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A Realist Approach to *Merck KGaA v. Integra*

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A Realist Approach to *Merck KGaA v. Integra*

By Daniel A. Lev*

I. INTRODUCTION

¶1 The patent bargain has been described as a balance between the public good that results from full disclosure of scientific research and a private property right.¹ Physical property rights are well-defined and as a result the economic and legal concerns surrounding them are well-understood.² However, the property right at issue in the patent bargain is not readily fenced off to prevent trespass.³ There are only two ways to uphold such a property right: by “keeping it under the mattress” or by providing legal remedies to the owner against trespassers.⁴ Intellectual property law encourages both types of protection, but the prospect of reverse engineering provides a powerful incentive to enter the patent bargain.⁵

¶2 An increasing body of data supports the notion that disclosure is economically beneficial. These studies go beyond the anecdotal observation that cultures with strong intellectual property rights protections have historically excelled technologically and economically.⁶ More recent studies of growth in the developing world support theoretical and historical approaches to the patent bargain as a growth engine.⁷ Although dissent remains as vigorous as ever,⁸ the idea that some balance of individual property

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¹ Katherine J. Strandburg, *What Does the Public Get? Experimental Use and the Patent Bargain*, 2004 WIS. L. REV. 81, 82 (2004).

² In his 2003 tome on intellectual property, Professor Landes stated: “The economics of property rights in physical property are now well understood, and its basic elements can be summarized fairly briefly.” WILLIAM M. LANDES & RICHARD A. POSNER, *THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW* 11 (2003).

³ *Id.* at 12-20 (constrasting the cost-benefit differences between tangible physical property and intangible intellectual property).

⁴ *Id.*

⁵ *Id.* at 21-22 (discussing the high costs of protecting patent assets that are easily imitated).

⁶ Economic historians have noted the grant of “open letters” (“*litterae patentes*” in Latin) in 15th Century Venice and 17th Century England, both times of rapid economic expansion in those countries. Paul A. David, *Intellectual Property Institutions and the Panda’s Thumb: Patents, Copyrights, and Trade Secrets in Economic Theory and History* in GLOBAL DIMENSIONS OF INTELLECTUAL PROPERTY RIGHTS IN SCIENCE AND TECHNOLOGY 19, 44-48 (Mitchel B. Wallerstein, Mary E. Moguee & Roberta A. Schoen eds., 1993). *Contra* ERIC SCHIFF, *INDUSTRIALIZATION WITHOUT NATIONAL PATENTS: THE NETHERLANDS, 1869-1912; SWITZERLAND, 1850-1907* (1971) (presenting a historical analysis of economic expansion in countries without patent rights that, nonetheless, achieved a high degree of economic expansion).

⁷ See SHAHID ALIKHAN & RAGHUNATH MASHELKAR, *National Economic Development Strategy and Intellectual Property*, INTELLECTUAL PROPERTY AND COMPETITIVE STRATEGIES IN THE 21ST CENTURY 55-87 (2004).

⁸ Intellectual property laws, particularly patent laws, have been the subject of intense political debate during many phases of economic and legal development. See David, *supra* note 6, at 230-32. See also Fritz

rights and public disclosure increases the benefits to society and is economically efficient has prevailed.⁹

¶3 However, one area where the public has had relatively free reign is in conducting research that builds on the inventions disclosed in granted patents. The reason for this right to research arises from two theories of innovation – one is analogous to the fair use doctrine in copyright law and one based on the ultimate value that arises from improvement innovations.¹⁰ These dual theories have given rise to two legal doctrines, each of which encompasses aspects of both theories — the common law research exemption and the statutory exemption.

¶4 This comment focuses on the recent Supreme Court decision in *Merck KGaA v. Integra Lifesciences*.¹¹ The decision primarily pertains to the exemption from patent infringement liability for research activities related to pharmaceutical development contained in 35 U.S.C. § 271(e)(1). Justice Scalia’s unanimous opinion announced a textualist interpretation of the statute that overruled a narrow formalistic interpretation by a three-judge panel of the Federal Circuit in 2003.¹²

¶5 By examining the Federal Circuit’s doctrinal development regarding both the common law and the statutory research exemption, it will first be shown how these doctrines informed the split panel decision. Second, the Federal Circuit’s normative approach will be considered – particularly whether the decision was consistent with precedential interpretations of the research exemption. In this section, the decision is analyzed in terms of legal realism and the contentious circumstances of the case. Third, while the Supreme Court’s decision is strictly based on the plain language of the statute, the economic realities of the research exemption support this interpretation over that of the Federal Circuit panel majority.¹³ Prospectively, *Merck KGaA v. Integra Lifesciences* indicates that textualism with respect to the patent law should be adhered to whenever possible – restricting policy decisions to the enacted statute. The modest conclusion is for the Federal Circuit to be mindful of normative tendencies, particularly when not in concert with textualist analysis, and recognize that economic realities often preclude such normative proscriptions.

Machlup & Edith Penrose, *The Patent Controversy in the Nineteenth Century*, 10 J. ECON. HIST. 1-29 (1950).

⁹ See Arti K. Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norm of Science*, 94 NW. U. L. REV. 77, 136-51 (1999) (discussing the competing economic and social interests involved in balancing the patent bargain in the context of biomedical technology). See also Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698, 700-701 (1998) (describing how the narrowing of the experimental use exemption through “pro-patent” doctrines is detrimental to innovation in bio-pharmaceutical technology).

¹⁰ Strandburg, *supra* note 1, at 120-23.

¹¹ *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005).

¹² *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003) (Rader, J., writing for the majority) (Newman, J., dissenting-in-part).

¹³ Judge Newman’s dissent contained some of the same basic features of Justice Scalia’s opinion. *Id.* at 872.

A. The “Fair Use” Common Law Research Exemption¹⁴

¶6 The common law research exemption began with *Whittemore v. Cutter*, in which Justice Story now famously quipped “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.”¹⁵ In 1813, Justice Story, sitting on the Circuit Court for the District of Massachusetts, recognized that two types of activities were not subject to the patent right to exclude: (1) innate human curiosity and (2) experiments to decipher the patented invention. Defining “philosophical experiments” and “ascertaining the sufficiency of the machine” has been the focus of the common law research exemption doctrine ever since.¹⁶

¶7 The Federal Circuit clarified its position with a decisively “pro-patent” opinion early in its history.¹⁷ In *Roche v. Bolar*,¹⁸ the court held that pure “scientific inquiry” was protected by the safe harbor, but only insofar as it lacks “definite, cognizable, and not insubstantial commercial purposes.”¹⁹ The *Roche* court significantly narrowed the common law exemption and established a commercial purpose threshold.²⁰ The Federal Circuit affirmed its narrow commercial purpose interpretation six times in the twenty intervening years between *Roche* and *Integra*.²¹

¶8 While technically in line with the Federal Circuit’s focus on commercial purposes, *Madey v. Duke* represents a severe limitation of the experimental use doctrine, wherein even non-profit and educational research is infringement when a distant commercial purpose exists.²² The court’s ruling merely reverses summary judgment, but the decision lays out a legal framework wherein “the experimental use defense persists albeit in the very narrow form articulated” in *Embrex* and *Roche*,²³ which “clearly do[] not immunize use that is *in any way* commercial in nature.”²⁴ The court eviscerated the educational use defense, stating that the “business” of Duke University was educational.²⁵ This

¹⁴ See JANICE M. MUELLER, *The Evanescent Experimental Use Exemption from United States Patent Infringement Liability: Implications for University and Nonprofit Research and Development*, 56 BAYLOR L. REV. 917, 925-37 (2004) (presenting a comparison of the fair use doctrine in copyright law to the development of the common law research exemption in patent law).

¹⁵ 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (No. 17,600).

¹⁶ See DONALD S. CHISUM, 5 CHISUM ON PATENTS § 16.03 (2005).

¹⁷ See *id.* at § 16.03[1][b] (discussing the history of the research exemption from *Whittemore* until the founding of the Federal Circuit, in which “[r]elatively few decisions actually excused the making and use of patented products or processes on the basis of experimental or nonprofit purpose”).

¹⁸ *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 856 (1984).

¹⁹ *Id.* at 863.

²⁰ The Federal Circuit’s decision in *Roche* was part of the impetus for Congress to pass the Hatch-Waxman Act’s statutory safe harbor for generic drug development. See *infra* notes 28 and 29.

²¹ See, e.g., *Embrex, Inc. v. Serv. Eng’g Corp.*, 216 F.3d 1343, 1349 (Fed. Cir. 2000) (holding that the research exemption is not available when a commercial goal is present, no matter how attenuated); *Madey v. Duke Univ.*, 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 959 (2003) (discussed in text *infra*). See also *Hoechst-Roussel Pharm., Inc. v. Lehman*, 109 F.3d 756, 763 (Fed. Cir. 1997) (discussing *Roche* doctrine in concurrence).

²² *Madey*, 307 F.3d at 1362-63.

²³ *Id.* at 1361.

²⁴ *Id.* at 1362 (emphasis added).

²⁵ The court elaborated on this point, stating, “[M]ajor research universities, such as Duke, often sanction and fund research projects with arguably no commercial application whatsoever. However, these projects

established a subjective test that looks to “the alleged infringer’s legitimate business, regardless of commercial implications.”²⁶ The experimental use principle has been refined to the proposition that experimental, educational, or non-profit uses do not infringe patent rights when the damages and gains realized by these uses are de minimis²⁷ — a proposition that accomplishes what many view as its purpose within the patent bargain.²⁸

B. The Plain Language of 35 U.S.C. § 271(e)(1)

¶9 In 1984, partly in response to what it perceived as problems with the Federal Circuit’s application of the common law research exemption,²⁹ Congress enacted the statutory safe harbor for experimental uses related to the development of generic drugs.³⁰ The “Drug Price Competition and Patent Term Restoration Act of 1984,” also known as the Hatch-Waxman Act, enacted two major statutory revisions that together represented a compromise between generic drug manufacturers and large pharmaceutical companies — the “innovators.”³¹ The generic drug manufacturers were given earlier entry to the market by exempting the research necessary for them to submit an abbreviated new drug application (ANDA) from patent infringement.³² And patented pharmaceuticals that are the subject of a new drug application (NDA) could apply for an extension of the standard patent term by the amount of time required by the FDA to approve the application.³³

¶10 The Hatch-Waxman amendment to the infringement provisions of the Patent Act is fairly ambiguous.³⁴ Section 271 generally creates a Federal cause of action against “whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.”³⁵ One of the main exceptions to this rule is contained in § 271(e),³⁶ which states

unmistakably further the institution’s legitimate business objectives, including educating and enlightening students and faculty participating in these projects.” *Id.*

²⁶ *Id.* On remand the district court allowed the jury to decide the issue of whether Duke was entitled to a research exemption under the clarified standard from the Federal Circuit. *Mayed v. Duke Univ.*, 336 F. Supp. 2d 583, 592 (M.D.N.C. 2004).

²⁷ CHISUM, *supra* note 16, at § 16.03[a].

²⁸ See, e.g., Rai, *supra* note 9; Michael S. Mireles, *An Examination of Patents, Licensing, Research Tools, and the Tragedy of the Anticommons in Biotechnology Innovation*, 38 U. MICH. J.L. REFORM 141 (2004).

²⁹ See *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1568 (1997) (discussing the legislative history of 35 U.S.C. § 271(e)).

³⁰ H.R. REP. 98-857(II), at 27 (August 1, 1984) (“the provisions of § 202 of the bill [that adds subsection (e) to 35 U.S.C. § 271] have the net effect of reversing the holding of the court in *Roche Products, Inc. v. Bolar Pharmaceutical Co.*”). See also Holly Soehnge, *The Drug Price Competition and Patent Term Restoration Act of 1984: Fine-Tuning the Balance Between the Interests of Pioneer and Generic Drug Manufacturers*, 58 FOOD & DRUG L.J. 51 (2003).

³¹ Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

³² *Id.* at 1588.

³³ *Id.*

³⁴ In his treatise on patent law, Professor Chisum notes that “Section 271(e)(1)’s awkward wording has vexed the courts.” CHISUM, *supra* note 16, at § 16.03[1][d][iii].

³⁵ 35 U.S.C. § 271(a) (2005).

³⁶ Other than the research exemption, the only third-party exception within 35 U.S.C. § 271 exempts products transformed by subsequent processes or incorporated into other products from liability for “import[ing] into the United States or offer[ing] to sell, sell[ing], or us[ing] within the United States a

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.³⁷

¶11 This language provides considerable latitude in statutory interpretation. It opens with the inclusive language “make, use, offer to sell, or sell” which has become equivalent to every commercial act of infringement.³⁸ The final clause is clearly directed to the Federal Food, Drug, and Cosmetic Act (FDCA), but is textually not so limiting — “a Federal law which regulates the manufacture, use, or sale of drugs.”³⁹

¶12 The intervening language is the most ambiguous in the statute and the subject of the *Merck* dispute, at least at the Supreme Court. What is the plain meaning of “solely for uses reasonably related to the development and submission of information”?⁴⁰ “Solely” would seem to indicate that a narrow set of acts qualify for the exemption. However, the “reasonably related” requirement broadens the exemption and introduces jurisprudential flexibility.⁴¹ Qualifying acts are further limited to “the development and submission of information.” The “submission of information” under a law regulating drugs is relatively unambiguous, but the development of that information encompasses a broad swath of activities that are not easily definable, and not clarified by a reasonableness test.

¶13 Past opinions have delineated certain uses that fell under the reasonably related test for the development of information. In 1994, the New Jersey district court gave considerable latitude to the statutory language and focused on the specific research involved in the product and patent at issue.⁴² The Federal Circuit upheld the research exemption when the patented invention was primarily used to develop a generic formulation of the patented drug.⁴³

¶14 An alternative structural interpretation of § 271(e)(1) has also been advanced by some district courts. In 2001, the Southern District of New York held that the text of the Hatch-Waxman amendment did not indicate a Congressional intent to restrict its

product which is made by a process patented in the United States” 35 U.S.C. § 271(g).

³⁷ 35 U.S.C. § 271(e)(1) (2005).

³⁸ See Soehnge, *supra* note 30, at 58.

³⁹ 35 U.S.C. § 271(e)(1).

⁴⁰ *Id.*

⁴¹ *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104, 107-08 (D. Mass. 1998) (holding that the phrase “solely for uses reasonably related” is less restrictive than other phrases Congress could have chosen, such as “use is solely for purposes reasonably related.”).

⁴² *NeoRx Corp. v. Immunomedics, Inc.*, 877 F. Supp. 202 (D.N.J. 1994).

⁴³ *Schering Corp. v. Geneva Pharm., Inc.*, 339 F.3d 1373 (Fed. Cir. 2003), *aff’d* 275 F. Supp. 2d 534 (D.N.J. 2002).

application to generic drugs, or drug patents in general.⁴⁴ Absent Congressional intent to the contrary, other subsections of § 271 support an interpretation of § 271(e)(1) to apply to all inventions – the limiting factor being whether the information is ultimately developed for or submitted to a Federal agency.⁴⁵

¶15 The most important decision to interpret § 271(e)(1) prior to *Merck KGaA v. Integra Lifesciences* concerned whether medical devices fell under the statutory exemption.⁴⁶ In *Eli Lilly & Co. v. Medtronic*, the Federal Circuit held Class III medical devices are within the scope of the statutory exemption.⁴⁷ Judge Nies wrote the decision for a unanimous panel that looked to the legislative history, specifically the fact that Congress intended to overrule *Roche* by enacting § 271(e)(1).⁴⁸ The court went on to reason that neither *Roche* nor the FDCA were restricted to drug research and approvals. Thus, the statutory exemption is likewise not restricted to drug approvals.⁴⁹

¶16 The Supreme Court agreed to hear *Eli Lilly* to consider the scope of the statutory research exemption.⁵⁰ The Court agreed with the Federal Circuit's broad interpretation of the statutory exemption after finding no Congressional purpose to limit the doctrine in the legislative history and, more importantly, no reason to limit the doctrine based on the text of the enacted law.⁵¹ Under this backdrop the Federal Circuit and the Supreme Court considered the matter at hand. Once again the highest patent court and the supreme judicial body were set to determine whether a certain type of research — in this case pre-clinical developmental drug research — is exempt from patent infringement liability.

II. MERCK KGAA, INTEGRA LIFESCIENCES, AND RGD PEPTIDES

¶17 The use of the RGD tripeptide – named such because it consists of arginine (R), glycine (G), and aspartic acid (D) — was initially discovered in 1982 by Dr. Michael Pierschbacher at the La Jolla Cancer Research Foundation (LJCRF).⁵² The first paper and corresponding patent did not specify the RGD domain as the critical component of the cell adhesion method.⁵³ Rather, the Pierschbacher paper described the primary structure of a novel protein known as the cell attachment factor of human plasma fibronectin.⁵⁴ The specific mechanism of cellular adhesion was not known at this time.⁵⁵

⁴⁴ Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., No. 95 Civ. 8833(RPP), 2001 WL 1512597, at *2 (S.D.N.Y. Nov. 28, 2001).

⁴⁵ *Id.*

⁴⁶ *Eli Lilly & Co. v. Medtronic, Inc.*, 872 F.2d 402 (Fed. Cir. 1989).

⁴⁷ *Id.* at 406.

⁴⁸ *Id.* at 404-05.

⁴⁹ *Id.* at 405-06.

⁵⁰ *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990).

⁵¹ *Id.* at 666-69.

⁵² The La Jolla Cancer Research Foundation was renamed the Burnham Institute in 1996.

⁵³ Michael D. Pierschbacher, Erkki Ruoslahti, Johan Sundelin, Peter Lind & Per A. Peterson, *The Cell Attachment Domain of Fibronectin*, 257 J. BIOL. CHEM. 9593 (1982). See also U.S. Patent No. 4,517,686.

⁵⁴ Pierschbacher, *supra* note 53, at 9594 (“A computer search for homologies of the sequence of the cell attachment fragment with published amino acid sequences revealed no statistically significant homologies with any other protein nor with any of the short sections of the sequence of fibronectin previously published.”).

⁵⁵ The lack of a credible mechanism for the necessity of the RGD domain raises a possible enablement issue into the patent chain, but this concern was satisfied by a 1984 Nature article. Michael D. Pierschbacher & Erkki Ruoslahti, *Cell Attachment Activity of Fibronectin Can be Duplicated by Small*

¶18 The oldest patent in the chain at issue was for a biologically derived cell surface receptor capable of binding to a peptide containing RGD.⁵⁶ Subsequent LJCRF patents claimed the use of RGD-containing peptides in promoting cell adhesion.⁵⁷ The most expansive patent claims alleged against Merck's use of RGD peptides were issued in 1997 in U.S. Patent No. 5,695,997.⁵⁸

¶19 In 1987, Dr. David Cheresh of the Scripps Research Institute⁵⁹ reported the recognition of RGD peptides by cell surface receptor proteins, also known as "integrins," in a line of human cancer cells.⁶⁰ In 1988, Merck KGaA began funding Dr. Cheresh's research into the role of integrins in angiogenesis.⁶¹ As a result of this research, Cheresh discovered that blocking $\alpha_v\beta_3$ integrins on endothelial cells inhibits angiogenesis and, ultimately, tumor growth.⁶² The blocking agents, or antagonists, reported by Cheresh were a murine monoclonal antibody and a cyclic RGD peptide,⁶³ which was provided by Merck.⁶⁴ These preliminary results led Merck to renew its funding for three years beginning in 1995, with a specific goal of developing potential drug candidates.⁶⁵ This research identified two cyclic RGD peptides,⁶⁶ for which Merck began the process of obtaining regulatory approval in 1996.⁶⁷

Synthetic Fragments of the Molecule, 309 NATURE 30 (1984) ("We conclude from these results and from the data presented below that the Arg-Gly-Asp must be maintained to preserve activity, while some variation at the [adjacent] position occupied by the serine residue is compatible with [cell adhesion] activity.").

⁵⁶ U.S. Patent No. 4,789,734 (1985) contains the single claim:

A substantially purified cell surface receptor derived from mesenchymal tissue and capable of binding to a peptide containing the amino acid sequence Arg-Gly-Asp, comprising a glycoprotein composed of at least two polypeptides of about 115 and 125 kD, respectively, as determined by SDS-PAGE under reducing conditions which selectively binds to vitronectin, but not to fibronectin.

⁵⁷ In addition to the '734 patent, the other four patents in suit are U.S. Patent Nos. 4,988,621, 4,792,525, 4,879,237, and 5,695,997.

⁵⁸ Claim 1 is an exemplary claim in the '997 patent: "A method of altering cell attachment activity of cells, comprising: contacting the cells with a substantially pure soluble peptide including RGD_X where X is an amino acid and the peptide has cell attachment activity."

⁵⁹ Then known as the Scripps Clinic and Research Foundation.

⁶⁰ See David A. Cheresh & John R. Harper, *Arg-Gly-Asp Recognition by a Cell Adhesion Receptor Requires Its 130-kDa α Subunit*, 262 J. BIOL. CHEM. 1434 (1987); Jeffrey W. Smith & David A. Cheresh, *The Arg-Gly-Asp Binding Domain of the Vitronectin Receptor*, 263 J. BIOL. CHEM. 18726 (1988); and David A. Cheresh, Jeffrey W. Smith, Helen M. Cooper & Vito Quaranta, *A Novel Vitronectin Receptor Integrin ($\alpha_v\beta_x$) is Responsible for Distinct Adhesive Properties of Carcinoma Cells*, 57 CELL 59 (1989).

⁶¹ *Telios Pharm., Inc. v. Merck KGaA*, No. 96-CV-1307, 1997 U.S. Dist. LEXIS 24187, at *3-5 (S.D. Cal. Sept. 11, 1997).

⁶² In 1994, Cheresh reported the reversal of tumor growth in chicken embryos. See Peter C. Brooks, Anthony M.P. Montgomery, Mauricio Rosenfeld, Ralph A. Reisfeld, Tianhua Hu, George Klier & David A. Cheresh, *Integrin $\alpha_v\beta_3$ Antagonists Promote Tumor Regression by Inducing Apoptosis of Angiogenic Blood Vessels*, 79 CELL 1157 (1994) [hereinafter Brooks, *Antagonists*]; Peter C. Brooks, Richard A.F. Clark & David A. Cheresh, *Requirement of Vascular Integrin $\alpha_v\beta_3$ for Angiogenesis*, 264 SCIENCE 569 (1994).

⁶³ Brooks, *Antagonists*, *supra* note 62 at 1162.

⁶⁴ *Id.*

⁶⁵ *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 198 (2005). See also Brief for the Petitioner at 12, *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005) (No. 03-1237).

⁶⁶ *Merck*, 545 U.S. at 198.

⁶⁷ *Id.* at 199.

A. *Integra Wins over the Jury After Consideration of the Common Law and Statutory Research Exemption*

¶20 In 1996, Telios Pharmaceuticals,⁶⁸ Integra, and Burnham learned of the Merck-Scripps research agreement and approached Merck to negotiate a mutually beneficial license agreement.⁶⁹ After Merck declined the license, the patent owners filed suit in the Southern District of California against Merck, Scripps, and Cheresh for patent infringement.⁷⁰ After the district court denied Merck's motion for summary judgment based on the statutory research exemption,⁷¹ a jury trial was held.⁷² The district court denied Merck's post-trial motion to dismiss,⁷³ but agreed that its pre-1995 basic research activities fell under the common law research exemption.⁷⁴ The jury then awarded Integra \$15 million in damages based on a reasonable royalty calculation.⁷⁵ After the district court denied Merck's post-trial motion for a judgment as a matter of law, Merck appealed to the Federal Circuit.⁷⁶

B. *The Federal Circuit Splits over § 271(e)(1)*

¶21 The panel of Judges Newman, Rader, and Prost heard arguments and then issued a split decision that upheld the trial court, with Judge Rader writing for the majority and Judge Newman dissenting in part.⁷⁷ The majority opinion takes up the issue of whether 35 U.S.C. § 271(e)(1) should be extended to provide a safe harbor for pre-clinical research on experimental drug compounds. The majority engaged in textual interpretation with a focus on the limiting word "solely":

At the outset, this statutory language *strictly limits* the exemption "solely" to uses with a reasonable relationship to FDA procedures. The term "solely" places a constraint on the inquiry into the limits of the exemption.

⁶⁸ Telios Pharmaceuticals, Inc., was founded in 1987 to commercialize integrin-mediated cell adhesion for tissue regeneration. Telios filed bankruptcy in 1995 and was acquired by Integra Lifesciences Corp. later that year. See Brief for the Petitioner at 20, *supra* note 65; *Bankruptcy Court Confirms Reorganization Plan*, Standard & Poor's Daily News (July 20, 1995), 1995 WLNR 578102.

⁶⁹ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 863 (Fed. Cir. 2003).

⁷⁰ *Id.* See also *Telios Pharm., Inc. v. Merck KGaA*, No. 96-CV-1307, 1997 U.S. Dist. LEXIS 24187, at *4 (S.D. Cal. Sept. 11, 1997).

⁷¹ *Telios*, 1997 U.S. Dist. LEXIS 24187, at *2, *5.

⁷² At trial, Merck did not contest the district court's claim construction, which held its cyclic RGD peptides were within the scope of the Integra patents. *Integra*, 331 F.3d at 861. Subsequently, "the district court granted Scripps' and Dr. Cheresh's motion to dismiss." *Id.* at 863.

⁷³ *Id.* at 864.

⁷⁴ *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 199 (2005).

⁷⁵ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 862 (Fed. Cir. 2003). The Federal Circuit found the damage calculation to be erroneous and the reasonable royalty rate was reduced on remand. Because of an earlier date of hypothetical negotiation and the overall value of Telios in its sale to Integra, the damages were reduced to \$6.375 million. *Integra Lifesciences I, Ltd. v. Merck KGaA*, No. 96CV1307-B(AJB), 2004 WL 2284001, at *4-9 (S.D. Cal. Sept. 7, 2004).

⁷⁶ *Integra*, 331 F.3d at 862.

⁷⁷ *Id.*

The exemption cannot extend at all beyond uses with the reasonable relationship specified in § 271(e)(1).⁷⁸

¶22 Thus, the court narrowly interpreted the operative language, “reasonably related to the development and submission of information,” to “[a]ctivities that...directly produce information for the FDA,” with limited exceptions for “activities that are not themselves the experiments that produce FDA information.”⁷⁹ The court held that Dr. Cheresch’s work did not qualify, because it “was not clinical testing to supply information to the FDA, but only general biomedical research to identify new pharmaceutical compounds.”⁸⁰

¶23 Despite this narrow statutory interpretation, the majority opinion was clearly informed by the legislative history of the Hatch-Waxman Act. Judge Rader declared that “the express objective of the 1984 Act was to facilitate the immediate entry of safe, effective generic drugs into the marketplace upon expiration of a pioneer drug patent.”⁸¹ Ultimately, Judge Rader countered Merck’s interpretation by stating that § 271(e)(1) “was meant to reverse the effects of *Roche* under limited circumstances”⁸²

¶24 Judge Newman dissented from the majority’s interpretation of the common law and statutory research exemptions.⁸³ Her approach was based on the following factors: (1) policy concerns centered on the roots of the patent system; (2) *stare decisis* of both the common law and statutory research exemption; and (3) a textual interpretation of the statute in view of the legislative intent.

¶25 In Judge Newman’s view, the basic policy behind the patent system is the fundamental patent bargain.⁸⁴ She admonishes the majority for “disapprov[ing] and essentially eliminat[ing] the common law research exemption”:⁸⁵

⁷⁸ *Id.* at 866 (emphasis added) (further noting that “the statutory language limits the reach of that relationship test”).

⁷⁹ *Id.*

⁸⁰ *Id.* Judge Rader further noted, “The FDA has no interest in the hunt for drugs that may or may not later undergo clinical testing for FDA approval.” *Id.*

⁸¹ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 866-67 (Fed. Cir. 2003). *See also* *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1568 (Fed. Cir. 1997) (“[T]he Drug Price Competition and Patent Term Restoration Act of 1984...legislation designed to benefit makers of generic drugs, research-based pharmaceutical companies, and not incidentally the public.”); *Allergan, Inc. v. Alcon Laboratories, Inc.*, 324 F.3d 1322, 1326 (Fed. Cir. 2003) (“To attain a balance between the interests of brand name pharmaceutical companies and generic drug manufacturers, Congress, as part of the Hatch-Waxman Act, legislated that a generic drug manufacturer may, without liability for infringement, use a drug claimed in a patent or a method of using a drug claimed in a patent in order to prepare an application for FDA approval of a generic drug.”); *Bayer AG v. Elan Pharm. Research Corp.*, 212 F.3d 1241, 1249 (Fed. Cir. 2000) (“[T]he Act specifically provides an ANDA applicant immunity from allegations of infringement for acts that are necessary in preparing an ANDA.”).

⁸² *Integra*, 331 F.3d at 867. The rule promulgated by the Federal Circuit is best summarized by Judge Rader: “[The Act] does not, for instance, expand the phrase ‘reasonably related’ to embrace all stages of development of new drugs merely because those new products will also need FDA approval.” *Id.*

⁸³ *Id.* at 872.

⁸⁴ *Id.* at 873 (citing the two competing “purpose[s] of a patent system” as “provid[ing] a financial incentive to create new knowledge” and “serv[ing] to add to the body of published scientific/technological knowledge”).

⁸⁵ *Id.*

The requirement of disclosure of the details of patented inventions facilitates further knowledge and understanding of what was done by the patentee, and may lead to further technologic advance. The right to conduct research to achieve such knowledge need not, and should not, await expiration of the patent. That is not the law, and it would be a practice impossible to administer.⁸⁶

¶26 Judge Newman, herself a research chemist, appears deferential to the considerable scientific progress made by Dr. Cheresh, which significantly improved the biological understanding of cell adhesion, the role of RGD peptides, and angiogenesis.⁸⁷

¶27 The basic structure of the argument is that the common law research exemption promotes the progress of science and technology by “requir[ing] full disclosure of the invention, including details of enabling experiments and technical drawings and best modes and preferred embodiments, even commercial sources of special components.”⁸⁸ However, Judge Newman recognizes that there must be a limit to the common law research exemption.⁸⁹ In this respect, Judge Newman analogizes the common law exemption to the fair use doctrine in copyright law, and is particularly adverse to restricting the doctrine purely on the basis of “an ultimate goal or hope of profit.”⁹⁰

¶28 Returning to Justice Story’s famous words in *Whittemore*, Judge Newman explains that “philosophical experiments” in this context “was referring to ‘natural philosophy,’ the term then used for what we today call ‘science’.”⁹¹ The allowance of a flexible common law exemption for research that falls under one of the two *Whittemore* categories has become a fundamental aspect of our patent system.⁹² Historically, the courts “have applied the research exemption when no commercial purpose was demonstrated for the research.”⁹³ Since the exemption has been a part of the common law for nearly 200 years, presumably its doctrinal effects have been incorporated into the economics of the patent system.⁹⁴ Furthermore, “[a] rule that this information cannot be

⁸⁶ *Id.*

⁸⁷ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 874 (Fed. Cir. 2003) (“As this research progressed, so did the scientific understanding of these peptide products . . .”).

⁸⁸ *Id.* at 875-76 (“Were all research using RGD peptides prohibited until the *Integra/Telios* patents expired, not even the patent owner would benefit, for the patented products had failed in *Telios*’ hands, leaving the patents valueless until Scripps and Merck made their discoveries as to the cyclic peptides and their anti-angiogenic properties.”).

⁸⁹ *Id.* at 876 (“Setting the boundaries of a common law exemption requires careful understanding of the mechanisms of the creation, development, and use of technical knowledge, and of today’s complexity of interactions among invention and innovating fruits of invention.”).

⁹⁰ *Id.*

⁹¹ *Id.* at 875, note 8.

⁹² *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 875 n.8 (Fed. Cir. 2003) (noting Justice Story’s second annunciation of this principle in *Sawin v. Guild*, 21 Fed. Cas. 554 (C.C.D. Mass. 1813)).

⁹³ *Id.* (citing *Chesterfield v. United States*, 141 Ct.Cl. 838 (1958) and *Ruth v. Stearns-Roger Manufacturing Co.*, 13 F. Supp. 697 (D.Colo. 1935)).

⁹⁴ *Id.* (“Today’s accelerated technological advance is based in large part on knowledge of the details of patented inventions and how they are made and used.”). In footnote 10, Judge Newman recognizes the “sweeping” rule created in the recent *Madey* decision. *Id.* at 878, n.10 (“I do not disagree with that decision on its facts; I disagree only with its sweeping dictum, and its failure to distinguish investigation into patented things, as has always been permitted, and investigation using patented things, as has never been permitted.”).

investigated without permission of the patentee is belied by the routine appearance of improvements on patented subject matter”⁹⁵

¶129 Judge Newman’s dissent further criticizes the majority opinion for basing its decision heavily on 35 U.S.C. § 271(e)(1) when both parties conceded that the statutory exemption applies to Merck’s Investigational New Drug (IND) Application.⁹⁶ Nonetheless, she agrees with Judge Rader that “the § 271(e)(1) safe harbor [does not] reach back down the chain of experimentation to embrace development and identification of new drugs,”⁹⁷ but disagrees with the application of this principle.⁹⁸ Judge Newman also reads into the statutory exemption a legislative intent to restrict its application to generic drugs,⁹⁹ but finds this inconsistent with the Supreme Court’s decision in *Eli Lilly*,¹⁰⁰ which significantly broadened the reasonableness test.¹⁰¹

C. Scalia’s Textualist Merck Opinion

¶130 Consistent with his broad textualist reading of 35 U.S.C. § 271(e)(1) in *Eli Lilly*,¹⁰² Justice Scalia, writing for a unanimous court, reversed the Federal Circuit majority opinion.¹⁰³ Scalia interprets the reasonableness test without the deference Judge Rader gave to the limiting modifier “solely.”¹⁰⁴ With respect to the appropriate interpretation of the reasonableness test, the court “decline[s] to read the ‘reasonable relation’ requirement so narrowly as to render § 271(e)(1)’s stated protection of activities leading to FDA approval for all drugs illusory.”¹⁰⁵ Justice Scalia gives short shrift to any myopic reading of legislative intent,¹⁰⁶ instead establishing:

Properly construed, § 271(e)(1) leaves adequate space for experimentation and failure on the road to regulatory approval: At least where a drugmaker has a reasonable basis for believing that a patented compound may work,

⁹⁵ *Id.* at 875.

⁹⁶ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 877 (Fed. Cir. 2003).

⁹⁷ *Id.* (quoting the majority opinion at 865-66). Neither Judge Rader nor Judge Newman cite to any authority for reading legislative history into statutes like 35 U.S.C. § 271. *See Texaco, Inc. v. Hasbrouck*, 496 U.S. 543, 569 n.27 (1990) (“Unlike scholarly commentators, we have a duty to be faithful to congressional intent when interpreting statutes, and are not free to consider whether, or how, the statute should be rewritten.”).

⁹⁸ *Integra*, 331 F.3d at 877 (noting “the territory that the Scripps/Merck research traversed, from laboratory experimentation to development of data for submission to the FDA, was either exempt exploratory research, or was immunized by § 271(e)(1)”).

⁹⁹ *Id.*

¹⁰⁰ *Id.*

¹⁰¹ *Eli Lilly & Co. v. Medtronic, Inc.* 496 U.S. 661 (1990).

¹⁰² *See Id.*

¹⁰³ *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005).

¹⁰⁴ *Id.* at 202 n.6 (“Although the Court of Appeals’ opinion suggests in places that § 271(e)(1)’s exemption from infringement is limited to research conducted in clinical trials...we do not understand it to have adopted that position.”).

¹⁰⁵ *Id.* at 202 (“As an initial matter, we think it apparent from the statutory text that § 271(e)(1)’s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of *any* information under the FDCA.”).

¹⁰⁶ *Id.* (“Congress did not limit § 271(e)(1)’s safe harbor to the development of information for inclusion in a submission to the FDA; nor did it create an exemption applicable only to the research relevant to filing an ANDA for approval of a generic drug.”).

through a particular biological process, to produce a particular physiological effect, and uses the compound in research that, if successful, would be appropriate to include in a submission to the FDA, that use is “reasonably related” to the “development and submission of information under...Federal law.”¹⁰⁷

¶31 Justice Scalia finds support for his interpretation in economic policy concerns and the nature of the FDA and the pharmaceutical industry. He notes the uncertainty attendant to the development of new drug compounds,¹⁰⁸ wherein the only way to “know at the outset that a particular compound will be the subject of an eventual application to the FDA [is] if the active ingredient in the drug being tested is identical” to an FDA approved drug.¹⁰⁹ This uncertainty has been recognized by the FDA, whose regulations “provide only that ‘[t]he amount of information on a particular drug that must be submitted in an IND’” depends on many factors.¹¹⁰ Furthermore, Justice Scalia cites the Government’s amicus brief, on behalf of the FDA, in support of the proposition that “the use of patented compounds in preclinical studies is protected under § 271(e)(1) as long as there is a reasonable basis for believing that the experiments will produce ‘the types of information that are relevant to an IND or NDA.’”¹¹¹ Justice Scalia also discounts Judge Rader’s normative policy arguments with respect to the extension of the rule to research tools, because the issue was never raised by *Integra* and need not be a focus of this case.¹¹²

III. A REALIST APPROACH TO *MERCK* AND THE STATUTORY EXEMPTION

¶32 The statutory research exemption has been a contentious issue ever since Congress intervened in what it perceived as a narrowing of the common law doctrine by the Federal Circuit.¹¹³ In light of the Supreme Court’s decision, it is important to reassess the state of the statutory and common law research exemptions and the gloss imparted to the doctrines by the Federal Circuit. The Supreme Court’s holding has broad implications that should inform the Federal Circuit’s view of this and similar doctrines going forward. As the number of articles published in the two years between the Federal Circuit’s decision and the Supreme Court ruling attests, the importance of the decision cannot be underestimated for its legal and economic impact.

¹⁰⁷ *Id.* (quoting 35 U.S.C. § 271(e)(1)).

¹⁰⁸ *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 207 (2005) (“many of the uncertainties that exist with respect to the selection of a specific drug exist as well with respect to the decision of what research to include in an IND or NDA”).

¹⁰⁹ *Id.* Justice Scalia implies that restricting § 271(e)(1) to generic drugs is inconsistent with the legislative record, which specifically rules out applying the Hatch-Waxman Act solely to “identical” drug formulations, instead opting for the less restrictive modifier “the same as the listed drug.” H.R. REP. 98-857(I), at 21.

¹¹⁰ *Merck*, 545 U.S. at 207 (quoting 21 C.F.R. § 312.22(b)).

¹¹¹ *Id.* at 2383-84 (quoting Brief of United States as *Amicus Curiae* at 23).

¹¹² *Id.* at 2382 n.7 (agreeing with Judge Newman’s opinion that studying a research tool is different from using the tool in research).

¹¹³ H.R. REP. NO. 98-857(II), at 27.

A. *The Positivists Have It*

¶33 Most of the scholarly research on the research exemptions has been concerned with the positive effects of changes in the patent law, assuming that any changes in the law result in behavioral changes in the market for patented inventions. In *Integra Lifesciences v. Merck KGaA*, the Federal Circuit panel majority adopted the positive view that its decision would change the manner in which research would be conducted.¹¹⁴ The majority explicitly stated that they were trying to protect “the exclusive rights of patentees owning biotechnology tool patents.”¹¹⁵ Returning to the original conception of the common law exemption, as reflected in the legislative history,¹¹⁶ the Federal Circuit applied a *de minimis* test to Merck’s actions.¹¹⁷

¶34 This rationale is a normative interpretation that values strong protections for patent rights and recognizes the role industry-forcing doctrines can have.¹¹⁸ By protecting the rights of research tool patent owners, the Federal Circuit extended its research exemption rule through dicta to “express a view about whether, or to what extent, § 271(e)(1) exempts from infringement the use of ‘research tools’ in the development of information for the regulatory process.”¹¹⁹ Therefore, the Supreme Court’s ruling should be a boon to companies “willing to use patented research tools without a license while the research tool industry is left wondering what value remains in their patents.”¹²⁰

¶35 In line with the majority decision at the Federal Circuit, many commentators viewed the *Integra* decision through a positivist lens.¹²¹ Professor Dreyfuss argues that the decision encroaches on the norms of scientific research and proposes a waiver system in response.¹²² The positivist component of this argument builds on Professor Eisenberg’s theory that the norms of science, e.g. the societal benefits obtained from an open exchange of ideas, are damaged by overzealous patent protection.¹²³ The proposed

¹¹⁴ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 866-68 (Fed. Cir. 2003).

¹¹⁵ *Id.* at 867 (focusing on the fact that “patented tools often facilitate general research to identify candidate drugs, as well as downstream safety-related experiment on those drugs”).

¹¹⁶ H.R. REP. NO. 98-857(II), at 30 (justifying the constitutionality of the Hatch-Waxman Act because simply “test[ing] the drug for purposes of submitting data to the FDA for approval” is no more than a *de minimis* interference with the patentee’s rights).

¹¹⁷ *Integra*, 331 F.3d at 867.

¹¹⁸ *Id.*

¹¹⁹ In his decision overruling this decision, Justice Scalia did not address the issue of research tool patents. He noted that “[r]espondents have never argued the RGD peptides were used at Scripps as research tools, and it is apparent from the record that they were not.” *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 205 n.7 (2005).

¹²⁰ Stanton J. Lovenworth & Melissa P. Cohen, *The Research Tool Conundrum: ‘Merck’ Decision Leaves Open Questions on Boundaries of Safe Harbor*, N.Y. L.J., October 17, 2005, at 4 (noting that the *Merck* decision “most certainly invites further suits to clarify the outer boundaries of the safe harbor and whether and to what extent § 271(e)(1) exempts the use of research tools”).

¹²¹ See, e.g., Tanuja V. Garde, *Supporting Innovation in Targeted Treatments: Licenses of Right to NIH-Funded Research Tools*, 11 MICH. TELECOMM. & TECH. L. REV. 249 (2005); Strandburg, *supra* note 1; Alison Ladd, Note, *Integra v. Merck: Effects on the Cost and Innovation of New Drug Products*, 13 J.L. & POL’Y 311 (2005); Tao Huang, Note, *The Experimental Purpose Doctrine and Biomedical Research*, 11 MICH. TELECOMM. & TECH. L. REV. 97 (2004).

¹²² See Rochelle Dreyfuss, *Protecting the Public Domain of Science: Has the Time for an Experimental Use Defense Arrived*, 46 ARIZ. L. REV. 457, 470-71 (2004).

¹²³ See Rebecca S. Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 Yale L.J. 177 (1987) (discussing the possibility of synchronizing the doctrines of basic scientific research and patent law).

waiver system is similar and complementary to compulsory licenses proposals,¹²⁴ except the waivers would only be available to academic institutions and would be subject to limitations on future disclosure and commercialization of innovations.¹²⁵

¶36 An alternative proposal by Professor Strandburg sides with Judge Newman's dissenting opinion in *Merck*, particularly the distinction drawn between "experimenting with" and "experimenting on" patented technology.¹²⁶ The focus of this proposal is again a positivist view that the panel majority decision will significantly affect research activity and unnecessarily resorts to "linguistic gymnastics" to protect research tools.¹²⁷ Professor Sandburg's analysis finds that research tool patent owners would be able to control the progress of research to the detriment of scientific progress under the panel majority's decision.¹²⁸

B. Legal Realism and the Future of the Research Exemption

¶37 The imparting of a de minimis qualification to § 271(e)(1) represents the normative consideration that a patent is an absolute property right for which easements should not be granted unless they are de minimis. The Federal Circuit's language in this respect can only be read as a normative proscription, because the statutory text contains no references to the extent of the alleged infringement. In the context of the legislative history, de minimis infringement is neither the more general statutory purpose nor the justification and explanation of any single provision of the statute.¹²⁹ Generic drug approval certainly does not have a de minimis impact on the pharmaceutical industry. Rather, the de minimis argument is raised as one among a few counterarguments to the contention that § 271(e)(1) violates the takings clause of the Fifth Amendment.¹³⁰ Presumably this view assures patent owners that their rights are secure and encourages patenting activity.¹³¹

¶38 The Federal Circuit should take heed of the second Supreme Court opinion to interpret this paragraph of the patent law with a strict textualist approach.¹³² Table 1

¹²⁴ A compulsory license scheme would force an arms length negotiation between the holder of a patent right and a license right. See *Garde*, *supra* note 121, at 280-83.

¹²⁵ Dreyfuss, *supra* note 122, at 472-72.

¹²⁶ Strandburg, *supra* note 121, at 88-90. See also Kevin Iles, *A Comparative Analysis of the Impact of Experimental Use Exemptions in Patent Law on Incentives to Innovate*, 4 NW. J. TECH. AND INTELL. PROP. 61, 82 (2005) ("a distinction must be drawn between experimenting with a patented invention and experimenting on a patented invention so as to protect the interests of the research tool patentee").

¹²⁷ Strandburg, *supra* note 121, at 85. One of the main positivist worries after the Federal Circuit's decision was that research activity would move overseas to countries where research exemptions were more firmly embedded in the patent law. See Ladd, *supra* note 121, at 353-55.

¹²⁸ Strandburg, *supra* note 121, at 146-50.

¹²⁹ The general purpose of the statute as recited by Congress is "to make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs." H.R. REP. NO. 98-857(I), at 14.

¹³⁰ H.R. REP. NO. 98-857(II), at 29 ("It is alleged by some witnesses that the provisions of the bill which permit the limited testing of drugs while they are on patent in order assist in the preparation of an abbreviated new drug application is a 'taking' without just compensation in violation of the requirements of the Fifth Amendment.").

¹³¹ William M. Landes & Richard A. Posner, *An Empirical Analysis of the Patent Court*, 71 U. CHI. L. REV. 111, 128 (2004) (concluding that the "pro-patent leanings" of the Federal Circuit "has had a significant effect on patent activity").

¹³² Other than *Merck KGaA v. Integra Lifesciences*, the Supreme Court considered the statutory research exemption in *Eli Lilly & Co. v. Medtronic, Inc.* and adopted a similarly broad textualist view in a decision authored by Justice Scalia. 496 U.S. 661 (1990).

illustrates the level of disagreement among the court's judges over the appropriate interpretation of this doctrine.¹³³ For example, one of the initial cases at the Federal Circuit to deal with the research exemption and generic drugs noted:

We do not read the statute as implying any such limitation. In the first place, if the language is clear, the plain meaning of the statute will be regarded as conclusive. While legislative history may aid our understanding of the function and purposes of the statute, and in cases of doubt assist in interpretation of the language, when the legislature has clearly spoken the law, the court's duty is to enforce it as written. The statute at issue here only requires that the making, using or selling of the patented invention be solely for uses reasonably related to FDA approval.¹³⁴

¶39 Table 1 illustrates that this view has been the norm in the Federal Circuit's interpretation of the statutory exemption since 1990. The *Integra* decision was an outlier in narrowing the applicability of the research exemption. In every other case, the Federal Circuit has acknowledged the broad textualist view it announced and the Supreme Court affirmed in *Eli Lilly*.¹³⁵

¶40 Perhaps in *Integra* the Federal Circuit saw potential abuse of a broad research exemption by innovator pharmaceutical companies,¹³⁶ or was concerned about diminishing the utility of research tools patents.¹³⁷ Regardless of the rationale, the court looked to facts beyond whether the Cheres data was reasonably likely to be submitted to the FDA, which was conceded by the parties.

C. *The Research Exemption Aligns with Economic Realities in the Pharmaceutical Industry*

¶41 If one accepts the positivist approach to the research exemption, will *Merck v. Integra* lead to a boom in fearless innovator research? Infringement liability will still protect the patent owner after FDA approval and will limit outright decisions to infringe.¹³⁸ In fact, the product in question would likely have infringed according to the

¹³³ Professors John Allison and Mark Lemley conducted an empirical study of all patent infringement decisions at the Federal Circuit during the 1989 term and discovered only minor differences in the overall results between two groups of judges – one with prior patent experience and one without. The differences were more significant when broken down by doctrine. John R. Allison & Mark A. Lemley, *How Federal Circuit Judges Vote in Patent Validity Cases*, 27 FLA. ST. U. L. REV. 745 (2000).

¹³⁴ *Teletronics Pacing Systems, Inc. v. Ventritex, Inc.*, 982 F.2d 1520, 1524 (Fed. Cir. 1992).

¹³⁵ *Eli Lilly & Co. v. Medtronic, Inc.*, 872 F.2d 402 (Fed. Cir. 1989), *aff'd*, 496 U.S. 661 (1990).

¹³⁶ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 867 (Fed. Cir. 2003) (“The safe harbor does not reach any exploratory research that may rationally form only a predicate for future FDA clinical tests.”).

¹³⁷ *Id.* (explaining that the decision avoids “swallow[ing] the whole benefit of the Patent Act for some categories of biotechnological inventions”).

¹³⁸ Eric E. Johnson, *Calibrating Patent Lifetimes*, 22 SANTA CLARA COMPUTER & HIGH TECH. L.J. 269, 290 (2006) (“Where the pharmaceutical industry ... maintains tremendous incentive to innovate despite having patent duration effectively shortened by approximately one-third, there is strong reason to believe that the incentive provided by the patent system may be much more than is necessary for this or other industries.”).

district court's claim construction, but Merck had not marketed it yet.¹³⁹ This raises the interesting question of whether Merck's due diligence was inadequate. Very few firms will take advantage of the ruling's expansion of the doctrine, because the threat of post-clinical litigation is too great to risk expending resources on development. Therefore, the positivist view, while technically accurate, is of little consequence to the pharmaceutical industry.

¶42 The Supreme Court's position is also supported by the economic realities of the pharmaceutical industry. While the Court did not cloud its textualist argument with economic concerns, there are overtones of these considerations. As it is with any bill that has a seminal impact on an important industry, Congress was clearly concerned about the economics of the pharmaceutical industry when it passed the Hatch-Waxman Act.¹⁴⁰

¶43 Four arguments support the premise that the Supreme Court's *Merck* decision is economically preferable to the Federal Circuit's approach to the research exemption. First, the facts of *Merck* and evidence from the industry demonstrate that licenses are not effective in pre-clinical drug research. Second, a broader research exemption will not significantly affect the future value of most drug patents. Third, the burden of a limited exemption stifles research into new drug uses, and the market value of innovator research is arguably more important than generic research. Finally, the concern about the impact on research tool patents is minimized by two factors: the sanctioned research is *into*, not *using*, patented technology and patents have a smaller impact on research tools and instruments than on drug development.

¶44 Licenses are a fundamental part of the rents obtained from intellectual property, but their appropriability is highly industry dependent. Merck KGaA sponsored the Scripps research without seeking a license from Integra or Burnham.¹⁴¹ This could have occurred because Merck believed that it could rely on the common law research exemption, which pre-*Madey* would have encompassed most investigational research at educational and non-profit institutions. It is also possible that Merck was not aware of the RGD patent portfolio. But that is difficult to rely on as a due diligence defense, because the specific RGD sequence was broadly claimed in the '734 patent and Dr. Cheresch's decision to use RGD peptides was clearly informed by the Burnham work.¹⁴² Presuming that Merck conducted the appropriate due diligence prior to launching its research program, we can assume that either the company held an honest belief that a research exemption would apply or the applicable patents were invalid or not infringed.

¶45 The costs of obtaining a license prior to investigational work were significant given the uncertainty associated with early stage drug development. Institutional costs and other externalities could have significantly increased the amount Merck expended over the ten years it supported Cheresch's research. Additionally, Merck would risk willful infringement if a license were sought and denied. The Federal Circuit decision would

¹³⁹ Merck contested the district court's claim construction that its cyclic RGD peptide was within the scope of Integra's claims. The Federal Circuit reviewed this holding de novo and affirmed the district court's claim construction. See *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 868-69 (Fed. Cir. 2003).

¹⁴⁰ H.R. REP. 98-857(II), at 4 (discussing the anti-competitive effects of the FDA's generic drug approval process at the time of the Hatch-Waxman bill).

¹⁴¹ Brief for the Petitioner at 21, *supra* note 65.

¹⁴² Cheresch repeatedly cites to the work of Pierschbacher et al. in his scientific publications. See *supra* notes 60 and 62.

require Merck and Cheresch to obtain a license from the patent owners even before conducting experiments to determine whether RGD peptides inhibit angiogenesis. This presents a significant hurdle to the development of new applications for existing compounds, which is the precise issue attacked in the anti-commons approach.¹⁴³

¶46 Like many other industries, most of the innovation in the pharmaceutical industry depends on existing disclosures and represents incremental improvements to existing technology.¹⁴⁴ In recent years, innovation activity has shifted away from models of absolute novelty to a model of routine exploitation of existing technology, particularly in the biopharmaceutical context.¹⁴⁵ This type of innovation places greater emphasis on the interactive and collective nature of innovation processes, which are fueled by access to existing disclosures.¹⁴⁶ The research exemptions improve access to existing technologies and do not limit appropriability of existing patent rights once the innovative technology is marketed.¹⁴⁷ As Judge Newman notes, the prevalence of improvements to existing technology in the pharmaceutical industry belies the assumption that licensing activity increases appropriability of existing rights.¹⁴⁸

¶47 As noted by Landes and Posner, “incremental increases in patent protection are unlikely to influence inventive activity significantly and incremental reductions might actually enhance economic welfare.”¹⁴⁹ Ultimately, if pharmaceutical firms do not seek licenses as part of their development models, the Federal Circuit’s insistence on this behavior does not serve the patent owners or the public good. The patent owners will not be served because the industry is not likely to be forced into this behavior, as demonstrated by Merck’s pre-development activities. Social welfare will be diminished by avoidance and circumvention of liability, which will not efficiently allocate the best resources, i.e. existing disclosures, to the task of new drug development.

¶48 In addition to the behavioral economic view, the present discount value of existing patent rights is relatively unaffected by the *Merck* research exemption. At a discount rate of 10%,¹⁵⁰ the present value of a patent right with a twenty-year term, assuming there is a market for the invention, is 85% of its value with perfect appropriability.¹⁵¹ However, one cannot assume that pioneer drug compound patents have a twenty-year term. Even

¹⁴³ See Mireles, *supra* note 28, at 178 (“The licensing of research tools that may have a broad application to many research problems also provides substantial risks to private firms.”). See also Eisenberg & Heller, *supra* note 9, at 699.

¹⁴⁴ See Dominique Foray, *Knowledge Distribution and the Institutional Infrastructure: The Role of Intellectual Property Rights*, in INTELLECTUAL PROPERTY RIGHTS AND GLOBAL COMPETITION 77 (1995).

¹⁴⁵ *Id.* (citing a study by Hermitte and Joly of innovation in the biotech sector).

¹⁴⁶ *Id.* at 112.

¹⁴⁷ Critics of stronger patent laws for drug innovations have pointed to the predominance of academic and federal drug R&D in producing therapeutic innovations, largely under the protective blanket of a research exemption. See LANDES, *supra* note 2, at 313.

¹⁴⁸ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860, 878 (Fed. Cir. 2003).

¹⁴⁹ LANDES, *supra* note 2, at 327. The value of patent rights account for only 10-15% of national R&D expenditures and have a fairly limited impact on innovative activity. *Id.* (citing data from Zvi Griliches, Ariel Pakes & Bronwyn H. Hall, *The Value of Patents as Indicators of Inventive Activity*, in ECONOMIC POLICY AND TECHNICAL PERFORMANCE 97, 120 (Partha Dasgupta and Paul Stoneman eds. 1987)).

¹⁵⁰ The cost of capital in the pharmaceutical industry hovers around 9-12%. See Henry G. Grabowski & John M. Vernon, *Returns to R&D on New Drug Introductions in the 1980s*, 13 J. HEALTH ECON. 383, 386-87 (1994).

¹⁵¹ LANDES, *supra* note 2, at 296.

with the patent-term restoration component of the Hatch-Waxman Act,¹⁵² the average effective term of a pharmaceutical patent is about eleven years,¹⁵³ which reduces the present value of the invention to 65%. Overall R&D costs make up about 30% of the present value of drug innovations, and the internal rate of return in the pharmaceutical industry is about 11% on R&D investments.¹⁵⁴ The issue is not whether this level of appropriability is fair to the patent owner, but whether the research exemption has a significant effect on the present value of the patent right. This issue concerns at least two important factors: incorporation of the exemption in the discount rate and effect on supply and demand elasticity.

¶49 Assuming the discount rate patentees use when assessing the market for a pharmaceutical treatment is relatively empirical, the research exemptions are incorporated. The most accurate and safest discount rate to apply – the one most relevant to investors – is the historical rate obtained from a regressive analysis based on empirical data, with fewer inherent assumptions than a rate obtained *ab initio*.¹⁵⁵ Since the research exemption has been a long-standing part of the existing law and is a *de facto* characteristic of the pharmaceutical industry, any historical analysis that incorporates data older than 2003, arguably until the Supreme Court’s 2005 decision, will incorporate this assumption.

¶50 Residual demand elasticity, as a ratio of supply and demand elasticity to overall supply, is the most important factor in pricing models for patented products,¹⁵⁶ because uncertainty in demand determines the marginal cost for imitators — whether they nominally infringe the patent or circumnavigate the claims by designing around their scope. In general, demand elasticity is low in the pharmaceutical industry, presumably because of the difficulty of imitating a drug compound patent.¹⁵⁷ The situation in reality is not so simple, because the rules of patentability often restrict patent protection to a narrow family of compounds, thereby increasing potential for circumventing a patent’s claim by developing a novel compound with comparable bioactivity.

¹⁵² The Drug Price Competition and Patent Term Restoration Act of 1984 provided for the latter as well as the former, which is the subject of this comment. Basically, the Act amended the Food Drug and Cosmetic Act to allow for extension of the statutory patent term by the amount of time required for a new drug to navigate the FDA approval process. Pub. L. No. 98-417.

¹⁵³ See Michelle Meadows, *Greater Access to Generic Drugs*, FDA CONSUMER, available at http://www.fda.gov/fdac/features/2003/503_drug.html. Analysis of the revenue and cash flow activity of patented new drug compounds supports an empirical eleven-year monopoly – the year in which revenues and cash flows reach their peak. See also Grabowski, *supra* note 150, at 391.

¹⁵⁴ Notably, pharmaceutical returns are not much higher than the cost of capital, indicating a “model of rivalrous R&D competition” by pharmaceutical firms. Henry Grabowski, John Vernon & Joseph DiMasi, *Returns on R&D for 1990s New Drug Introductions*, http://www.dklevine.com/archive/grabow-randd_returns.pdf, at 2 (March 2002). See also Grabowski, *supra* at note 150, at 400-402 (noting that nearly all studies find internal rate of return in the pharmaceutical industry are within 1% of net cost of capital); F.M. Scherer, *The Link Between Gross Profitability and Pharmaceutical R&D Spending*, 20 HEALTH AFFAIRS 216 (2001) (studying profitability in the pharmaceutical industry empirically).

¹⁵⁵ See Richard Gilbert & Carl Shapiro, *Optimal Patent Length and Breadth*, 21 RAND J. ECON. 106 (1990); Paul Klemperer, *How broad should the scope of patent protection be?*, 21 RAND J. ECON. 113 (1990).

¹⁵⁶ The patentee’s profit-maximizing ratio equals $[\epsilon_d/s + \epsilon_s(1-s)/s]/[\epsilon_d/s + \epsilon_s(1-s)/s - s]$; where ϵ_d and ϵ_s are the demand and supply elasticities, respectively, and s is the patentee’s output. Therefore, lower supply and demand elasticity lead to higher profits for the patentee. See LANDES, *supra* note 1, at 299.

¹⁵⁷ N. Edward Coulson & Bruce C. Stuart, *Insurance Choice and the Demand for Prescription Drugs*, 61 S. ECON. J. 1146, 1146-57 (1995) (demand in the pharmaceutical industry is nearly inelastic).

¶51 The research exemption can increase the potential for designing around existing patents through decreased research and development costs when imitators take advantage of patent disclosures. This type of activity is not necessarily within the scope of *Merck*, because simply using a patented compound as a research tool without a reasonable expectation of a submission to the FDA was not considered by the Court.¹⁵⁸ Even so, it is not likely that this activity has a significant impact on supply and demand elasticity for the patented product. Consider the RGD peptide example: Whereas Integra employed RGD peptides as cell adhesion promoters, its competitors and imitators would experience a marginal cost commensurate with developing competitive cell adhesion promoters. The demand elasticity for cell adhesion promoters would be unaffected by Cheresh's research exemption.

¶52 Ultimately, the research exemption encourages the creation of new markets for already granted patents. This increases the future appropriability of unanticipated value as a result of the research exemption and does not affect residual demand elasticity in the existing market. The research exemption encourages innovation, which in turn increases social benefits, with little effect on the value of the private right. Scalia's decision establishes a more specific rule and sets forth a textualist position with respect to the patent laws that decreases the uncertainty the rent seeker will encounter. Uncertainty in experimental use doctrine discourages innovation and diminishes appropriability of patented inventions.¹⁵⁹

IV. CONCLUSION

¶53 *Merck KGaA v. Integra Lifesciences* represents one case in a continuing struggle over the position of the research exemption in U.S. patent law. This issue may not be solved soon, with the common law doctrine perhaps dependent on panel composition, although a majority of judges favor a narrow interpretation.¹⁶⁰ In a broader context, *Merck v. Integra* also reinforces the Supreme Court's textualist interpretation of the Patent Act. This should be a welcome indicator to firms who were startled by the Federal Circuit's earlier decision.

¶54 In the future, the Federal Circuit should be mindful of the judges' normative tendencies and adhere to the plain language of the statute when it requires interpretation. The statutory research exemption is entrenched in the Patent Act and must be given its broadest interpretation within the Congressional design. Additionally, the court may

¹⁵⁸ *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 206 (2005) ("It does not follow . . . that § 271(e)(1)'s exemption from infringement categorically excludes either (1) experimentation on drugs that are not ultimately the subject of an FDA submission or (2) use of patented compounds in experiments that are not ultimately submitted to the FDA.").

¹⁵⁹ JOHN W. SCHLICHER, *PATENT LAW, LEGAL AND ECONOMIC PRINCIPLES* § 8.50 (2005) ("[N]othing in the current Patent Act or any earlier Patent Act ... suggests that it is also the purpose of patent law to permit an inventor to capture the value of all subsequent complementary inventions or to permit a patent owner to prohibit experiments necessary to develop substitute inventions."). See also Iles, *supra* note 126, at 82 (noting the current commercial/non-commercial distinction is incongruous with economic realities in R&D).

¹⁶⁰ A detailed study of the panel dependence of research exemption decisions is probably unfeasible for lack of data and beyond the scope of this paper. A number of researchers have begun empirical legal realist studies of the Federal Circuit's jurisprudence. See, e.g., R. Polk Wagner & Lee Petherbridge, *Is the Federal Circuit Succeeding? An Empirical Assessment of Judicial Performance*, 152 U. PA. L. REV. 1105 (2004).

consider economic rationales, because a patent is fundamentally an economic monopoly. Ultimately, the Supreme Court's decision in *Merck* is supported by the economic reality of the pharmaceutical industry, in which risk and capital costs are high and concomitant returns are realized by the most agile firms.

Table 1. Summary of Federal Circuit's § 271(e)(1) Decisions.

Judge	Case	Issue	Holding
<u>Rader</u> , Prost	<i>Integra</i> ¹⁶¹ (2003)	Preclinical research of a new drug	Restricted to clinical trial data
<u>Newman</u> (dissenting)	<i>Integra</i> ¹⁶² (2003)	Preclinical research of a new drug	Common law exemption applies to preclinical research and § 271(e)(1) to clinical tests
<u>Rader</u> , Mayer, Michel	<i>Abtox</i> ¹⁶³ (1997)	Tests data on Class II device used for raising capital	Underlying purpose of test is irrelevant if data could reasonably be for FDA
<u>Clevenger</u> , Cowen, Archer	<i>Intermedics</i> ¹⁶⁴ (1993)	Relevance of commercial potential	Irrelevant as long as related to FDA submission
<u>Rader</u> , Mayer, Plager	<i>Chartrex</i> ¹⁶⁵ (1993)	Display at trade shows and use in consumer studies	Do not lose § 271(e) exemption by engaging in other activities
<u>Plager</u> , Michel, Rich	<i>Telectronics</i> ¹⁶⁶ (1992)	Class II medical devices	§ 271(e) includes medical devices, not restricted by legislative history
<u>Nies</u> , Cowen, Archer	<i>Eli Lilly</i> (1990) ¹⁶⁷	Class III medical devices	<i>Roche</i> doctrine not limited to drugs, § 271(e) overruled <i>Roche</i>

¹⁶¹ *Integra Lifesciences I, Ltd. v. Merck KGaA*, 331 F.3d 860 (Fed. Cir. 2003).

¹⁶² *Id.* at 872.

¹⁶³ *Abtox, Inc. v. Exitron, Corp.*, 122 F.3d 1019 (Fed. Cir. 1997).

¹⁶⁴ *Intermedics, Inc. v. Ventritex Co., Inc.*, 991 F.2d 808 (Fed. Cir. 1993).

¹⁶⁵ *Chartrex Int'l PLC v. M.D. Pers. Prods. Corp.*, 5 F.3d 1505 (Fed. Cir. 1993).

¹⁶⁶ *Telectronics Pacing Systems, Inc. v. Ventritex, Inc.*, 982 F.2d 1520 (Fed. Cir. 1992).

¹⁶⁷ *Eli Lilly & Co. v. Medtronic, Inc.*, 872 F.2d 402 (Fed. Cir. 1989), *aff'd*, 496 U.S. 661 (1990).