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INTEGRA v. MERCK: EFFECTS ON THE COST AND INNOVATION OF NEW DRUG PRODUCTS

*Alison Ladd**

INTRODUCTION

The rising cost of pharmaceutical drugs is a concern of most consumers.¹ Americans reportedly spent \$125 billion on drugs in 1999.² The cost to discover and develop a new drug is similarly significant and is estimated at nearly \$1.7 billion.³ Drugs are distinct from most other products entering the marketplace in that they must undergo extensive premarket approval by the Food and Drug Administration (FDA) pursuant to the Federal Food, Drug, and Cosmetics Act (FDCA) before reaching consumers.⁴ FDA approval is a lengthy process and takes, on average, 8.2 years.⁵ Given that the cost of research and development cannot be

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¹ David Noonan, *Why Drugs Cost So Much*, NEWSWEEK, Sept. 25, 2000, at 22.

² *Id.*

³ Ann M. Thayer, *Blockbuster Model Breaking Down: Pharma Industry Reaches New Sales Peak, Despite Rising Costs and Bigger Challenges for Drug R&D*, MODERN DRUG DISCOVERY, June 2004, at 23.

⁴ 21 U.S.C. §§ 301-395 (2004).

⁵ CONGRESSIONAL BUDGET OFFICE STUDY, HOW INCREASED COMPETITION FROM GENERIC DRUGS HAS AFFECTED PRICES AND RETURNS IN THE PHARMACEUTICAL INDUSTRY 33 (July 1998) [hereinafter CBO STUDY].

recovered unless and until FDA approval is obtained, the research and development costs for a new drug result in a negative cash flow for pioneer drug companies.⁶ Consequently, only one out of 5,000 possible new drugs is approved for sale and use.⁷

The Patent Act provides pioneer, or innovative, drug companies with the right to patent new drugs.⁸ Patents enable pioneer drug companies to preclude others from making, using, importing, offering for sale, or selling their drugs in the United States.⁹ Further, patents provide pioneer drug companies with exclusive access to the marketplace, allowing the recovery of drug development costs.¹⁰ Problematically, however, the FDA approval process overlaps with the patent terms of new drugs and effectively shortens the period of market exclusivity enjoyed by these products. Pioneer drug companies thus face a reduced period in which to turn profits and recover research and development costs.¹¹ As a result, drug companies seek to recover these costs from consumers through higher product prices.¹²

When the patent rights related to a new drug expire, generic drugs are permitted to enter and compete in the marketplace.¹³ Generic drugs can be sold at much cheaper prices than their brand name counterparts, in part because their manufacturers can make use of existing research in developing drug formulas rather than originating this knowledge base. Through patent laws requiring

⁶ *Id.* at 14-15.

⁷ PHARMACEUTICAL AND RESEARCH MANUFACTURERS OF AMERICA (PHRMA), PHARMACEUTICAL INDUSTRY PROFILE 3 (2003), *available at* <http://www.phrma.org/publications/publications/2004-03-31.937.pdf> [hereinafter PHRMA PROFILE 2003].

⁸ 35 U.S.C. § 101 (2004).

⁹ 35 U.S.C. § 154(a)(1) (2002) (“Every patent shall . . . grant to the patentee . . . the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States . . .”).

¹⁰ CBO STUDY, *supra* note 5, at 3.

¹¹ *Id.* at 3-4

¹² Sarah E. Eurek, *Hatch-Waxman Reform and Accelerated Market Entry of Generic Drugs: Is Faster Necessarily Better?*, 2003 DUKE L. & TECH. REV. 18, 18 (2003).

¹³ *See* CBO STUDY, *supra* note 5, at 2.

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full disclosure of patented inventions, generic drug manufacturers can obtain the patent submissions of brand name drugs and acquire the information necessary to develop and manufacture generic versions.¹⁴ Having benefited from lower development costs, generic drugs may enter the market with lower prices than their brand name rivals.¹⁵ Prior to 1984, however, generic drugs were prevented from entering the marketplace immediately upon the expiration of brand name drug patents and were required to undergo premarket approval by the FDA prior to sale.¹⁶ Patent law prohibited generic drug companies from engaging in premarket approval activities, including the manufacture or use of brand name drugs during their patent terms.¹⁷ Thus, premarket testing by generic drug manufacturers was delayed until the brand name patent had expired.¹⁸

In 1984, in recognition of the need to control drug prices, Congress passed the Drug Price Competition and Patent Term Restoration Act.¹⁹ Commonly referred to as the “Hatch-Waxman Act,” after its two congressional sponsors, the legislation was intended to address the issue of rising drug prices by controlling the practices of brand name manufacturers and enabling generic

¹⁴ 35 U.S.C. § 112 (1975) states:

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

Id.

¹⁵ Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1677 (2003).

¹⁶ *See Roche Products, Inc. v. Bolar Pharm. Co.*, 733 F.2d 858 (Fed. Cir. 1984) (holding that performance of experiments to derive FDA required test data, conducted with a view to the adaptation of the patented invention to the experimenter’s business is a violation of the rights of the patentee to exclude others from using his patented invention).

¹⁷ *Id.*

¹⁸ *Id.*

¹⁹ The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

manufacturers to participate more actively in the market.²⁰ Section 202 of the Act, codified as 35 U.S.C. § 271(e)(1),²¹ facilitates quicker market access for generic manufacturers.²² Section 271(e)(1) has become known as the “safe harbor” provision to patent infringement, as it exempts from patent infringement all activities related to the gathering of information required for compliance with federal laws that regulate drugs and veterinary biological products.²³

Courts have struggled to define the scope of the safe harbor provision.²⁴ Recently, the Federal Circuit in *Integra LifeSciences I, Ltd. v. Merck KGaA*²⁵ narrowed the scope of section 271(e)(1) by excluding from the safe harbor all activities related to the preclinical development of new drugs.²⁶ The court held that the

²⁰ H.R. REP. NO. 98-857(I) (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647; *see also* Jaclyn L. Miller, *Drug Price Competition and Patent Term Restoration Act: The Elimination of Competition Between Drug Manufacturers*, 5 DEPAUL J. HEALTH CARE L. 91 (2002).

²¹ 35 U.S.C. § 271(e)(1) (2003). This section states:

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

Id.

²² H.R. REP. NO. 98-857(I), at 14 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647.

²³ 35 U.S.C. § 271(e)(1) (2003).

²⁴ *See* *Scripps Clinic & Research Found. v. Baxter Travenol Lab., Inc.*, 7 U.S.P.Q.2d 1562 (D. Del. 1988) (stating that the scope of 35 U.S.C. § 271(e)(1) “presents a question of law that has no clear answer”).

²⁵ *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003).

²⁶ The term “preclinical development,” as used by the *Integra* court, refers to the experiments that identified the best drug candidate “to subject to *future*

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safe harbor does not reach “any exploratory research that may rationally form a predicate for future clinical tests.”²⁷ This decision suggests that safe harbor protection is limited to generic drug manufacturers that seek FDA approval for products that compete with existing brand name drugs.²⁸ The restriction of the safe harbor to generic drugs means that liability may be imposed on brand name drug manufacturers for activities they perform during the period preceding FDA approval. This disparity greatly affects the research and development of brand name drugs, as they must undergo a more rigorous FDA approval process than their generic competitors. As a result, brand name drug companies must confront costly burdens to pharmaceutical innovation.

This note will examine the implications of the *Integra* decision for the discovery and development of new drugs. Part I discusses the interpretation of the safe harbor exemption in cases preceding the *Integra* decision. These decisions clarified the types of patents that are covered under the safe harbor²⁹ and announced a “reasonably related use” test to guide the application of the exemption.³⁰ Part II discusses the narrowing of the safe harbor exemption by the Federal Circuit in *Integra*. Part III examines the impact of the *Integra* decision on new drug innovation, with an emphasis on the difficulties posed by the patent licensing process. This section also explores the ways in which *Integra* has affected the landscape of patent infringement exemptions and patent term restoration and, more generally, competition between innovative and generic drug manufacturers. Finally, the note concludes that *Integra* may lead to a reduction in innovative research and development in the United States and suggests that it may be time

clinical testing under the FDA processes.” *Id.* at 865-67 (emphasis added).

²⁷ *Id.* at 867.

²⁸ *Id.* (“The § 271(e)(1) safe harbor covers those pre-expiration activities ‘reasonably related’ to acquiring FDA approval of a drug already on the market.”).

²⁹ *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990); *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997).

³⁰ *Intermedics, Inc. v. Ventritex Co., Inc.*, 26 U.S.P.Q.2d 1524 (Fed. Cir. 1993); *Elan Transdermal, Ltd. v. Cygnus Therapeutic Sys.*, 24 U.S.P.Q.2d 1926 (N.D. Cal. 1992).

to consider amending the Hatch-Waxman Act to broaden the scope of the safe harbor and lengthen patent term extensions for innovative drug manufacturers.

I. THE HISTORY OF JUDICIAL INTERPRETATION OF 35 U.S.C. § 271(E)(1)

The Hatch-Waxman Act's primary purpose is twofold: "to make available more low cost generic drugs by establishing a generic approval procedure for pioneer drugs"³¹ and "to create a new incentive for increased expenditures for research and development of certain products which are subject to premarket government approval."³² Although the first of these goals is restricted to the regulation of drug products, the second goal is unclear in scope. The language of the safe harbor provision in section 271(e)(1) is similarly unclear with regard to the provision's applicability to products other than drugs. In order to determine the scope of the safe harbor, courts have turned to the plain language and legislative history of the statute.³³ Using these tools of statutory interpretation, courts have determined both the types and uses of patents covered by the safe harbor.

A. Summary of the Hatch-Waxman Act

In enacting the Hatch-Waxman Act, Congress explained that Title I of the Act would make available lower-priced generic versions of drugs by allowing for an abbreviated approval process for generic drugs, while Title II, by creating an additional patent term, would "act as a spur to develop innovative and, ultimately, less costly treatment for diseases."³⁴ The two titles of the legislation attempted to balance the interests of generic and

³¹ H.R. REP. NO. 98-857(I), at 14 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647.

³² *Id.* at 15.

³³ *United States v. Clark*, 454 U.S. 555, 560 (1982); *see Alexander v. Sandoval*, 532 U.S. 275 (2001).

³⁴ H.R. REP. NO. 98-857(I), at 20 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2653.

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innovative drug manufacturers.³⁵ The act proposed two sets of changes: first, it implemented an abbreviated approval process for generic drugs, and second, it established patent term extensions for innovative drugs.³⁶ The intended purpose of these changes was to foster greater competition in the drug industry and provide access to lower-cost generic drugs.³⁷

The abbreviated approval process for generic drugs eliminated the duplicative testing previously required for FDA approval of generic drugs.³⁸ This abbreviated process is intended to extend approval to generic drugs, provided that the generic version is the same as the original drug or is so similar that the FDA can conclude that additional safety and effectiveness testing is unnecessary.³⁹ In filing for FDA approval, the generic applicant is required to make a certification to the FDA regarding each patent that claims the brand name drug or method for its use.⁴⁰ The four possible certifications are: I) the patent information has not been filed; II) the patent has expired; III) the date on which the patent will expire; and IV) the patent is invalid or will not be infringed by the applicant's generic drug.⁴¹ Under the first or second options, the time of generic approval is not limited, as there is not a current valid patent covering the generic drug for which approval is sought. In contrast, under the third option, approval of the generic drug occurs only upon the expiration of the existing patent on the brand name drug. When making a certification under the fourth option, known as a Paragraph IV certification, the applicant is required to give notice to each owner of every patent covering a brand name drug that the generic manufacturer asserts to be invalid

³⁵ CBO STUDY, *supra* note 5, at 3.

³⁶ *Id.*

³⁷ 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, 51-52 (2003).

³⁸ CBO STUDY, *supra* note 5, at 3.

³⁹ H.R. REP. NO. 98-857(I), at 14-15 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647-48.

⁴⁰ 21 U.S.C. § 355(j)(2)(A)(vii) (2003).

⁴¹ *Id.*

or not infringed.⁴² This notification requirement is designed to protect holders of valid drug patents by allowing the patent holder to sue the generic applicant for infringement.⁴³ If an infringement action is timely brought within forty-five days after notice of Paragraph IV certification, the generic approval process is stayed for a thirty-month period.⁴⁴ Yet, upon a successful Paragraph IV certification, the generic applicant receives 180 days of market exclusivity.⁴⁵

To balance the interests of generic and innovative drug manufacturers, the Hatch-Waxman Act also provides for patent term restoration for certain products that are subject to premarket government approval.⁴⁶ A patent term extension, or restoration, is intended to provide innovative manufacturers with an opportunity to make up the portion of the patent term that is lost during the regulatory approval of the patented drug.⁴⁷ There are several notable limitations on the extensions afforded by the patent term restoration provision. First, extensions cannot exceed five years.⁴⁸ Additionally, extensions are capped at fourteen years from a product's initial approval by the FDA.⁴⁹ Moreover, a patent term extension can only be applied to the earliest patent claiming a particular product.⁵⁰

In providing innovative drug manufacturers with the benefit of patent term restoration, Congress also sought to prevent the de facto extension of an innovative drug's patent term through delay

⁴² 21 U.S.C. § 355(j)(2)(B) (2003); H.R. REP. NO. 98-857(I), at 24 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2657.

⁴³ *Id.*

⁴⁴ 21 U.S.C. § 355(j)(5)(B)(iii) (2003).

⁴⁵ *Id.* § 355(j)(5)(A)(iv) (2003).

⁴⁶ H.R. REP. NO. 98-857(I), at 15 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2648. The products which can gain the benefit of patent term restoration include human drugs, animal drugs, medical devices, and food and color additives. *Id.*

⁴⁷ Sarah M. Yoho, *Reformation of the Hatch-Waxman Act, an Unnecessary Resolution*, 27 NOVA L. REV. 527, 536 (2003).

⁴⁸ 35 U.S.C. § 156(g)(6)(A) (2002).

⁴⁹ *Id.* § 156(c)(3) (2002).

⁵⁰ *Id.* § 156(c)(4) (2002).

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in the approval of generic drugs following the patent term's expiration.⁵¹ This de facto extension of the innovative drug's patent term was created because a generic manufacturer could not begin the testing necessary for FDA approval of the generic drug product prior to the expiration of the innovative drug's patent, given that such testing was considered an infringing use.⁵² Thus, the patent holder retained exclusivity on the market after the expiration of the drug patent while the generic manufacturer was testing its generic drug for FDA approval. Section 202 of the Act, later codified as 35 U.S.C. § 271(e)(1), eliminates de facto extensions by providing that "it shall not be an act of infringement to make, use, or sell a patented invention solely for uses reasonably related to the development and submission of information under a federal law which regulates the approval of drugs."⁵³ This provision is known as the safe harbor for patent infringement.

B. Types of Patented Inventions Covered by the Safe Harbor

In order to determine which patented inventions receive protection under the safe harbor provision, one must consider the Hatch-Waxman Act in its entirety. The phrase "patented invention," as used in section 271(e)(1), is in no way limited to drug-related inventions.⁵⁴ The safe harbor exemption should

⁵¹ H.R. REP. NO. 98-857(I), at 46 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2679.

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

Id.

⁵² *Roche Products, Inc. v. Bolar Pharm. Co.*, 733 F.2d 858 (Fed. Cir. 1984).

⁵³ H.R. REP. NO. 98-857(I), at 45 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2678.

⁵⁴ 35 U.S.C. § 100(a) (1999); *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 556 (1990). The only types of patented inventions to which the statute does not apply are those pertaining to a new animal drug or veterinary biological product "which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques." 35 U.S.C. § 271(e)(1) (2003).

therefore be applied to any patented invention that would be infringed in the course of conducting activities related to the development and submission of information required by a federal law that regulates drugs and veterinary biological products.⁵⁵ Section 271(e)(1) makes no specific reference to other items covered by the FDCA, such as medical devices, food additives, or color additives.⁵⁶ By contrast, the patent term extension applies to drugs, medical devices, food additives, and color additives.⁵⁷ Yet, the definitions set forth in the FDCA for medical devices, food additives, and color additives are defined separately and distinctly from the definitions of drugs.⁵⁸ Section 271(e)(1), therefore, does

⁵⁵ *Id.*

⁵⁶ 35 U.S.C. § 271(e)(1) (2003).

⁵⁷ *Id.* § 156(f) (2004).

⁵⁸ 21 U.S.C. § 321 (2004).

The term ‘device’ . . . means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is —

(1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

21 U.S.C. § 321(h).

The term ‘food additive’ means any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the

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not appear to cover medical devices, food additives, or color additives. Thus, the safe harbor exemption applies to only some of the products that receive the benefit of patent term restoration.⁵⁹

In *Eli Lilly & Co. v. Medtronic, Inc.*, the U.S. Supreme Court considered whether Medtronic's testing and marketing of an implantable cardiac defibrillator, a medical device used in the treatment of heart patients, was exempt from patent infringement

conditions of its intended use; except that such term does not include— (1) a pesticide chemical residue in or on a raw agricultural commodity or processed food; or (2) a pesticide chemical; or (3) a color additive; or (4) any substance used in accordance with a sanction or approval granted prior to the enactment of this paragraph pursuant to this Act, the Poultry Products Inspection Act or the Meat Inspection Act of March 4, 1907; (5) a new animal drug; or (6) an ingredient described in paragraph (ff) in, or intended for use in, a dietary supplement.

21 U.S.C. § 321(s).

The term 'color additive' means a material which— (A) is a dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived, with or without intermediate or final change of identity, from a vegetable, animal, mineral, or other source, and (B) when added or applied to a food, drug, or cosmetic, or to the human body or any part thereof, is capable (alone or through reaction with other substance) of imparting color thereto; except that such term does not include any material which the Secretary, by regulation, determines is used (or intended to be used) solely for a purpose or purposes other than coloring.

21 U.S.C. § 321(t)(1).

The term 'drug' means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C).

21 U.S.C. § 321(g)(1).

⁵⁹ See H.R. REP. NO. 98-857(I), at 20-37 (1984), reprinted in 1984 U.S.C.C.A.N. 2647, 2653-70.

under section 271(e)(1).⁶⁰ Focusing on what it perceived to be the intended purpose of the exemption, the Court applied the safe harbor to medical devices.⁶¹ The Supreme Court explained that, in using the language “the development and submission of information *under* a Federal law” to reference those preapproval activities that would be exempt under the safe harbor, Congress intended to refer to all activities related to “compliance with a comprehensive scheme of regulation.”⁶² The Court emphasized that if Congress had intended the safe harbor to apply exclusively to drug patents, there were “infinitely more clear and simple ways of expressing that intent.”⁶³ The Court considered the patent term restoration and patent infringement exemption provisions of the Hatch-Waxman Act to be a single legislative package⁶⁴ and reasoned that Congress could not have intended for the benefits of both provisions to apply to drugs, but only the patent term extension to apply to medical devices.⁶⁵

⁶⁰ *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990). Eli Lilly brought a patent infringement action to enjoin Medtronic’s testing and marketing of an implantable cardiac defibrillator. *Id.* Medtronic’s defense was that its alleged infringing activities were for the purpose of developing and submitting information for premarket approval of a medical device and was therefore exempt under 35 U.S.C. § 271(e)(1). *Id.*

⁶¹ *Id.*

⁶² *Id.* at 666-67.

⁶³ *Id.*

⁶⁴ *Id.* at 670 n.3.

⁶⁵ *Id.* at 672-73.

It seems most implausible to us that Congress, being demonstrably aware of the *dual* distorting effects of regulatory approval requirements in this entire area—dual distorting effects that were roughly offsetting, the disadvantage at the beginning of the term producing a more or less corresponding advantage at the end of the term—should choose to address both those distortions only for drug products; and for other products . . . should enact provisions which not only leave in place an anticompetitive restriction at the end of the monopoly term but simultaneously expand the monopoly term itself, thereby not only failing to eliminate but positively aggravating distortion of the 17-year patent protection

Id.

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The decision in *Eli Lilly* discusses medical devices generally.⁶⁶ The FDCA, however, has established three classes of medical devices: Class I, Class II, and Class III.⁶⁷ Of these three classes, only Class III is subject to rigorous premarket approval.⁶⁸ Class I

⁶⁶ *See id.* at 667-69.

⁶⁷ 21 U.S.C. § 360c (2004). Class I devices, or general control devices, are those for which the controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device. *Id.* § 360c(a)(1)(A).

Class II devices, or special controls devices, are those which cannot be classified as a Class I device because the general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device. A Class II device requires sufficient information to establish special controls to provide such assurance, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines (including guidelines for the submission of clinical data in premarket notification).

Id. § 360c(a)(1)(B).

Class III devices require premarket approval. Class III devices are those which cannot be classified as a Class I device because insufficient information exists to determine that the application of general controls are sufficient to provide reasonable assurance of the safety and effectiveness of the device, and cannot be classified as a Class II device because insufficient information exists to determine that the special controls would provide reasonable assurance of its safety and effectiveness. A Class III device that is purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or presents a potential unreasonable risk of illness or injury, is subject premarket approval to provide reasonable assurance of its safety and effectiveness.

Id. § 360c(a)(1)(C).

⁶⁸ 21 U.S.C. § 360e (2004). Class III devices require an approved application for premarket approval. *Id.* § 360e(a)(2). An application for premarket approval consists of full reports of all information, published or known or which should reasonably be known to the applicant, concerning investigations which have been made to show whether or not such device is safe and effective; a full statement of the components, ingredients, and properties and of the principle or principles of operation, of such device; a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and, when relevant, packing and installation of, such device; an identifying reference to any performance standard which would be applicable to

and Class II devices are subject to an abbreviated approval process.⁶⁹ The Federal Circuit clarified the safe harbor exemption as it applies to medical devices in *Abtox, Inc. v. Exitron Corp.*⁷⁰ In that case, the court considered whether the safe harbor exemption applied to a patented device used to sterilize medical instruments.⁷¹ The court determined that the safe harbor applies to Class II medical devices, even though their abbreviated premarketing approval process precludes them from being eligible for patent term extensions.⁷²

One court has argued for symmetry in the eligibility requirements for patent term restoration and the safe harbor exemption.⁷³ In *Infigen, Inc. v. Advanced Cell Technology, Inc.*, the District Court for the Western District of Wisconsin held that only those patents whose terms were eligible for patent term

any aspect of such device if it were a class II device, and either adequate information to show that such aspect of such device fully meets such performance standard or adequate information to justify any deviation from such standard; samples of such device and of components thereof, except where the submission of such samples is impracticable or unduly burdensome, the requirement may be met by the submission of complete information concerning the location of one or more such devices readily available for examination and testing; specimens of the labeling proposed to be used for such device; and any other information relevant to the subject matter of the application. *Id.* § 360e(c)(1).

⁶⁹ 21 U.S.C. §§ 351, 352, 360f (2004). All classes of devices cannot be an adulterated, misbranded, or banned device. *Id.* Manufacturers or importers of Class I devices must give notice to the FDA, as well as maintaining records and reports to assure that the device is not adulterated or misbranded or to otherwise assure its safety and effectiveness. 21 U.S.C. §§ 360h, 360i (2004). Class II devices require promulgation of performance standards and, postmarket surveillance, patient registries, development and dissemination of guidelines recommendations, and other appropriate actions 21 U.S.C. §§ 360c(a)(1)(B), 360d (2004).

⁷⁰ *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997).

⁷¹ *Id.*

⁷² 35 U.S.C. § 156 (2002); See Courtenay C. Brinckerhoff, *Can the Safe Harbor of 35 U.S.C. § 271(e)(1) Shelter Pioneer Drug Manufacturers?*, 53 FOOD DRUG L.J. 643, 654 (1998).

⁷³ *Infigen, Inc. v. Advanced Cell Tech., Inc.*, 65 F. Supp. 2d 967 (W.D. Wis. 1999).

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extensions would be immune from infringement under the safe harbor.⁷⁴ The court argued that “the patent term extension is the quid pro quo for the protection from infringement actions and vice versa.”⁷⁵ Thus, under *Infigen*, research conducted to support FDA approval is not immune from infringement liability for patents that cannot benefit from patent term restoration. The decision in *Infigen* ignores the Supreme Court precedent established in *Eli Lilly*.⁷⁶ The Supreme Court did not inextricably link the type of patents covered by the safe harbor to those eligible for term extensions.⁷⁷ To the contrary, the Court recognized that there could be situations in which a patent gains the benefit of a term extension without the disadvantage of infringement exemption, and others in which the disadvantage will be suffered without the benefit.⁷⁸

C. Types of Uses Covered by the Safe Harbor

In addition to determining the types of patents protected by the safe harbor of section 271(e)(1), courts were also charged with interpreting which infringing uses of patented subject matter merited the benefit of the safe harbor. In *Scripps Clinic & Research Found. v. Genentech, Inc.*, the Northern District of California became the first court to consider the types of uses covered by the safe harbor exemption.⁷⁹ The court focused on the “solely for” language of section 271(e)(1).⁸⁰ The section, by its plain language, allows for an infringement exemption for the use of a patented invention “solely for uses reasonably related to the

⁷⁴ *Id.* at 980.

⁷⁵ *Id.*

⁷⁶ *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990).

⁷⁷ *Id.*

⁷⁸ *Id.* at 671-73.

⁷⁹ *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379 (N.D. Cal. 1987). Scripps Clinic brought an infringement action on their patented protein, Factor VIII:C, that causes human blood to clot. *Id.* Genentech argued that their uses of Factor VIII:C, though not solely for the purposes related to FDA testing, had some reasonable relationship to such purposes and therefore did not infringe under section 271(e)(1). *Id.*

⁸⁰ *Id.* See *supra* note 21 for language of the statute.

development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.”⁸¹ The court determined that in order for an infringing use to be exempt, the use of the patent need only be related to the generation of information that would meet the FDA’s requirements for drug approval.⁸² However, if the use is also related to other ventures, such as preparations for patent filings or agreements in preparation for commercial manufacturing, the use of the patent will no longer be exempt from infringement.⁸³

This interpretation was soon criticized for limiting the safe harbor to activities that are “solely related” rather than “reasonably related” to FDA approval.⁸⁴ Courts subsequently adopted a test for infringing uses that seized on the “reasonably related” language rather than the “solely for” language of section 271(e)(1).⁸⁵

The test for a reasonably related use was set forth by the Northern District of California in *Intermedics, Inc. v. Ventritex, Inc.*⁸⁶ Intermedics alleged that various activities in connection with the development of Ventritex’s implantable defibrillator were acts of infringement.⁸⁷ These activities included the manufacture of the

⁸¹ 35 U.S.C. 271(e)(1) (2003).

⁸² *Scripps Clinic*, 666 F. Supp. 1379.

⁸³ *See id.* at 1396.

⁸⁴ *Scripps Clinic & Research Found. v. Baxter Travenol Lab., Inc.*, 7 U.S.P.Q.2d 1562, 1565 (D. Del. 1988). The issue before the court was “whether any foreign activities can be ‘reasonably related’ to FDA drug approval.” *Id.* The court looked to the legislative history of section 271(e)(1) and found that it did not “provide guidance on what activities are ‘reasonably related’ to FDA drug approval.” *Id.* The court then criticized the decision in *Scripps v. Genentech* for “interpret[ing] the statute to only cover activities that were ‘solely related’ to FDA approval and did not consider what acts are ‘reasonably related’ to it.” *Id.*, citing *Scripps v. Genentech*, 666 F. Supp. 1379, 1396 (N.D. Cal. 1987).

⁸⁵ *Elan Transdermal, Ltd. v. Cygnus Therapeutic Sys.*, 24 U.S.P.Q.2d 1926, 1932-33 (N.D. Cal. 1992) (explaining that the word “solely” in § 271(e)(1) modifies “uses” not “reasonably related”); *Intermedics v. Ventritex Co.*, 26 U.S.P.Q.2d 1524 (Fed. Cir. 1993).

⁸⁶ *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269, 1281 (N.D. Cal. 1991).

⁸⁷ *Id.* at 1282; *see supra* Part I.B for discussion of the safe harbor as it applies to medical devices.

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defibrillator, its sale to hospitals, and the demonstration of the device at trade shows.⁸⁸ The court found that all of these activities were reasonably related to the performance of clinical trials necessary for FDA approval of the defibrillator.⁸⁹ The court looked to Congress's acknowledgement that the types and quantities of information required by the FDA for approval will not always be clear.⁹⁰ Thus, the court held that the "reasonably related" language was intended to provide latitude to those who seek FDA approval in making judgments about the nature and extent of otherwise infringing activities.⁹¹ The court recognized that the exemption should not be lost because activities either fail to generate information that interests the FDA or generate more information than is necessary.⁹²

The reasonably related use test broadened the scope of section 271(e)(1). The test set out by the *Intermedics* court asks whether the use in question could reasonably contribute to the generation of information of the type that would likely be required for FDA approval.⁹³ This test, by not limiting the exemption to infringing uses that actually result in information for submission to the FDA, provides innovators with a more generous safe harbor with which to protect themselves against infringement allegations. Further, this test gives safe harbor to drug manufacturers that use a patented invention to obtain information relevant to FDA approval, even if the information gained from the infringing use is also used for other purposes.⁹⁴

⁸⁸ *Intermedics*, 775 F. Supp. at 1282.

⁸⁹ *Id.* at 1282-88.

⁹⁰ *Id.* at 1280.

⁹¹ *Id.*

⁹² *Id.*

⁹³ *Id.*

⁹⁴ See *Teletronics Pacing Sys. v. Ventritex, Inc.*, 982 F.2d 1520, 1524 (Fed. Cir. 1992) (explaining that there is not a requirement in the statute [35 U.S.C. § 271(e)(1)] that disclosure of information to persons other than the FDA would "repeal" the exemption to patent infringement); see also *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019, 1030 (Fed. Cir. 1997) (finding that the statutory language [of 35 U.S.C. § 271(e)(1)] allows the would-be infringer "to use its data for more than FDA approval").

Although this test disregards the word “solely” as it appears in the statute, it is clear from the legislative history that information obtained from infringing uses need not be submitted to the FDA in order to qualify for the exemption.⁹⁵ Until the decision in *Integra*, the decisions discussing the exempted uses of a patented invention under the safe harbor gave little or no significance to the word “solely” in favor of a broad “reasonably related” test. Under this interpretation, innovative drug developers were given more leeway in their research activities, given that the fruits of their research activities would retain the protection of the safe harbor, even if the resulting information had possible uses other than FDA submission.

II. *INTEGRA LIFESCIENCES I, LTD. V. MERCK KGAA*

Before *Integra*, courts generally gave broad reach to the activities and types of patents that could be covered under the safe harbor.⁹⁶ Specifically addressing the applicability of the safe

⁹⁵ H.R. REP. NO. 98-857(I), at 45 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2678 (“A party which develops such information, but decides not to submit an application for approval, is protected as long as the development was done to determine whether or not an application for approval would be sought.”). The court in *Intermedics* elaborated on what they considered Congress’ intent to actually have been. *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269, 1280 (N.D. Cal. 1991). The court states that the phrase “reasonably related” “reflects Congress’ acknowledgement that it will not always be clear to parties setting out to seek FDA approval for their new product exactly which kinds of information, and in what quantities, it will take to win that agency’s approval.” *Id.* The court went on to state:

[W]e do not believe that Congress intended a party to lose the exemption simply because it turns out, after the fact, that some of that party’s otherwise infringing ‘uses’ either failed to generate information in which the FDA was interested or generated more information that turned out to be necessary to secure FDA approval.

Id.

⁹⁶ *See* *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990); *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997); *Telectronics Pacing Sys. v. Ventritex, Inc.*, 982 F.2d 1520 (Fed. Cir. 1992); *Nexell Therapeutics, Inc. v. AmCell Corp.*, 199 F. Supp. 2d 197 (D.De. 2002); *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833, 2001 U.S. Dist. LEXIS 19361

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harbor to innovative drug development, the Southern District of New York in *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*⁹⁷ found that the use of a patented invention for research and development of a new drug can be afforded the protection of the safe harbor.⁹⁸ The court looked to Congress's stated desire to encourage innovation and bring new drugs to the market in a quicker fashion.⁹⁹ Nearly two years later, the Federal Circuit in *Integra* denied safe harbor to the research and development of new drugs, effectively narrowing the protection afforded to innovative drug manufacturers.¹⁰⁰ The *Integra* decision brings the scope of the exemption back in line with the initial interpretation by *Scripps Clinic & Research Found. v. Genentech, Inc.*¹⁰¹ As previously discussed, the *Scripps* court focused on the "solely for" limitation of the statute, rejecting a broad construction that would immunize "any use of a patented invention so long as some aspect of that use is reasonably related to FDA testing."¹⁰² This "solely for" test was later rejected by other district courts, which adopted the reasonably related use test set forth by the Northern District of California in *Intermedics*.¹⁰³

(S.D.N.Y. Nov. 27, 2001); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104 (D. Mass. 1998); *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269 (N.D. Cal. 1991).

⁹⁷ *Bristol-Myers*, 2001 U.S. Dist. LEXIS 19361.

⁹⁸ *Id.* at *19-20.

⁹⁹ *Id.* at *10.

¹⁰⁰ *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003).

¹⁰¹ *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379 (N.D. Cal. 1987).

¹⁰² *Id.* at 1396.

¹⁰³ *Nexell Therapeutics, Inc. v. Amcell Corp.*, 1999 F. Supp. 2d 197, 204-5 (D. Del. 2002) (stating that activities only exceed the scope of the §271(e)(1) exemption when they have no objectively reasonable application towards obtaining FDA approval); *Bristol-Myers*, 2001 U.S. Dist. LEXIS 19361, at *12-13 (denying summary judgment on the basis that a reasonable jury could conclude uses of the patented invention were reasonably related to the submission of information to the FDA); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104, 107 (D. Mass. 1998) ("Uses . . . may be related to FDA approval, and yet be conducted for purposes other than, or in addition to, obtaining FDA approval.").

A. District Court Decisions Prior to Integra v. Merck

The decision in *Integra* is a clear break from the line of cases dealing with the infringement exemption for preclinical drug discovery.¹⁰⁴ *Integra* was the first appellate court decision to address the safe harbor since the U.S. Supreme Court's decision in *Eli Lilly*.¹⁰⁵ In the thirteen years between *Eli Lilly* and *Integra*, three district courts addressed the application of the safe harbor to preclinical development of innovative products.¹⁰⁶ Each of the three courts concluded that the safe harbor applied to these activities.¹⁰⁷ Because the Federal Circuit has exclusive appellate jurisdiction over patent cases, *Integra* overrules each of these district court decisions, even though there was no disagreement among the district courts regarding the applicability of the safe harbor to preclinical development.¹⁰⁸

In *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, the District Court of Massachusetts became the first court to apply the safe

¹⁰⁴ *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990); *Nexell Therapeutics, Inc. v. AmCell Corp.*, 199 F. Supp. 2d 197 (D.De. 2002); *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833, 2001 U.S. Dist. LEXIS 19361 (S.D.N.Y. Nov. 27, 2001); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104 (D. Mass. 1998); *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269, 1280 (N.D. Cal. 1991).

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

¹⁰⁶ *Nexell Therapeutics*, 199 F. Supp. 2d at 197; *Rhone-Poulenc*, 2001 U.S. Dist. LEXIS at *1; *Amgen*, 3 F. Supp. 2d at 104.

¹⁰⁷ *Nexell Therapeutics*, 199 F. Supp. 2d at 205; *Rhone-Poulenc*, 2001 U.S. Dist. LEXIS at *19-20; *Amgen*, 3 F. Supp. 2d at 111.

¹⁰⁸ 35 U.S.C. § 145 (2002) (covering the right to a civil action to obtain a patent); 35 U.S.C. § 146 (2002) (granting the remedy of a civil action to any party to a patent interference dissatisfied with the decision of the Board of Patent Appeals and Interferences on the interference); 35 U.S.C. § 154(b) (2002) (deals with the adjustment of patent terms); 28 U.S.C. § 1295(a)(4)(C) (1999) (stating in pertinent part that “[t]he United States Court of Appeals for the Federal Circuit shall have exclusive jurisdiction of an appeal from a decision of a district court to which a case was directed pursuant to section 145, 146, or 154(b) of title 35”); 28 U.S.C. § 1292(c)(2) (1992) (stating in pertinent part that “[t]he United States Court of Appeals for the Federal Circuit shall have exclusive jurisdiction of an appeal from a judgment in a civil action for patent infringement”).

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harbor to an innovative drug product.¹⁰⁹ In that case, Hoechst had used Amgen's patented protein product, erythropoietin (EPO), to facilitate the development of GA-EPO, a competing but novel product.¹¹⁰ The court held that the safe harbor exemption applied to a variety of Hoechst's activities, which it deemed relevant to the FDA approval process.¹¹¹ The court emphasized that the use of a patented invention must be reasonably related to FDA approval, but need not be for the exclusive purpose of FDA approval.¹¹² The court also clarified that to fall within the safe harbor of section 271(e)(1), the making, using, or selling of a patented invention must be "in ways that objectively bear reasonable prospects of yielding information that might be relevant in the FDA approval process."¹¹³

Three years later, the District Court for the Southern District of New York in *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.* followed and expanded upon the decision in *Amgen*.¹¹⁴ There, the court held that the use of patented intermediates by Bristol-Myers Squibb (BMS) in the development of new drugs was exempt from infringement under the safe harbor.¹¹⁵ The court found that it was objectively reasonable for BMS to believe that there was a "decent prospect" that the use of the patented intermediates would contribute, in a relatively direct manner, to the generation of information upon which the FDA could base approval of the newly discovered drug.¹¹⁶ The court reasoned that even though each use of the patented intermediates by BMS in

¹⁰⁹ *Amgen*, 3 F. Supp. 2d at 104.

¹¹⁰ *Id.* at 106.

¹¹¹ *Id.* at 113. Hoechst's activities included a multitude of studies on GA-EPO that the company argued were required for FDA approval, including purity studies, consistency studies, characterization studies, and viral clearance tests. These studies were done in comparison with Amgen's EPO product. *Id.* at 109-11.

¹¹² *Id.* at 108.

¹¹³ *Id.*

¹¹⁴ *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833, 2001 U.S. Dist. LEXIS 19361 (S.D.N.Y. Nov. 27, 2001).

¹¹⁵ *Id.* at *19.

¹¹⁶ *Id.* at *19-20, quoting *Intermedics, Inc. v. Ventritex, Inc.*, 775 F. Supp. 1269, 1280 (N.D. Cal. 1991).

early stage research might not have yielded information that could be submitted to the FDA, the uses related to this preliminary activity could facilitate the generation of information that later would be submitted.¹¹⁷ Furthermore, the court determined that eligibility for the safe harbor exemption should not be delayed until after a candidate drug has been selected or designated as the subject of an application for FDA approval.¹¹⁸ The court explained that if selection or filing of a candidate drug were required, the exemption would never apply because the underlying research and development necessary for FDA approval could never be undertaken.¹¹⁹

Finally, in *Nexell Therapeutics, Inc. v. AmCell Corp.*, the District Court of Delaware considered the application of the safe harbor to an innovative product.¹²⁰ *Nexell* differs from the two

¹¹⁷ *Id.* at *25.

¹¹⁸ *Id.* at *23.

¹¹⁹ *Id.* at *23-24. In response to Rhone-Poulenc Rorer's argument that the § 271(e)(1) exemption only applies after a particular drug candidate has been selected or filed with the FDA, Bristol-Myers Squibb argued that the exemption must apply to all activities reasonably related to an actual or possible FDA application:

It would be nonsensical for the exemption to apply only in the development process after a drug candidate was identified, or after a drug candidate was actually filed with the FDA. If so, the exemption would never be reached because the underlying preliminary research and development work could not be undertaken.

Id. at *23. The court also looked to the report of the Special Master, who had been appointed to the case, given the district court judge's absence due to major surgery. *Id.* at *2. The report found that the uses of the patented invention were reasonably related to an FDA application:

(1) even where each such use does not directly result in an FDA application being filed, so long as the use was made in order to determine whether or not an application for approval would be sought; and (2) even though each such use of the patented intermediates may not directly yield information that could be submitted to the FDA, but relates to a preliminary activity that may facilitate or be useful in generating information that could be submitted to the FDA.

Id. at *24.

¹²⁰ *Nexell Therapeutics, Inc. v. AmCell Corp.*, 199 F. Supp. 2d 197 (D.De. 2002).

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previous cases in that it deals with a medical device rather than a drug.¹²¹ Nexell argued that AmCell had used its patented antibodies in the development of a magnetic cell-separating device.¹²² The court found that AmCell's diverse activities were either exempt because they were carried out in relation with ongoing FDA trials or were insulated from infringement liability because they were conducted pursuant to the FDA approval process.¹²³ The *Rhone-Poulenc*, *Hoechst*, and *Nexell* cases signaled a preference for a broad interpretation of the safe harbor provision—a trend that has been largely reversed by the Federal Circuit's decision in *Integra*.

B. Integra v. Merck

On July 18, 1996, Integra filed a complaint against Merck for patent infringement in the Southern District of California. Integra owns five patents related to a short tri-peptide known as an RGD peptide.¹²⁴ These peptides are known to bind to $\alpha_v\beta_3$ receptors on the surface of cells.¹²⁵ A researcher at Scripps Research Institute

¹²¹ *Id.*

¹²² *Id.* at 198.

¹²³ *Id.* at 207-8. Amcell's activities included sending information to physicians to recruit clinicians to participate in FDA studies; maintaining a booth at the American Society of Hematology featuring a display of the device; advertising in medical journals; soliciting clinicians through Amcell's website; and providing the device to FDA-approved clinical investigators. *Id.* at 199.

¹²⁴ U.S. Patent No. 5,695,997 (issued Dec. 9, 1997); U.S. Patent No. 4,988,621 (issued Jan. 29, 1991); U.S. Patent No. 4,879,237 (issued Nov. 7, 1989); U.S. Patent No. 4,792,525 (issued Dec. 20, 1988); U.S. Patent No. 4,789,734 (issued Dec. 6, 1988).

¹²⁵ *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 862 (Fed. Cir. 2003). RGD peptides are a short tri-peptide segment of fibronectin (an adhesive protein) having the amino acid sequence Arg-Gly-Asp (in single-letter notation, RGD). *Id.* The RGD peptide sequence promotes beneficial cell adhesion by interacting with $\alpha_v\beta_3$ receptors on cell surface proteins called integrins. *Id.* The RGD sequence attaches to the $\alpha_v\beta_3$ receptors on the surfaces of cells. *Id.* at 862-63. This bond adheres the cells to the substrate containing RGD. *Id.* at 863. Inducing better cell adhesion and growth promotes wound healing and biocompatibility of prosthetic devices. *Id.* In addition, blood vessels grow new branches due to controlled interactions with integrins. *Id.*

(Scripps) discovered that blocking these $\alpha_v\beta_3$ receptors could have therapeutic uses in inhibiting tumor growth.¹²⁶ Following this discovery, Merck KGaA (Merck) entered into an agreement with Scripps to fund “the necessary experiments to satisfy the biological bases and regulatory (FDA) requirements for the implementation of clinical trials” using a certain cyclic RGD peptide developed at Scripps, or derivatives thereof.¹²⁷ A derivative of this peptide was later chosen for clinical development.¹²⁸ In its case before the Southern District of California, Integra asserted that the agreement between Merck and Scripps was commercial in nature and that research conducted pursuant to that agreement was an infringement of its patents.¹²⁹ After trial, a jury found Merck liable for the infringement of four of Integra’s patents.¹³⁰

Merck appealed to the Federal Circuit from the jury’s verdict of infringement.¹³¹ The company asserted that the district court had erroneously interpreted section 271(e)(1).¹³² In its review of the lower court’s interpretation of the statute, the Federal Circuit

¹²⁶ *Id.* at 863.

¹²⁷ *Id.* Merck KGaA began funding research at Scripps in 1988 when Dr. Cheresh, a researcher at Scripps, identified a monoclonal antibody that had activity as an inhibitor of integrin activity. *Id.* The collaboration was enlarged in 1995 when Dr. Cheresh discovered that a Merck-provided peptide, having the sequence c(RGDfV), inhibits new blood vessel growth by interaction with a specific integrin. *Id.* In this collaboration, cyclic RGD peptides were synthesized and studied. *Id.* It was found that some cyclic RGD peptides have anti-angiogenic properties, of interest for the treatment of a host of diseases, including cancer, macular degeneration, and rheumatoid arthritis. *Id.* “Angiogenic” refers to the process of generating new blood vessels, a process essential to tumor growth. *Id.* The purpose of the collaborative research was to (1) assess the potential efficacy of the peptides as therapeutic agents; (2) discover the mechanism of the action of the peptides; and (3) shed light on the histopathology, toxicology, circulation, diffusion, and half-life of the peptides in the blood stream. *Id.* The ultimate goal of the research was to find a product that would be sufficiently effective in the treatment of angiogenic disease that could be developed and brought to market. *Id.* at 873-74.

¹²⁸ *Id.* at 863.

¹²⁹ *Id.*

¹³⁰ *Id.*

¹³¹ *Id.* at 864.

¹³² *Id.*

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announced that the term “solely” limits the safe harbor exemption from extending beyond uses of patented inventions that are reasonably related to those specified in section 271(e)(1).¹³³ The court further explained that the limitation created by the term “solely” was essential because “activities that do not directly produce information for the FDA are already straining the relationship to the central purpose of the safe harbor.”¹³⁴ The safe harbor’s central purpose was explained as an express objective to facilitate the immediate entry of generic drugs into the marketplace.¹³⁵ The court thus held that “[t]he safe harbor does not reach any exploratory research that may rationally form a predicate for future FDA clinical tests.”¹³⁶

Two rationales support the court’s holding. First, the court noted that the FDA has no interest in the general “hunt” for new drugs.¹³⁷ Rather, it is concerned with specific drugs for which approval is being sought.¹³⁸ Second, the court held that Congress had narrowly tailored the safe harbor in order to ensure only a de minimis impact on patent holders’ rights.¹³⁹ This de minimis impact was protected by limiting safe harbor protection to those activities that are reasonably related to the FDA approval of a drug already on the market.¹⁴⁰ The court therefore concluded that Merck’s activities, which were not related to a drug already on the market, did not fall under the safe harbor.¹⁴¹

The court also argued that if the safe harbor exemption was

¹³³ *Id.* at 866. Section 271(e)(1) allows exemption from infringement for patented inventions “solely for uses reasonably related to the development and submission of information under a Federal law which regulates . . . drugs or veterinary biological products.” 35 U.S.C. § 271(e)(1) (2003).

¹³⁴ *Integra*, 331 F.3d at 866.

¹³⁵ *Id.* at 866-67.

¹³⁶ *Id.* at 867.

¹³⁷ *Id.* at 866. In using the word “hunt” the court elaborated upon its meaning by saying that “the FDA does not require information about drugs other than the compound featured in an Investigational New Drug application.” *Id.*

¹³⁸ *Id.*

¹³⁹ *Id.* at 867.

¹⁴⁰ *Id.*

¹⁴¹ *Id.*

expanded to include Merck's activities, it would "effectively vitiate the exclusive rights of patentees owning biotechnology tool patents."¹⁴² The court explained that many patents cover tools that are used to facilitate general research to identify candidate drugs and to test the safety of those newly identified drugs.¹⁴³ The court acknowledged that such tools fall within the safe harbor when used for clinical testing required for FDA approval, yet argued that they would hold little commercial benefit to the patent holder if they fell within the safe harbor when used to support general research.¹⁴⁴ The court then held that if section 271(e)(1) was "exaggerated," it "would swallow the whole benefit of the Patent Act for some categories of biotechnological inventions."¹⁴⁵

III. THE PROBLEMATIC EFFECTS OF THE *INTEGRA* DECISION

The decision in *Integra* poses new challenges for the innovative drug industry. Problematically, *Integra* has created a greater need for innovators to license patents for research and development. With little or no protection from the safe harbor, innovators will face great liability from the owners of research tool patents, which are essential to innovative research. This is especially likely, given that the common-law research exemption has recently been narrowed and that no statutory experimental use exemption exists in the United States. The patent term restorations provided by the Hatch-Waxman Act have proved similarly unavailing in aiding the recovery of research and development costs by innovative drug manufacturers, as they fail to cover the entire period lost to the regulatory approval process. Finally, the cumulative effect of these problems could stifle competition or, alternatively, drive innovators to perform their research abroad, where patent laws are more amenable to innovative research.

¹⁴² *Id.* (explaining that patented tools facilitate general research in identifying and testing the safety of new drugs).

¹⁴³ *Id.*

¹⁴⁴ *Id.*

¹⁴⁵ *Id.*

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A. *Integra* Creates Problems for Patent Licensing

Integra has established that the safe harbor does not reach down the chain of experimentation to embrace preclinical drug discovery.¹⁴⁶ Yet *Integra* fails to elaborate at what point research moves from the preclinical research phase to a development stage that is reasonably related to FDA approval and, thus, becomes eligible for the infringement exemption. Specifically, the court fails to enunciate which forms of experimentation reasonably contribute to the production of information for FDA approval such that the safe harbor would apply.¹⁴⁷ Although the court did not expressly limit the safe harbor exemption to generic drugs, it failed to discuss the applicability of the safe harbor to innovators prior to submission of a new drug candidate to the FDA.¹⁴⁸ The decision in *Rhone-Poulenc* indicated that the designation or filing of a candidate drug is not a prerequisite to obtaining exemption under the safe harbor.¹⁴⁹ Yet the *Integra* court seems to suggest that this might now be the case.¹⁵⁰

The *Integra* court expressly acknowledged that the cumulative effect of the number of patent licenses required to develop a drug can be substantial.¹⁵¹ In addition to the high costs associated with obtaining numerous licenses, manufacturers also might face the resistance of patentees who refuse to license their technologies, thereby blocking entire research programs.¹⁵² Moreover, innovative drug companies will face the problematic concern of predicting which patents they must license prior to embarking on a

¹⁴⁶ *Id.*

¹⁴⁷ Charles Raubicheck, *Integra v. Merck: A Mixed Bag for Research Tool Patents*, 21 NATURE 1099, 1100 (Sept. 2003).

¹⁴⁸ *Integra*, 331 F.3d at 867; see also Raubicheck *supra* note 147.

¹⁴⁹ *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer*, No. 95 Civ. 8833, 2001 U.S. Dist. LEXIS 19362, at *23 (Nov. 27, 2001).

¹⁵⁰ *Integra*, 331 F.3d at 866-67.

¹⁵¹ *Id.* at 871.

¹⁵² See Nicholas Groombridge & Sheryl Calabro, *Integra LifeSciences v. Merck – Good for Research or Just Good for Research Tool Patent Owners?*, 22 BIOTECHNOLOGY L. REP. 462, 470 (2003).

new research project.¹⁵³ The unresolved issue of what, if any, activity by innovative researchers is covered by the safe harbor leaves the innovative drug industry in a precarious situation. This uncertainty requires innovators to make educated guesses regarding which patents they must license in order to perform the necessary research to develop new drugs. In seeking to protect the rights of patent holders, *Integra* may have created a curious set of circumstances: the use of a patented invention for drug discovery will result in liability for patent infringement, whereas the use of the same invention after designation of a candidate drug will be immune.¹⁵⁴ Researchers thus will be saddled with questions regarding how licensing can be effectuated if, as research and development activities progress, their activities unknowingly move from being susceptible to infringement liability to being immune under the safe harbor.

Further, innovation may be hindered by the numerous patents that must be used in order to develop a new drug.¹⁵⁵ A company's research potential hinges on the company's ability to access existing patents.¹⁵⁶ Pharmaceutical development requires the use of a large number of basic research tools and laboratory techniques. The potential liability associated with and the cost of innovative research is greatly increased by a rise in the number of patents pertaining to research tools.¹⁵⁷ Given that research tool patents

¹⁵³ *See id.*

¹⁵⁴ Paul Fehlner, *Not Such a Safe Harbor After All*, 10 No. 6 ANDREWS INTEL. PROP. LIT. REP. 18 (July 22, 2003).

¹⁵⁵ Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 7 (2001).

¹⁵⁶ Kyla Dunn, *A Look at . . . Patents & Biotech*, WASH. POST, Oct. 1 2000, at B3 (summarized statement of Robert Lanza, the vice president of medical and scientific development of a small biotech company called Advanced Cell Technology) ("[A] company's research can be determined not only by what it would most like to accomplish, but by which patents it is able to access."). Research tools have been defined by the National Institutes of Health's Working Group on Research Tools as "the full range of resources that scientists use in the laboratory." Mueller, *supra* note 153, at 11-12.

¹⁵⁷ *See* Mueller, *supra* note 155, at 7-9; *see also* Donald R. Ware, *Research Tool Patents: Judicial Remedies*, 38 AIPLA Q.J. 267, 270 (2002).

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cover a vast range of products and processes necessary for identifying and evaluating new drug products,¹⁵⁸ manufacturers must now secure multiple licenses to perform innovative research on new drugs.¹⁵⁹

However, researchers experience acute difficulties in accessing patented research tools in the biotechnology and pharmaceutical industries.¹⁶⁰ Researchers in these industries generally require access to a greater number of proprietary research tools to conduct their research than their counterparts in other fields.¹⁶¹ Research tool patents, which now cover an increasing number of processes, expose innovative drug companies to potential patent infringement liability and may entitle patent holders to injunctive relief.¹⁶² Moreover, patentees are free to refuse licenses to their research tools and are likely to refuse requests for licenses from both competitors and small companies.¹⁶³ Even when a patent holder is amenable to licensing, license negotiation is time consuming and the price demanded by the patent holder can sometimes prevent successful negotiations.¹⁶⁴ Licensing costs and risks may prove so great as to impede, postpone, or even halt the development of new

¹⁵⁸ Natalie M. Derzko, *In Search of a Compromised Solution to the Problem Arising from Patenting Biomedical Research Tools*, 20 SANTA CLARA COMPUTER AND HIGH TECH L.J. 347, 349-50 (2004). See also Mueller, *supra* note 155, at 11.

¹⁵⁹ Groombridge & Calabro, *supra* note 152, at 470.

¹⁶⁰ See Mueller, *supra* note 155, at 11-12; see also Brief for the United States as *Amicus Curiae*, *Merck KGaA v. Integra LifeSciences I, Ltd.*, 125 S.Ct. 237 (2004) (No. 03-1237), available at <http://www.usdoj.gov/osg/briefs/2004/2pet/6invt/2003-1237.pet.ami.inv.html> ("If licensing were always a realistic solution, however, Section 271(e)(1) would be altogether unnecessary, because a researcher could always license any patented technology.").

¹⁶¹ *Id.*

¹⁶² Ware, *supra* note 157, at 270.

¹⁶³ Desmond Mascarenhas, *Negotiating the Maze of Biotech "Tool Patents"*, 16 NATURE BIOTECH. 1371 (Dec. 1998). The author explains that "large corporations often do not feel it is worth spending the time negotiating a license with a small outfit whose product may never even succeed in getting to the marketplace." *Id.* He also indicates that patent holders tend to ignore attempts by competitors to license their technologies. *Id.*

¹⁶⁴ *Id.*; Mueller, *supra* note 155, at 16.

drugs.¹⁶⁵

Patent holders of biological research tools have attempted to maximize the benefits of their patents by seeking licensing royalties based on the sale of commercial products that are discovered and brought to market using those tools.¹⁶⁶ These royalties are known as “reach-through royalties,”¹⁶⁷ as they give the research tool patent owner the right to royalties on subsequent discoveries.¹⁶⁸ Reach-through royalty licenses are common, given that they are more profitable and easier to enforce than licenses based solely on the sale or use of the research tool.¹⁶⁹ As a matter of public policy, however, patents should not be used to prohibit research activities beyond what their patent specifications disclose and claim.¹⁷⁰ Indeed, the U.S. Supreme Court has held that the grant of a patent license is limited to the payment of royalties on products within the scope of the patent.¹⁷¹ This restriction is intended to prevent a patentee’s extending the monopoly of his patent to derive a benefit not attributable to the patent’s teachings.¹⁷²

The *Integra* court argued that the expansion of the safe harbor to include the preclinical development of new drugs “would effectively vitiate the exclusive rights of patentees owning biotechnology tool patents.”¹⁷³ Yet the plain wording of the safe

¹⁶⁵ Mueller, *supra* note 155, at 7.

¹⁶⁶ Gerald J. Flattmann & Jonathon M. Kaplan, *Licensing Research Tool Patents*, 20 NATURE BIOTECH. 945 (Sept. 2002).

¹⁶⁷ Michelle Cai, *Madey v. Duke Univ.: Shattering the Myth of Universities’ Experimental Use Defense*, 19 BERKELEY TECH. L.J. 175, 180 (2004).

¹⁶⁸ Derzko, *supra* note 158, at 357; Cai, *supra* note 167.

¹⁶⁹ See Derzko, *supra* note 158, at 357.

¹⁷⁰ David Alban, *Rambus v. Infineon: Patent Disclosures in Standard-Setting Organizations*, 19 BERKELEY TECH. L.J. 309, 318 (2004); see also 6-19 CHISUM ON PATENTS §19.04 (2004).

¹⁷¹ *Zenith Radio Corp. v. Hazeltine Research, Inc.*, 395 U.S. 100 (1969).

¹⁷² *Id.*

¹⁷³ *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 867 (Fed. Cir. 2003).

[P]atented tools often facilitate general research to identify candidate drugs, as well as downstream safety-related experiments on those new

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harbor provision of section 271(e)(1) appears to protect the use of patented research tools in the development of a drug so long as the use is reasonably related to submission of information to the FDA for regulatory approval.¹⁷⁴ The plain wording of the statute is very broad and does not limit the type of patented inventions it encompasses.¹⁷⁵ There is no limitation in the statute that requires the patented invention to be the same as the product undergoing regulatory review,¹⁷⁶ as would be the case with the testing of a generic drug for FDA approval prior to the expiration of the brand name drug's patent. Indeed, the U.S. Supreme Court in *Eli Lilly* found that the phrase "patented invention," as used in the statute, includes all inventions, not simply drug-related inventions, let alone generic drugs.¹⁷⁷ *Integra's* determination that the safe harbor applies only to FDA approval of drugs already on the market and not to the development of new drugs runs contrary to established Supreme Court precedent¹⁷⁸ and the plain wording of section 271(e)(1).

Complex and restrictive licensing of research tool patents threatens to impede new drug discovery and development.¹⁷⁹ Both scientific progress and new drug innovation are at stake. Under the present system, reach-through royalties reduce the profits of innovative drug companies that seek to recover the costs of new

drugs. Because the downstream clinical testing for FDA approval falls within the safe harbor, these patented tools would only supply some commercial benefit to the inventor when applied to general research. Thus, exaggerating § 271(e)(1) out of context would swallow the whole benefit of the Patent Act for some categories of biotechnological inventions.

Id.

¹⁷⁴ 35 U.S.C. § 271(e)(1) (2003).

¹⁷⁵ *Id.*

¹⁷⁶ 35 U.S.C. § 271(e)(1); *see also* *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 664-68 (1990).

¹⁷⁷ *Eli Lilly*, 496 U.S. at 665.

¹⁷⁸ *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 867 (Fed. Cir. 2003). This apparent transgression from Supreme Court precedent was noted in *Integra* by Judge Newman in her dissent. *Id.* at 877, *citing Eli Lilly*, 496 U.S. at 661 ("[T]he statute has been interpreted as of broader scope.").

¹⁷⁹ Flattmann, *supra* note 166, at 945-46.

drug research and development.¹⁸⁰ Although the *Integra* court did not opine on the legitimacy of reach-through royalties, it did acknowledge the cost to innovative drug companies of licensing research tool patents.¹⁸¹ However, by interpreting the safe harbor to exclude the use of research tool patents in the preclinical development of new drugs, the *Integra* decision diminishes the incentive for drug manufacturers to innovate.¹⁸² With frightening consequences, the *Integra* decision overlooks Congress's stated intent of encouraging innovation and accelerating the introduction of new drugs to the market.¹⁸³

B. The Narrowing of Patent Infringement Research Exemptions

Critics argue that patents on drug discovery tools stifle research and innovation.¹⁸⁴ For example, research tool patent holders may impede technological progress by limiting the use of their tools to research that is most beneficial to them at the expense of new drug research and development that is beneficial to society.¹⁸⁵ This argument is bolstered by the fact that a common law experimental

¹⁸⁰ See Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources: Final Notice, 64 Fed. Reg. 72090, 72091 (Dec. 23, 1999).

¹⁸¹ *Integra*, 331 F.3d at 871 (“[T]he number of patent licenses needed to develop a drug may also affect the value placed on any single technology used in the development process. The cumulative effect of such stacking royalties can be substantial, particularly when reach-through royalties come into play.”(citation omitted)).

¹⁸² See *id.* at 873 (Newman, J., dissenting) (“The right to conduct research to achieve . . . knowledge need not, and should not, await expiration of [a] patent.”); *Id.* at 875 (Newman, J., dissenting) (“[T]he patent system both contemplates and facilitates research into patented subject matter, whether the purpose is scientific understanding or evaluation or comparison or improvement. Such activities are integral to the advance of technology.”).

¹⁸³ *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, 2001 U.S. Dist. LEXIS 19361 at *9 n.6 (S.D.N.Y. Nov. 27, 2001).

¹⁸⁴ Eric K. Steffe & Timothy J. Shea, Jr., *Drug Discovery Tools and the Clinical Research Exemption from Patent Infringement*, 22 BIOTECHNOLOGY L. REP. 369, 373 (2003).

¹⁸⁵ See Katherine J. Strandburg, *What Does the Public Get?: Experimental Use and the Patent Bargain*, 2004 WIS. L.REV. 81, 123 (2004).

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use exemption to patent law has been essentially eliminated.¹⁸⁶ Judge Newman, in her dissent in *Integra*, explained that the essential elimination of the common law research exemption is “ill-suited to today’s research-founded, technology-based economy.”¹⁸⁷ Judge Newman noted that technological progress and innovation would be hampered if even basic research were subject to infringement liability.¹⁸⁸ She argued that there is a recognized distinction between “research” and “development.”¹⁸⁹ Although Judge Newman agreed with the *Integra* majority that the safe harbor provision does not embrace the development and identification of new drugs,¹⁹⁰ she argued that the common law research exemption should apply to these early research activities and that the statutory immunity of section 271(e)(1) should be triggered at the point at which the research exemption ends.¹⁹¹

¹⁸⁶ See *id.* at 84. Although this note is not meant to be an analysis of the current state of the common law research exemption, a brief history of the doctrine is provided to give the reader some background. The common law research exemption was first developed by Justice Story when he stated that “it could never have been the intention of the legislature to punish a man who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects.” *Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813). Justice Story further distinguished infringing activity from that of exempted research by holding that infringing activity “must be the making with an intent to use for profit,” whereas research is for “the mere purpose of philosophical experiment, or to ascertain the verity and exactness of the specification.” *Sawin v. Guild*, 21 F. Cas. 554, 555 (C.C.D. Mass. 1813). Since its development, the common law experimental use defense has been very narrow and strictly limited. *Madey v. Duke*, 307 F.3d 1351, 1362 (Fed. Cir. 2002). The exemption is limited to actions performed for “amusement, to satisfy idle curiosity, or for strictly philosophical inquiry.” *Id.* When activities have the slightest commercial implication they do not fall under the common law experimental use exemption. *Id.* Moreover, activities in keeping with the legitimate business of the alleged infringer also have been held to not qualify for the experimental use exemption. *Id.*

¹⁸⁷ *Integra*, 331 F.3d at 873 (Newman, J., dissenting).

¹⁸⁸ See *id.* at 875-77.

¹⁸⁹ *Id.* at 876.

¹⁹⁰ *Id.* at 877.

¹⁹¹ See *id.* at 876.

The extension of the now limited common-law research exemption to embrace early research would promote innovation by allowing drug companies more freedom to operate. Recently, the House Judiciary Committee recommended a proposed bill to the U.S. House of Representatives in an attempt to codify such a research exemption.¹⁹² The proposed legislation provides that the manufacture or use of a patented invention solely for research or experimentation will not constitute an act of patent infringement unless the patented invention has the primary purpose of research or experimentation.¹⁹³ The proposal was intended to “create an incentive for the research and experimentation activities that fuel this country’s inventive genius and our vibrant economy.”¹⁹⁴ Thus the proposed legislation was designed to promote innovation by allowing research *on* a patented invention while retaining the prohibition against research *using* a patented invention.¹⁹⁵ Although the proposed legislation would not exempt research tools from patent infringement, it is a step in the right direction.

Research exemptions similar to those proposed in Congress exist in many foreign countries.¹⁹⁶ In most of Europe, experimentation on the subject of a patented invention is exempt from infringement, while experimentation using a patented invention to achieve other results falls outside the exemption.¹⁹⁷ The enactment of a similar research exemption in the United States

¹⁹² 136 Cong. Rec. H7498 (1990). This proposed legislation was entitled Title IV, Research, Experimentation and Competitiveness, of the Patent Competitiveness and Technological Innovation Act of 1990.

¹⁹³ *Id.* at H7499.

¹⁹⁴ *Id.*

¹⁹⁵ *Id.* Research exemption legislation for research into the subject matter of a patented invention is in accord with Judge Newman’s opinions set forth in *Integra. Integra*, 331 F.3d at 875-78 (Newman, J., dissenting). Judge Newman disagreed with the majority’s implication that *Integra*’s patents were research tools. *Id.* at 878. She argued that the defendants merely investigated the subject matter of *Integra*’s patents to develop improved RGD peptides, and therefore, should be immune from infringement under the common law research exemption. *Id.* at 875-78.

¹⁹⁶ See generally David L. Parker, *Patent Infringement Exemptions for Life Science Research*, 16 HOUS. J. INT’L. L. 615, 648-56 (1994).

¹⁹⁷ *Id.* at 656.

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would promote further innovation resulting from the investigation of and improvement on patented subject matters, and, simultaneously, protect the rights of research tool patent holders.

A research, or experimental use, exemption in U.S. patent law could be analogized to the fair use doctrine of copyright law. The fair use doctrine, statutorily enacted in the 1976 Copyright Act, provides that certain socially beneficial uses of copyrighted works, such as research, criticism, and news reporting, will not give rise to liability for copyright infringement.¹⁹⁸ The fair use doctrine has been recognized as necessary to stimulate the production of new copyrightable works.¹⁹⁹ The doctrine has even been expanded to encompass unlicensed commercial uses.²⁰⁰ Rather than emphasizing the commercial nature of the use, the fair use doctrine focuses on whether the use furthers the goals of copyright law to promote science and the arts by developing new copyrightable works.²⁰¹ “Such works thus lie at the heart of the fair use doctrine’s guarantee of breathing space within the confines of copyright, and the more transformative the new work, the less will be the significance of other factors, like commercialism, that may weigh

¹⁹⁸ 17 U.S.C. § 107 (1992). Stating in pertinent part:

... [T]he fair use of a copyrighted work... for purposes such as criticism, comment, news reporting, teaching, ... scholarship, or research, is not an infringement of copyright. In determining whether the use made of a work in any particular case is a fair use the factors to be considered shall include—(1) the purpose and character of the use, including whether such use is of a commercial nature or is for nonprofit educational purposes; (2) the nature of the copyrighted work; (3) the amount and substantiality of the portion used in relation to the copyrighted work as a whole; and (4) the effect of the use upon the potential market for or value of the copyrighted work.

Id.

¹⁹⁹ See *Campbell v. Acuff-Rose Music, Inc.*, 510 U.S. 569, 575 (1994) (“[F]air use of copyrighted materials has been thought necessary to fulfill copyright’s very purpose, ‘to promote the Progress of Science and useful Arts.’”) (quoting U.S. CONST. art. I, § 8, cl. 8).

²⁰⁰ *Id.* at 572, 594 (explaining that the commercial nature of the use of a copyright does not render that use presumptively unfair).

²⁰¹ *Id.* at 579.

against a finding of fair use.”²⁰² An expanded experimental use doctrine in patent law would lessen or alleviate the restrictions on research and development imposed by research tool patents and would likewise promote the goal of innovation.²⁰³

Notably, the creation of too broad a research exemption for the purpose of promoting innovation may result in the absence of meaningful patent protection for drug discovery tools and a corresponding increase in trade secrets.²⁰⁴ An increase in trade secrets would both reduce public dissemination of research information and inhibit innovation.²⁰⁵ Innovation will be most spurred by facilitating the transfer of research tools. The National Institutes of Health (NIH) has released guidelines regarding the dissemination of research tools developed with NIH funds.²⁰⁶ The NIH has recognized that restrictions on the availability of research tools can stifle new discoveries and limit future avenues of research and product development to the immediate detriment of science and the long-term detriment of product development and public health.²⁰⁷ Thus, NIH discourages reach-through licensing on the basis that such royalty obligations can only dampen incentives for commercial development.²⁰⁸

An alternative solution, especially for research tools not developed with NIH funding, is the creation of a compulsory licensing program for tools not readily available for licensing on

²⁰² *Id.*

²⁰³ See Mueller, *supra* note 155, at 43.

²⁰⁴ Steffe & Shea, *supra* note 184, at 374. A “trade secret” is information, including a formula, pattern, compilation, program, device, method, technique, or process, that derives independent economic value, actual or potential, from not being generally known to, and not being readily ascertainable by proper means by, other persons who can obtain economic value from its disclosure or use, and is the subject of efforts that are reasonable under the circumstances to maintain its secrecy. 1-1 MILGRIM ON TRADE SECRETS § 1 (2004).

²⁰⁵ Steffe & Shea, *supra* note 184, at 374.

²⁰⁶ NAT’L INST. OF HEALTH, REPORT OF THE NATIONAL INSTITUTES OF HEALTH (NIH) WORKING GROUP ON RESEARCH TOOLS (June 4, 1998), at <http://www.nih.gov/news/researchtools/index.htm>.

²⁰⁷ *Id.*

²⁰⁸ *Id.*

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reasonable terms.²⁰⁹ Compulsory licensing might be effectuated in two situations: 1) where a patent holder refuses to license with the result of restraining trade or lessening competition, and 2) where the patent holder refuses to license and also does not use the patented invention.²¹⁰ Thus, compulsory licensing would balance the patent holder's exclusive right against the public interest in promoting commercialization of inventions and greater competition in drug innovation.²¹¹ Furthermore, compulsory licensing is consistent with the intellectual property obligations of member countries of the World Trade Organization.²¹² Compulsory licensing would discourage research tool patent holders from keeping their tools for in-house or personal research only.²¹³ Additionally, the enactment of legislation that requires compulsory licensing for research tool patents would establish a clear policy regarding licensing techniques and help to ensure that innovative drug companies will not be burdened by excessive licensing costs. Unfortunately, if a low-cost means of licensing research tool patents is not developed, the effects of *Integra* and the cost of stacking licenses on drug development will become prohibitive, resulting in less innovation and fewer new drugs.

C. The Problem of Inefficient Patent Term Restoration

In order to promote innovative research and discovery, the Hatch-Waxman Act provides for patent term extensions for innovative drugs whose patent terms are encroached upon by the

²⁰⁹ See Mueller, *supra* note 155, at 58.

²¹⁰ Kurt M. Saunders, *Patent Nonuse and the Role of Public Interest as a Deterrent to Technology Suppression*, 15 HARV. J. LAW & TECH. 389, 435 (2002).

²¹¹ *Id.*

²¹² Agreement on Trade-Related Aspects of Intellectual Property Rights, Art. 31(b), available at http://www.wto.org/english/docs_e/legal_e/27-trips.pdf (providing that compulsory licensing shall only be permitted if "the proposed user has made efforts to obtain authorization from the right holder on reasonable commercial terms and conditions and that such efforts have not been successful within a reasonable period of time") (last visited Feb. 7, 2004).

²¹³ Strandburg, *supra* note 185, at 139.

FDA approval process.²¹⁴ The patent term is essential for innovative drug companies that seek to recover the costs of new drug research and development once drugs reach the market.²¹⁵ It is also necessary for the recovery of costs related to the research and development of drugs that either fail the approval process or fail in the market.²¹⁶ Similarly, by allowing pioneer drug companies sufficient time to market their new drugs without competition from generics, the patent term enables the development of new products for the generics to copy and, therefore, encourages competition from generic manufacturers.²¹⁷

Unfortunately, drug patents do not provide the monopoly over a market that one might expect.²¹⁸ Because more than one drug can have the same or similar effects, different drug companies may have patents on competing drugs and share the consumer market.²¹⁹ A breakthrough drug usually exists between one and six years on the market before a therapeutically similar drug is patented and introduced.²²⁰ In addition, drugs are also forced to compete with alternative, non-drug therapies.²²¹

The Hatch-Waxman Act seeks to encourage innovation by allowing for patent term extensions for innovative drug patents to offset the portion of the patent term used during the FDA approval

²¹⁴ *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 870 (Fed. Cir. 2003).

²¹⁵ PHARMACEUTICAL AND RESEARCH MANUFACTURERS OF AMERICA (“PHARMA”), *DELIVERING ON THE PROMISE OF PHARMACEUTICAL INNOVATION: THE NEED TO MAINTAIN STRONG AND PREDICTABLE INTELLECTUAL PROPERTY RIGHTS* 7 (Apr. 22, 2002), available at <http://www.phrma.org/publications/policy//2002-06-24.436.pdf> [hereinafter *DELIVERING ON THE PROMISE*]. The average cost to develop a new prescription drug, including the costs of research and development failures, is nearly \$1.7 billion. Thayer, *supra* note 3, at 23.

²¹⁶ Mandy Wilson, *Pharmaceutical Patent Protection: More Generic Favored Legislation May Cause Pioneer Drug Companies to Pull the Plug on Innovation*, 90 KY. L.J. 495, 498-99 (2001); see also CBO STUDY, *supra* note 5, at 3.

²¹⁷ *DELIVERING ON THE PROMISE*, *supra* note 215, at 11.

²¹⁸ CBO STUDY, *supra* note 5, at 7.

²¹⁹ *Id.* at 3.

²²⁰ *Id.* at xi.

²²¹ *Id.*

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process.²²² However, several limitations on patent term extensions hinder the achievement of this goal. First, patent term extensions cannot exceed five years.²²³ Second, the period between product approval and patent term expiration may not exceed fourteen years.²²⁴ Patent term restorations are also limited to a single patent whenever the drug is covered by multiple patents.²²⁵ Due to these restrictions, patent term extensions average about three years for new drugs.²²⁶ This is only a fraction of the average time spent on the approval process.²²⁷ Thus, the patent term extensions fail to restore the actual time and cost lost by innovative drug companies.

The caps placed on patent term restoration have become increasingly burdensome in light of lengthening FDA approval periods.²²⁸ Due to additional preclinical screening of new drug candidates and the larger clinical trials required by the FDA, FDA approval times have increased.²²⁹ Given the delays associated with the FDA approval process, policy makers should consider amending the Hatch-Waxman Act to provide for more meaningful patent term extensions. In order to provide incentives for innovation, patent term restoration should be extended to include the entire clinical approval process.²³⁰ Patent term restoration under the current rules assures that new drug products will receive

²²² See 35 U.S.C. § 156 (2002).

²²³ *Id.* § 156(g)(6)(A) (2002).

²²⁴ *Id.* § 156(c)(3) (2002).

²²⁵ *Id.* § 156(c)(4) (2002).

²²⁶ CBO STUDY, *supra* note 5, at 39.

²²⁷ *Id.* at 17 (noting that the total development time after clinical testing begins before reaching FDA approval is, on average, 8.2 years).

²²⁸ *Id.*

²²⁹ Jill Wechsler, *Pharmaceutical Pricing and Innovation Key Issues for 2003*, PHARMACEUTICAL TECHNOLOGY, Jan. 2003, at 28, available at www.pharmtech.com/pharmtech/data/articlestandard/pharmtech/022003/42759/article.pdf; see also Henry Grabowski & John Vernon, *Longer Patents for Increased Generic Competition in the US: The Waxman-Hatch Act After One Decade*, 10 PHARMACO-ECONOMICS, 110, 122 (Supp. 2 1996).

²³⁰ In fact, the European Community has a more favorable incentive for drug development. Patent time lost during the clinical development period in the European Community is eligible for 100% restoration versus 50% in the United States. See Grabowski & Vernon, *supra* note 229.

below-average effective patent terms, making it more difficult for drug manufacturers to recover the costs of research and development and generate profits to fund further innovation.

Inefficient patent term restoration is not the only obstacle to recouping the cost of developing new drugs. Even with the limited patent term extensions, generic drugs have reduced the total returns from marketing a new drug by approximately \$27 million.²³¹ The percentage of generic drugs on the market has greatly increased as a result of the Hatch-Waxman Act: from 13 percent in 1980 to 58 percent in 1994.²³² Once generic drugs become available, brand name drugs quickly lose more than 40 percent of their market.²³³ By limiting drug patent terms to fourteen years from FDA approval and increasing the share of the market for generic drugs, the Hatch-Waxman Act has effectively diminished the incentive to innovate. *Integra*, by precluding the application of the safe harbor to new drug products,²³⁴ has further eroded the incentive to innovate by increasing liability for and the cost of innovative research and development.

D. The Stifling of Competition Between Innovative and Generic Drugs Companies

In addition to creating higher costs for new drug research (and, ultimately, higher costs for consumers), *Integra* might also lead to abuses of the Hatch-Waxman Act. One of the purposes of the Hatch-Waxman Act is to allow generic drugs access to the market immediately upon the expiration of the brand name drug's patent.²³⁵ Yet the Act also provides pioneer drug manufacturers with a means of delaying the FDA approval of generic alternatives.²³⁶ In order to obtain FDA approval, a generic drug

²³¹ CBO STUDY, *supra* note 5, at 38.

²³² *Id.* at 37.

²³³ *Id.*

²³⁴ *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 867 (Fed. Cir. 2003).

²³⁵ See Miller, *supra* note 20.

²³⁶ Larissa Burford, *In Re Cardizem & Valley Drug Co.: The Hatch-Waxman Act, Anticompetitive Actions, and Regulatory Reform*, 19 BERKELEY

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company must file an Abbreviated New Drug Application (ANDA) with the FDA.²³⁷ The ANDA must do two things: 1) certify that the corresponding new drug patent has already expired, when it is to expire, or that it is invalid or is not infringed,²³⁸ and 2) notify the patent holder of the submission of the ANDA.²³⁹ Upon notice, the patent holder has forty-five days to file a patent infringement suit against the generic applicant.²⁴⁰ If an infringement suit is filed within the forty-five day period, the approval of the generic drug is automatically postponed for thirty months.²⁴¹ These stays are advantageous to pioneer drug companies because they provide for more than two additional years of patent exclusivity.

The exclusion of new drugs from the safe harbor may

TECH. L.J. 365, 368-69 (2004).

²³⁷ 21 U.S.C. § 355(j) (2003).

²³⁸ *Id.* § 355(j)(2)(A)(vii) (2003) states:

[A]n abbreviated application for a new drug shall contain a certification . . . that such patent has expired, of the date on which such patent will expire, or that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted

Id.

²³⁹ *Id.* § 355(j)(2)(B)(i) (2003) states:

[A]n applicant who makes a certification [under 21 U.S.C. § 355(j)(2)(A)(vii)] . . . shall include in the application a statement that the applicant will give the notice required . . . to each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice

Id.

²⁴⁰ *Id.* § 355(j)(5)(B)(iii) (2003) states:

[I]f the applicant made a certification [under 21 U.S.C. § 355(j)(2)(A)(vii)] . . . the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice . . . is received. If such an action is brought . . . the approval shall be made effective upon the expiration of the thirty-month period.

Id.

²⁴¹ *Id.*

encourage pioneer drug companies to seek protection for their products by filing patent infringement suits to trigger the thirty-month stay on the generic drug's approval. By this means, pioneer drug companies can ensure longer market exclusivity to recover research and development costs and make a profit.²⁴² Abuse of the Hatch-Waxman Act in this manner can be attributed to insufficient patent term restoration and has become so prevalent as to prompt investigations by the Federal Trade Commission.²⁴³ In light of this, courts will be faced with frivolous lawsuits and consumers will be denied quicker access to cheaper generic alternatives.

Innovative drug companies have employed a variety of tactics to delay the sale of generic drugs. One such tactic involves the negotiation of agreements between innovative and generic companies whereby generic companies receive a large payout in exchange for not releasing their products, thus enabling pioneer companies to maintain their market share.²⁴⁴ With a similar goal in mind, innovative companies have also begun to introduce their own generics into the market prior to the expiration of their brand-name drug patents.²⁴⁵ Although this strategy does not preclude market access by other generics upon patent expiration, it has been noted that drugstores usually buy the first low-cost alternative to brand name drugs and rarely switch to other products once customers grow accustomed to the offered generic product.²⁴⁶ Both of these tactics risk possible antitrust violations, given that they substantially reduce market competition.²⁴⁷ Increased liability protection for new drugs at the research and development stage will assist in reducing the cost of bringing new drugs to market and will potentially decrease the incentive for pioneer drug companies

²⁴² See Eureka, *supra* note 12, at 18.

²⁴³ *Id.*

²⁴⁴ Laura Giles, *Promoting Generic Drug Availability: Reforming the Hatch-Waxman Act to Prevent Unnecessary Delays to Consumers*, 75 ST. JOHN'S L. REV. 357, 370 (2001).

²⁴⁵ Grabowski & Vernon, *supra* note 229, at 114; Catherine Yang, *The Drugmakers vs. The Trustbusters: The FTC is Eyeing Big Companies' Tactics Against Makers of Generics*, BUSINESS WEEK, Sept. 5, 1994, at 67.

²⁴⁶ Yang, *supra* note 245.

²⁴⁷ See Giles, *supra* note 244; see Yang, *supra* note 245.

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to employ anticompetitive tactics. Presently, such violations of antitrust laws are likely attributable to the insufficient protection afforded to innovative research.

E. The Possible Loss of Research and Development to Foreign Countries

Without instituting some form of protection for innovative research, whether by applying a research exemption to new drug development or by implementing a low-cost research tool licensing program, the United States runs the risk of losing its innovative pharmaceutical industry to foreign markets. Many foreign countries have broader research exemptions than does the United States.²⁴⁸ For example, Japanese patent law provides for a general statutory experimental use exception that permits the use of any patented invention for experiment or research.²⁴⁹ Broad research exemptions in foreign patent law enable innovative drug companies to perform preclinical research abroad, beyond the reach of liability from U.S. patents on research tools. Alternatively, innovative drug companies might turn to countries with poor patent systems. Thus, if preclinical pharmaceutical research is not protected by a statutory safe harbor or by common law research exemptions, innovative drug companies may be enticed to perform their innovative research abroad.

The relocation of innovative research to foreign countries has been facilitated by recent interpretations regarding the scope of section 271(g) of the Patent Act. Section 271(g) states that anyone who imports into the United States products made by a process that is patented in the United States will be liable for patent infringement.²⁵⁰ Two district court decisions have held that

²⁴⁸ Groombridge & Calabro, *supra* note 152, at 471.

²⁴⁹ Jennifer A. Johnson, *The Experimental Use Exception in Japan: A Model for U.S. Patent Law?*, 12 PAC. RIM L. & POL'Y 499 (2003).

²⁵⁰ 35 U.S.C. § 271(g) (2003). It states:

Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during

infringement by importation under section 271(g) applies only to patented processes that produce physical, manufactured products and not to those that merely generate information.²⁵¹ Recently, the Federal Circuit affirmed these holdings in *Bayer AG v. Housey Pharmaceuticals, Inc.*²⁵² The Federal Circuit decisively held that infringement under section 271(g) “is limited to physical goods that were manufactured and does not include information generated by a patented process.”²⁵³ Thus, section 271(g) provides extraterritorial protection for manufactured products and creates a loophole for research tool patents whose use results only in information on possible drug candidates.²⁵⁴ This interpretation of section 271(g) allows innovative drug companies to perform the research necessary to identify possible drug candidates abroad and to make use of the research results in the United States once the safe harbor applies.

The availability of broader research exemption patent laws overseas, when viewed in tandem with judicial support for the importation of information obtained using U.S. process patents (including research tool patents), signals the potential loss of U.S.-based innovative research in the future. Encouraging companies to conduct new drug development abroad will create a flow of

the term of such process patent.

Id.

²⁵¹ *Bayer AG v. Housey Pharmaceuticals, Inc.*, 169 F. Supp. 2d 328, 330 (D. Del. 2001) (“Upon a plain reading of the statute, the court finds that Section 271(g) addresses only products derived from patented *manufacturing processes*, i.e., methods of actually making or creating a product as opposed to methods of gathering information about, or identifying, a substance worthy of further development.”) (emphasis in original); *Synaptic Pharmaceutical Corp. v. MDS Panlabs, Inc.*, 265 F. Supp. 2d 452 (D.N.J. 2002) (holding that the importation into the United States of reports on the results of diagnostic assays performed abroad were not infringed under 35 U.S.C. § 271(g)).

²⁵² *Bayer AG v. Housey Pharmaceuticals, Inc.*, 340 F.3d 1367 (Fed. Cir. 2003).

²⁵³ *Id.* at 1368

²⁵⁴ See Richard J. Warburg & Stephen B. Maebius, *Warning – Research Dollars at Risk!*, LEGAL TIMES, Mar. 24, 2003, available at http://www.foley.com/files/tbl_s31Publications/FileUpload137/1300/2003-24-03.pdf.

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money, jobs, and new technology out of the United States.²⁵⁵ Currently, the U.S. pharmaceutical industry invests a greater percentage of capital in research than do other American industries.²⁵⁶ As a key driver of economic growth, the pharmaceutical industry is a significant source of new, highly-skilled jobs.²⁵⁷ The industry is one of this country's largest employers, with approximately 223,000 employees nationwide.²⁵⁸ The loss of the pharmaceutical research and development industry to foreign countries would therefore have a deleterious effect on the U.S. economy. To prevent an exodus of innovative research, a broader research exemption or a low-cost research tool licensing program must be established.

CONCLUSION

Although *Integra* may have brought the safe harbor back in line with Congress's original intent of allowing generic manufacturers swifter access to the marketplace, it has done so with serious detriment to innovative drug discovery. Congress clearly stated that one of the purposes of the Hatch-Waxman Act was to make available more low-cost generic drugs available.²⁵⁹ It is clear, however, that Congress also intended to create a new incentive for increased expenditures for research and development.²⁶⁰ The intended net effect of these two purposes is thrown off balance by *Integra*.

Even before the decision in *Integra*, the incentive to innovate could be viewed as having been diminished as a result of the Hatch-Waxman Act. The patent term extensions provided by the Hatch-Waxman Act still resulted in pioneer drug companies

²⁵⁵ Brief *Amicus Curiae* of Wyeth in Support of Defendant-Appellant's Petition for Panel Rehearing and En Banc Rehearing, *Integra LifeSciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003) (No. 02-1052, -1065) at 9.

²⁵⁶ PHRMA PROFILE 2003, *supra* note 7, at 11.

²⁵⁷ *Id.* at 17.

²⁵⁸ *Id.*

²⁵⁹ H.R. REP. NO. 98-857(I), at 14 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647.

²⁶⁰ *Id.* at 15.

realizing far shorter actual patent terms than innovators in other industries.²⁶¹ Shorter patent terms mean less time to recover the cost of the development of new drugs. Recovering the cost of development is especially important because drug development is risky. Indeed, only one out of 5,000 potential new drugs developed ever gains FDA approval²⁶² and the cost of developing a single drug can be more than half a billion dollars.²⁶³ The Hatch-Waxman Act, by facilitating the rapid entrance of generics into the marketplace, has, in turn, complicated the recovery of research and development costs by pioneer drug companies.

The *Integra* decision ushered in an even bleaker environment for innovation. By denying the safe harbor protection to the preclinical development of new drugs, the decision exposes innovative drug companies to enormous patent liability. This liability results from the necessity of utilizing numerous patented research tools to develop new drugs. Without establishing clear guidelines regarding when innovative drug development may be protected by the safe harbor, *Integra* provides pioneer drug companies with little information as to when and for how long research tools must be licensed. This uncertainty may result in the necessity to license access to these tools on the basis of reach-through royalties. Problematically, however, reach-through royalties reduce a manufacturer's recovery of already-high research and development costs. To avoid the high cost of accessing necessary research tools, innovative companies may choose to perform innovative research abroad, given that the importation of information resulting from overseas research activities does not carry infringement liability.²⁶⁴ Or worse yet, innovative companies may choose not to conduct research at all.

The importance of the *Integra* decision to the pharmaceutical industry is evidenced by ongoing efforts to seek review of the decision. Merck filed a petition for a panel rehearing or rehearing *en banc* by the Federal Circuit. Several other domestic innovative

²⁶¹ DELIVERING ON THE PROMISE, *supra* note 215, at 9.

²⁶² PHRMA PROFILE 2003, *supra* note 7, at 3.

²⁶³ See Thayer, *supra* note 3, at 23.

²⁶⁴ See discussion *supra* Part III.E.

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pharmaceutical companies similarly urged review of the decision.²⁶⁵ Furthermore, the legal and policy implications compelled the Association of the Bar of the City of New York to support the *en banc* review.²⁶⁶ On December 3, 2003, the Federal Circuit denied *en banc* review.²⁶⁷ Merck filed a petition for writ of certiorari on March 2, 2004.²⁶⁸ Two amicus briefs as well as the briefs of the parties were subsequently filed with the Supreme Court.²⁶⁹ On October 4, 2004, the Supreme Court invited the Acting Solicitor General to file a brief expressing the views of the United States.²⁷⁰ The United States filed an amicus brief on December 10, 2004 supporting review of the decision.²⁷¹ On January 7, 2005, the petition for a writ of certiorari was granted, as was Eli Lilly's motion for leave to file an amicus brief.²⁷² Depending on the ultimate decision of the U.S. Supreme Court, it

²⁶⁵ Brief *Amicus Curiae* of Eli Lilly; Combined Petition for Panel Rehearing and Rehearing En Banc of Defendant-Appellant Merck KGaA, Integra LifeSciences I, Ltd. v. Merck KGaA, 331 F.3d 860 (Fed. Cir. 2003) (No. 02-1054, -1065); Brief *Amicus Curiae* of Wyeth in Support of Defendant-Appellant's Petition for Panel Rehearing and En Banc Rehearing, Integra LifeSciences I, Ltd. v. Merck KGaA, 331 F.3d 860 (Fed. Cir. 2003) (No. 02-1052, -1065).

²⁶⁶ Petition of *Amicus Curiae* the Association of the Bar of the City of New York for Rehearing En Banc, Integra LifeSciences I, Ltd. v. Merck KGaA, 331 F.3d 860 (Fed. Cir. 2003) (No. 02-1052, -1065).

²⁶⁷ Integra LifeSciences I, Ltd. v. Merck KGaA, No. 02-1052, 02-1065, 2003 U.S. App. LEXIS 26547 (Fed. Cir. 2003).

²⁶⁸ Integra LifeSciences I, Ltd. v. Merck KGaA, 331 F.3d 860 (Fed. Cir. 2003), *petition for cert. filed* (U.S. Mar. 2, 2004) (No. 03-1237).

²⁶⁹ Merck KGaA v. Integra LifeSciences I, Ltd., No. 03-1237 (U.S. 1999), *available at* <http://www.supremecourtus.gov/docket/03-1237.htm>.

²⁷⁰ Merck KGaA v. Integra LifeSciences I, Ltd., No. 03-1237, 125 S.Ct. 237 (Oct. 4, 2004).

²⁷¹ Brief for the United States as *Amicus Curiae*, Merck KGaA v. Integra LifeSciences I, Ltd., 125 S.Ct. 237 (2004) (No. 03-1237), *available at* <http://www.usdoj.gov/osg/briefs/2004/2pet/6invt/2003-1237.pet.ami.inv.html> (concluding that petition for a writ of certiorari should be granted because "the court of appeals' restrictive interpretation of Section 271(e)(1) will likely hinder the development of important and medically valuable new drugs.")

²⁷² Merck KGaA v. Integra LifeSciences I, Ltd, 2005 U.S. LEXIS 614, 73 U.S.L.W. 3396 (2005).

may be time to consider possible legislation to determine the scope of the safe harbor as it applies to innovative drug discovery, particularly in light of the recent interpretation of 35 U.S.C. § 271(g) as excluding from infringement liability the importation of information gained from the use of patented inventions.²⁷³ The nation's economy and health are in serious danger without clarification of the patent laws as they apply to innovative drug discovery.

²⁷³ See discussion *supra* Part III.E.