

INTEGRA V. MERCK: LIMITING THE SCOPE OF THE § 271(E)(1) EXCEPTION TO PATENT INFRINGEMENT

By George Fox

Congress enacted 35 U.S.C. § 271(e)(1) as part of the Drug Price Competition and Patent Term Restoration Act of 1984, better known as the Hatch-Waxman Act.¹ One purpose of the Act was to reduce health care costs by providing incentives for drug manufacturers to bring more generic drugs to market.² Congress attempted to achieve this goal by providing an expedited Food and Drug Administration (FDA) approval process for generic drugs and by permitting generic drug manufacturers to seek such approval prior to the expiration the drug patents.³ Section 271(e)(1) is the statute that allows generic drug manufacturers to seek FDA approval prior to patent expiration.⁴

While the applicability of § 271(e)(1) is uncontested within the context of a drug manufacturer seeking FDA approval for a generic drug, courts and commentators have struggled to define its remaining scope.⁵ The legislative history of the Hatch-Waxman Act suggests that it should be very narrowly applied.⁶ Judicial interpretation, on the other hand, has resulted in a steady expansion in the types of activities that § 271(e)(1) can shel-

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1. Brian Coggio & F. Dominic Cerrito, *The Safe Harbor Provision of the Hatch-Waxman Act: Present Scope, New Possibilities, and International Considerations*, 57 FOOD & DRUG L.J. 161, 161-62 (2002).

2. See H.R. REP. 98-857, pt. 1, at 14-17 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2647-50.

3. *Id.*; see also Holly Soehnge, *The Drug Price Competition and Patent Term Restoration Act of 1984: Fine-Tuning the Balance Between the Interests of Pioneer and Generic Drug Manufacturers*, 58 FOOD & DRUG L.J. 51, 58 (2003).

4. See *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 671 (1990) (noting that section 271(e)(1) “allows competitors, prior to the expiration of a patent, to engage in otherwise infringing activities necessary to obtain regulatory approval”).

5. See, e.g., David Bloch, *If It's Regulated Like a Duck . . . Uncertainties in Implementing the Patent Exceptions of the Drug Price Competition and Patent Term Restoration Act*, 54 FOOD & DRUG L.J. 111, 120-26 (1999); Courtenay Brinckerhoff, *Can the Safe Harbor of 35 U.S.C. § 271(e)(1) Shelter Pioneer Drug Manufacturers?*, 53 FOOD & DRUG L.J. 643, 648-54 (1998); Coggio & Cerrito, *supra* note 1, at 162-69.

6. See H.R. REP. 98-857, pt. 2, at 24-25 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2708-09; Coggio & Cerrito, *supra* note 1, at 162.

ter.⁷ The recent decision of the Federal Circuit in *Integra Lifesciences I, Inc. v. Merck KGaA*,⁸ has the effect of undoing some of this expansion. Essentially overturning the findings of a district court in the Southern District of New York,⁹ the Federal Circuit held that research and development activities that concern the identification of new drug candidates for clinical trials are not protected by § 271(e)(1).¹⁰ Regardless of whether this is viewed as a positive or negative development, the strength of the Federal Circuit's decision is undermined by its lack of clarity. Furthermore, some of the language of the opinion leaves open other avenues for future expansion, even though the Federal Circuit was ostensibly trying to rein in § 271(e)(1)'s scope.

This Note takes a critical look at the Federal Circuit's decision, focusing on how it will affect the value of patents in the pharmaceutical industry. The Note begins with a discussion of the Hatch-Waxman Act, its legislative history, and some of the important judicial interpretations of § 271(e)(1). After a brief description of the *Integra* case, this Note discusses problems inherent in the court's statutory construction of § 271(e)(1) and in its distinction between research activities covered by the exemption and those that are not. The Note concludes that the Federal Circuit has reached the desirable result, but that its opinion may contribute to further expansion of the scope of § 271(e)(1) and a decrease in the value of research tool patents.

I. 35 U.S.C. § 271(E)(1): ANTECEDENTS, LEGISLATIVE HISTORY, AND JUDICIAL INTERPRETATION

Congress enacted § 271(e)(1) to facilitate the entry of generic drugs into the market immediately following the expiration of patent protection for corresponding pioneering drugs. The language of § 271(e)(1), however, is broadly written and does not unambiguously delineate the statute's scope.¹¹ 35 U.S.C. § 271(e)(1) provides:

7. Brinckerhoff, *supra* note 5, at 648-54; Coggio & Cerrito, *supra* note 1, at 162-69.

8. 331 F.3d 860 (Fed. Cir. 2003).

9. Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., No. 95 Civ. 8833(RRP), 2001 WL 1512597, at *4-*7 (S.D.N.Y. Nov. 28, 2001).

10. *Integra*, 331 F.3d at 867 (holding that "[e]xtending § 271(e)(1) to embrace new drug development activities would ignore its language and context with respect to the 1984 Act in an attempt to exonerate infringing uses only potentially related to information for FDA approval").

11. See *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 669 (1990) (criticizing the language of § 271(e)(1) as "not plainly comprehensible on anyone's view").

[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.¹²

Because of this broad language, a proper understanding of § 271(e)(1)'s scope requires knowledge about the structure of the Hatch-Waxman Act and the legislative history behind it.

The Hatch-Waxman Act was motivated by two overriding concerns: (1) the desire to reduce health care costs by encouraging the manufacture and sale of low-price generic drugs; and (2) a desire to protect the profit incentives that encourage innovative pharmaceutical companies to develop pioneering new drugs.¹³ These two goals are reflected in the structure of the Act, which consists of two titles.¹⁴ Title I creates an abbreviated new drug application ("ANDA") procedure designed to streamline the FDA approval process for generic versions of pioneering drugs.¹⁵ As it exists today, the ANDA procedure allows a generic drug manufacturer to avoid the time and expense associated with a new drug application ("NDA")¹⁶

12. 35 U.S.C. § 271(e)(1) (2000).

13. The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (codified in scattered sections of 35 U.S.C.).

14. H.R. REP. 98-857, pt. 1, at 16-18 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2649-51.

15. *Id.* Prior to enactment of the Hatch-Waxman Act, an ANDA process already existed for obtaining FDA approval of generic versions of pre-1963 FDA approved pioneering drugs. The Hatch-Waxman extended the ANDA process to the approval of generic versions of pioneering drugs approved by the FDA after 1962. Soehnge, *supra* note 3, at 53-54.

16. The FDA approval process for new drugs involves three clinical trial phases and a period of FDA review. The three clinical trial phases take an average of six years to complete and involve testing a candidate drug on at least 1000 human subjects. The FDA review period takes an additional two and a half years. During the mid-90s, the cost of obtaining FDA approval for a single new drug was between \$200 and \$500 million. Prior to the enactment of the Hatch-Waxman Act, generic drug manufacturers seeking approval for a generic drug (corresponding to a new drug approved by the FDA after 1962) were required to satisfy the requirements as a new drug applicant. Thus, the cost of approval was a major barrier to the entry of generic drugs into the market. *See generally* Diane Furman, *Pharmaceutical and Biotechnology Licensing and the Patent/Regulatory Background*, 514 PRACTICING L. INST., PAT., COPYRIGHT, TRADEMARKS, AND LITERARY PROP. COURSE HANDBOOK SERIES 7 (1998); Jaclyn Miller, *Drug Price Competition and Patent Term Restoration Act: The Elimination of Competition Between Drug Manufacturers*, 5 DEPAUL J. HEALTH CARE L. 91, 92-98 (2002); Brian Urevig, Note, *Hatch-Waxman—*

by submitting data demonstrating that its generic drug is both chemically identical and bioequivalent to a drug that has already received FDA approval.¹⁷

Title II of the Hatch-Waxman Act, which was designed to mitigate distortions in patent term created by the FDA regulatory process, contains two sections. Section 201 provides a single patent term extension for patents covering new drugs and medical devices that successfully obtain FDA approval.¹⁸ Congress provided the patent term extension to compensate for the decrease in patent term resulting from the time-consuming FDA approval process. The FDA approval process takes, on average, over eight years to complete, and thus substantially decreases the amount of patent life during which pharmaceutical companies and medical device manufacturers can profit from their inventions.¹⁹ Congress reasoned that restoring some of this lost patent life would maintain profit incentives for pioneering drug manufacturers and thereby ensure continued innovation in the pharmaceutical and medical device industries.²⁰

Section 202 of Title II, which was codified as § 271(e)(1), counterbalances the benefits that patent term extension provides for pharmaceutical companies. Under § 271(e)(1), manufacturers of generic drugs and medical devices are allowed to use a patented invention prior to the expiration of its patent term, provided that the use is solely for the purpose of obtaining FDA approval.²¹ Both sections attempt to remedy distortions in the patent term resulting from the FDA's regulation of drug marketing.²² The

Thoughtful Planning or Just Piling On: A Consideration of the Federal Trade Commission's Proposed Changes, 4 MINN. INTELL. PROP. REV. 367, 369-73 (2003).

17. Bioequivalence concerns the dosage and rate of absorption of a drug. Two formulations of a drug (e.g., two different pills) will be bioequivalent if, when taken in the prescribed amount, they deliver about the same drug dosage at about the same rate. Urevig, *supra* note 16, at 374 n.49.

18. H.R. REP. 98-857, pt. 2, at 21 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2705.

19. Miller, *supra* note 16, at 107.

20. H.R. REP. 98-857, pt. 2, at 6, *reprinted in* 1984 U.S.C.C.A.N. at 2690; H.R. REP. 98-857, pt. 1, at 17-18 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2650-55. The patent term restoration provisions of Title II allow restoration of one-half the time spent testing the product for safety and efficacy and all of the time spent during FDA regulatory review, subject to the constraints that the period of restoration can be reduced if the applicant did not act with due diligence during the regulatory review period and that the amount of post-FDA approval patent term (including the extension) cannot be longer than fourteen years. Miller, *supra* note 16, at 106.

21. See 35 U.S.C. § 271(e)(1) (2000); Coggio & Cerrito, *supra* note 1, at 161-62.

22. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 671-73 (1990); Bloch, *supra* note 5, at 111-12.

patent term extension provisions reduce “front end distortion” resulting from the effective loss of patent term that occurs during the FDA approval process. The § 271(e)(1) exemption reduces “back end distortion” resulting from the de facto extension of patent term that would otherwise occur if generic drug manufacturers had to delay seeking FDA approval until after the expiry of the patent covering the pioneering drug.²³

Unlike the ANDA and the patent term extension provisions of the Hatch-Waxman Act, § 271(e)(1) was not legislation that Congress had been considering for several years. Rather, its inclusion was stimulated by the Federal Circuit’s decision in *Roche v. Bolar*,²⁴ which issued only a few months prior to the Act’s passage.²⁵ In *Bolar*, the defendant wanted to market a generic version of Roche’s patented drug flurazepam-hcl.²⁶ Reasoning that the commercial success of a generic drug is dependent upon how quickly it enters the market after the controlling patent expires, Bolar decided to import a small amount of flurazepam-hcl and initiate the tests required for FDA approval before Roche’s patent expired.²⁷ Roche sued and the Federal Circuit held that, even though Bolar had no intention of marketing generic flurazepam-hcl until after Roche’s patent expired, the mere use of the drug for business-related purposes established an act of patent infringement.²⁸ Describing the purpose of § 271(e)(1) with reference to *Bolar*, the House Committee on Energy and Commerce stated:

The purpose of sections § 271(e)(1) and (2) is to establish that experimentation with a patented drug product, when the purpose is to prepare for commercial activity which will begin after a valid patent expires, is not a patent infringement . . . In *Roche Products, Inc. v. Bolar Pharmaceutical Co., Inc.* ___ F.2d ___ (Fed. Cir., April 23, 1984), the Court of Appeals for the Federal Circuit held that the experimental use of a drug product prior to the expiration of a patent claiming that drug product constitutes patent infringement, even though the only purpose of the experiments is to seek FDA approval for the commercial sale of the drug after the patent expires. It is the Committee’s view that experimental activity does not have any adverse economic impact on the patent owner’s exclusivity during the life of a patent, but

23. Bloch, *supra* note 5, at 111-12.

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

25. H.R. REP. 98-857, pt. 1, at 45-46, *reprinted in* 1984 U.S.C.C.A.N. at 2678-79.

26. 733 F.2d at 860.

27. *Id.*

28. *Id.* at 863, 865.

prevention of such activity would extend the patent owner's commercial exclusivity beyond the patent expiration date.²⁹

More to the point, § 271(e)(1) was introduced as having "the net effect of reversing the holding of the court in *Roche Products, Inc. v. Bolar Pharmaceutical Co., Inc.*"³⁰

Other aspects of the Hatch-Waxman Act's legislative history also support the idea that § 271(e)(1) was enacted for the limited purpose of reversing *Bolar*. For example, when the Committee on the Judiciary met to consider the bill, Representative Moorhead proposed an amendment to limit the § 271(e)(1) exception to the last year of a patent term extension period.³¹ Representative Moorhead's amendment would have restricted the application of § 271(e)(1) to only those patents which received a patent term extension.³² At the same time, however, the amendment would have prevented generic manufacturers from marketing their generic drugs immediately after patent expiration.³³ This is because it takes an average of two years to receive FDA approval after filing an ANDA.³⁴ The Committee rejected Congressman Moorhead's amendment for two reasons, stating:

First, the only activity which will be permitted by the bill is a limited amount of testing so that generic manufacturers can establish the bioequivalency of a generic substitute. The patent holder retains the right to exclude others from the major commercial marketplace during the life of the patent. Thus, the nature of the interference with the rights of the patent holder is not substantial. Second, the Committee accepted the public policy rationale of our sister Committee on Energy and Commerce. They reasoned that without section 202 [§ 271(e)(1)] generic manufacturers would be required to engage in these bioequivalency tests after the expiration of the patent. This would result in delays of about two years after the expiration of the patent before a generic could go to market. Thus, the Committee on Energy and Commerce reasoned that section 202 of the bill was essential to implement the policy objective of getting safe and effective

29. H.R. REP. 98-857, pt. 1, at 45-46, *reprinted in* 1984 U.S.C.C.A.N. at 2678-79.

30. H.R. REP. 98-857, pt. 2, at 27 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2711.

31. *Id.* at 8, *reprinted in* 1984 U.S.C.C.A.N. at 2692.

32. *See id.*

33. *Id.* at 8-9, 29-30, *reprinted in* 1984 U.S.C.C.A.N. at 2692-93, 2713-14.

34. *See id.* at 8, *reprinted in* 1984 U.S.C.C.A.N. at 2692.

generic substitutes on the market as quickly as possible after the expiration of the patent.³⁵

With regard to discerning congressional intent, these statements could hardly be clearer. The “only activity” allowed under § 271(e)(1) is activity taken by “generic manufactures” for the purpose of establishing bio-equivalency—the very same activity that the Federal Circuit found to be infringing in *Bolar*. In addition, when the Committee on Energy and Commerce released its report on the bill, the report included a section entitled “Minority Views of Mr. Bliley” which criticized the loss of patent rights caused by § 271(e)(1).³⁶ The patent rights that concerned Representative Bliley appear to be limited, however, to only those rights at issue in *Bolar* since his critique discusses no other type of patent rights.³⁷ Thus, Congressional opponents and proponents alike shared the view that § 271(e)(1) has a limited scope confined the facts and circumstances presented in *Bolar*.

Since the Hatch-Waxman Act passed into law in 1984, many courts have had the opportunity to interpret its scope. Perhaps the most important case is *Eli Lilly & Co. v. Medtronic, Inc.*,³⁸ a Supreme Court opinion that directly confronts the ambiguity in the scope of § 271(e)(1) and provides a model approach for resolving such issues. In *Medtronic*, the Court held that § 271(e)(1) was applicable to not only pharmaceutical drugs but also to medical devices.³⁹ In reaching its decision, the Court considered the purpose of the Hatch-Waxman Act—to mitigate the two unintended distortions in patent term length caused by pre-market regulatory approval requirements.⁴⁰ The Court reasoned that the patent term extension and the § 271(e)(1) provisions of the Hatch-Waxman Act counterbalance one another and that, since patent term extension is available for medical devices, § 271(e)(1) must also apply to medical devices.⁴¹

Recent court decisions have relied on *Medtronic* to both limit and expand the scope of § 271(e)(1).⁴² In *Infigen, Inc. v. Advanced Cell Technology, Inc.*, for example, a district court found that patent infringement could not be immunized by § 271(e)(1) unless the patent at issue is eligible for

35. *Id.*

36. H.R. REP. 98-857, pt. 1, at 74-75 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2684-85.

37. *Id.*

38. 496 U.S. 661 (1990).

39. *Id.* at 664, 679.

40. *Id.* at 669-70.

41. *Id.* at 670-73.

42. *See* Coggio & Cerrito, *supra* note 1, at 167-69.

patent term extension.⁴³ In contrast, the district court in *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, found that all patents, not just those eligible for patent term extension, are potentially subject to the § 271(e)(1) exception.⁴⁴ Some practitioners have expressed concern that the decision of the *Bristol* court, if followed by other courts, could undermine or even eliminate the value of many patents.⁴⁵

II. THE *INTEGRA* CASE

A. Factual History

The *Integra* case provided the Federal Circuit with an opportunity to resolve conflicting opinions regarding the scope of § 271(e)(1) and to address concerns about the insufficient protection afforded to research tool patents.⁴⁶ The plaintiff, *Integra*, owns a series of patents covering short amino-acid sequences, known as peptides, which include the three amino-acid sequence “RGD,” and methods of using such peptides to regulate cellular adhesion.⁴⁷ Modulation of cellular adhesion can induce cellular migration, which is necessary for processes such as wound healing.⁴⁸ Al-

43. 65 F. Supp. 2d 967, 980 (W.D. Wis. 1999). The district court stated that: As *Eli Lilly [& Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990)] holds, however, § 271(e)(1) is to be read in conjunction with § 156. When that is done, it becomes apparent that § 271(e)(1) applies only to those patents identified in § 156(a)(4) and (5) that, among other things, cover certain specified products (including drug products, see § 156(f)) that were subject to a regulatory review period before their commercial marketing or use.

Id.

44. No. 95 Civ. 8833(RPP), 2001 WL 1512597, at *2 (S.D.N.Y. Nov. 28, 2001). The court found that:

[n]othing in the text of Section 271(e)(1) indicates that Congress intended to restrict the scope of the term “patented invention” to those products covered by Section 156. As the U.S. Supreme Court noted, “The term patented invention in 271(e)(1) is defined to include all inventions, not drug-related inventions alone. . . . *Eli Lilly v. Medtronic*, 496 U.S. 661, 665 (1990).”

Id.

45. Coggio & Cerrito, *supra* note 1, at 169-70.

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

47. “RGD” refers to a three amino acid peptide having the sequence arginine-glycine-aspartic acid. The patents at issue in the case were US Patent Nos. 4,789,734; 4,879,237; 4,988,621; 5,695,997; and 4,792,525. *Id.* at 862.

48. See R. Rudolph & D. Cheresch, *Cell Adhesion Mechanisms and their Potential Impact on Wound Healing and Tumor Control*, 17(3) CLINICAL PLASTIC SURGERY 457 (1990).

though Integra's predecessor, Telios, believed that the RGD peptides could be used therapeutically to stimulate wound healing, it was never able to develop its patented technology into a drug candidate suitable for clinical trials.⁴⁹

In separate studies, scientists at Scripps Oceanographic Institute ("Scripps") discovered that inhibition of cellular adhesion can suppress angiogenesis, the process of growing new blood vessels.⁵⁰ Inhibition of angiogenesis is believed to be a promising cancer therapy because tumor growth is limited by blood supply.⁵¹ In order to identify angiogenesis inhibitors, Merck paid the scientists at Scripps to screen a library of drug candidates for angiogenesis-inhibiting activity.⁵² Of the drug candidates provided by Merck, a particularly promising angiogenesis inhibitor emerged—EMD 66203, a cyclic peptide which includes an RGD sequence.⁵³

Upon the identification of EMD 66203, Merck entered into an agreement with Scripps to fund studies on the specificity, efficacy, and toxicity of EMD 66203 and several of its derivatives, including EMD 85189 and 121974.⁵⁴ The purpose of the agreement was to gather data required by the FDA as part of an Investigatory New Drug ("IND") application.⁵⁵ Scripps examined, among other things, the histopathology, toxicology, circulation, diffusion, and half-life of the three peptides in the bloodstreams of mice, as well as the best mode of administering the peptides for optimum therapeutic effect.⁵⁶ Based on their results, the Scripps scientists identified EMD 121974 as the best candidate for clinical trials, and Merck filed a corresponding IND application in 1998.⁵⁷

The Merck-Scripps angiogenesis collaboration began in 1994.⁵⁸ When Integra learned of the agreement, it offered to license its RGD-peptide pat-

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

50. *Id.* at 863.

51. B.P. Eliceiri & D.A. Cheresh, *Adhesion Events in Angiogenesis*, 13(5) CURRENT OPINIONS IN CELL BIOLOGY 563 (2001).

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

53. *Id.*

54. *Id.*

55. *Id.* In order to enter into human clinical trials with a new and previously unapproved drug, the party seeking approval must first file an IND application. 21 C.F.R. § 312.20(b) (2003). The FDA uses information in the initial IND application to determine whether the new drug is sufficiently safe and effective to justify testing it on human subjects. *Id.* § 312.22(a), (b).

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

57. *Id.* at 863, 874.

58. *Id.* at 863.

ents to Merck.⁵⁹ Despite extensive negotiations, a licensing agreement was never reached and Integra ultimately filed suit for patent infringement against Merck and Scripps.⁶⁰ Merck responded by claiming that Integra's RGD patents were either limited to linear peptides or entirely invalid, and that its work with Scripps was protected by § 271(e)(1).⁶¹ The jury found that Merck had infringed several of Integra's patents, and the district court concluded that the § 271(e)(1) exemption did not cover the work performed for Merck at Scripps.⁶² Based on the finding of infringement, the jury awarded Integra with a reasonable royalty of \$15 million.⁶³

B. The Federal Circuit's Analysis

On appeal, Merck argued that the district court erred in construing the claims of Integra's patents, in interpreting § 271(e)(1), and in refusing to reconsider the damages award.⁶⁴ The Federal Circuit affirmed the district court's claim construction.⁶⁵ The court reasoned that Integra's claims covered both linear and circular peptides because (1) the claims were not explicitly limited to "linear" peptides, and (2) prior art relating to circular peptides was cited in the patents.⁶⁶

The Federal Circuit also upheld the lower court's decision that § 271(e)(1) did not protect the work that Scripps had performed for Merck.⁶⁷ According to the court, the § 271(e)(1) exception to infringement is not broad enough to encompass research and development efforts.⁶⁸ In arriving at its decision, the court focused on the language of § 271(e)(1), with particular emphasis on the word "solely" and the phrase "for uses reasonably related to the development and submission of information [for the FDA]."⁶⁹ The court first reasoned that the term "solely" placed a significant constraint on the scope of the exemption.⁷⁰ Then, to understand

59. *Id.*

60. *Id.*

61. *Id.*

62. *Id.* at 863-64.

63. *Id.*

64. *Id.* at 864.

65. *Id.* at 868.

66. *Id.*

67. *Id.*

68. *Id.* at 867.

69. *Id.* at 866.

70. *Id.* The emphasis on the term "solely" is interesting because it harkens back to earlier decisions in which the courts narrowly construed the language of § 271(e)(1). *See* Brinkerhoff, *supra* note 5, at 649-50 (discussing how courts have shifted away from their earlier emphasis on the "solely" language towards an emphasis on the "reasonably related" language).

which limited uses are “reasonably related” to developing and submitting information for FDA approval, the court considered the Hatch-Waxman Act’s objective of “facilitat[ing] the immediate entry of safe, effective generic drugs into the marketplace upon expiration of a pioneering drug patent.”⁷¹ Observing that generic drug manufacturers need only perform safety and effectiveness tests on a generic drug and submit the results to the FDA as part of the ANDA process, the court held that uses are “reasonably related” to FDA requirements only if the information generated by the use is considered by the FDA when it evaluates an application for drug approval.⁷² As a result, the court concluded that uses which merely identify a compound that is a good candidate for clinical trials fall outside the scope of § 271(e)(1).⁷³ The court substantiated its decision by noting that the alternative holding—that § 271(e)(1) protects research and development activities that occur prior to clinical trials—would strip the value from research tool patents used in biomedical research.⁷⁴

Finally, the Federal Circuit agreed with Merck that the district court erred by refusing to reconsider the damages award.⁷⁵ The court held that the jury award of \$15 million was not supported by substantial evidence, and it remanded the issue to the district court for proceedings to determine what a “reasonable royalty” would be at a time prior to Merck’s first infringement of Integra’s patents.⁷⁶

C. Judge Newman’s Dissent

In dissent, Judge Newman indicated that she would have overturned the district court’s finding that Merck infringed Integra’s patents.⁷⁷ Although Judge Newman agreed with the majority in finding that both linear and cyclic peptides were encompassed by Integra’s patents, she contended that Merck’s research is protected by the long-standing experimental use doctrine.⁷⁸ According to Judge Newman, Merck’s research did not simply involve using Integra’s RGD peptides to modulate cellular adhesion.⁷⁹ Rather, the research was focused on creating new and improved RGD peptides having pharmaceutically useful properties.⁸⁰ She suggested that al-

71. *Integra*, 331 F.3d at 866-67.

72. *Id.* at 867.

73. *Id.*

74. *Id.*

75. *Id.*

76. *Id.* at 869-72.

77. *Id.* at 872-78 (Newman, J., dissenting).

78. *Id.* at 877 (Newman, J., dissenting).

79. *Id.* (Newman, J., dissenting).

80. *Id.* (Newman, J., dissenting).

lowing this type of experimental use is an essential means for promoting scientific advancement.⁸¹

III. DISCUSSION

To fully understand the implications of the Federal Circuit's decision in *Integra*, it is important to understand that the facts of *Integra* differ strikingly from those presented in *Bolar*, the case that inspired Congress to enact § 271(e)(1). In *Bolar*, the defendant sought to obtain FDA approval to market a generic version of flurazepam-hcl, which was Roche's patented, FDA approved, and commercially successful sleeping medication.⁸² *Integra*, unlike Roche, never produced an FDA approved drug. Indeed, even though *Integra* had acquired patent protection for RGD peptides and their use in modulating cellular adhesion, *Integra* was never able to develop its patented inventions further.⁸³ Consequently, Merck was not in the same position as *Bolar*. Merck was trying to develop and market a new drug rather than trying to get FDA approval for a generic drug. This difference is significant for two reasons. First, Merck was not in competition with *Integra* and thus could have licensed *Integra*'s RGD-related patents. In contrast, Roche would never have voluntarily eroded its monopoly position in the flurazepam-hcl market by licensing its patents to *Bolar*.⁸⁴ Second, the FDA approval process is much more extensive for new drugs as compared to generic drugs.⁸⁵ As a result, any activity that Merck undertook to obtain FDA approval of its RGD-peptide anti-cancer drug was necessarily greater than the activity that a generic drug manufacturer would undertake to bring a generic drug to market. These differences take Merck outside the legislative intent of Congress in enacting § 271(e)(1).

The Federal Circuit, however, did not distinguish Merck as a new drug manufacturer falling outside the ambit of § 271(e)(1). Instead, by ignoring the differences that exist between new drug manufacturers and generic drug manufacturers, the court blurred the distinction between research that should and should not be protected by the § 271(e)(1) exception. The majority adopted the standard that research is "reasonably related" to obtaining FDA approval, and hence protected by § 271(e)(1), if it consists of the

81. *Id.* (Newman, J., dissenting).

82. *Roche Prods., Inc. v. Bolar Pharm. Co., Inc.*, 733 F.2d 858, 860 (Fed. Cir. 1984).

83. *Integra*, 331 F.3d at 873.

84. *See* discussion *infra* Part IIIB3.

85. Obtaining FDA approval for a new drug takes eight and one-half years on average, while the approval process for a generic drug takes two and one-half years on average. Miller, *supra* note 16, at 104.

type of research in which a generic drug manufacturer would engage.⁸⁶ The court then applied the standard to the activities of Merck, a new drug manufacturer, rather than limiting its application to generic drug manufacturers.⁸⁷ The majority's treatment of Merck's research activities is confusing because it side-steps the issue of whether § 271(e)(1) should ever be used to protect the activities of new drug manufacturers. The subsequent discussion uses legislative history, policy arguments, and a critique of existing case law to argue that new drug manufacturers should not be protected by § 271(e)(1).

A. The Federal Circuit Failed To Clearly Distinguish Between Research Exempted by § 271(e)(1) and Exploratory Research

In describing the work that Scripps performed for Merck as part of their collaboration, the majority suggests that there were two distinct phases: an early phase during which a collection of drugs were screened for the ability to inhibit angiogenesis, and a later phase during which the specificity, efficacy, and toxicity of EMD 66203 and some of its derivatives were analyzed.⁸⁸ This distinction is important because there is a credible argument that testing the specificity, efficacy, and toxicity of drug candidates is "reasonably related" to obtaining FDA approval. To satisfy the requirements of an IND application, the party seeking FDA approval will typically provide an extensive array of experimental data that addresses, among other things, the histopathology, toxicology, circulation, diffusion, and half-life of the drug in the bloodstream of laboratory animals.⁸⁹ Since the information that Merck and Scripps obtained from the second phase of research was the type that is typically submitted as part of an IND, the second phase of research was, in fact, "reasonably related" to obtaining FDA approval.

The Federal Circuit nonetheless ignored the differences between the two research phases and labeled all of the Scripps-Merck collaborative studies as the "development and identification of new drugs."⁹⁰ One reason why the court may have ignored the differences between the two research phases is that the second phase was not exclusively devoted to obtaining information that would go into an IND application. As indicated in the dissent, the second phase of research evaluated not only the specificity, efficacy, and toxicity of EMD 66203, but also the anti-angiogenesis capa-

86. *Integra*, 331 F.3d at 865-67.

87. *Id.* at 867.

88. *See id.* at 863.

89. 21 C.F.R. § 312.23(a)(8) (2003).

90. *Integra*, 331 F.3d at 865-66.

bilities of a number of compounds derived from EMD 66203.⁹¹ Assuming that the EMD 66203 derivatives were not evaluated for anti-angiogenesis activity during the first phase of research, their evaluation during the second phase necessarily amounted to additional drug candidate identification, which is the type of research that the court clearly found to be outside of the § 271(e)(1) exception.⁹²

Although the court may have had good reasons for concluding that the research performed by Scripps was outside the § 271(e)(1) exception, it is unfortunate that the court did not explicitly recognize that the work related to the filing of an IND application had, at the very least, a claim to being reasonably related to obtaining FDA approval. Instead, the court looked toward the legislative intent behind the Hatch-Waxman Act, specifically its emphasis on generic manufacturers, and reasoned that any experimentation outside the requirements of an ANDA application must be beyond the scope of § 271(e)(1).⁹³ In reaching its decision, the court thus ignored the fact that Merck was seeking regulatory approval of a new drug, not a generic drug, and that the FDA requires new drug manufacturers to provide greater amounts of experimental data prior to regulatory approval. This latter point raises the question of whether a new drug manufacturer could ever be eligible for the § 271(e)(1) exception.⁹⁴

91. *Id.* at 873-74 (Newman, J., dissenting).

92. *Id.* at 866-67.

93. *Id.*

94. That the Federal Circuit considers new drug manufacturers, like Merck, eligible for the § 271(e)(1) exception is implicit in the *Integra* decision, which states that: "Merck may, nonetheless, escape liability for patent infringement if its uses of the *Integra* inventions falls within the strict limits of § 271(e)(1). To qualify for exemption, Merck must show its activities were 'solely for uses reasonably related to the development and submission of information' to the FDA." *Id.* at 866. On the other hand, it has also been argued that the Federal Circuit's opinion in *Integra* suggests that § 271(e)(1) may be limited to situations involving generic drugs. Nicholas Groombridge & Sheryl Calabro, *Integra Lifesciences v. Merck—Good For Research Or Just Good For Research Tool Patent Owners*, 22 BIOTECHNOLOGY L. REV. 462 (2003). Groombridge and Calabro note that:

The majority opinion in *Integra* does not squarely hold that applicability of § 271(e)(1) is limited to generic drugs to be the case, but it comes very close to doing so. Specifically, the opinion states that "the context of this safe harbor keys its use to facilitating expedited approval of patented pioneer drugs already on the market" and that the proper interpretation of the provision "does not . . . expand the phrase 'reasonably related' to embrace the development of new drugs because those new products will also need FDA approval." Thus, it appears that in the view of the *Integra* majority at least, § 271(e)(1) simply does not apply outside the generic drug context.

Id. at 469.

B. The § 271(e)(1) Exception Was Never Intended To Protect The Activities Of New Drug Manufacturers

1. Statutory Construction of § 271(e)(1)

A cursory examination of the language of § 271(e)(1) suggests that the statute protects the activities of both generic and new drug manufacturers. Under § 271(e)(1), it is not an act of infringement “to make, use, or sell a patented invention” for the sole purpose of developing and submitting information under a federal law that regulates the manufacture, use, or sale of drugs.⁹⁵ The Supreme Court has held that the term “patented invention” includes *all* inventions, and not just drug-related inventions.⁹⁶ The Court reached this conclusion after observing that 35 U.S.C. § 100(a) states: “When used in this title unless the context otherwise indicates . . . [t]he term ‘invention’ means invention or discovery.”⁹⁷ Based on this broad, all-encompassing statutory construction, the conclusion naturally follows that § 271(e)(1) covers pharmaceutical inventions that do not lead to an FDA approved drug, so long as the invention is being used to “develop and submit information” for FDA approval. As such, a new drug manufacturer’s efforts to develop drugs based on preexisting, patented technology theoretically fall within the scope of § 271(e)(1).

Nevertheless, the term “patented invention” may take on new meaning in the context of § 271(e)(1).⁹⁸ In *Medtronic*, the Supreme Court acknowledged that the plain meaning of § 271(e)(1) remained ambiguous, even though it interpreted the phrase “patented invention” to include all inventions.⁹⁹ To better define the scope of the statute, the Court turned to the structure and text of the Hatch-Waxman Act.¹⁰⁰ Observing that the Act was designed to address two off-setting distortions in patent term, the Court endorsed an interpretation of § 271(e)(1) that creates a “perfect product fit” between the patent term extension provisions and the § 271(e)(1) provisions of the Act.¹⁰¹ According to the Court:

All of the products eligible for a patent term extension were subject to [§ 271(e)(1)], since all of them—medical devices, food

95. 35 U.S.C. § 271(e)(1) (2000).

96. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 665 (1990).

97. *Id.*

98. *Cf.* 35 U.S.C. § 100(a) (stating that “[w]hen used in this title *unless the context otherwise indicates* . . . [t]he term ‘invention’ means invention or discovery”) (emphasis added).

99. 496 U.S. at 669.

100. *Id.*

101. *Id.* at 669-74.

additives, color additives, new drugs, antibiotic drugs, and human biological products—are subject to premarket regulatory approval under various provisions of the FDCA [Food, Drug, and Cosmetic Act]. . . . And the products subject to premarket approval under the FDCA . . . that are not made eligible for a patent term extension under § 201—new animal drugs and veterinary biological products—are excluded from [§ 271(e)(1)] as well.¹⁰²

The Court recognized, however, that there might be “relatively rare” situations in which a patentee would benefit from the patent term extension provisions of the Hatch-Waxman Act without being subjected to the § 271(e)(1) exception, and vice versa.¹⁰³ But the Court stated that, absent a good reason, it could not readily imagine such situations.¹⁰⁴

Despite the Supreme Court’s endorsement of the “perfect product fit” interpretation of the patent term extension and § 271(e)(1) exception provisions of the Hatch-Waxman Act, other courts have held otherwise.¹⁰⁵ In *Abtox, Inc. v. Exitron Corp.*, for example, the Federal Circuit held that patented class II medical devices, which are not eligible for patent term extension, are nonetheless subject to the § 271(e)(1) exception.¹⁰⁶ The *Abtox* court reasoned that the Supreme Court’s decision in *Medtronic* was based on two somewhat conflicting lines of reasoning: first, that the term “patented invention” encompasses all inventions; and second, that § 271(e)(1) and the patent term extension provisions of the Hatch-Waxman Act are ideally applicable to the same sets of inventions.¹⁰⁷ Because the Supreme Court acknowledged that there might be cases in which only one of the provisions applied, however, the *Abtox* court concluded that the critical holding in *Medtronic* was that the term “patented invention” encompasses all inventions.¹⁰⁸ The *Abtox* court went on to state that § 271(e)(1) “does not look to the underlying purposes or attendant

102. *Id.* at 673-74.

103. *Id.* at 671-72.

104. *Id.* at 672 n.4.

105. See *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997) (Rader, J.); *Chartex Intern. PLC v. M.D. Personal Products Corp.*, 5 F.3d 1505 (Fed. Cir. 1993) (unpublished, Rader, J.); *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833(RPP), 2001 WL 1512597 (S.D.N.Y. Nov. 28, 2001) (citing to the Federal Circuit’s opinions in *Abtox* and *Chartex*).

106. *Abtox*, 122 F.3d at 1027-30. Class III medical devices require FDA approval prior to marketing, and thus are eligible for patent term extension, while Class I and II medical devices do not require FDA approval prior to marketing. *Id.*

107. *Id.* at 1028-29.

108. *Id.* at 1029.

consequences of the activity . . . as long as the use is reasonably related to FDA approval.”¹⁰⁹

The *Abtox* court’s reading of *Medtronic*, and thus its construction of § 271(e)(1), subverts the Supreme Court’s opinion and is at odds with any reasonable reading of the legislative history of the Hatch-Waxman Act. If the Supreme Court in *Medtronic* had believed that questions about the applicability of § 271(e)(1) could be resolved simply by concluding that the term “patented invention” encompasses all inventions, it would not have devoted most of the opinion to an analysis of the structure of the Act.¹¹⁰ Furthermore, as discussed above, the clear intent behind the Act was to stimulate the entry of generic drugs into the marketplace while protecting the interests of new drug manufacturers.¹¹¹ Protection of the interests of new drug manufacturers was accomplished by providing term extensions for patents that yield FDA approved drugs.¹¹² Stimulation of the manufacture and sale of generic drugs, on the other hand, was accomplished in part by providing a *limited* exception to patent infringement, thereby allowing generic drug manufacturers to apply for FDA approval prior to the expiration of pioneering drug patents.¹¹³ Many courts and commentators have explicitly recognized that the competing interests of generic drug manufacturers and new drug manufacturers provide the foundation for understanding the Hatch-Waxman Act.¹¹⁴ By concluding that § 271(e)(1) is applicable to *any* invention that may be used to gather information for submission to the FDA, the *Abtox* court expanded the scope of § 271(e)(1) well beyond the limited exception intended by Congress.

109. *Id.* at 1030.

110. The Court devoted two sentences in the *Medtronic* opinion to the meaning of the term “patented invention” and over five pages to its analysis of the structure of the Hatch-Waxman Act. See 496 U.S. 661, 665, 669-74 (1990).

111. H.R. REP. 98-857, pt. 1, at 14-18 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647-51; H.R. REP. 98-587, pt. 2, at 4-6 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2688-90.

112. H.R. REP. 98-857, pt. 1, at 14-18, *reprinted in* 1984 U.S.C.C.A.N. at 2647-51; H.R. REP. 98-587, pt. 2, at 4-6, *reprinted in* 1984 U.S.C.C.A.N. at 2688-90.

113. H.R. REP. 98-857, pt. 1, at 14-18, *reprinted in* 1984 U.S.C.C.A.N. at 2647-51; H.R. REP. 98-587, pt. 2, at 4-6, *reprinted in* 1984 U.S.C.C.A.N. at 2688-90.

114. See, e.g., *Allergan, Inc. v. Alcon Labs., Inc.*, 324 F.3d 1322, 1325-26 (Fed. Cir. 2003); *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1568-69 (Fed. Cir. 1997); *Infigen, Inc. v. Advanced Cell Tech., Inc.*, 65 F. Supp. 2d 967, 979-80 (W.D. Wis. 1999); *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269, 1272-73 (N.D. Cal. 1991); see also Soehnge, *supra* note 3, at 53-59.

2. *Applying § 271(e)(1) to the Activities of New Drug Manufactures Runs Contrary to the Statute's Legislative History*

When a statute is ambiguous, legislative history may be used to guide statutory interpretation.¹¹⁵ Furthermore, even if the language of a statute is unambiguous, when the "plain meaning" of the text is clearly contrary to Congressional intent, a court may interpret the statute in light of the legislative history.¹¹⁶ The Supreme Court observed that § 271(e)(1) is ambiguously worded, thus providing a justification for using the legislative history of the Hatch-Waxman Act to interpret § 271(e)(1).¹¹⁷ A construction of § 271(e)(1) that reads "patented invention" to mean *any* patented invention creates a serious conflict between the statute and Congress' intent for § 271(e)(1) to be a narrow exception having "the net effect of reversing the holding of the court in *Roche Products, Inc. v. Bolar Pharmaceutical Co., Inc.*"¹¹⁸

At least one court has tried to argue that the legislative history of the Hatch-Waxman Act supports a broad reading of § 271(e)(1). According to the court in *Bristol-Myers*, the House report's statement that § 271(e)(1) allows only "a limited amount of testing so that generic manufacturers can establish the bioequivalency of a generic substitute" is contradicted by other statements in the legislative history, and is thus insufficient to outweigh the "plain language" of the statute.¹¹⁹ The court's primary basis for this conclusion is the House Committee's rejection of Representative Moorhead's proposed amendment limiting the applicability of § 271(e)(1) to the last year of a patent term extension period.¹²⁰ The *Bristol-Myers* court reasoned that the rejection supports a broad reading of § 271(e)(1) because Congress knew about the broad language of the statute, but nevertheless chose not to amend it.¹²¹ This conclusion, however, is unwarranted. One of the two reasons that the House Committee on the Judiciary provided for rejecting the Moorhead amendment was that the FDA approval

115. *Wis. Pub. Intervenor v. Mortier*, 501 U.S. 597, 610 n.4 (1991); *Blanchard v. Bergeron*, 489 U.S. 87 (1989); *Train v. Colo. Pub. Interest Research Group, Inc.*, 426 U.S. 1, 10 (1976).

116. *Garcia v. United States*, 469 U.S. 70, 75 (1984) (holding that the plain meaning of a statute can be limited by legislative history, albeit only upon "the most extraordinary showing of contrary intentions").

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

118. H.R. REP. 98-857, pt. 2, at 27, *reprinted in* 1984 U.S.C.C.A.N. at 2711.

119. *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833 (RPP), 2001 WL 1512597 at *3 n.6 (S.D.N.Y. Nov. 28, 2001).

120. *Id.*

121. *Id.*

process for generic drugs takes about two years.¹²² Consequently, the proposed amendment could not have satisfied § 271(e)(1)'s explicit goal of getting generic drugs to market *as soon as possible* following patent expiration.¹²³ Furthermore, Representative Bliley's statements indicate that even those Representatives opposed to § 271(e)(1) believed that its scope did not extend beyond the facts presented in *Bolar*.¹²⁴

The *Bristol-Myers* court's other observations similarly fail to identify statements in the legislative history that contradict the clear indications that § 271(e)(1)'s scope should be construed very narrowly.¹²⁵ In addition, the findings of the *Bristol-Myers* court run contrary to the legislative history of § 271(e)(1) as viewed by both the Supreme Court in *Medtronic* and the Federal Circuit in *Integra*.¹²⁶

3. *Applying § 271(e)(1) to the Activities of New Drug Manufacturers Undermines the Rationale of the Statute*

To better understand why Congress enacted § 271(e)(1), it is helpful to consider why the problem in *Bolar* arose in the first place. *Bolar* could never have obtained a license to use Roche's patented and highly profitable drug, flurazepam-hcl, because Roche, as a monopolist in the flurazepam-hcl market, could expect to maximize its profits by excluding competitors from the market for as long as possible.¹²⁷ Because companies like

122. H.R. REP. 98-857, pt. 2, at 8-9, *reprinted in* 1984 U.S.C.C.A.N. at 2692-93.

123. *Id.*

124. H.R. REP. 98-857, pt. 1, at 74-75 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2684-85.

125. *See* *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833 (RPP), 2001 WL 1512597 at *3 n.6 (S.D.N.Y. Nov. 28, 2001). It seems that the court's dismissal of legislative history in *Bristol-Myers* is motivated primarily by a belief in the "plain language" approach to statutory construction, given that the court's final argument is a citation to Justice Scalia's concurring opinion in *Crosby v. National Foreign Trade Council*, 530 U.S. 363, 390-91 (2000), which argued that the only reliable indicators of Congressional intent are the words of the bill that were voted into law.

126. *See* *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 669-73 (1990); *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 866-67 (Fed. Cir. 2003).

127. *Cf.* Urevig, *supra* note 16, at 377-78 (discussing recent antitrust litigation arising from settlement agreements between new drug manufacturers and generic manufacturers in which the pioneering drug manufacturers are willing to pay generic manufacturers to stay out of the market). The antitrust litigation described by Urevig suggests that there is no amount of money that a profit-maximizing generic drug manufacturer could pay a new drug manufacturer in order to license a patented drug for the purpose of seeking FDA approval for a generic version. To provide such a license, a new drug manufacturer would be expected to charge a licensing fee equivalent to its predicted loss in profits caused by giving up a monopoly position and allowing a low-cost competitor into the market immediately following patent expiration. The introduction of a low-price generic drug into

Bolar could neither license patented drugs nor use the drugs for the limited purpose of obtaining FDA approval without infringing the corresponding patents, it was simply impossible for generic drugs to enter the market immediately after patent expiration. Congress correctly reasoned that the only way to achieve the goal of immediate entry was to provide generic drug manufacturers with a limited exemption to patent infringement such as that provided by § 271(e)(1).¹²⁸

The rationale behind Congress' enactment of § 271(e)(1), and its concomitant reversal of *Bolar*, is simply inapplicable in the context of new drug manufacturers like Merck. Integra, having failed to produce an FDA-approved drug based on its RGD-peptide patents, actively sought to license its patents to Merck.¹²⁹ Presumably because Merck did not want to pay Integra's asking price, the negotiations broke down.¹³⁰ The court's conclusion that Merck's use of Integra's RGD peptides could be protected by § 271(e)(1), provided that the use occurs during clinical trials and is reasonably related to obtaining FDA approval,¹³¹ is thus problematic. The Federal Circuit has, in effect, granted Merck unlimited license to use Integra's patented inventions in clinical trials. But Integra's sole means of profiting from its inventions is through licensing agreements. Unlike Roche, Integra has no pharmaceutical products to sell.¹³² The court's ruling thus results in a substantial diminution of patent rights, despite its acknowledgement that the § 271(e)(1) exception was intended to have "only a *de minimis* impact on the patentee's right to exclude."¹³³ Furthermore, allowing unfettered use of Integra's patented RGD-peptide technology during clinical trials does not advance the goal of the Hatch-Waxman Act,

the market, however, would result in a loss in manufacturer surplus. Consequently, the generic manufacturer would have to pay all of its profits to the new drug manufacturer plus a sum of money corresponding to the lost surplus. Since the payment covering lost surplus would cause the generic drug manufacturer to lose money, it would not make sense for the generic drug manufacturer to enter into the licensing agreement in the first place. *See also* Burford, 19 BERKELEY TECH. L.J. 365 (2004).

128. *See* H.R. REP. 98-857, pt. 2, at 8-9 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2692-93.

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

130. *Id.*

131. *See id.* at 866-67. The court held that "Merck may, nonetheless, escape liability for patent infringement if its uses of the Integra inventions fall within the strict limits of § 271(e)(1)" and that "the district court correctly confined the § 271(e)(1) exemption to activity that 'would contribute (relatively directly)' to information the FDA considers in approving a drug." *Id.*

132. *Id.* at 867, 876.

133. *Id.* at 867.

even though it may result in a new drug being brought to market at a reduced cost to Merck.¹³⁴

A second problem with the broad reading of “patented invention” in § 271(e)(1) is that it allows all inventions to be used for the purpose of obtaining FDA approval, even if the inventions, such as research tools, are unrelated to the product being tested for approval. In rendering its opinion in *Integra*, the Federal Circuit stated that “expansion of § 271(e)(1) to include the Scripps Merck activities would effectively vitiate the exclusive rights of patentees owning biotechnology tool patents. After all, patented tools often facilitate general research to identify candidate drugs, as well as downstream safety-related experiments on those new drugs.”¹³⁵ Ironically, under the reading of § 271(e)(1) endorsed by the Federal Circuit, methods or tools which can be used to synthesize or evaluate therapeutic drugs during clinical trials no longer have to be licensed during clinical trials.¹³⁶ Thus, the Federal Circuit’s holding reduces the value of research tool patents that might be used during clinical trials and decimates the value of research tool patents that are used primarily in the context of clinical trials. Needless to say, the resulting loss of licensing revenue far exceeds the type of *de minimis* infringement that Congress permitted when it enacted § 271(e)(1).

4. *The Experimental Use Exception Does Not Protect Activities that Fall Within the Legitimate Business Interests of an Accused Infringer*

In dissent, Judge Newman argued that Merck’s research and development activities should be protected by the common-law experimental use

134. See H.R. REP. 98-857, pt. 1, at 14-15 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2647-48 (stating that “[t]he purpose of Title I of the bill is to make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962”). The Report further stated that:

[t]he purpose of Title II of the bill is to create a new incentive for increased expenditures for research and development of certain products which are subject to premarket government approval. The incentive is the restoration of some of the time lost on patent life while the product is awaiting pre-market approval.

Id.

135. 331 F.3d at 867.

136. *Id.* at 866 (holding that Merck could escape liability for patent infringement by showing that “its activities were ‘solely for uses reasonably related to the development and submission of information’ to the FDA,” even though Merck had infringed five of *Integra*’s patents, only one of which was directed to RGD peptides). The remaining four patents were directed to methods of using RGD peptides. Compare U.S. Patent No. 4,792,525 with U.S. Patent Nos. 4,789,734; 4,879,237; 4,988,621; and 5,695,997.

exception, if not by § 271(e)(1). Her dissent focused on the interplay between scientific advancement and patent law rather than the more technical issues of statutory construction.¹³⁷ The issues raised by Judge Newman are quite important. It may not be desirable for our increasingly technical society to prevent scientists from conducting research in a particular field simply because someone has a broad patent in that area.¹³⁸ This is a big concern in the area of biotechnology, in particular, since many biotech patents are directed to pioneering technology not yet sufficiently developed to yield pharmaceutical drug candidates. Consider, for example, the large number of DNA patents, most of which claim poorly characterized genes that are potentially related to one or more diseases.¹³⁹ By providing too much protection to early stage inventions, broad patents may have a stifling influence on future research efforts.¹⁴⁰

Although the issues raised by Judge Newman are important, this application of the common law experimental use exception to Merck's activities runs counter to established law.¹⁴¹ It is undisputed that Merck's research and development activities were related to its business interests—the development and sales of pharmaceutical drugs.¹⁴² In contrast, the experimental use exception, while arguably applicable to university-based scientific pursuits, was never applied to experimentation that fell within the legitimate business interests of an alleged infringer.¹⁴³ Consequently, Merck has no legitimate experimental use claim.¹⁴⁴ Merck's inability to

137. See *Integra*, 331 F.3d at 872-78 (Newman, J., dissenting).

138. Rebecca Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017 (1989); Janice Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1 (2001).

139. See, e.g., Julian Borger, *Rush to Patent Genes Stalls Cures for Disease*, GUARDIAN (Dec. 15, 1999), at www.guardian.co.uk/genes/article/0,2763,191864,00.html.

140. Eisenberg, *supra* note 138, at 1048-65. However one commentator argues that investments can be seen as a scarce resource. See Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265, 275-78 (1977) (comparing patents to mining prospects and arguing that because investment in innovation is limited, it can be seen as a scarce resource). Thus, Kitch argues, investment in innovation is limited, so broad patent protection for pioneering inventions increases the overall level of innovation in society by reducing the amount of duplicative investment in innovation. *Id.*

141. See *Pitcairn v. United States*, 547 F.2d 1106, 1125-26 (Ct. Cl. 1976) (holding that experiments that are in line with the alleged infringer's legitimate business interests are not protected by the experimental use defense).

142. See *Integra*, 331 F.3d at 876.

143. *Roche Prods., Inc. v. Bolar Pharm. Co., Inc.*, 733 F.2d 858, 862-63 (Fed. Cir. 1984); *Pitcairn*, 547 F.2d at 1125-26.

144. Merck's attorneys explicitly stated that the experimental use defense was not relevant to the lawsuit. *Integra*, 331 F.3d at 863 n.2.

successfully assert an experimental use defense is desirable because Merck could have licensed Integra's patents and internalized the cost into the price of its marketed pharmaceutical drugs. A holding that Merck's activities are protected by the experimental use doctrine would greatly reduce the value of countless patents that relate to technology still being developed.¹⁴⁵ While it can be argued that such patents inhibit scientific advances, expanding the experimental use exception in the manner advocated by Judge Newman amounts to a dramatic change in existing law—a change that could have far reaching consequences. As such, the re-evaluation and modification of the scope of the experimental use doctrine is a task best left to Congress.

IV. CONCLUSION

By holding that § 271(e)(1) does not protect developmental research activities, the Federal Circuit in *Integra* reversed a judicial trend of expanding the statute's scope. Although this is a desirable outcome, the court's reasoning lacks clarity because it made no distinction between research that is required for entry into clinical trials and research that is focused on identifying new drug candidates. The court supposed that activities related to obtaining approval for both generic and new drugs are within the scope of § 271(e)(1), but then used legislative history to justify a standard for activities "reasonably related" to obtaining regulatory approval that had been exclusively targeted towards generic drug manufacturers. While activities that take place during clinical trials are protected by § 271(e)(1), pre-clinical activities mandated by the FDA are not. Furthermore, the court ignored the obvious discrepancy between the focus of § 271(e)(1)'s legislative history on generic drug manufacturers and its application to pioneering drug manufacturers like Merck. Implicit in the opinion is a "plain meaning" approach to statutory construction that fails to match up with the legislative intent behind § 271(e)(1). As a result, the court implies that the scope of § 271(e)(1) will expand in new directions, such as towards the protection of otherwise infringing uses of research tool patents during clinical trials. The court's decision can only hurt the value of research tool patents and early-stage pharmaceutical patents like the ones owned by Integra.

145. This, in turn, could lead to a decrease in investment in innovation. See Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law*, 5 J. ECON. PERSPS. 29, 30-31 (1991) (arguing that a company's inability to profit from an early stage invention by obtaining patent protection and licensing the patented technology to other companies that can then improve the invention and successfully market it decreases incentives for companies to invest in innovation).

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