., PANDEMIC FLU FACT SHEET (2004), http://www.hhs.gov/nvpo/pandemics/dhhs.html (last visited Dec. 8, 2005).

7 *See* THE CTRS. FOR DISEASE CONTROL AND PREVENTION, AVIAN INFLUENZA VACCINES (2005), http://www.cdc.gov/flu/avian/gen-info/vaccines.htm (last visited Dec. 8, 2005).

8 For discussions of the real world problem of licensing multiple patents for a single stream of research, *see* Mueller, *supra* note 1, at 6-9; *see also* Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698 (May 1, 1998). Heller and Eisenberg's seminal article focuses on the undesirable result that occurs when "a user needs to access multiple patented inputs to create a single useful product," and compares such patents to "tollbooth[s] on the road to product development, adding to the cost and slowing the pace of downstream biomedical innovation." *Id.* at 699. R

9 Influenza viruses (including, controversially, the unusually deadly 1918 strain) have been reconstructed in the laboratory from their constituent genes. *See, e.g.*, Terrence M. Tumpey et al., *Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus*, 310 SCIENCE 77 (Oct. 7, 2005). The ethical implications of publication of the gene sequences of the 1918 strain are discussed in Philip A. Sharp, *1918 Flu and Responsible Science*, 310 SCIENCE 17 (Oct. 7, 2005).

10 The terms "upstream" and "downstream" respectively refer to earlier and later parts of the research and development process, or "stream" of research. The results of an experiment performed early on, or upstream, may be needed in order to make informed decisions about what experiments to perform later, or downstream. In pharmaceutical research, for example, the initial screening of possible drug candidates in the laboratory would be upstream of later, downstream, clinical trials.

"clinical research tool," are absolutely required for the development of VaxDev's bird flu vaccine, and we will further assume that VaxDev and ResTool, after much haggling, were unable to reach a mutually acceptable licensing agreement.

The bird flu vaccine hypothetical will serve as a framework for analyzing the impact of recent decisions of the Court of Appeals for the Federal Circuit ("CAFC") and the Supreme Court on the too-common real world situation in which a drug developer must license and use multiple patented inventions in both the earlier laboratory and later clinical phases of the same research stream. By tracing the jurisprudential history of exemptions from patent infringement liability under both statute and common law,[11] we will see that the strict patent protection traditionally enjoyed by research toolmakers has given way to broad "fair use" protection for the pharmaceutical industry. The Court's broad construction of statutory safe harbor provisions has arguably created a situation that may require wholesale re-drafting of relevant sections of the patent code in order to protect the research tool industry from rampant unlicensed use of its patented inventions. Carefully drafted and well thought-out statutory provisions will provide a continued economic incentive to the development of research tools, while providing a safe harbor for some legislatively defined, limited, and necessary reasonable uses.

II. BACKGROUND

A. *Safe Harbors from Infringement Under Common Law and Statute*

1. The Experimental Use Exception: An Elusive Common Law Safe Harbor

Though the patent protection balance has traditionally and by design[12] weighed most heavily on the side of patentees, a somewhat elusive common law exemption from infringement liability has, at least in theory, provided a safe harbor[13] for non-commercial experimental researchers since the early 1800s. In 1813 in *Whittemore v. Cutter*, Justice Story stated that, "it could never have

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[11] Most recently in Merck KGaA v. Integra Lifesciences I, Ltd., 125 S.Ct. 2372 (2005).

[12] The power of Congress "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to . . . Inventors . . . the exclusive Right to their . . . Discoveries" was discussed by James Madison in Federalist No. 43; the identical language was ratified in Article I, Section 8 of the Constitution. THE FEDERALIST NO. 43, at 219 (James Madison) (William R. Brock ed., 2000); U.S. CONST. art. I, § 8, cl. 8.

[13] Black's Law Dictionary defines "safe harbor" as "a provision (as in a statute or regulation) that affords protection from liability or penalty." BLACK'S LAW DICTIONARY, 8TH ED. Here, I will also refer to the common law experimental use exemption as the "common law safe harbor." Statutory safe harbor is discussed at length *infra*.

been the intention of the legislature to punish a man, who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects."[14] Just a few months after *Whittemore* was decided, Justice Story had occasion to gloss his oft-quoted language, explaining in *Sawin v. Guild* that infringement should be triggered only where the alleged infringer intends to derive economic gain from his experiments.[15]

Under the rationale of *Whittemore*, hypothetical research tool patentee ResTool would likely be successful in an infringement action brought against vaccine developer VaxDev for unlicensed use of either ResTool's preclinical or clinical research tool. Since VaxDev's goal is to produce a commercial vaccine, its unlicensed use of ResTool's patented inventions goes far beyond the "philosophical experiment" contemplated by Justice Story. In the absence of a mutually acceptable license agreement, short of abandoning its vaccine research, VaxDev would be forced to pay ResTool's high license fee or to risk litigation by infringing ResTool's patents. Either choice would ultimately result in consumers paying an unnecessarily high cost for a necessary vaccine.

3. Contemporary CAFC Jurisprudence Interprets the Common Law Experimental Use Exemption Very Narrowly

The VaxDev / ResTool hypothetical presents a case in which patented inventions are used for clearly commercial ends. However, even uses that are facially non-commercial have historically faced a high bar for showing that "merely philosophical" experiments have been conducted by the alleged infringer. The common law experimental use exemption as a defense "has been frequently raised but rarely sustained,"[16] and the CAFC recently made clear that the experimental use defense is so "narrow and strictly limited"[17] that except in the case of true

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[14] This frequently quoted passage appears at 29 F. Cas. 1120, 1121 (C.C.D. Mass. May 1813) (No. 17,600).

[15] *See* 21 F. Cas. 554, 554 (C.C.D. Mass. Oct. 1813) (No. 12,391) ("This court has already had occasion to consider the clause in question, and upon mature deliberation, it has held that the [infringing act] must be the making with *an intent to use for profit* . . . .") (Story, J.) (emphasis added).

[16] Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017, 1019; *see also* Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 17-18 (stating that the common law experimental use exemption "has rarely been applied in favor of an accused infringer.").

[17] Madey v. Duke Univ., 307 F.3d. 1351, 1362 (Fed. Cir. 2002). In support of this

"dilettante affairs,"[18] the defense will generally fail even if no direct economic gain is sought by the infringer.

In *Madey v. Duke University*, when Madey, a research physicist, moved his free electron laser ("FEL") laboratory from Stanford to Duke University, he brought with him two patents that he then practiced at Duke as part of the FEL laboratory's research.[19] Madey served as director of the FEL laboratory at Duke from 1989 until 1997, when he was removed from that position after a dispute over management of the laboratory—Duke contended that Madey mismanaged the FEL laboratory, while Madey contended that Duke wanted him to make inappropriate use of the some of the laboratory's equipment in violation of federal funding guidelines.[20] After resigning his professorship at Duke altogether in 1998, Madey sued the university for infringement of his two patents.[21]

Moving for summary judgment in the district court, Duke asserted that its use of Madey's patents was exempt from infringement liability under the common law research use exemption of *Whittemore*.[22] Quoting Justice Story, the district court agreed, explaining that:

> [a]lthough the scope of the defense has recently been the issue of much debate . . . the experimental use defense remains viable and may be asserted [where] the allegedly infringing use of the patent is made for experimental, non-profit purposes only . . . . Given this standard, for Plaintiff to overcome his burden of establishing actionable infringement in this case, he must establish that Defendant has not used the equipment at issue "solely for an experimental or other non-profit purpose." More specifically, Plaintiff must sufficiently establish that Defendant's use of the patent had "definite, cognizable, and not insubstantial commercial purposes."[23]

In its reversal of the district court's summary judgment decision in

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proposition, the court cites Roche Prods., Inc. v. Bolar Pharm. Co., Inc., 733 F.2d. 858, 863 (Fed. Cir. 1984), and Embrex, Inc. v. Service Engineering Corp., 216 F.3d 1343, 1349 (Fed. Cir. 2000).

18 See *Roche*, 733 F.2d. at 863 (noting that a commercially harmful infringing act "is no dilettante affair such as Justice Story envisioned"). *See infra* Part I.C. for a full discussion of *Roche*.

19 *Madey v. Duke Univ.*, 307 F.3d at 1352.

20 *Id.* at 1352-53.

21 *Id.* at 1353.

22 Madey v. Duke Univ., 266 F. Supp 2d 420, 425 (M.D.N.C. 2001).

23 *Id.* at 425 (citing Embrex, Inc. v. Service Engineering Corp., 216 F.3d 1343, 1349 (Fed. Cir. 2000) in support of the district court's recognition of the experimental use exemption, and quoting respectively, CHISUM ON PATENTS § 16.03[1] (2000) and Roche Prods. v. Bolar Pharm. Co., 733 F.2d 858, 863 (Fed. Cir. 1984) (other internal citations and quotations omitted)).

favor of Duke, the CAFC corrected two misinterpretations of its previous holdings concerning experimental use.[24] First, the CAFC explained that the common law experimental use exemption, if properly construed as a *defense*, requires assertion and establishment of non-commercial use by the accused infringer, and does not shift the burden of establishing commercial use to the plaintiff.[25] Second, and more important for the present discussion, the CAFC explained that its decision in *Embrex* was meant to limit the experimental use defense strictly to "actions performed to satisfy idle curiosity, or strictly for philosophical inquiry"[26] and that the defense is unavailable if a potentially infringing use has even "the slightest commercial implication."[27]

Again returning to the hypothetical travails of VaxDev and ResTool, it is clear that after *Madey*, unlicensed use of either ResTool's preclinical virus production tool or its clinical antibody detection tool by VaxDev would still result in infringement liability in a suit brought by ResTool. The CAFC's view of the common law experimental use exemption is perhaps even narrower than Justice Story's, and under the rationale of *Madey*, VaxDev would again be forced to choose between paying an unreasonably high license fee, infringing ResTool's patents, or abandoning vaccine development.

3. The Federal Circuit First Narrowly Construed the Experimental Use Exemption in *Roche v. Bolar*

The CAFC's antipathy toward "fair use"[28] defenses to infringement has its origin not in the "philosophical experiments" or "idle curiosity" contemplated by the common law research exemption, but rather in the realm of big business as carried out by multinational drug companies. In *Roche v. Bolar*,[29] the complicated interplay of the patent law and federal administrative regulations came to the fore in the context of generic drug development. At issue in *Roche* was the de facto patent term extension that arose when a drug maker maintained a monopoly on its branded drug after its patent term had expired, as a result of the generic manufacturer's need to seek FDA approval before marketing the

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24 307 F.3d at 1361.

25 *Id.*

26 *Id.* at 1362.

27 *Id.*

28 For a discussion likening the experimental use exemption in patent law to "fair use" in copyright law, *see* WILLIAM M. LANDES & RICHARD A. POSNER, *The Economics of Patent Law*, *in* THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 315, 315-16 (2003).

29 Roche Prods. v. Bolar Pharm. Co., 733 F.2d 858 (Fed. Cir. 1984).

generic version.[30] This inequity made it clear that a per se exclusionary right or monopoly on use was probably not reasonable given the regulations governing the pharmaceutical industry. Such a per se rule appears in the text of 35 U.S.C. § 271(a), which states in relevant part that:

> [e]xcept as otherwise provided in this title [35 USCS §§ 1 et seq.], whoever without authority . . . *uses* . . . any patented invention, within the United States . . . during the term of the patent therefore, infringes the patent.[31]

In *Roche*, Bolar, a generic drug company, used flurazepam hcl, the patented active ingredient found in Roche's sleeping pill Dalmane, in experiments relating to future FDA approval of a generic version of the drug, to be sought after the expiration of Roche's patent term.[32] Roche sued Bolar, arguing that under § 271(a), Bolar's use of flurazepam hcl constituted infringement.[33] The district court found Bolar's use to be non-infringing, reasoning that Bolar gained "no benefit during the term of the patent," that "post-expiration delay in competition unintentionally imposed by FDA regulation is not a right or benefit granted by the patent law," and, finally, that "Roche [could] point to no substantial harm it [would] suffer from Bolar's FDA studies before the patent expire[d]."[34] When Roche appealed, Bolar raised two main arguments. Bolar first argued that under the common law experimental use exemption, its use was de minimis and non-infringing, and second argued that public policy considerations, e.g., the prompt availability of cheap generic drugs, demanded an exception to the infringement liability imposed by § 271(a).[35]

In its reversal of the district court's decision, the CAFC vigorously rejected both arguments. Citing the decision of the Court of Claims in *Pitcairn v. United States*, the CAFC first dispatched the experimental use argument, explaining that "no case had permitted a pattern of systematic exploitation for the purpose of furthering the legitimate business interests of the

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[30] I will refer to this as "back end" patent term extension. Dramatic "front end" patent term shortening also occurred for pioneer drug makers seeking initial regulatory approval. According to the court in *Roche*, "because most FDA-required testing [was] done after a patent issue[d], the remaining effective life of patent protection [had been] as low as 7 years." 733 U.S. at 864 (citing NATIONAL ACADEMY OF ENGINEERING, THE COMPETITIVE STATUS OF THE U.S. PHARMACEUTICAL INDUSTRY, 79-80 (1983)). *See infra* Part I.D. for a more complete discussion of patent term extension.

[31] 35 U.S.C. § 271(a) (second emphasis added).

[32] 733 F.3d at 860.

[33] *Id.*

[34] Roche Prods., Inc. v. Bolar Pharm. Co., 572 F. Supp. 255, 258 (E.D.N.Y. 1983).

[35] Roche Prods., Inc. v. Bolar Pharm. Co., 733 F.2d 858, 862 (Fed. Cir. 1984).

infringer."[36] This rationale was squarely in line with that of Justice Story in *Whittemore* and *Sawin*, and represented the hard-line position on experimental use that the CAFC would maintain going forward toward *Madey*. When considering Bolar's second argument, that an exception to the mandate of § 271(a) should be created on public policy grounds, the court demurred, "declin[ing] the opportunity . . . to engage in legislative activity proper only for the Congress."[37]

It was clear that under *Roche*, decided in 1984, just as under *Whittemore* and *Sawin*, decided in 1813, a patentee's right to exclude unlicensed use remained nearly absolute. Revisiting hypothetical companies ResTool and VaxDev, it is equally clear that under *Roche*, the federal courts would have been unlikely to allow any unlicensed use of either of ResTool's patented inventions, regardless of the economic and administrative burden imposed on VaxDev.

4. Congress Steps In: The Hatch-Waxman Act

Congress, aware of the patent term problems articulated in *Roche*, sought to create a statutory safe harbor for generic drug companies engaged in experimental use in anticipation of FDA approval, and to ameliorate the lengthy front end regulatory delays suffered by manufacturers of new "pioneer" drugs. The resulting legislation was enacted as part of the Drug Price Competition and Patent Term Restoration Act of 1984 ("the 1984 Act"), commonly referred to as the Hatch-Waxman Act.[38]

The 1984 Act addressed multiple administrative problems facing both pioneer and generic drug manufacturers. First, Section 101 of the Act[39]created the Abbreviated New Drug Application ("ANDA"), which allowed generic drug manufacturers to gain fast FDA approval for their drug if its active ingredient had been previously approved.[40] This eased the economic burden on manufacturers of generics, allowing them to bring their drugs to market in a shorter time. Next, Section 201 of the Act[41] eased the burden on pioneer drug manufacturers by extending the patent term of any product that "has been subject to a regulatory review period before its commercial marketing or use."[42] Finally, Section

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[36] *See id.* at 863-64 (citing Pitcairn v. United States, 547 F.2d 1106 (Ct. Cl. 1976)).
[37] *Id.*
[38] 98 Stat. 1585 (1984).
[39] Codified as 21 U.S.C. § 355(j).
[40] 35 U.S.C. § 355(j) (2005).
[41] Codified as 35 U.S.C. § 156(a).
[42] 35 U.S.C. § 156(a)(4) (2005).

202 of the Act[43] sought to end de facto extension of patent terms for pioneer drug manufacturers by providing a safe harbor for experimental use by generic drug manufacturers in anticipation of FDA approval. The safe harbor provision states in relevant part that:

> [i]t shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a *patented invention* . . . solely for uses *reasonably related* to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.[44]

Since the Hatch-Waxman provisions were signed into law, it has become apparent that the language of § 271(e)(1), though crafted to do away with the specific problem of de facto patent term extension, can be interpreted much more broadly than Congress likely intended. Judicial interpretation of these clauses over the last fifteen years has caused the balance of statutory protection between toolmakers and drug developers to shift significantly.[45] While the CAFC has favored interpretations of 35 U.S.C. § 271(e)(1) that offer strong protection for researchers, the Supreme Court has favored interpretations that result in an extremely broad safe harbor for researchers, though, ironically, only in commercial settings.

B. *After Hatch-Waxman: The CAFC and the Supreme Court Interpret § 271(e)(1)*

1. The Supreme Court Takes Aim at the "Inelegant" Drafting of § 271(e)(1) in *Eli Lilly v. Medtronic*

The first landmark decision construing the text of § 271(e)(1) came in 1990 in *Eli Lilly & Co. v. Medtronic, Inc.*[46] The underlying case involved an action for infringement in which Lilly sought an injunction to prevent Medtronic from "testing and marketing . . . an implantable cardiac defibrillator, a *medical device* used in the treatment of heart patients."[47] Lilly prevailed at trial after convincing the district court that the safe harbor exemption

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[43] Codified as 35 U.S.C. § 271(e)(1).

[44] 35 U.S.C. § 271(e)(1) (2005) (emphasis added).

[45] For the purposes of this paper, I will divide § 271(e)(1) into a "patented invention" clause, considered in *Eli Lilly v. Medtronic*, 496 U.S. 661 (1990), and a "reasonably related" clause, considered in *Merck v. Integra*, 125 S.Ct. 2372 (2005). See emphases in the passage from § 271(e)(1) quoted in the text *supra*.

[46] 496 U.S. 661 (1990).

[47] *Id.* at 664 (emphasis added).

of § 271(e)(1), given its original relation to patented drugs, did not apply to medical devices. Medtronic subsequently prevailed on appeal to the CAFC, which reversed, holding that "by virtue of § 271(e)(1), respondent's activities could not constitute infringement if they had been undertaken to develop information reasonably related to the development and submission of information necessary to obtain regulatory approval . . . ."[48] The Supreme Court granted certiorari to clarify whether the safe harbor created under § 271(e)(1) applied to drugs only, or indeed to any patented invention.[49]

In *Lilly*, the Court first construed the plain meaning of the phrase "patented invention" as it appears in the text of § 271(e)(1).[50] Per Justice Scalia, the Court explained that under 35 U.S.C. § 100(a), the phrase "patented invention" is not limited to "drug-related inventions,"[51] and must include *all* inventions unless otherwise specified.[52] The Court also reasoned that since the 1984 Act was passed to remediate both de facto extension of patent terms for pioneer drug developers and de facto shortening of patent terms for generic drug developers,[53] it was hard to believe that Congress would have intended an outcome allowing a company to reap the advantage of the legislated patent term extension conferred by § 156(a), but not suffer the disadvantage of § 271(e)(1)'s safe-harbor for "fair use" by others during the patent term.

Thus, in *Lilly* the Supreme Court opened the § 271(e)(1) safe harbor to *any* invention, not just the generic drug inventions originally contemplated by the 1984 Act. The Court in *Lilly* arguably reached a sensible result, acknowledging the need for consistency in patent term duration that inspired the 1984 Act. However, its broad reading of § 271(e)(1)'s "patented invention" clause would later, when applied in conjunction with an equally broad reading of the "reasonably related" clause, give rise to sweeping protection from infringement actions that Congress

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48 *Id.*; *see also* 35 U.S.C. § 100(a) (stating that "[t]he term 'invention' means invention or discovery).

49 496 U.S. at 664.

50 *Id.* at 665.

51 *Id.*

52 *Id.*

53 As mentioned *supra*, requiring a generic drug company to wait until a patent expires to start research results in de facto "back end" extension of the patent term for the patentee, while the patentee's own research pending FDA approval results in a de facto "front end" shortening of the patent term. The Hatch-Waxman Act sought to remedy both of these inequities.

likely did not anticipate.[54]

2. *Integra v. Merck*: The CAFC Narrowly Construes the "Reasonably Related" Clause of § 271(e)(1)

While the line of cases beginning with *Roche* and ending with *Madey* allowed the CAFC to articulate its narrow interpretation of the common law research exemption of *Whittemore*, *Integra v. Merck*[55] allowed the court to quell any hope among potential infringers that the "reasonably related" clause of 35 U.S.C. § 271(e)(1) might constitute a *statutory* exemption for experimental use.[56]

While *Madey* dealt with academic research at least facially removed from the commercial realm, *Integra* dealt with the big business of drug discovery, an explicitly commercial activity that had never been protected under the common law. At stake in *Integra* was Integra's right to protect its patents on a class of peptides[57] used in research by Dr. David Cheresh, a scientist at the Scripps Research Institute, a leading academic biomedical research institution. RGD[58] peptides are peptides derived from proteins that bind to integrins,[59] which are among the many classes of proteins that reside on the surface of human cells. Integrins have been implicated in a variety of basic biological processes, including cell migration and adhesion,[60] and are attractive drug targets because these basic processes of cellular interaction play important roles in more complex biological processes of special importance to humans. These include such diverse processes as tumor angiogenesis (the process by which tumors acquire a blood supply),[61] immune function,[62] and virus entry into human cells.[63]

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54 The Court perhaps presaged its revisiting of § 271(e)(1) fifteen years later in *Merck v. Integra*, noting in dictum that "[n]o interpretation we have been able to imagine can transform § 271(e)(1) into an elegant piece of statutory draftsmanship." *Lilly*, 496 U.S. at 679.

55 Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860 (Fed. Cir. 2003).

56 For a discussion likening the Hatch-Waxman Act provisions discussed here to an extension of the experimental use doctrine, *see* LANDES & POSNER, *supra* note 28, at 315. R

57 Peptides are simply oligomers (short chains) of amino acids, and are generally either derived from proteins or synthesized in the laboratory from individual amino acids.

58 R, G, and D are standard one-letter abbreviations for the amino acids arginine, glycine, and aspartic acid, respectively.

59 Edward F. Plow, Thomas A. Haas, Li Zhang, Joseph Loftus, and Jeffrey W. Smith, *Ligand Binding to Integrins*, 275 J. BIOL. CHEM. 21785 (Jul. 21, 2001). For a brief and less technical discussion of integrins and their ligands, *see* WIKIPEDIA, INTEGRIN, http://en.wikipedia.org/wiki/Integrin (last visited Dec. 8, 2005).

60 *Id.*

61 *See, e.g.*, Peter C. Brooks, Richard A.F. Clark, and David A. Cheresh, *Requirement of Vascular Integrin $\alpha_v\beta_3$ for Angiogenesis*, 264 SCIENCE 569 (Apr. 22, 1994). Importantly, RGD peptides inhibit angiogenesis by binding to integrins, preventing tumors from acquiring a blood supply, and thereby preventing tumor growth.

Because integrins are involved in such diverse and important biological processes, study of these proteins and their ligands is of potentially great importance to both public health and commercial drug development, and recognition of this importance arose directly out of Cheresh's research.[64] After discovering the role of integrins in tumor angiogenesis, Cheresh and Scripps began to receive funding from Merck KGaA, a German pharmaceutical company.[65] Experiments initiated through the Scripps-Merck collaboration first included *in vitro* experiments designed to test basic properties of the RGD peptides provided to Cheresh by Merck, and later included *in vivo* experiments designed to test the therapeutic utility of the compounds in animals.[66] Many of these experiments made use of Integra's patented RGD peptides as controls.[67] After Integra became aware of Merck's use of its inventions, the two companies unsuccessfully attempted to negotiate a licensing arrangement; when these negotiations failed, Integra sued Merck.[68] Merck, *inter alia*, asserted the defense of non-infringement under the safe harbor provision of 35 U.S.C. § 271(e)(1).[69]

Though Merck sought the safe harbor protection of § 271(e)(1) under the theory that commercializing its therapeutic RGD peptides would require FDA approval, Integra argued that any use of its patented peptides that, like much of the Scripps research, pre-dated clinical trials, could not be specifically tied to an FDA submission under the statute's "reasonably related" clause.[70] At trial, a jury agreed, awarding Integra $15 million in damages, under a jury instruction construing the "reasonably related" clause narrowly and requiring the jury to find that Merck had infringed unless, "there was a decent prospect that the accused activities would contribute, relatively directly, to the generation of the kinds of information that are likely to be relevant in the

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62 *See, e.g.*, Estelle S. Harris, Thomas M. McIntyre, Stephen M. Prescott, and Guy A. Zimmerman, *The Leukocyte Integrins*, 275 J. BIOL. CHEM. 23409 (Jul. 21, 2001).

63 *See, e.g.*, Adam L. Feire, Heidi Koss and Teresa Compton, *Cellular Integrins Function as Entry Receptors for Human Cytomegalovirus via a Highly Conserved Disintegrin-like Domain*, 101 PROC. NATL. ACAD. SCI. U.S.A. 15470 (Oct. 26, 2004).

64 *See supra* note 61. R

65 Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860, 863 (Fed. Cir. 2003).

66 *Id.*

67 *Id.*

68 Integra's initial suit named Merck, Scripps, and Cheresh, requesting monetary damages from Merck and declaratory judgment against Scripps and Cheresh; the declaratory judgment claims against Scripps and Cheresh were dismissed by the district court. 331 F.3d at 863.

69 *Id.*

70 *See supra* Part I.D.

processes by which the FDA would decide whether to approve the product in question."[71]

The CAFC affirmed the district court's decision against Merck, adopting the district court's narrow interpretation of the "reasonably related" clause,[72] and adding that "the safe harbor does not reach *any* exploratory research that may form a predicate for future FDA clinical test"[73]—thus drawing a bright line between those downstream experiments whose results would ultimately be included in an FDA submission, and those upstream experiments whose results would not. This bright line served to vigorously protect research tool patentees from any unlicensed use which might occur and then be defended by vague assertions of reasonable relatedness to some far-removed and speculative FDA submission.

In deciding *Integra*, the CAFC was explicitly aware of the negative effect that broadening the safe harbor could have on research tool patentees, stating that "the 1984 Act was meant to reverse the effects of *Roche* under limited circumstances, not to deprive entire categories of inventions of patent protection."[74] Returning to our bird flu hypothetical, after *Integra*, VaxDev could likely claim the protection of § 271(e)(1)'s safe harbor for its use of ResTool's clinical research tool, but its use of the preclinical tool would almost certainly still be infringing under the CAFC's rationale because such a use would be too far removed from FDA submission to meet the "reasonably related" requirement. *Integra* would thus have been a partial win for VaxDev given the decreased transaction costs associated with having to haggle over licensing of only one tool rather than two.

3. *Merck v. Integra*: The Supreme Court Broadly Construes the "Reasonably Related" Clause of § 271(e)(1)

Successfully petitioning for certiorari, Merck put the interpretation of the "reasonably related" clause into the hands of the Supreme Court.[75] *Merck v. Integra* attracted no fewer than twenty-one briefs of amicus curiae, with research toolmakers predictably and appropriately lining up alongside respondent Integra, and pioneer drug makers joining ranks with petitioner

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[71] See the Supreme Court's decision in *Merck v. Integra*, 125 S.Ct. 2372 (2005), *infra*, for the most comprehensive summary of the facts and procedural history of *Integra v. Merck*.

[72] 331 F.3d at 867.

[73] *Id.* (emphasis added.)

[74] *Id.*

[75] 125 S.Ct. at 2380 (2005).

Merck.[76] While research tool amici like Invitrogen cautioned the Court that "[a]pplication [o]f § 271(e)(1) [t]o [r]esearch [t]ools [w]ould [d]evastate [f]uture [r]esearch [a]nd [d]evelopment [o]f [n]ew [d]rugs,"[77] the pioneer drug makers warned that "[c]lassification of patents into categories such as 'tools' and prohibiting application of the safe harbor has no basis in the language of § 271(e)(1)"[78] and that declining to apply the § 271(e)(1) use exemption to research tool patents would leave "an aspiring drug discoverer . . . shipwrecked outside the safe harbor . . . ."[79] The Court, though explicitly declining to face the research tool issue head on, reversed, creating a situation in which the fears of the research tool amici would soon be put to the test.

If Justice Scalia thrust the Court's bayonet into the belly of § 271(e)(1) in *Lilly*,[80] he pulled out its viscera in *Merck v. Integra*. In *Lilly*, the Court, while criticizing the drafting of § 271(e)(1), construed its "patented invention" clause to include *any* invention used "solely for uses *reasonably related* to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products."[81] In *Merck*, the Court had the opportunity to evaluate the CAFC's narrow construction of the "reasonably related" clause, and its reversal of that court's decision has left research tool patentees sitting on an uncertain landscape, perhaps with dark clouds looming overhead.

The Court unanimously declined to adopt the CAFC's interpretation of § 271(e)(1), explaining that inherent in the process of scientific experimentation on potential new drugs is uncertainty as to what compounds initially tested might some day end up as part of an FDA submission.[82] For this reason, Justice Scalia explained,

> to construe § 271(e)(1) as the Court of Appeals did, not to protect research conducted on patented compounds for which an [FDA submission] is not ultimately filed is effectively to limit assurance of exemption to the activities necessary to seek

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[76] *See, e.g.*, Brief for Invitrogen Corp. et al. as Amici Curiae in Support of Respondents, Merck KGaA v. Integra Lifesciences I, 125 S.Ct. 2372 (2005) (No. 03-1237), 2005 WL 682093 [hereinafter Invitrogen Brief], and Brief of Amici Curiae Eli Lilly Co. et al. in Support of Petitioner, Merck KGaA v. Integra Lifesciences I, 125 S.Ct. 2372 (2005) (No. 03-1237), 2005 WL 435888 [hereinafter Lilly Brief].

[77] Invitrogen Brief, *supra* note 76, at *9. R

[78] Lilly Brief, *supra* note 76, at *18. R

[79] *Id.* at *17.

[80] *See supra* Part II.A.

[81] Eli Lilly v. Medtronic, 496 U.S. 661, 665 (1990); 35 U.S.C. § 271(e)(1) (1984).

[82] Merck KGaA v. Integra Lifesciences I, Ltd., 125 S.Ct. 2372, 2382-83 (2005).

> approval of a generic drug . . . [t]he statutory text does not require such a result.[83]

The Court instead adopted a broad view of the "reasonably related" clause, explaining that proper construction of § 271(e)(1) required protection of experiments like Cheresh's, because " 'development and submission of information' to the FDA does not become more attenuated (or less reasonable) simply because the data from [a particular] experiment are left out of the submission that is ultimately passed along to the FDA."[84] Despite this broad pronouncement, the Court explicitly declined, by way of a footnote, to "express a view about whether, or to what extent, § 271(e)(1) exempts from infringement the use of 'research tools' in the development of information for the regulatory process."[85]

Taken at face value, however, the Court's decision represents a true reversal of fortune for research toolmakers and drug developers. After *Merck*, research toolmakers previously immunized against experimental use by the CAFC's decisions in *Madey* and *Integra* may find themselves vulnerable to a new strain of safe harbor jurisprudence that renders almost any commercial experimental use non-infringing, as long as that use can be tied to a future FDA submission. For the first time since 1813, the fate of our hypothetical vaccine developer and former patent infringer, VaxDev, has shifted completely, with its unlicensed use of ResTool's preclinical research tool now rendered immune to any action for infringement, as long as VaxDev can show some relevance, no matter how attenuated, to future federal regulatory approval.

4. The Aftermath of *Merck v. Integra*: A Rough Road Ahead for Research Tool Patentees?

Public reaction following *Merck* may prove to be predictive of a great deal of confusion still to come. While some construed the decision as "a big win for discovery drug companies" and construed the Court's holding to mean that "activities . . . like using biotech research tools for drug discovery are not categorically excluded from the exemption,"[86] others immediately adopted the opposing

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[83] *Id.* at 2383.
[84] *Id.*
[85] *Id.* at 2382 n.7.
[86] Eli Kintisch, *Supreme Court Rules on Patent Suits*, ScienceNow, Jun. 13, 2005, http://sciencenow.sciencemag.org/cgi/content/full/2005/613/2 (quoting Attorney Kevin Noonan of McDonnell Boehnen Hulbert & Berghoff LLP) (last visited Oct. 18, 2005). A truncated version of the quotation appears in Eli Kintisch, *Supreme Court on Drug Research*, 308 SCIENCE 1725 (Jun. 17, 2005).

view. Invitrogen, for example, despite its earlier warnings of "devastation,"[87] issued a press release stating that the Court's decision "leaves research tool patents unaffected," even going as far as stating that since the Court declined to address the research tools issue, "[w]e believe . . . that the ruling will not have a material effect on Invitrogen's business."[88]

However, not long after *Merck* was decided, indications quickly appeared suggesting that such optimism may have been gravely misplaced. In *Classen Immunotherapies v. Biogen IDEC*, decided just a month after *Merck* in the District of Maryland, the district court interpreted *Merck*'s holding in the broadest possible manner, dismissing Classen's claims against Biogen IDEC ("Biogen") and GlaxoSmithKline ("GSK") when the defendants successfully argued that their allegedly infringing acts of research tool use fell within the safe harbor provision of § 271(e)(1) as construed in *Lilly* and *Merck*.[89]

In *Classen*, Biogen and GSK, together with Merck & Co., Inc.,[90] Chiron Corp., and Kaiser-Permanente,[91] were sued by Classen for infringement of four patents related to protocols for evaluating vaccine administration schedules.[92] Relying on the Court's decision in *Merck*, Biogen and GSK sought to have the portions of the complaint alleging infringement of Classen's patents dismissed.[93] The *Classen* court held that under *Lilly* and *Merck*, "§ 271(e)(1)'s exemption 'extends to all uses of patented inventions that are reasonably related to the development and submission of *any* information under [federal law],'" and that because defendants were studying "risks associated with various vaccination schedules . . . reasonably related to the development and submission of [such] information . . . , GSK and Biogen's motion to dismiss . . . [should] be granted."[94]

Importantly, Biogen and GSK's alleged acts of infringement occurred after the vaccines under study had already been approved

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[87] *See supra* note 76. **R**

[88] Press Release, Invitrogen Corp., U.S. Supreme Court Decision in Merck KGaA v. Integra LifeSciences Leaves Research Tool Patents Unaffected (Jun. 14, 2005), http://phx.corporate-ir.net/phoenix.zhtml?c=61498&p=irol-newsArticle&ID=720161 (last visited Dec. 8, 2005).

[89] Classen Immunotherapies, Inc. v. Biogen IDEC, 381 F. Supp. 2d 452 (D. Md. 2005).

[90] Merck & Co., Inc., is a New Jersey corporation, and should not be confused with the German pharmaceutical company Merck KGaA of *Merck v. Integra*.

[91] I focus here only on the safe harbor aspect of the opinion, which concern only Biogen and GSK.

[92] *Id.* at 453.

[93] *Id.* at 455.

[94] *Id.* at 456 (quoting Merck KGaA v. Integra Lifesciences I, Ltd., 125 S.Ct. 2372, 2380 (2005)) (emphasis in original).

by the FDA, and, unlike the RGD peptides in *Merck* which the Court declined to consider as research tools,[95] it was not possible to construe Classen's vaccine evaluation protocols as having been "objects of study," or indeed as anything other than research tools.

The district court in *Classen* turned the Supreme Court's holding in *Merck* on its head by construing it to mean that as long as the "reasonably related" requirement is fulfilled by *any* invention present in the experimentation at issue, no infringement by *other* inventions used in the same set of experiments can be claimed. In other words, because the vaccines under study themselves qualified for safe harbor, so did the patented protocols used to study them. This reasoning is at odds with the plain text of the portion of Justice Scalia's opinion quoted by the district court, which states that:

> [w]here a drugmaker has a reasonable basis for believing that a patented compound may work, through a biological process, to produce a particular physiological effect, and *uses the compound* in research that, if successful, would be appropriate to include in a submission to the FDA, *that use* is reasonably related to the development and submission of information under Federal law.[96]

The natural interpretation of this passage is that patented inventions (in *Merck*, patented compounds) under study are *themselves* exempt from infringement when such study is reasonably related to an FDA submission. To construe the Court's language as the *Classen* court did is to say that not only was Merck KGaA's use of RGD peptides exempt from infringement under § 271(e)(1), but indeed that *any* patented invention (protocol, instrument, reagent, etc.) used in the same stream of experimentation was also exempt. Such an interpretation of *Merck* is indeed the research toolmaker's worst nightmare, as it would expand § 271(e)(1)'s safe harbor into a single, broad research exemption that, as Justice Story might find ironic, applies only to commercial use.

III. CONCLUSIONS

A. *The § 271(e)(1) Safe Harbor in the Post-*Merck *World*

We have tracked the progress of the licensing and infringement battle of two fictional companies, ResTool and

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[95] *See supra* Part II.C.

[96] *Classen*, 381 F. Supp. 2d at 456 n.2 (emphasis added) (quoting *Merck KGaA*, 125 S.Ct. at 2383) (internal quotation marks omitted).

VaxDev, meant to represent research tool patentee and drug developer, respectively. Table 1 shows how the balance of power has shifted over time, with a patent system that once entirely favored the patentee now favoring the former infringer. While ResTool would have received complete protection from unlicensed commercial use of its research tool patents during the first 170 years of the U.S. patent system's existence, the tables have turned dramatically since the 1984 Act's introduction of 35 U.S.C. § 271(e)(1).

The aftershocks following the *Merck* decision, as exemplified by *Classen*, are not likely to dissipate in the short term. On the legislative front, though Congress is currently undertaking major patent reform as it considers the Patent Reform Act of 2005, the bill contains no reference to § 271(e)(1), and does not in any way modify § 271(a)'s general prohibition on infringing use.[97]

TABLE 1: SAFE HARBOR AND EXPERIMENTAL USE FROM MAY 1812 THROUGH NOV. 2005.[98]

	Pre-Clinical Research Tool		Clinical Research Tool	
Case/Year	ResTool	VaxDev	ResTool	VaxDev
Sawin v. Guild (1813)	X		X	
Roche v. Bolar (1984)	X		X	
Hatch-Waxman / 1984 Act introduces 35 U.S.C. § 271(e)(1)				
Integra v. Merck (2003)	X			X
Merck v. Integra (2005)		X		X

The question remains what effect the *Merck* decision will have on the research tool industry in general. One might argue that appropriate pricing of research tools for initial purchase could help research toolmakers to compensate for lost licensing revenues. For example, many research tools, especially complex instruments and consumable reagents that require huge sunk costs for production, are not easily made in-house by potential infringers, and therefore, in most cases, must be purchased. Even a large multinational drug maker is unlikely to take up the manufacture of centrifuges, DNA sequencers, fluorescently labeled monoclonal antibodies, or any other product that would be more cheaply and easily obtained by simple purchase even at high price points. Further, simpler tools such as pipettors may be even more

[97] Patent Reform Act of 2005, H.R. 2795, 109th Cong. (2005), *available at* http://www.abanet.org/intelprop/home/PatentAct2005.pdf (last visited Dec. 8, 2005).

[98] An "X" indicates the probable winner of an infringement suit in which ResTool argues against unlicensed use of both its pre-clinical and clinical research tools, according to the precedent of the indicated case.

unlikely to be pirated by drug development companies, as their use in research and development is ubiquitous, and these companies lack the economy of scale of specialized manufacturers. Put more simply, in many cases, it may be cheaper to pay to use an invention than to pirate it, and a toolmaker afraid of potential non-payment of license fees could simply raise the initial cost to its drug developer client.

The foregoing analysis belies, however, some of the complexities of the problem facing research tool patentees after *Merck*. Tools that *are* easily pirated, such as gene sequences and written protocols, present difficult problems reminiscent of those facing the movie and music industries, where such matters are governed by copyright law. While the entertainment industry may sometimes be able to recoup losses from piracy of easily copied intellectual property through pricing, this creates a free rider problem, with end users who engage in piracy getting the benefit of the invention for free while raising the cost for honest users.[99] In addition, though raising prices at first seems an obvious way to avoid losses, the movie and music industries provide examples of how unauthorized use can have the effect of lowering rather than raising prices since the percentage of honest users will decrease as prices rise.[100] Despite rampant piracy, unauthorized duplication of movies and music remains illegal under copyright law, with pirates at even the lowest level likely engaging in a cost-benefit analysis that considers potential penalties for unauthorized use. In contrast, *Merck* and its progeny, at present limited to *Classen*, suggest that a large and economically meaningful part of formerly unauthorized use is now explicitly protected by law.

The solution to the research tool problem, if taken on legislatively, will likely not be a simple one. One obvious possibility would be to give § 271(e)(1) what it lacks—reference to a specific class or classes of inventions, and/or a specific segment of the research stream, e.g., pre-clinical or clinical experiments, that would qualify for safe harbor protection. For example, the phrase "patented invention *itself under study for future regulatory approval*" might be more

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[99] For example, a manufacturer of an operating system or an office application might try to predict how much piracy will occur, and then divide the total cost of piracy across the total number units produced, raising the price of each unit and compensating the manufacturer *ex ante* for unauthorized use.

[100] *See, e.g.*, Kate Kelly, Ethan Smith, & Ethan Wonacott, *Going Legit: Movie Industry Tries to Fight DVD Pirates with Lower Prices*, Wall Street Journal Classroom Edition, May 2005, http://www.wsjclassroomedition.com/archive/05may/medi_piracy.htm (last visited Dec. 8, 2005), and Charles Goldsmith, *Apple's iPod Success Isn't Sweet Music for Record Company Sales*, Bloomberg News, Nov. 2, 2005, http://quote.bloomberg.com/apps/news?pid=nifea&&sid=AHP5Ko1pozM0# (last visited Dec. 8, 2005).

effective than the more general "patented invention" that currently exists in § 271(e)(1). Similarly, the phrase "*as part of a clinical trial* reasonably related" rather than the more general "reasonably related" would provide a level of specificity and clarity that the statute currently lacks. Such revisions would, however, have to overcome the immense political influence and lobbying power of the pioneer drug industry,[101] which does not promise to be an easy task.

B. *Safe Harbor Patent Reform and Chisum's "Neutral Principles"*

In addition to the legislative difficulties they present, such patchwork additions to the patent code are also likely to be an inefficient way of solving a complicated problem. Such additions run counter to certain "neutral principles" that respected patent law professor Donald Chisum urges might be applied in order to efficiently achieve true patent reform.[102] Three of these neutral principles—*simplicity*, *zero-based budgeting*, and *cost sensitivity*—are particularly applicable to the present discussion.

Simplicity requires that a proposed change make the current system simpler rather than more complex.[103] While my suggested amendments may decrease complexity by narrowing the scope of § 271(e)(1), it is possible they could also increase complexity in unpredictable ways, as the jurisprudential history of § 271(e)(1) itself suggests. This is an undesirable result according to Chisum, who explains that increased complexity increasingly taxes the system by raising administrative costs.[104] For example, the more complex § 271 becomes through addition of new statutory language, the more likely infringement litigation is to ensue, as parties seek to determine how courts will interpret the added language, and to exploit new loopholes that may have arisen inadvertently as a result of patchwork re-drafting. Added linguistic complexity would therefore increase the burden on the federal district courts, the CAFC, and ultimately the Supreme Court—clearly an undesirable result from an efficiency perspective.

The principle of *zero-based budgeting* builds upon the simplicity notion by requiring fundamental change of a general rule if that

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[101] *See, e.g.*, Elizabeth Drew, *Selling Washington,* THE New York Review of Books, Jun. 23, 2005, at 22, *available at* http://www.nybooks.com/articles/18075 (last visited Dec. 8, 2005).

[102] Donald S. Chisum, *Reforming Patent Law Reform*, 4 J. MARSHALL REV. INTELL. PROP. L. 336, 341-43 (2005) (suggesting that patent reform can sometimes be better accomplished by re-drafting relevant portions of the patent code, rather than by adding band-aid-like modifications of language and adding new provisions that introduce exceptions to existing provisions).

[103] *Id.* at 341-42.

[104] *Id.* at 342.

rule is problematic, rather than "creating exceptions to solve the immediate problem,"[105] as occurred in 1984 when § 271(e)(1) was appended to 35 U.S.C. § 271. Introduction of § 271(e)(1) itself violated the zero-based budgeting principle by creating an exception (safe harbor for uses reasonably related to FDA submission) to solve an immediate problem (de facto patent term extension). This increase in statutory complexity indeed increased administrative costs, as parties attempted to fit possibly infringing uses into the semantics of the new statutory provision, and courts sought to define the boundaries of the new provision, as seen in *Merck* and *Classen*. As the failed experiment of § 271(e)(1) suggests, adherence to the zero-based budgeting principle may require wholesale redrafting of § 271, a task which, as noted earlier, is not presently visible on Congress's horizon.[106]

Finally, and perhaps most importantly, *cost sensitivity* requires consideration of the direct and indirect impact of the statute on all interested parties.[107] This means that re-drafting must take into account the plight of research toolmakers and the general public in addition to that of the interest group with the largest immediate financial stake—in this case the pioneer drug industry. As we have seen, a statutory scheme that encourages either judicial approval of license-free use of patented inventions or increased infringement litigation will clearly not accomplish this goal, suggesting that both inaction and simple amendment are undesirable approaches to the safe harbor problem. It is hard to argue that § 271(e)(1) was drafted with the interests of the highest payer in mind, since the Hatch-Waxman Act arose precisely as a response to the inequities that rewarded a few large players at the expense of their smaller competitors. However, it now appears that despite Congress's best intentions, § 271(e)(1) is simply not equal to its complex task.

It is likely that when cases like *Classen* are appealed and rise through the appellate system, the CAFC and the Supreme Court will speak specifically to the research tool issue, and will perhaps narrow the holding of *Merck* to apply only to inventions *under study* in anticipation of regulatory approval. Whether the solution to the research tool problem lies with the Congress or with the courts remains to be seen, but it seems likely that the Supreme Court's

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105 *Id.*

106 *See supra* note 97. R

107 Chisum, *supra* note 102, at 342. R

decision in *Merck v. Integra*, especially if it continues to spawn progeny like *Classen*, will spur the interested parties to action.

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