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Biotechs Beware: Safe Harbor No More?

Shawn C. Troxler¹

I. Introduction

The Presidential election of 2000 forever will be known as one of the most highly contested elections in United States' history. After the final tally, a mere 537 votes decided the presidency.² One of the key issues at the heart of the election was the high cost of prescription drugs, especially for senior citizens.³ Both candidates hoped to lower prescription drug prices and, at the same time, facilitate the entry of generic drugs into the marketplace to drive down prices.⁴ Coincidentally, nearly twenty years earlier, Congress faced a similar debate. That debate led to the creation of The Drug Price Competition and Patent Term

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² CNN, *How We Got Here: A Timeline of the Florida Recount* (Dec. 13, 2000), at <http://www.cnn.com/2000/ALLPOLITICS/stories/12/13/got.here/index.html> (on file with the North Carolina Journal of Law & Technology).

³ In the third presidential debate on October 17, 2000, both candidates answered questions on how they would reform current Medicaid problems and lower the cost of prescription drugs. George W. Bush replied:

The purchasing powers—and I'm again [sic] price controls. I think price controls would hurt our ability to continue important research and development. Drug therapies are replacing a lot of medicine as we used to know it. One of the most important things is to continue the research and development component, and so I'm against price controls. Expediting drugs through the FDA makes sense, of course. Allowing the new bill that was passed in the Congress made sense to allow for, you know, drugs that were sold overseas to come back, in other countries, to come back into the United States. That makes sense.

CNN, *Campaign 2000: Vice President Gore and Governor Bush Participate in Third Debate Sponsored by the Commission of Presidential Debates* (Oct. 17, 2000), at <http://www.cnn.com/ELECTION/2000/debates/transcripts/u221017.html> (on file with the North Carolina Journal of Law & Technology).

⁴ *Id.*

Restoration Act ("Hatch-Waxman Act"),⁵ which dramatically affected the patent and food and drug laws as well as the manner in which the pharmaceutical industry operated.

Congress enacted the Hatch-Waxman Act in 1984 essentially to reverse the Federal Circuit's decision in *Roche Products, Inc. v. Bolar Pharmaceuticals Co.*⁶ In *Roche*, the Federal Circuit concluded that a generic drug manufacturer's use of a patented drug to obtain information needed for the regulatory approval of its generic drug constituted patent infringement.⁷ This decision prevented generic drug manufacturers from using patented drugs to gather the information needed to obtain pre-market approval for generic drugs, thereby delaying the marketing of any generic drugs until the relevant patents had expired. The pre-market approval process of pharmaceuticals is a lengthy process that requires the drug manufacturers to comply with various statutes, regulations, and guidelines set forth by the Food and Drug Administration ("FDA").⁸ The result of the *Roche* decision was that a patentee would continue to enjoy commercial exclusivity in a practical sense, even after the patent had expired.⁹

Congress hoped to remedy this situation by enacting legislation that would allow generic drug manufacturers to use patented drugs to obtain pre-market approval, including "bioequivalency testing."¹⁰ Generic drug manufacturers perform

⁵ Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified at 15 U.S.C. §§ 68(b)-(c), 70(b) (1994); 21 U.S.C. §§ 301, 355, 360(c) (1994); 28 U.S.C. § 2201 (1994); 35 U.S.C. §§ 156, 271, 282 (1994)).

⁶ 733 F.2d 858 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 856 (1984); *see* H.R. REP. NO. 98-857, pt. 2, at 45 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2467, 2711 ("The provisions of Section [271(e)] have the net effect of reversing the holding of the court in *Roche*.").

⁷ *Roche*, 733 F.2d at 863.

⁸ *See generally* Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended 21 U.S.C. §§ 301-399 (1994)) (providing that the purpose of this section is to protect consumers from dangerous food and drug products and to set enforcement standards which will be used to safeguard the public health).

⁹ Such a result would also hinder the purpose of the patent, which is to "promote the progress of science and useful arts . . ." U.S. CONST. art. I, § 8; cl. 8.

¹⁰ *See* H.R. REP. NO. 98-857, pt. 1, at 14-15 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647-48.

bioequivalency testing to ensure that the generic drug contains the same amount of active ingredient as the patented drug.¹¹ To this end, Congress enacted 35 U.S.C. § 271(e)(1), which created a safe harbor by exempting from infringement all conduct “reasonably related to the development and submission of information” necessary to obtain regulatory approval.¹² As a result, it was estimated that, by the end of 2002, generic drugs would account for over two-thirds of all prescriptions written and approximately twenty billion dollars in retail.¹³

This Recent Development examines the Federal Circuit’s recent decision in *Integra Lifesciences I, Ltd. v. Merck KGaA*¹⁴ and argues that the Federal Circuit properly narrowed the scope of the exemption provided by the § 271(e)(1) safe harbor provision. Additionally, this Recent Development proposes that the Supreme Court should grant certiorari and affirm the *Integra* decision because it is consistent with the legislative intent of § 271(e)(1). Moreover, this Recent Development proposes that Congress should enact a statute codifying the common law research exemption to bring the state of patent law in accord with twenty-first century principles.

II. The Safe Harbor Provision

A. Section 271(e)(1)

Congress enacted § 271(e)(1) as a safe harbor provision to ensure that generic drugs would be ready for market as soon as any

¹¹ See *Am. Bioscience, Inc. v. Shalala*, 142 F. Supp. 2d 1, 3 (D.D.C. 2000) (citing *United States v. Generix Drug Corp.*, 460 U.S. 453, 455 (1983)) (“A generic drug contains the same active ingredients, but not necessarily the same inactive ingredients, as a brand-name prescription drug.”).

¹² 35 U.S.C. § 271(e)(1) (2001).

¹³ C. DANIEL MULLINS ET AL., DEP’T OF HEALTH & HUMAN SERVS., PROJECTIONS OF DRUG APPROVALS, PATENT EXPIRATIONS, AND GENERIC ENTRY FROM 2000 TO 2004, at <http://aspe.os.dhhs.gov/health/reports/Drug-papers/Mullins-Palumbo%20paper-final.htm> (Sept. 27, 2003) (on file with the North Carolina Journal of Law & Technology).

¹⁴ 331 F.3d 860 (Fed. Cir. 2003).

relevant patents expired.¹⁵ Section 271(e)(1) provides [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.¹⁶

Although the scope of the exemption was initially limited to the manufacture of drugs, the protection afforded by the section has since been expanded.

B. Expansion of the Safe Harbor Provision

The first dramatic expansion came in the landmark case, *Eli Lilly & Co. v. Medtronic, Inc.*¹⁷ In *Eli Lilly*, the Federal Circuit held that the law was not limited to “drugs” but included medical devices subject to FDA approval.¹⁸ In affirming the Federal Circuit’s decision, the Supreme Court broadened the scope of § 271(e)(1) even further.¹⁹ The Court focused on the phrase “a Federal law which regulates the manufacture, use, or sale of drugs,” and considered whether this phrase referred to “an isolated statutory section” or “to an entire Act.”²⁰ The Court concluded that the phrase applied to all products subject to approval under the Federal Food, Drug, and Cosmetics Act.²¹ If Congress had intended to include only drug patents, the Court reasoned, it easily could have done so by stating that in the statute.²² Additionally, the Court held that “[t]he phrase ‘patented invention’ in §

¹⁵ See *Teletronics Pacing Sys., Inc. v. Ventritex, Inc.*, 982 F.2d 1520, 1525 (Fed. Cir. 1992) (concluding that the intent of Congress was to “allow [generic manufacturers] to be in a position to market their products as soon as . . . legally permissible”).

¹⁶ 35 U.S.C. § 271(e)(1).

¹⁷ 872 F.2d 402 (Fed. Cir. 1989), *aff’d*, 496 U.S. 661 (1990).

¹⁸ *Id.* at 406.

¹⁹ *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 679 (1990).

²⁰ *Id.* at 665–66.

²¹ 21 U.S.C. § 360(e) (2002); *Eli Lilly*, 496 U.S. at 679.

²² *Eli Lilly*, 496 U.S. at 669.

271(e)(1) is defined to include all inventions, not drug-related inventions alone.²³ As a result of *Eli Lilly*, the safe harbor provision encompasses not only drugs, but also medical devices, food additives, color additives, and human biological products.²⁴

Initial § 271(e)(1) jurisprudence also focused on the interpretation of other key terms and phrases in the safe harbor provision. The original focus was on the word “solely” and whether the infringing “uses” related “solely” to seeking regulatory approval.²⁵ This interpretation helped to narrow the scope of § 271(e)(1) in early federal decisions. However, federal courts have since concluded that “solely” is correctly read as modifying “uses,” and is not determinative, expanding the protections of § 271(e)(1).²⁶

Recent federal district court decisions involving § 271(e)(1) have addressed whether particular conduct is “reasonably related” to obtaining regulatory approval.²⁷ In *Amgen v. Hoechst Marion Roussel*,²⁸ the District Court of Massachusetts concluded that the phrases “solely for uses reasonably related” and “use solely for purposes reasonably related” were not the same, the latter being more restrictive.²⁹ Generally these decisions have concluded that only uses reasonably related to gathering data for regulatory approval are within the safe harbor.³⁰ Such an analysis greatly

²³ *Id.* at 665.

²⁴ *Id.* at 670–71.

²⁵ See generally *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379, 1395–96 (N.D. Cal. 1987) (concluding that “to establish entitlement to the statutory exemption, the defendant must demonstrate that it made and used plasma-derived and recombinant Factor VIII:C preparations solely for the purpose of meeting FDA reporting requirements”).

²⁶ *Elan Transdermal, Ltd. v. Cygnus Therapeutic Sys.*, 24 U.S.P.Q.2d (BNA) 1926, 1932–33 (N.D. Cal. 1992).

²⁷ See *Abtox, Inc. v. Exitron Corp.*, 888 F. Supp. 6, 8–9 (D. Mass. 1995) (concluding that § 271(e)(1) requires a two-step analysis: (i) only otherwise infringing uses are analyzed under the section; and (ii) only those infringing uses that are not reasonably related to obtaining regulatory approval are outside of the safe harbor).

²⁸ 3 F. Supp. 2d 104 (D. Mass. 1998).

²⁹ *Id.* at 107.

³⁰ See, e.g., *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269, 1280 (N.D. Cal. 1991) (asking whether “it [would] have been reasonable, objectively, for a

expanded the protection available to alleged patent infringers.

The most recent and broadest reading of § 271(e)(1) was rendered by the District Court for the Southern District of New York in *Bristol-Myers Squibb Co. v. Rhône-Poulenc Rorer, Inc.*³¹ In this case, the court held that Bristol-Myers' research using Rhône-Poulenc Rorer's patented chemical intermediates to investigate and identify potential new drug candidates was protected by the safe harbor provision.³² The court concluded that § 271(e)(1) protects all research, including synthesis of new drug candidates, their initial testing, and the determination of whether drug candidates should be pursued.³³ Thus, the court concluded that the § 271(e)(1) exemption includes all patents covering all inventions that are involved in the FDA approval process.³⁴ The recent Federal Circuit decision in *Integra*, therefore, comes at a time of increasing judicial reluctance to narrow the scope of the safe harbor provision.

C. *Integra Lifesciences I, Ltd. v. Merck KGaA*³⁵

In *Integra*, the patentee, Integra, owned patents relating to a peptide sequence that promoted beneficial cell adhesion to substrates by interacting with $\nu\beta$ receptors on cell surface proteins.³⁶ Integra alleged that Merck, which funded research that used Integra's research tools for identifying compounds that would block the same receptors, infringed its patents.³⁷ Merck discovered that blocking these receptors would inhibit the formation of new

party in defendant's situation to believe that there was a decent prospect that the 'use' in question would contribute . . . to the generation of kinds of information that was likely to be relevant in the process by which the FDA would decide whether to approve the product").

³¹ No. 95 C 8833, 2001 WL 1512597 (S.D.N.Y. Nov. 28, 2001).

³² *Id.* at *7-8.

³³ *Id.* at *8.

³⁴ *See id.* at *6 (concluding that Bristol-Myers' experiments would contribute to the generation of kinds of information that was likely to be relevant in the FDA approval process).

³⁵ 331 F.3d 860 (Fed. Cir. 2003).

³⁶ *Id.* at 862.

³⁷ *Id.* at 863.

blood vessels and possibly halt tumor growth.³⁸

1. The Majority Opinion

At trial, the District Court for the Southern District of California held that the § 271(e)(1) exemption did not apply to the Merck-sponsored research.³⁹ The Federal Circuit affirmed, focusing its analysis on the legislative intent.⁴⁰ The Federal Circuit noted that the House Committee that initiated the safe harbor provision expressly described the pre-market approval activity as “a limited amount of testing so that generic manufacturers can establish the bioequivalency of a generic substitute.”⁴¹ Such an infringement would only be “de minimis.”⁴² The Federal Circuit concluded that because § 271(e)(1) is limited to activities that are “solely for uses reasonably related to the development and submission of information” to the FDA, the exemption “cannot extend at all beyond uses with the reasonable relationship specified in § 271(e)(1).”⁴³ Moreover, the court stated that § 271(e)(1) “simply does not globally embrace all experimental activity that at some point, however attenuated, may lead to an FDA approval process.”⁴⁴

Additionally, the court concluded that extending § 271(e)(1) to encompass new drug development would not limit the exemption to instances of de minimis infringement.⁴⁵ Furthermore, the Federal Circuit recognized that a broad interpretation of § 271(e)(1) would “effectively vitiate the exclusive rights of patentees owning biotechnology tool patents.”⁴⁶ The court stated that an expansive reading of § 271(e)(1) “would swallow the benefit of the Patent Act for some categories of

³⁸ *Id.*

³⁹ *Id.* at 863–64.

⁴⁰ *Id.* at 872.

⁴¹ *Id.* at 865 (citing H.R. REP. No. 857, pt. 2, at 8 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2467, 2692).

⁴² *Id.* at 867.

⁴³ *Id.* at 866.

⁴⁴ *Id.* at 867.

⁴⁵ *Id.*

⁴⁶ *Id.*

biotechnological inventions.”⁴⁷ Finally, the court held that the Merck-sponsored research was not embraced by the language and context of the safe harbor provision.⁴⁸

2. The Dissent

In her dissent, Judge Newman explained that pursuant to the “common-law” research exemption, the subject matter of patents might be studied “in order to understand it, or to improve upon it, or to find a new use for it, or to modify or ‘design around’ it.”⁴⁹ Otherwise, a patentee would stop the “advancement of technology” in a certain field.⁵⁰ In Judge Newman’s view, Merck took a patented product that was of no value in Integra’s hands and improved it.⁵¹ The fact that profits were the ultimate goal or hope of a research effort should not preclude a research effort from the safe harbor exemption.⁵² “The better rule is to recognize the exemption for research conducted in order to understand or improve upon or modify the patented subject matter.”⁵³ Although Judge Newman agreed with the majority that § 271(e)(1) does not embrace the “development and identification of new drugs,” she argued that Merck’s research either was exempt exploratory

⁴⁷ *Id.*

⁴⁸ *Id.* at 868.

⁴⁹ *Id.* at 875 (Newman J., dissenting). The common law research exemption, developed in case law since 1813, creates an exception for patent infringement “solely for research, academic, or experimental purposes.” *Id.* See *Whittemore v. Cutter*, 29 F. Cas. 1120 (C.C.D. Mass. 1813) (No. 17,600) (stating that the availability of this common law exception to infringement turns on whether a use for profit was evident or in keeping with the alleged infringer’s legitimate business, and that even “commercial overtones” may take an infringer’s activity out of the exemption); *Madey v. Duke Univ.*, 307 F.3d 1351, 1362 (Fed. Cir. 2002) (concluding that use is disqualified from the exemption if it has the slightest commercial implication).

⁵⁰ *Integra*, 331 F.3d at 875 (Newman J., dissenting).

⁵¹ See *id.* at 876. “Were all research using RGD peptides prohibited until the *Integra/Telios* patents expired, not even the patent owner would benefit, for the patented products had failed in *Telios*’ hands, leaving the patents valueless until *Scripps* and *Merck* made their discoveries . . .” *Id.*

⁵² *Id.*

⁵³ *Id.*

research or was immunized by § 271(e)(1).⁵⁴ “It would be strange to create an intervening kind of limbo, between exploratory research subject to exemption, and the FDA statutory immunity, where the patent is infringed and the activity can be prohibited.”⁵⁵ Judge Newman concluded that such an arrangement would defeat the purposes of both exemptions, and “the law does not favor such an illogical outcome.”⁵⁶

3. Criticism of the *Integra* Majority

The Federal Circuit’s decision in *Integra* marked a dramatic reversal in the trend to broadly interpret the scope of drug development activities exempted from patent infringement by § 271(e)(1).⁵⁷ Until the *Integra* decision, “the courts, the bar, and industry generally shared the view” that the safe harbor provision exempted any and all activity, including early-stage drug research, that led to the submission of data for FDA approval.⁵⁸ Although the Federal Circuit achieved the proper outcome, the court’s conclusion that § 271(e)(1) does not apply to the use of research tools is open to criticism.⁵⁹

⁵⁴ *Id.* at 877.

⁵⁵ *Id.*

⁵⁶ *Id.*

⁵⁷ See, e.g., *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990); *Bristol-Myers Squibb Co. v. Rhône-Poulenc Rorer, Inc.*, No. 95 C 8833, 2001 WL 1512597 (S.D.N.Y. Nov. 28, 2001); *Amgen v. Hoechst Marion Roussel*, 3 F. Supp. 2d (D. Mass. 1998).

⁵⁸ Carl B. Massey, Jr. & Paul C. Kimball, *Federal Circuit Narrows FDA “Research Exemption” Safe Harbor Under § 271(e)(1): Research Tool Patents Revived*, (June 24, 2003), at Womble Carlyle, <http://www.wcsr.com/CM/News%20Bites/News%20Bites1662.asp> (on file with the North Carolina Journal of Law & Technology); see *Bristol-Myers*, 2001 WL 1512597, at *7–8 (concluding that the § 271(e)(1) exemption included all patents covering all inventions that are used in the FDA approval process).

⁵⁹ A research tool may be defined very broadly to include the “full range of resources that scientists use in the laboratory,” including “cell lines, monoclonal antibodies, reagents, animal models, growth factors, . . . cloning tools, . . . methods, laboratory equipment and machines, databases and computer software.” Janice M. Mueller, *No “Dilettante Affair”*: *Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 11 (2001) (citing NATIONAL INSTITUTES OF

The Federal Circuit's analysis of the reasonable relationship between the use of research tools to identify drug candidates and the possible submission of information to the FDA is troubling. For instance, a mere two years earlier Merck's use of patented research tools would have been exempted under the safe harbor provision according to the District Court for the Southern District of New York.⁶⁰ That court concluded that there was a "decent prospect" that the use of the patented tools would somewhat contribute to the generation of information sought by the FDA.⁶¹ Such analysis is correct, as the plain language of the statute does not require a showing that the new product would actually be submitted to the FDA. Additionally, the use of patented research tools to produce new drug candidates appears to have a proximate relationship that is "reasonably related" to the submission of drug information to the FDA. Research tools play an integral part in the "stream" of drug development, and such use is not unforeseeable in this process.⁶² Nonetheless, the Federal Circuit never cited nor addressed previous decisions relating to research-tool infringement.⁶³ Perhaps, then, the strength of the *Integra* majority's rationale lies in its acknowledgement of the

HEALTH, REPORT OF THE NATIONAL INSTITUTES OF HEALTH WORKING GROUP ON RESEARCH TOOLS 3, at <http://www.nih.gov/news/researchtools/index.htm> (June 4, 1998) [hereinafter NIH Research Tools Report]). However, a research tool may also be narrowly defined, and this Recent Development limits such an analysis to those "patented tools used in the development of new biotechnological or pharmaceutical products that do not themselves physically incorporate the tool." *Id.* at 14.

⁶⁰ See *Bristol-Myers Squibb Co.*, 2001 WL 1512597, at *7-8 (holding that the use of patented research tools to identify drug candidates was exempt under the safe harbor provision).

⁶¹ *Id.* at *6.

⁶² See generally Mueller, *supra* note 59, at 11 ("The problem of access to patented research tools is currently more acute and better documented in biotechnology than in any other scientific field. Biotechnology is research intensive. A high percentage of basic research tools and laboratory techniques of biotechnology are subject to proprietary restraints such as patents or material transfer agreements."); Stephen Maebius et al., *Preclinical Use of Research Tools Is Infringement*, 25 NAT'L L. J. 14 (concluding that often a screening research tool is only performed once to identify a drug candidate).

⁶³ See *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003).

legislative intent of the Act.

4. Reverting the Safe Harbor Back to Its Legislative Intent

The *Integra* majority's proper focus on the legislative history marked the first time in many safe harbor decisions that the Federal Circuit considered congressional intent when ruling on the application of the safe harbor provision.⁶⁴ Previous interpretations of § 271(e)(1), including that of the Supreme Court, demonstrated the courts' willingness to ignore the statute's legislative history in favor of its plain language and reluctance to imply limitations the statute does not require.⁶⁵ For example, in *Eli Lilly*, the Court held that if Congress intended to include only drug patents, it could easily have done so by drafting the statute to read "[i]t shall not be an act of infringement to . . . use . . . a patented drug invention"⁶⁶ In reaching its decision, the *Integra* majority acknowledged that the objective of the Hatch-Waxman Act was to "facilitate the immediate entry of safe effective generic drugs into the marketplace upon expiration of a pioneer drug patent."⁶⁷ The court further indicated that § 271(e)(1) should apply only to bioequivalence testing of generic versions of patented drugs, since such testing developed as a consequence of the Act.⁶⁸ However, the plain language of the statute states no such limit. In contrast,

⁶⁴ See generally *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019, 1027–30 (Fed. Cir. 1997) (considering the plain language of the statute and the Supreme Court's decision in *Eli Lilly* before deciding that the statute applies to all medical devices, regardless of FDA classification); *Intermedics, Inc. v. Ventritex, Inc.*, 991 F.2d 808, 1993 WL 87405, at *5 (Fed. Cir. Feb. 22, 1993) (concluding that the defendant's reliance on § 271(e)(1) is not precluded by manifestation of an intent to commercialize upon FDA approval, and stating that "[i]f the statutory language is clear, the plain meaning of the statute controls").

⁶⁵ See generally *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990); *Abtox*, 122 F.3d at 1019–30 (Fed. Cir. 1997) (considering the plain language of the statute and the Supreme Court's decision in *Eli Lilly* before deciding that the statute applies to all medical devices, regardless of FDA classification).

⁶⁶ *Eli Lilly*, 496 U.S. at 667.

⁶⁷ *Integra*, 331 F.3d at 866–67.

⁶⁸ *Id.* at 865 (citing H.R. REP. No. 98-857, pt. 2, at 8 (1984), reprinted in 1990 U.S.C.C.A.N. 2647, 2692).

the court's language seems to speak for itself—only activities within a similar category of clinical testing are exempt under § 271(e)(1).

Additionally, the *Integra* majority focused on the legislative intent to “vitate” the rights of patentees owning research tool patents.⁶⁹ The legislative history clearly provides that Congress did not intend the enactment of the safe harbor provision to interfere significantly with the rights of the patent holder.⁷⁰ Congress intended only a de minimis or negligible encroachment on the rights of the patentee.⁷¹ The *Integra* majority concluded that allowing the use of a research tool in general research to identify a candidate drug would thereby deprive the patentees of the benefits of patent protection.⁷² Such complete infringement is obvious, as the research tool achieves its utility when used in the discovery of new products and technology.⁷³ By concentrating on the legislative history of the Act, the *Integra* majority provided a just basis for the narrowing of the scope of the exemption to reflect its originally intended purpose.

5. A Narrow or Broad Safe Harbor Provision?

The majority and dissenting opinions in *Integra* appear to reflect two schools of thought on the scope of the safe harbor provision: a narrow interpretation to reflect the congressional intent and a broad approach to facilitate modern biotechnological research.⁷⁴ Proponents of a narrow safe harbor provision, reflected in *Integra*'s majority opinion, argue that a broadened safe harbor provision would leave many patentees uncompensated and without

⁶⁹ *Id.* at 867.

⁷⁰ See H.R. REP. No. 98-857, pt. 2, at 28, 30 (1984), *reprinted in* 1984 U.S.C.C.A.N. at 2714.

⁷¹ See *id.*

⁷² See *Integra*, 331 F.3d at 867.

⁷³ See generally Mueller, *supra* note 59, at 10–17 (defining what a research tool is and describing possible uses).

⁷⁴ See generally *id.* at 49–66 (discussing the benefits and drawbacks of a broadened versus narrow experimental use exemption and its application on the use of research tools).

sufficient incentives to develop new technology.⁷⁵ In essence, if all non-consensual patent users were given a complete exemption from liability, biotechnology companies could potentially keep their technology as trade secrets, thus detracting from the legislative intent of the statute.⁷⁶

However, proponents of a broadened § 271(e)(1), reflected in Judge Newman's *Integra* dissent,⁷⁷ argue that the doctrine should be expanded in a way that will maximize the development of important new therapeutic products.⁷⁸ This development of new biotechnology products coincides with the constitutional underpinnings of the patent system, which is "to promote the progress of . . . the useful arts."⁷⁹ As Judge Newman argued, by preventing the research use of inventions disclosed in a patent, such restrictions would frustrate public policy and hamper scientific research.⁸⁰ Such debate has continued since the enactment of § 271(e)(1) nineteen years ago and reflects the original interests of competing drug companies in constructing the

⁷⁵ See Rich J. Warburg et al., *Patentability and Maximum Protection of Intellectual Property in Proteomics and Genomics*, 22 BIOTECHNOLOGY L. REP. 264, 270–72 (2003) (concluding that if the current views of activities exempted under the safe harbor provision as expressed by the district court [in *Bristol-Myers*] prevail, companies may benefit by making its technology protected as a trade secret, and noting that such concerns may facilitate more companies to maintain its technology as a trade secret rather than seeking patent protection).

⁷⁶ See *id.*

⁷⁷ *Integra*, 331 F.3d at 872 (Newman J., dissenting).

⁷⁸ See Mueller, *supra* note 59, at 7 (quoting NIH Research Tools Report, *supra* note 59) ("[T]he stacking of intellectual property obligations as successive tools are used in the course of an extended research project has the potential to impede or even preclude the development of new and better diagnostic therapeutic products."); see also Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons Biomedical Research*, 280 Sci. 698, 699 (1998).

⁷⁹ U.S. CONST. art. I, § 8, cl. 8.

⁸⁰ See *Integra*, 331 F.3d at 876 (Newman J., dissenting) (stating "[t]hat is how the patent system has always worked: the patent is infringed by and bars activity associated with development and commercialization of infringing subject matter, but the research itself is not prohibited, nor is comparison of the patented subject matter with improved technology or with designs whose purpose is to avoid the patent").

Hatch-Waxman Act.⁸¹ Although both sides present sound arguments, perhaps the *Integra* decision will provide a chance to strike an equitable balance between the two factions.

III. Reconciling *Integra* with Twenty-First Century Principles

A. Certiorari to the Supreme Court

In the recent past, the Supreme Court has rendered itself nearly invisible in patent law.⁸² *Eli Lilly*⁸³ is the only Supreme Court ruling on § 271(e)(1).⁸⁴ The “structural arrangements in the early federal judiciary dictated, or at least facilitated, substantial Supreme Court involvement in patent law.”⁸⁵ Nevertheless, structural reorganization of patent law jurisdiction over the past two decades has conferred on the Supreme Court increasingly greater discretion to move to the margins of patent law.⁸⁶

One author has proposed that the Supreme Court should follow a “Managerial Model,” making the Court a monitor that steps in to resolve intercircuit conflicts.⁸⁷ Although patent law has

⁸¹ ORRIN HATCH, *SQUARE PEG: CONFESSIONS OF A CITIZEN SENATOR* 70–81 (2002). Senator Hatch explains how the discussions and negotiations between the generic drug manufacturing representatives and the “brand companies” were often heated. During one point, Senator Hatch exclaimed, “If you guys don’t stop it, I’m going to kill somebody.” However, Senator Hatch later admitted that this outburst may have been additionally provoked from a throbbing tooth which needed root canal surgery.

⁸² *E.g.*, Mark Janis, *Patent Law and the Age of the Invisible Supreme Court*, 2001 U. ILL. L. REV. 387, 387 (2001).

⁸³ *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990).

⁸⁴ *See generally* Janis, *supra* note 82, at 415 (“The *Eli Lilly* case furnishes even a less satisfying illustration of the Supreme Court’s involvement in substantive patent law decision making.”).

⁸⁵ Janis, *supra* note 82, at 389.

⁸⁶ *See id.* at 392 (“By designating the Federal Circuit a court of appeals, Congress also ensured that decisions of the Federal Circuit were reviewable at the Supreme Court by a grant of certiorari.”).

⁸⁷ *Id.* at 408. The author also analyzes two other models: an interventionist and an invisible model. In the interventionist model, the Supreme Court would be inspired and impelled to guard the balance between incentivizing private invention and preserving integrity, while routinely exercising certiorari

no true intercircuit conflicts, the Supreme Court should give special consideration to dissents in the Federal Circuit and “use the presence of dissents as the major model impetus for Supreme Court review.”⁸⁸ Additionally, the Managerial Model calls for the Supreme Court to grant certiorari in patent cases to “review substantive patent issues only where there is a compelling issue of the allocation of power among institutional actors at stake.”⁸⁹ *Integra* provides an excellent opportunity for the Supreme Court to act under this model.

Further review of *Integra*, upon certiorari, would give the Supreme Court the opportunity to clarify the statute and determine its scope. In affirming the Federal Circuit’s decision in *Integra*, the Court could affirmatively revert the safe harbor provision back to its intended purpose of providing a safe harbor only to generic drug manufacturers. The Court could establish that clinical testing, which relates to the bioequivalence testing of a generic drug, is the lone activity exempt under § 271(e)(1).⁹⁰ Such a decision would help restore the protection once offered to patentees of various biotechnological products. Thus, the Court could limit the scope of § 271(e)(1) and definitively reverse the trend that it first established thirteen years earlier.

jurisdiction in patent cases in order to write new patent jurisprudence. In the invisible model, the Supreme Court would allay all authority of substantive law issues to the Federal Circuit. Under this model, few patentees would ever see the Supreme Court intercede in patent jurisprudence. *Id.*

⁸⁸ Helen W. Nies, *Dissents at the Federal Circuit and Supreme Court Review*, 45 AM. U. L. REV. 1519, 1520 (1996).

⁸⁹ Janis, *supra* note 82, at 408. The author advocates that decisions concerning patent law standards should be understood in terms of the allocation of decision-making authority, such as delegating the work of articulating and refining these standards to the Federal Circuit or the Patent and Trademark Office (PTO). *Id.* Additionally, the author states that in cases involving other “questions of administrative law, such as whether the Federal Circuit should accord . . . deference to PTO decisions, or procedure, . . . may be expected to conform with a managerial model, in which the Supreme Court intervenes as arbiter of a power struggle among patent law institutions.” *Id.* at 410.

⁹⁰ See 35 U.S.C. § 271(e)(1) (2001); H.R. REP. NO. 98-857, pt. 2, at 27 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2692.

B. Congressional Intervention . . . Again

Aside from the safe harbor provision provided by § 271(e)(1), case law in the United States also favors a narrow infringement exemption for research. This common law research exemption, developed in case law since 1813, creates an exception for patent infringement “solely for research, academic, or experimental purposes.”⁹¹ Availability of this common law exemption hinges on whether the research use of a patented invention is in any way commercial or within the legitimate business of the alleged infringer. Research does not qualify for an exemption if the infringement is undertaken in the “guise of scientific inquiry but has definite, cognizable, and not insubstantial commercial purposes.”⁹² Additionally, if the infringing use is in the furtherance of the alleged infringer’s legitimate business, then the research exemption does not apply.⁹³ Therefore, federal courts must perform tedious analyses to determine if the infringing use has any commercial overtones while performed in function with

⁹¹ See *Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (No. 17,600) (“[I]t could never have been the intention of the legislature to punish a man, who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects.”). The Federal Circuit’s only significant holding on the common law research exemption came in *Roche Prod., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858 (Fed. Cir. 1984). In *Roche*, the Federal Circuit held that the research exemption does not exempt activities that are legitimate business interests or have some other commercial purpose. *Id.* at 863.

⁹² *Madey v. Duke Univ.*, 307 F.3d 1351, 1362 (Fed. Cir. 2002) (quoting *Embrex, Inc. v. Serv. Eng’g Corp.*, 216 F.3d 1343, 1349 (Fed. Cir. 2000)); see *Sawin v. Guild*, 21 F. Cas. 554, 555 (C.C.D. Mass. 1813) (No. 12,391) (concluding that patent infringement must concern “the making [of the invention] with an intent to use for profit, and not for the mere purpose of philosophical experiment In other words, that the making must be with an intent to . . . deprive the owner of the lawful rewards of his discovery”).

⁹³ See *Madey*, 307 F.3d at 1362 (Fed. Cir. 2002) (“[S]o long as the act is in furtherance of the alleged infringer’s legitimate business and is not solely for amusement . . . the act does not qualify for the very narrow and strictly limited experimental use defense.”).

the alleged infringer's business activities.⁹⁴ "[I]n the case of biotechnological research, however, the line between commercial and noncommercial research is increasingly blurred; virtually all scientific research, particularly biotechnological research could be interpreted as within the legitimate business of the user or as having some commercial purpose."⁹⁵ Thus, this blurring of the line in biotechnological research and the confusion generated from federal court decisions as to what activities are exempt under § 271(e)(1) has left this area of patent law somewhat unsettled.

To avoid the confusion of what constitutes an activity exempt under § 271(e)(1) and to protect up-stream patent holders, Congress should pass legislation similar to the Proposed Patent Competitiveness and Technological Innovation Act of 1990 ("PPCTIA").⁹⁶ The PPCTIA provided,

It shall not be an act of infringement to make or use a patented invention solely for research or experimentation purposes unless the patented invention has a primary purpose of research or experimentation. If the patented invention has a primary purpose of research or experimentation, it shall not be an act of infringement to manufacture or use such invention to study, evaluate, or characterize such invention or to create a product outside the scope of the patent covering such invention. This subsection does not apply to a patented invention to which subsection (e)(1) applies.⁹⁷

The purpose of the PPCTIA was to remove confusion in general patent law, "reduce unnecessary litigation as well as threats of litigation," and to avoid the negative effect on research and

⁹⁴ See generally *id.* at 1355-63 (providing a detailed analysis of whether Duke University's use of Madey's patented equipment during research was exempt under the common law experimental use exemption).

⁹⁵ David L. Parker, *Patent Infringement Exemptions for Life Science Research*, 16 Hous. J. INT'L L. 615, 619 (1994).

⁹⁶ H.R. REP. NO. 101-960(I), 101st Cong., 2d Sess. 1 (1990). The PPCTIA was Congress' attempt to codify the common law research exemption.

⁹⁷ *Id.* at 65-66.

innovation.⁹⁸ This proposed legislation would encourage research and experimentation by providing that the making and using of a patented invention solely for research or experimentation would not constitute an act of infringement unless the patented invention had research and experimentation as its primary purpose.⁹⁹ The House report accompanying the PPCTIA explained that if the primary purpose of the invention was research or experimentation, “such as a transgenic mouse for cancer research or a laboratory implement such as a microscope,” then it would not be an act of infringement to “(1) study, characterize, or evaluate the invention; or (2) use the invention to create a product outside the scope of the patent.”¹⁰⁰ Nevertheless, the PPCTIA did not pass, and eventually was shelved.¹⁰¹

Today, similar legislation could potentially remedy the uncertainty and controversy surrounding § 271(e)(1). Codification of such legislation would promote the constitutional goal of promoting innovation and allowing research on a patented invention, i.e., research to create an improvement or “design around” that invention, while retaining the prohibition against

⁹⁸ *Id.* at 43–44.

⁹⁹ *Id.* at 41.

¹⁰⁰ *Id.* The report closes with a list of activities that would not constitute patent infringement under the proposed Act:

- (1) testing an invention to determine its sufficiency or to compare it to prior art;
- (2) tests to determine how the patented invention works;
- (3) experimentation on a patented invention for the purpose of improving on it or developing a further patentable invention;
- (4) experimentation for the purpose of “designing around” a patented invention;
- (5) testing to determine whether the invention meets the tester’s purposes in anticipation of requesting a license; and
- (6) academic instructional experimentation with the invention.

Id. at 44–45.

¹⁰¹ H.R. REP. NO. 101-960(I), 101st Cong., 2d Sess. 1 (1990); see Eyal H. Barash, *Experimental Uses, Patents, and Scientific Progress*, 91 Nw. U. L. REV. 667, 697 (1997). The author provides that some commentators were split on the utility and appropriateness of the Act. Some argued it would erode the country’s carefully-crafted incentive system and would be devastating. Others thought this Act would protect university researchers from potential patent infringement lawsuits for using many other patented inventions.

research using a patented invention.¹⁰² Also, such a statute would draw a clear line as to what constitutes patent infringement during drug development. For example, in *Integra*,¹⁰³ Merck's use of a patented research tool would clearly be an act of infringement under the PPCTIA. Merck's utilization of Integra's patented research tool to identify compounds that would block a cell's surface protein receptors would constitute infringement because Integra's research tool had the primary purpose of research or experimentation. However, if Merck merely improved the research tool in some way, that activity would certainly be protected under this exemption. Additionally, as Judge Newman advocated, the legislation would relieve the courts from common law determination of whether the research use of the invention is in any way commercial or profit-driven.¹⁰⁴ Therefore, this re-conceptualization of the common law research exemption would reflect the commercial realities of the twenty-first century research and development process.¹⁰⁵

The recent *Integra* decision only confirms the uncertainty of safe harbor provision exemptions and reveals the need to reform the provision back to its original intent. Legislation like the PPCTIA would benefit not only the biotechnology industry but also help the courts to refine § 271(e)(1) to its stated purpose. Thus, although the PPCTIA was not passed in 1990, it is time for Congress to propose such legislation again.

IV. Ex Post Royalty

One short-term solution to alleviate the confusion generated by § 271(e)(1) is payment of an ex post royalty. Under this system, a generic drug manufacturer would be permitted to use a patented invention in exchange for an ex post royalty payment

¹⁰² U.S. CONST. art. I, § 8, cl. 8.

¹⁰³ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003).

¹⁰⁴ *See id.* at 876 (Newman J., dissenting). *See generally* *Madey v. Duke Univ.*, 307 F.3d 1351, 1355–63 (Fed. Cir. 2002).

¹⁰⁵ *See Integra*, 331 F.3d at 876 (Newman J., dissenting) (stating that the “ultimate goal or hope of profit from successful research should not eliminate the exemption.”); Mueller, *supra* note 59, at 37 (stating that “[p]rofit motive should no longer be held antiethical to the experimental use doctrine”).

based on the market value of the newly created product.¹⁰⁶ For example, a drug manufacturer would be allowed a nonconsensual use of a patented research tool in exchange for a royalty payment based on the approximate true value of the research tool to the tool user and the product developer.¹⁰⁷ The research tool patent owner would be entitled to a royalty stream, while the drug manufacturer would avoid the burdens of “pre-use license negotiations, up-front payments, and blocked access to the proprietary research tool.”¹⁰⁸

Although the utilization of a royalty approach may trigger patent misuse or antitrust concerns, the patent community supports such a system. Royalty system advocates contend that patent misuse does not occur if the royalties result from a bargained, arms-length transaction.¹⁰⁹ Additionally, recent Federal Circuit decisions regarding damages jurisprudence have expanded the notion of recoverable damages to encompass virtually any type of economic harm that was “reasonably foreseeable” from the infringement.¹¹⁰ A royalty would lead to less infringement litigation as well as fewer transactional costs, as such infringement would be recognized in return for substantial payment. Thus, the payment of royalties to a patentee would not only continue to protect its patent rights, but would also allow possible drug developers to lawfully infringe such patents while continuing to

¹⁰⁶ See Mueller, *supra* note 59, at 58 (proposing the adoption of “a reach-through royalty structure that would link the royalty payment with the ultimate commercial value of the products developed from the use of the patented research tool”).

¹⁰⁷ See *id.*

¹⁰⁸ *Id.*

¹⁰⁹ John H. Barton, *Patents and Antitrust: A Rethinking in Light of Patent Breadth and Sequential Innovation*, 65 ANTITRUST L. J. 449, 461 (1997) (“[I]f [reach-through royalties] are reasonable, they should be permitted and . . . insistence on such terms should not be read as an antitrust violation.”).

¹¹⁰ *King Instrument Corp. v. Prego*, 72 F.3d 855, 857 (Fed. Cir. 1995) (Nies, J., dissenting from denial of panel rehearing) (characterizing the 1995 Federal Circuit decision in *Rite-Hite* as having “expanded legal injury for patent infringement” and having worked a “fundamental change in patent rights”); see also *Rite-Hite Corp. v. Kelley Co.*, 56 F.3d 1538, 1546 (Fed. Cir. 1995) (*en banc*) (“If a particular injury was or should have been reasonably foreseeable by an infringing competitor in the relevant market, broadly defined, that injury is generally compensable absent a persuasive reason to the contrary.”).

facilitate advancements in technology.

V. Conclusion

The Federal Circuit's decision in *Integra* marked a dramatic reversal in the expansion of the scope of activities exempt under § 271(e)(1). The court's decision appeared to refocus the scope of the safe harbor provision to those purposes expressly provided in the legislative history of the Hatch-Waxman Act. Although the Federal Circuit's decision appeared to focus on the use of research tools in the development of drug products, the decision applies to all patentable subject matter, and it will definitively influence later federal decisions regarding § 271(e)(1).

While the Federal Circuit's decision restricted the scope of the safe harbor provision, the confusion surrounding what activities are exempt under § 271(e)(1) may continue. To remedy this confusion, the Supreme Court and Congress should take action to refocus the scope of § 271(e)(1) to its original intent, and facilitate the advancement of technology without significantly violating the rights of patent holders. Nonetheless, until the Supreme Court or Congress responds, many activities considered drug development and discovery may no longer be exempt under § 271(e)(1). Biotech companies that utilize patented technology in pre-clinical research, whether to develop new drugs or generics, should consider eliminating questionable activities, conduct traditional non-infringement activities, and, where needed, investigate licensing options.

