

RESEARCH TOOL PATENTS AFTER *INTEGRA* V. *MERCK*—HAVE THEY REACHED A SAFE HARBOR?

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INTRODUCTION

Biotechnology has become one of the key technologies of the 21st century. The rapid evolution of biomedical research has raised expectations of finding ever better treatment to an increased number of illnesses. Due to the complexity of biomedical research, researchers—scientists working in academia and in commercial enterprises alike—need access to numerous resources for their projects. Concerns have been expressed that increased patenting of upstream inventions, especially of research tools, has led to a situation of blocking patents and has impaired research and development of new or better therapeutic products.

Responding to these concerns, proposals have been made to facilitate access to the necessary inputs by excluding upstream inventions

from patentability¹ through: a more stringent application of the patentability requirements,² a broadening of the experimental use exemption,³ or compulsory licensing of research tools.⁴ Except for the exclusion of research tools from patentability,⁵ all approaches are worthy of closer consideration and should best be pursued consistent with each other and with the rationale of the patent system. Whereas an introduction of compulsory licensing provisions into U.S. patent law seems

1. See, e.g., Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 46 n.233, 47 (2001).

2. See, e.g., Cynthia D. Lopez-Beverage, *Should Congress Do Something About Upstream Clogging Caused by the Deficient Utility of Expressed Sequence Tag Patents?*, 10 J. TECH. L. & POL'Y 35 (2005) (arguing in favor of a heightened utility standard); Richard R. Nelson, *The Market Economy, and the Scientific Commons*, 33 RES. POL'Y 455, 466 (2004) (arguing in favor of a stricter application of the utility requirement to keep open the scientific commons: "A stricter interpretation here would require [a] more compelling demonstration of significant progress towards a particular practical solution than seems presently required . . . [and] would be a major contribution to protecting the commons."); Teresa M. Summers, *The Scope of Utility in the Twenty-First Century: New Guidance for Gene-Related Patents*, 91 GEO. L.J. 475 (2003) (arguing that the utility requirement should be used to restrict the number of patents granted for biotechnology invention and research tools); see also 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, 194-201 (2004) (analyzing the development of the utility standard and the suggestions of commentators to heighten the standard).

3. See, e.g., Natalie M. Derzko, *In Search of a Compromised Solution to the Problem Arising from Patenting Biomedical Research Tools*, 20 SANTA CLARA COMPUTER & HIGH TECH. L.J. 347 (2004); Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017 (1989); 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 (2004); Mueller, *supra* note 1.

4. See, e.g., Ruth E. Freeburg, *No Safe Harbor and No Experimental Use: Is it Time for Compulsory Licensing of Biotech Tools?*, 53 BUFF. L. REV. 351 (2005); Donna M. Gitter, *International Conflicts Over Patenting Human DNA Sequences in the United States and the European Union: An Argument for Compulsory Licensing and a Fair-Use Exemption*, 76 N.Y.U. L. REV. 1623 (2001).

5. As Mueller noted, an exclusion of certain technologies from patentability would constitute an ultimate measure that has always been avoided in the U.S. and would run "afoul of the developmental history of U.S. patent jurisprudence . . ." Mueller, *supra* note 1, at 47. Furthermore, even if U.S. tradition could be overcome, any exclusion from patentability would have to conform to the obligations under the TRIPS Agreement, especially to the non-discrimination requirement of Article 27. *Agreement on Trade-Related Aspects of Intellectual Property Rights*, art. 27.1, *Marrakesh Agreement Establishing the World Trade Organization*, Annex 1C, Apr. 15, 1994, 108 Stat. 4809, 4988, 1869 U.N.T.S. 299 (1994), available at http://www.wto.org/english/docs_e/legal_e/27-trips.pdf. An exclusion of research tools would likely constitute a violation of TRIPS. *Id.* See also the analysis with regard to extending the scope of the experimental use exemption to the use of research tools *infra* Part VII.C.2.b.

highly unlikely,⁶ courts and patent offices recently seem to have followed a more stringent application of the patentability requirements.⁷

The saga surrounding the *Integra v. Merck* cases has rekindled a heated debate about the proper scope of both common law exemption and the safe harbor provision, causing significant concern for owners of research tool patents. This Article will argue that the next judicial decision addressing the question of research tool patents should clarify that they are in a safe harbor because none of the two exemptions from infringement referenced above extends to the use of research tools in experiments in order to preserve the necessary incentives for their creation in the first place. Allowing access to research tools under any of the exemptions—though arguably having a positive short term effect—would endanger the development of sufficient innovative research technologies which may have a greater negative impact on the pace of biotechnological research than an occasional lack of access to needed resources.

This Article consists of nine sections. Section I will provide an introduction to the most relevant theoretical justifications of the patent system. Section II will give an overview of the development in the biotechnology sector with its competing interests. Section III will define research tools. Section IV will analyze the blocking effect of patents in the biotechnology sector. Section V will argue for a broadened common law experimental use exemption to alleviate some of the concerns among

6. The U.S. Patent Act never had a compulsory licensing provision. Barton reports that there was substantial debate on compulsory licensing in the 1950s, but that it was violently opposed at the time he wrote the article. John H. Barton, *Patents and Antitrust: A Rethinking in Light of Patent Breadth and Sequential Innovation*, 65 ANTITRUST L.J. 449, 458 (1977). He favors compulsory licensing provisions as they increase the leverage of sequential inventors to obtain licenses for dependent improvements, thus heightening the incentive to conduct follow-on research. *Id.* at 453–55. See also Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 839 n.2 (1990) (providing further references). Compulsory licensing is generally viewed as contrary to the U.S. patent policy. See, e.g., *Dawson Chem. Co. v. Rohm & Haas Co.*, 448 U.S. 176, 215 (1980) (describing compulsory licensing as “rarity” in U.S. patent system); Merges & Nelson, *supra*, at 911 (describing compulsory licensing as an “anathema” and repeatedly rejected by the IP community). *But cf. infra* Part VII.B.4.b.

7. In response to criticism especially with regard to its application of the utility requirement, the U.S. Patent & Trademark Office (USPTO) raised the standard for utility when it issued its new Utility Examination Guidelines in 2001. See 66 Fed. Reg. 1092-99 (Jan. 8, 2001). The Federal Circuit’s decision in *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005), further alleviated concerns when the court affirmed the Board of Patent Appeals and Interferences’ rejection of a patent application directed to Expressed Sequence Tags (ESTs) without known function as lacking specific and substantial utility. Furthermore, one decision designated precedential by the Board of Patent Appeals and Interferences in 2007 indicates that, following the Supreme Court’s decision in *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), the USPTO attempted to re-invigorate the non-obviousness requirement in the field of biotechnology. *Ex parte Kubin*, 2007 WL 2070495 (B.P.A.I. May 31, 2007).

academic researchers by exempting from infringements experimentation on patented inventions. Section VI will provide an analysis of the yet unclear scope of the safe harbor provision of § 271(e)(1) with respect to research tools. Section VII will show why the use of research tools should neither be exempted under the common law exemption nor the safe harbor provision. Section VIII will address borderline cases where the distinction between “research on” and “research with” a patented research tool may arguably become blurred. Section IX will conclude with an outlook.

I. THE RATIONALE OF THE PATENT SYSTEM

The U.S. patent system derives its origin from the constitutional grant of power to Congress “[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.”⁸ It is strongly based on economic considerations and predominantly justified with utilitarian principles.⁹ Several different theoretical approaches have been used to evaluate how the patent system stimulates the technological progress, such as, the incentive to invent, the incentive to disclose and the incentive to invest.¹⁰ European patent scholars additionally draw on equity considerations embodied in the reward theories.¹¹ Economic literature has discussed and critically analyzed each of the approaches,¹² so that only a brief introduction to the incentive and reward based theories will be given.¹³

8. U.S. Const., art. I, § 8, cl. 8. See Eisenberg, *supra* note 3, at 1024.

9. See DONALD S. CHISUM ET AL., PRINCIPLES OF PATENT LAW (2004), 1–50 (discussing the theoretical and philosophical origin of the patent system with numerous references); FREDERIC M. SCHERER, INDUSTRIAL MARKET STRUCTURE AND ECONOMIC PERFORMANCE 440 (1980); Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1595–1615 (2003) (finding agreement among commentators that the basic purpose of the patent system is utilitarian and discussing the different theories); Eisenberg, *supra* note 3, at 1024–28 (describing in detail the theories that patents encourage innovation); F. Scott Kieff, *Property Rights and Property Rules for Commercializing Inventions*, 85 MINN. L. REV. 697, 697–98 (2001) (finding that while rights-based or “natural law” approaches exert some influence on the theoretical debate, the predominant approach is utilitarian).

10. See CHISUM ET AL., *supra* note 9, at 38–71; R. CARL MOY, MOY’S WALKER ON PATENTS §§ 1:26–42 (2003); Eisenberg, *supra* note 3, at 1025–46. See, for example, Roberto Mazzoleni & Richard R. Nelson, *Economic Theories about the Benefits and Costs of Patents*, 32 J. ECON. ISSUES 1031 (1998), for an economic analysis of the different theories.

11. See RUDOLF KRASSER, PATENTRECHT [Patent Law] 34–35 (2004).

12. See, e.g., Eisenberg, *supra* note 3, at 1024–46; Mazzoleni & Nelson, *supra* note 10.

13. Other approaches shall be briefly mentioned but not be considered for the purpose of this Article. The natural rights theories follow the teaching of Locke, arguing that the inventor should own the invention as it is derived from his (mental) labor. See John Locke, *The Second Treatise of Government*, in TWO TREATISES OF GOVERNMENT 327–44 (Peter Laslett

A. Patents to Induce Inventions

The most familiar and most intuitive theory about the economic function of patents is that they induce useful inventive activity.¹⁴ The theory rests on the assumption that certain inventions would not have been made without the prospect of receiving exclusive rights which protect their commercialization.¹⁵ Absent patent protection, competitors could easily appropriate inventions and may then have the competitive advantage that they did not have to bear the costs of invention.¹⁶

B. Patents as Incentive to Invest

The “incentive to invest” theory focuses on a patent’s function to induce investment for the development and commercialization of inventions.¹⁷ Under this theory, the patent system is not so much needed to stimulate inventive activity; rather, it facilitates investment into costly and risky development processes that are necessary to transform a “mere” invention into a marketable product.¹⁸ This function is particularly important in the biotechnology sector where a patent on a promising compound or technology can attract capital for product development.¹⁹

ed., Cambridge Univ. Press 1960) (1690). The Hegelian approach takes the view that, because an invention is imbued with the personality and labor of its inventor, it belongs to him as a natural right, like his freedom or personal space. See MARGARET J. RADIN, REINTERPRETING PROPERTY 44–48 (1993); cf., Universal Declaration of Human Rights, G.A. Res. 217A, art. 27, § 2, U.N. GAOR, 3d Sess., 1st plen. Mtg., U.N. Doc. A/810 (Dec. 12, 1948), available at <http://www.un.org/Overview/rights.html> (“Everyone has the right to the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he is the author.”). Newer theories rely closely on economic analysis. See F. Scott Kieff, *Coordination, Property & Intellectual Property: An Unconventional Approach to Anticompetitive Effects and Downstream Access*, 56 EMORY L.J. 327 (2006) (focusing on the coordination function of intellectual property rights); Robert P. Merges, *A Transactional View of Property Right*, (Mar. 10, 2005), <http://ssrn.com/abstract=707202> (focusing on their function to allow transactions of the protected subject matter and thus facilitating a more efficient allocation of goods).

14. Mazzoleni & Nelson, *supra* note 10, at 1032.

15. *Id.* at 1032; see also SCHERER, *supra* note 9, at 379–99; Eisenberg, *supra* note 3, 1024–25.

16. Eisenberg, *supra* note 3, at 1024–25.

17. See, e.g., Kieff, *supra* note 9; Mazzoleni & Nelson, *supra* note 10, at 1039–41. The “incentive to commercialize” theories comprise Kitch’s “Prospect Theory” which views the patent as an important means to providing incentives for further investment to increase the value of the patent; by allocating a broad right at an early stage, the patentee can coordinate research and prevent wasteful duplication of resources. Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265, 276–77 (1977).

18. Kieff, *supra* note 9, at 708–12.

19. Investors are motivated by the prospect of filing continuation applications which may also cover other indications (e.g., detection assay for further disorders). See Patent Law Revision: Hearing on H.R. 2795 Before the Subcomm. on Courts, the Internet, and Intellectual

C. Patents as Reward for Inventive Activity

The reward theories consider it a principle of justice to reward the inventor for his contribution to the economic and technological progress resulting from his inventive activity.²⁰ Conferring an exclusive right was viewed as the simplest and most adequate way of rewarding the inventor for his contribution because an inventor's profits will depend on the usefulness (i.e. commercial value) of his invention and be paid by the people benefiting from the invention—its users.²¹

D. Patents as Incentive (Reward) for the Disclosure of Knowledge

The “incentive to disclose” argument rests on the premise that—but for the patent system—inventors would not disclose their invention but rather keep them a (trade) secret in order to prevent competitors from exploiting them.²² The disclosure of an invention by virtue of the mandatory publication of the patent application increases the technical knowledge available to the general public.²³ Furthermore, the disclosure prevents wasteful duplication of research as third parties can build upon the knowledge of the invention.²⁴ The focus of the theory is not that patents are needed to stimulate invention, but to stimulate the disclosure of knowledge and to facilitate its quick dissemination.²⁵

Property of the H. Comm. on the Judiciary, 109th Cong. 6 (2005) (statement of Robert Chess, Executive Chairman, Nektar Therapeutics, testifying on behalf of the Biotechnology Industry Organization), available at <http://www.promotetheprogress.com/ptpfiles/patentreform/houseoversight/091505/prepared/chess.pdf>.

20. See, e.g., Friedrich-Karl Beier, *Die herkömmlichen Patentrechtstheorien und die sozialistische Konzeption des Erfinderrechts* [The Conventional Theories of Patent Law and the Socialist Conception of Inventor's Rights], GRUR 1970, 1, 3–4.

21. Beier, *supra* note 20.

22. See, e.g., Eisenberg, *supra* note 3, at 1028–30 (with further references) (stating that the theory is more popular with the courts than with commentators and questioning the economic soundness of the theory with respect to inventions that could be exploited in secret without the fear of competition). European commentators see the disclosure theory as related to the reward theory; however, the general underlying policy of stimulating technological progress remains the same for both reward and incentive theory. Cf., e.g., Rüdiger Rogge, in GEORG BENKARD, PATENTGESETZ, GEBRAUCHSMUSTERGESETZ [Patent Law, Utility Law] (C.H. Beck'sche Verlagsbuchhandlung 10th ed., 2006), Einleitung, marginal note 2; KRASSER, *supra* note 11, at 35; Beier, *supra* note 20, at 4–5 (noting that knowledge contained in millions of patent specifications would not have been made widely available but for the patent system). But see Yusing Ko, *An Economic Analysis of Biotechnology Patent Protection*, 102 YALE L.J. 777, 796 (1992) (pointing out that the incentive may only work where secrecy is not a viable option because of the ease of reengineering the invention; otherwise the inventor would prefer the possibility of perpetual protection through secrecy instead of a limited patent term).

23. Mireles, *supra* note 2, at 153–54.

24. Martin J. Adelman, *Property Rights Theory and Patent-Antitrust: The Role of Compulsory Licensing*, 52 N.Y.U. L. REV. 977, 982 (1977).

25. Mazzoleni & Nelson, *supra* note 10, at 1039. The disclosure theory—at least if understood as part of the incentive approaches—loses its persuasiveness where an invention

II. THE BIOTECHNOLOGY INDUSTRY

Biotechnology has become one of the key technologies of the 21st century and has already made an invaluable contribution to medicine, agriculture, and industry in the past.²⁶ Some perceived it as the last sector of America's technical superiority.²⁷ Still in nascent stages in the 1980s, the biotechnology sector has considerably grown in the last decades, with an increase in market capitalization from \$45 billion in 1994 up to \$410 billion in December 2005.²⁸ The total number of patents granted for biotechnological inventions has increased from 2160 patents in 1989 to 7763 patents in 2002.²⁹ The share of patents granted to publicly traded biotech companies has seen an even bigger increase from 393 in 1995 to a peak of 1966 in 2002, before sharply declining back to 1434 by the end of 2005.³⁰ Additionally, the ownership structure has changed considerably: while the majority of the biotech patents were held by a small number of large companies in the 1995, ownership has atomized to include numerous small enterprises.³¹

The biotechnology industry is highly innovative and very research intensive. Spending on research and development by commercial enterprises has increased to \$19.8 billion in 2005, up from \$7 billion in 1994.³² In view of the high costs of product development, the Biotech-

can be easily reverse-engineered; in such cases, trade secret protection does not constitute a viable alternative to patent protection as the invention cannot be exploited without giving the invention away. *See Paulik v. Rizkalla*, 760 F.2d 1270, 1276 (Fed. Cir. 1985) (en banc) (finding it rare that an invention "cannot be deciphered more readily from its commercial embodiment than from the printed patent."). *But see* Richard C. Levin et al., *Appropriating the Returns from Industrial Research and Development*, 862 COWLES FOUND. DISCUSSION PAPERS 783, 794-95 (1987), available at <http://ideas.repec.org/p/cwl/cwldpp/862.html> (finding empirical evidence that trade secret protection is viewed as more effective than patents for many process inventions).

26. *See generally* BRUCE ALBERTS, *MOLECULAR BIOLOGY OF THE CELL* (Garland Science 2002) (1989). For an overview of individual biotechnological achievements, *see* BIOTECHNOLOGY INDUSTRY ORGANIZATION, *GUIDE TO BIOTECHNOLOGY 6-15* (2007), available at <http://bio.org/speeches/pubs/er/BiotechGuide.pdf> [hereinafter BIO, INDUSTRY GUIDE].

27. Tanuja V. Garde, *Supporting Innovation in Targeted Treatments: Licenses of Right to NIH-Funded Research Tools*, 11 MICH. TELECOMM. & TECH. L. REV. 249, 253 (2005).

28. BIO, INDUSTRY GUIDE, *supra* note 26, at 3.

29. Mireles, *supra* note 2, at 143 n.6.

30. *See* Saurabh Aggarwal et al., *Insights into U.S. Public Biotech Sector Using Patenting Trends*, 24 NATURE BIOTECHNOLOGY 643, 643 (2006). The peak is likely to be the delayed result of the investment bubble in 2000. *Id.* at 644. In 2002, approximately 50% of the patents were granted to small biotech enterprises; however, whereas the number of patents granted to big biotechnological companies remained roughly the same during the decline of patenting in 2002-2005, the numbers granted to small firms decreased by more than 40%. *Id.*

31. *Id.* at 650.

32. BIO, INDUSTRY GUIDE, *supra* note 26, at 3. According to PhRMA, the biopharmaceutical industry spent an estimated \$55.2 billion on R&D in 2006, with \$43.0 coming from PhRMA member companies. *See* PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF

nology Industry Organization (BIO) views patents as “the needed assurance for investors to risk the capital necessary in the long development process,” allowing not only recoupment of the investment but also the generation of profits.³³

A. *The Dynamics after 1980*

In 1980, two events spurred the development of the U.S. biotech industry: the U.S. Supreme Court’s landmark decision *Diamond v. Chakrabarty*³⁴ and the adoption of the Government Patent Policy Act of 1980, better known as the Bayh-Dole Act.³⁵

In *Diamond v. Chakrabarty*, the court was faced with the question of patenting “life” when it had to decide on whether a genetically engineered organism for biologically controlling and decomposing oil spills constituted patentable subject matter.³⁶ The claims had been rejected as being directed to a living organism, or, in the alternative, as being directed to a product of nature.³⁷ The Supreme Court reversed and determined that the genetically modified organism was not a product of nature and interpreted the statutory language of § 101, “manufacture” and “composition of matter,” broadly, so as to encompass genetically modified organisms.³⁸ The decision became famous for its sweeping statement that statutory subject matter “include[s] anything under the sun that is made by man” and has led to a significant increase of biotechnological inventions.³⁹

The Bayh-Dole Act was promulgated to increase public access to government funded inventions which were perceived as

AMERICA, PHARMACEUTICAL INDUSTRY PROFILE 2 (2007), available at <http://www.phrma.org/files/Profile%202007.pdf>.

33. Biotechnology Indus. Org., Intellectual Property, <http://bio.org/ip/> [hereinafter BIO, IP] (last visited Feb. 10, 2008). BIO describes its mission as being “the champion of biotechnology and the advocate for its member organizations—both large and small.” Biotechnology Indus. Org., Mission Statement, <http://bio.org/aboutbio/mission> (last visited Feb. 10, 2008).

34. *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

35. Government Patent Policy Act of 1980, 35 U.S.C. §§ 200–12 (2003).

36. *Diamond*, 447 U.S. at 307.

37. Initially, the claims were rejected as being directed to a living organism or, alternatively, to a product of nature and thus unpatentable under § 101. The Board of Patent Appeals reversed the product of nature rejection and upheld only the rejection of the claims as being directed to a living organism, which in turn was reversed by the predecessor of the Court of Appeal for the Federal Circuit, the Court of Customs and Patent Appeals. *In re Bergy*, 596 F.2d 952, 977 (C.C.P.A. 1979). The Commissioner of Patents and Trademark petitioned for certiorari.

38. *Diamond*, 447 U.S. at 308.

39. *Id.* at 309. The decision evoked a spirited dissent by four Justices which considered upholding a patent on a living organism as an expansion of the subject matter patentable under § 101 which should be left to Congress. *Id.* at 319–22 (Brennan, White, Marshall & Powell JJ., dissenting). See also Garde, *supra* note 27, at 254.

under-commercialized.⁴⁰ It allowed universities to apply for patents for inventions resulting from government funded research and to transfer them to industry for development, including by means of exclusive licensing.⁴¹ Further, the legislation was enacted due to decreasing investment in research and development and the fact that the U.S. industry was falling behind in productivity compared to foreign competitors.⁴² Subsequently, the role of university research changed profoundly as universities became more actively involved in “undertaking sophisticated commercially-focused, high-risk research.”⁴³ Academic research has become more closely linked to the commercialization of research results through university transfer of technology offices, spin-offs, incubating mechanisms, joint ventures with for-profit enterprises, or sponsored research.⁴⁴

Since the inception of the Bayh-Dole Act, university patenting has increased from less than 250 in 1980 to more than 3800 in 2004.⁴⁵ Addi-

40. In the congressional hearings on the Bayh-Dole Act, Senator Stevenson pointed out that less than five percent of government-owned patents had been commercialized in 1979. See 126 CONG. REC. S1, 994–99 (Feb. 6, 1980) (statement of Sen. Stevenson).

41. Policies and Objectives of the Bayh-Dole Act include:

- . . . to use the patent system to promote the utilization of inventions arising from federally supported research or development;
- to encourage maximum participation of small business firms in federally supported research and development efforts;
- to promote collaboration between commercial concerns and nonprofit organizations, including universities;
- to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise . . .

35 U.S.C. § 200 (2005).

42. See Garde, *supra* note 27, at 254 & n.18 (referencing the relevant legislative history).

43. U.S. DEPT. OF COMMERCE, THE ADVANCED TECHNOLOGY PROGRAM: REFORM WITH A PURPOSE 5 (2002), available at http://www.atp.nist.gov/secy_rept/contents.htm [hereinafter ATP REPORT]. See generally Ian M. Cockburn, *O Brave New Industry, That Has Such Patents in It! Reflections on the Economic Consequences of Patenting DNA*, in PERSPECTIVES ON THE PROPERTIES OF THE HUMAN GENOME PROJECT 385 (F. Scott Kieff ed., 2003).

44. See ATP REPORT, *supra* note 43, at 5–6. For more detailed view on the changes of the role of universities, see MARTIN KENNEY, BIOTECHNOLOGY: THE UNIVERSITY-INDUSTRIAL COMPLEX (Yale Univ. Press 1986) and Walter W. Powell & Jason Owen-Smith, *Universities and the Market for Intellectual Property in the Life Sciences*, 17 J. POL'Y ANALYSIS & MGMT. 253 (1998). With respect to the specific changes in biotechnology, see Peter Shorett et al., *The Changing Norms of the Life Sciences*, 21 NATURE BIOTECHNOLOGY 123 (2003).

45. W. Mark Crowell, *A Message From the President* in ASS'N OF UNIV. TECH. MANAGERS, AUTM U.S. LICENSING SURVEY: FY 2004 (Ashley J. Stevens, Frances Toneguzzo & Dana Bostrom eds., 2005), available at <http://www.autm.net/events/File/04AUTMSurveySum-USpublic.pdf> [hereinafter AUTM SURVEY]. Whereas universities held only 1.1% of corporate owned patents issued between 1969 and 1986, the number has risen threefold to 4.8 % in 1999, then falling to 4.18% in 2005. See U.S. Patent and Trademark

tionally, more than 3100 new products resulting from university or non-profit research have entered the market between 1998 and 2004.⁴⁶ Whereas the Bayh-Dole Act has been successful in reaching its purpose in increasing cooperation between university and industry and in increasing the commercialization of inventions resulting from federally supported research,⁴⁷ the transition of the universities' role has not been universally considered beneficial, and concerns about the long-term implication of increased university patenting have been raised.⁴⁸

B. Diverging Interests in the Industry

The biotechnology industry consists of a very heterogeneous mixture of firms with often diverging, and sometimes opposing, interests.⁴⁹ It has become fashionable to refer to biotechnology firms as either belonging to the group of "tool companies" or to the group of "product companies."⁵⁰ Classic product companies like Amgen, Biogen, Chiron, or Genentech have to overcome substantial risks to develop a compound into a drug and perform the clinical studies required for its market approval. The development of a successful pharmaceutical drug costs between \$800 million and \$1.2 billion and extends over a period of 12 to 15 years.⁵¹ If successful, the assumption of such risks is rewarded by

Office, U.S. Colleges and Universities—Utility Patent Grants 1969–2005 (2005) http://www.uspto.gov/web/offices/ac/ido/oeip/taf/univ/asgn/table_1_2005.htm.

46. AUTM SURVEY, *supra* note 45.

47. See, e.g., Lita Nelsen, *The Rise of Intellectual Property Protection in the American University*, 279 SCI. 1460, 1460 (1998) (considering the Bayh-Dole Act as "one of the most successful pieces of economic development and job creation legislation").

48. ADAM B. JAFFE & JOSHUA LERNER, *INNOVATION AND ITS DISCONTENTS: HOW OUR PATENT SYSTEM IS ENDANGERING INNOVATION AND PROGRESS AND WHAT TO DO ABOUT IT* 67 (2004) (considering the proximity of commercial development and basic academic research in biotechnology as an important cause of potential conflicts between rights of "initial" inventors and the process of cumulative accumulation); Rebecca S. Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 YALE L.J. 177 (1987) (criticizing the lack of distinction between fundamentals of basic (upstream) research and downstream development and viewing the patenting of upstream research results as impairing the technological and economic progress); Nelson, *supra* note 2, at 467–70 (considering the increased patenting by universities as a result of the Bayh-Dole Act as a major part of the problem of blocking access to scientific research results); see also Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROBS. 289, 290–91 (2003); Michelle Cai, *Madey v. Duke University: Shattering the Myth of Universities' Experimental Use Defense*, 19 BERKELEY TECH. L.J. 175, 179 (2004).

49. Joseph Straus, *Reach-Through Claims and Research Tools as Recent Issues of Patent Law*, in ESTUDIOS SOBRE PROPIEDAD INDUSTRIAL E INTELLECTUAL Y DERECHO DE LA COMPETENCIA, COLLECTION OF ARTICLES IN HONOUR TO ALBERTO BERCOVITZ RODRIGUEZ-CANO 921 (2005). For a good overview of the biotech industry in the U.S. with short profiles of some of the major players, see Aggarwal et al., *supra* note 30.

50. Cockburn, *supra* note 43, at 387.

51. *The Patent Reform Act of 2007: Hearing on H.R. 1908 Before the Subcomm. On Courts, the Internet, and Intellectual Property of the H. Comm. on the Judiciary*, 110th Cong.

commensurate returns from the sale of the proprietary product. By contrast, tool companies like Celera, Quiagen, Human Genome Sciences, or Millennium seek commercial return from the development of research technologies and their sale to product developers.⁵² Naturally, both groups have a different perception of the appropriate scope of research tool patents. For drug development companies, research tools are necessary inputs for their research, and consequently they are interested in having access at the lowest possible cost; for the tool companies, however, research tools represent their lifeblood, and the patents protecting them are often their only assets.⁵³

The significant role of research tools can also be deduced from the fact that research tool patents have been found to constitute the largest component in the patent portfolios of biotech and pharmaceutical companies, often amounting to more than 60% of the number of patents.⁵⁴

(2007) (testimony of Kevin Sharer, CEO and Chairman of the Board, Amgen, Inc.), available at <http://judiciary.house.gov/media/pdfs/Sharer070426.pdf>. A new study estimates the costs for the development of a successful biopharmaceutical also at \$1.2 billion. Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 *MANAGERIAL & DECISION ECON.* 469, 469 (2007) (The average capitalized costs of \$1241 million can be divided into \$615 million for the preclinical period and \$626 million for the clinical period.). See also CHRISTOPHER ADAMS & VAN V. BRANTNER, *SPENDING ON NEW DRUG DEVELOPMENT* (2005), available at <http://ssrn.com/paper=869765> (estimating the average cost of bringing a new pharmaceutical drug to the market to over \$1 billion); TUFTS CTR. FOR THE STUDY OF DRUG DEV., *OUTLOOK 2007* 10 (2007) <http://csdd.tufts.edu/infoservices/outlookpdfs/outlook2007.pdf> (estimating the average cost of a new biotechnology product at \$1.2 billion).

52. Straus, *supra* note 49, at 921. See also David Malakoff & Robert F. Service, *Genomania Meets the Bottom Line*, 291 *SCI.* 1193 (2001) (providing a detailed overview of the different categories of tool (and service) companies and the products (and services) they offer).

53. PHILIP W. GRUBB, *PATENTS FOR CHEMICALS, PHARMACEUTICALS, AND BIOTECHNOLOGY: FUNDAMENTALS OF GLOBAL LAW, PRACTICE AND STRATEGY* 412 (4th ed. 2004); Aggarwal et al., *supra* note 30 at 650. See also James H. Davis & Michele M. Wales, *The Effect of Intellectual Property on the Biotechnology Industry*, in *PERSPECTIVES ON THE PROPERTIES OF THE HUMAN GENOME PROJECT* 427–28 (F. Scott Kieff ed., 2003) (stating that enterprises in the biotechnological industry exert their competitive advantage solely due to intellectual property rights); FEDERAL TRADE COMMISSION, *TO PROMOTE INNOVATION: THE PROPER BALANCE OF COMPETITION AND PATENT LAW AND POLICY* ch. 3 at 20 (2003), available at <http://www.ftc.gov/os/2003/10/innovationrpt.pdf> [hereinafter *FTC REPORT*] (reporting that panelists stressed the importance of patenting research tools for biotechnological companies. “[I]f there’s anything you want to protect and incent with patents, it’s the research tool technology.”).

54. Michael M. Hopkins et al., *DNA Patenting: The End of an Era?*, 25 *NATURE BIOTECHNOLOGY* 185, 186 (2007). Besides an analysis of patent application and grant data, the surveyors interviewed representatives from 10 biotech firms, 10 pharma firms and 10 public sector research entities which were among the top 50 most active assignees in the field and collectively owned close to 30% of the patent families in the surveyed data set. See also Kevin E. Noonan et al., *Paradise Lost: The Uncertain Future of Research Tool Patents*, 15 *INTELL. PROP. & TECH. L.J.* 1, 8 n.53 (2003) (reporting that “most biotechnology intellectual property concerns reagents and methods for drug discovery and development”).

BIO describes intellectual property as the “key factor for economic growth and advancement in the biotechnology sector” and patents as a critical incentive for investment in the biotechnology industry.⁵⁵ Venture capital, a vital source of funding for the biotechnology industry, has influenced the industry significantly since the creation of the first biotechnological start-up company (Genentech) in 1975.⁵⁶ It still remains an important source of funding for biotechnological startup companies.⁵⁷ Once venture capitalists target a suitable market for investment, they will base their decision on a company’s ability to defend their technological market advantage through their patent rights.⁵⁸ The patent position of a company can have decisive influence on whether the company can continue on the market or whether it will disappear.⁵⁹

Drug development companies often form research cooperations with research tool companies, funding their research on specific compounds in exchange for access to the discovered compounds.⁶⁰ In the majority of cases, the discovered compounds, such as proteins, cell-lines, or receptors, will not become an active component of the final drug, but will “merely” function as research tools, for example, for the identification or isolation of suitable drug compounds or for the testing of their specific biological properties.⁶¹ Consequently, licensing their use in research is often the only way to extract economic return from the invention.

III. DEFINING BIOTECHNOLOGY RESEARCH TOOLS

The rapid progress in biotechnological research has provided many new insights into the functioning of the human body, the development of diseases, their causation, and possible methods for their treatment. A crucial means for gaining these insights and exploring the scientific relationship is the use of different types of research tools, whose availability has created a revolution in biomedical research and has turned the

55. BIO, IP, *supra* note 33.

56. Terry C. Bradford, *Evolving Symbiosis—Venture Capital and Biotechnology*, 21 NATURE BIOTECHNOLOGY 983, 983 (2003).

57. *Id.* at 984.

58. FTC REPORT, *supra* note 53, ch. 2 at 1 (“Biotechnology start-ups rely on their ability to patent their innovations to attract investment and continue innovating. . .”).

59. *Id.* ch. 3 at 18 (“The venture capital accessed through patents thus enables not-yet-profitable companies to ‘sustain . . . innovation through massive investments in research and development.’”); Eisenberg, *supra* note 3, at 1039.

60. An example is the cooperation of Merck KGaA and The Scripps Research Institute on the research on potential drug candidates that might inhibit angiogenesis which is the object of patent infringement litigation and the Supreme Court decision *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005). See *infra* Part VI.A.1–4.

61. Esther Pfaff, “Bolar” Exemptions—A Threat to the Research Tool Industry in the U.S. and the EU?, 38 IIC. 258, 260 (2007); Derzko, *supra* note 3, at 348.

research process “from one of controlled serendipity to one of extremely high probability of serendipity.”⁶² Research tools have played a significant role in promoting rapid technological development,⁶³ as well as in facilitating and accelerating the introduction of new diagnostic and therapeutic products and methods.⁶⁴

While there is no generally accepted definition of research tools,⁶⁵ the Federal Trade Commission (FTC) proposes the following narrow definition: “a technology that is used by pharmaceutical and biotechnology companies to find, refine, or otherwise design and identify a potential product of properties of a potential drug product. As such, it serves as a springboard for follow-on innovation.”⁶⁶

Essentially, the FTC definition distinguishes research tools from products with commercial application by the market they serve.⁶⁷ Research tools are sold generally to private and public scientists,⁶⁸ whereas the market for commercial applications consists of the general public.⁶⁹ However, this distinction does not take into consideration that research tools may also serve both markets and would seem to exclude research tools that have an additional commercial application beyond their use in a laboratory setting.⁷⁰ Therefore, the broader, more inclusive definition proposed by the National Institutes of Health will be adopted for the purpose of this Article:

We use the term “research tool” in its broadest sense to embrace the full range of resources that scientists use in the laboratory, while recognizing that from other perspectives the same resources may be viewed as “end products.” For our purposes, the

62. Robert Blackburn, *Research Tools in the Biotechnology Industry and the Hatch-Waxman Act*, Presentation at the 2001 High Technology Summit Conference University of Washington, Seattle, in Symposium Series No. 7, July 2002, at 28, available at <http://www.law.washington.edu/CASRIP/Symposium/Number7/1-Blackburn.pdf>.

63. See generally *infra* notes 75–82 and accompanying text.

64. Malakoff & Service, *supra* note 52; FTC REPORT, *supra* note 53, ch. 3 at 19 (“[A] panelist suggested that research tools have led to a considerable reduction in the cost and time required for the targeting of therapeutic antibodies during the initial stages of new drug research.”).

65. The very attempt to define a category of research tools has been criticized because it is sometimes impossible to distinguish between “things that are used only in the laboratory and things that might potentially be sold to non-research consumers.” Derzko, *supra* note 3, at 352. As an example, Derzko names a DNA sequence that, at first, is thought to be useful only for research purposes but ultimately turns out to be a diagnostic marker or to encode a therapeutic protein. *Id.*

66. FTC REPORT, *supra* note 53, ch. 3 at 18.

67. *Id.*

68. See Malakoff & Service, *supra* note 52.

69. See FTC REPORT, *supra* note 53 ch. 3 at 18.

70. Derzko, *supra* note 3, at 352. See also Mireles, *supra* note 2, at 149 (recognizing the fact without drawing any consequences).

term may thus include cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry libraries, drugs and drug targets, clones and cloning tools (such as PCR), methods, laboratory equipment and machines, databases and computer software.⁷¹

For purposes of this article, research tools that have no use but in research (i.e. research tools according to the FTC definition) will be referred to as “pure research tools” and research tools with a further commercial application will be referred to as “dual purpose research tools.”⁷² Regardless of how the term “research tool” is defined, it should be noted that the term is not neutral, but already reflects the perspective of a consumer and not of the manufacturer.⁷³ From the manufacturer’s perspective, research tools are end products, not merely intermediate products necessary for production of an end product.⁷⁴

Examples of patented research tools include the following:

(1) Recombinant DNA techniques.⁷⁵ The method and plasmids for gene cloning developed by Cohen and Boyer were deemed the founding technology for the biotechnology industry.⁷⁶ The respective patents were co-owned by Stanford University, University of California,

71. NATIONAL INSTITUTES OF HEALTH, REPORT OF THE NATIONAL INSTITUTES OF HEALTH (NIH) WORKING GROUP ON RESEARCH TOOLS (June 4, 1998), <http://www.nih.gov/news/researchtools/index.htm> [hereinafter NIH, RESEARCH TOOLS]. The Guidelines issued by NIH for recipients of NIH research grants use the terms “unique research resource” and “biomedical research resource” instead of research tools. The terms “research tools” and “materials” are used . . . interchangeably with “unique research resources.” Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources: Final Notice, 64 Fed. Reg. 72,090, 72,092 n.1 (Dec. 23, 1999). The notable difference from the definition of the NIH Research Tool Working Group, however, is that this definition does not include drugs or drug targets.

72. Derzko starts with the same distinction, however she uses the term “partial research tools” for dual purpose research tools. Derzko, *supra* note 3, at 353. However, dual use seems more appropriate as the other term would imply that the compound is only partially suitable for research, which is not the case.

73. Derzko, *supra* note 3, at 350. The different perspectives are already acknowledged in the summary of the NIH Report: “One institution’s research tool may be another institution’s end product.” See NIH, RESEARCH TOOLS, *supra* note 71. The report further showed that private firms were concerned with the broad definition of “research tools” due the difficulty of distinguishing between pure research tools and research tools considered to be a final product potentially sold to the general public. *Id.*

74. Derzko, *supra* note 3, at 350; Davis & Wales, *supra* note 53, at 434.

75. U.S. Patent No. 4,237,224 (filed Jan. 4, 1979) (issued Dec. 2, 1980) (directed to the method); U.S. Patent No. 4,468,464 (filed Nov. 9, 1978) (issued Aug. 28, 1984) (directed to plasmids).

76. See Tim Beardsley, *Big-Time Biology*, SCI. AM., Nov. 1994, at 90. Cohen and Boyer received the Lemelson-MIT Prize in 1996 and the Albany Medical Center Prize in Medicine in 2004 in recognition of this outstanding achievement.

San Francisco, Cohen, and Boyer, and widely licensed on non-exclusive and inexpensive terms.⁷⁷

(2) Polymerase chain reaction (PCR). PCR allows the selective and exponential amplification of DNA or RNA sequences using Taq-Polymerase.⁷⁸ The technology became a vital tool for researching and analyzing genes in biological samples; without it, the sequencing of the human genome would not have been possible.⁷⁹ The patents had been assigned by Cetus to Hoffmann-LaRoche who tied respective licenses to the purchase of other Hoffmann-LaRoche products. License terms diverged depending on the licensee and, since the terms were not nearly as welcoming as licenses to the Cohen-Boyer patents, have been met with criticism.⁸⁰

(3) Animal models, such as the Harvard Oncomouse.⁸¹ The mouse was genetically modified to be susceptible to developing cancer and is a useful tool in cancer research.

77. Merges & Nelson, *supra* note 6, at 906. For details and an analysis of the licensing situation, see NATIONAL RESEARCH COUNCIL, INTELLECTUAL PROPERTY RIGHTS AND THE DISSEMINATION OF RESEARCH TOOLS IN MOLECULAR BIOLOGY: SUMMARY OF A WORKSHOP HELD AT THE NATIONAL ACADEMY OF SCIENCES, FEBRUARY 15–16, 1996 42–44 (1997), available at http://books.nap.edu/openbook.php?record_id=5758&page=42 (use the forward button above the text to navigate to the other pages) [hereinafter NAS WORKSHOP RESEARCH TOOLS] and Irving N. Feit, *Biotechnology Research and the Experimental Use Exception to Patent Infringement*, 71 J. PAT. & TRADEMARK OFF. SOC'Y 819, 820 (1989).

78. For details on the invention of PCR, see PAUL RABINOW, MAKING PCR (1996). The inventor of Taq polymerase, Kary Mullis, shared the Nobel Prize for Chemistry in 1993 for the revolutionary work. NAS WORKSHOP RESEARCH TOOLS, *supra* note 78, at 43.

79. NAS WORKSHOP RESEARCH TOOLS, *supra* note 78, at 43 ("Tom Caskey, senior vice-president for research at Merck Research Laboratories and past-president of the Human Genome Organization, attributes much of the success of the Human Genome Project to PCR: 'The fact is that, if we did not have free access to PCR as a research tool, the genome project really would be undoable . . . Rather than bragging about being ahead, we would be apologizing about being behind.'").

80. Some participants of the NAS Workshop "Research Tools" reported that the costs for Taq-polymerase had made some research projects unfeasible. For small biotechnological entrant companies, the use of the PCR technology was too expensive and prevented them from developing further PCR research tools. NAS WORKSHOP RESEARCH TOOLS, *supra* note 78, at 44.

81. U.S. Patent No. 4,736,866 (filed June 22, 1984) (issued Apr. 12, 1988); European Patent No. 0169672 (filed June 24, 1985) (issued May 13, 1992) (both directed to transgenic non-human mammalian animals).

(4) Expressed Sequence Tags (ESTs).⁸² Expressed Sequence Tags (ESTs) are small pieces of cDNA with lengths of 200 to 500 bp.⁸³ They are primarily used for the discovery or identification of expressed genes, for the identification of coding regions in genomic sequences, or as a marker to locate a gene on a physical map of a genome.⁸⁴ The patentability of ESTs has been controversially debated⁸⁵ because the patent applications often disclosed only a general utility, such as the “use as a marker.”⁸⁶ However, the Federal Circuit’s decision in *In re Fisher*

82. According to John Doll, Director at the USPTO, more than 2,300 patents for gene sequences had been granted by the USPTO until May 2001. Henrik Holzapfel, *Die patentrechtliche Zulässigkeit der Benutzung von Forschungswerkzeugen* [The Admissibility of the Use of Biotechnological Research tools under Patent Law], in GRUR INT. 2006, 10, 11 n.3 (2006) [hereinafter Holzapfel, *Research Tools*]. Incyte Pharmaceuticals alone is reported to have filed more than 400,000 patent applications for gene sequences. Timothy A. Worrall, *The 2001 PTO Utility Examination Guidelines and DNA Patents*, 16 BERKELEY TECH. L.J. 123, 127–28 (2001). For information on relevant patent statistics and applicants’ strategies, see, for example, ALEXANDER R. KREFFT, PATENTE AUF HUMAN-GENOMISCHE ERFINDUNGEN [Patents on Human Genomic Inventions] 47–49 (2003); Martin Bobrow & Sandy Thomas, *Patents in a Genetic Age*, 409 NATURE 763 (2001); Molly A. Holman & Stephen R. Munzer, *Intellectual Property Rights in Genes and Gene Fragments: A Registration Solution for Expressed Sequence Tags*, 85 IOWA L. REV. 735 (2000); Joseph Straus, *Abhängigkeit bei Patenten auf genetische Information—ein Sonderfall?* [Dependency of Patents on Genetic Information—A Special Case?], GRUR 1998, 314; Worrall, *supra*.

83. They are produced either by reverse transcription of short mRNA sequences isolated from a mix of mRNA representing expressed genes or from random parts of cDNA taken from cDNA libraries. See Mark D. Adams et al., *Complementary DNA Sequencing: Expressed Sequence Tags and Human Genome Project*, 252 SCIENCE 1651, 1652 (1991). For more information on cDNA, see generally, Oak Ridge National Laboratory, Human Genome Project Information, http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml (last visited Mar. 5, 2008); National Center for Biotechnology Information, A Science Primer—Just the Facts: A Basic Introduction to the Science Underlying NCBI Resources, ESTs: Gene Discovery Made Easier, <http://www.ncbi.nlm.nih.gov/About/primer/est.html> (last visited Mar. 5, 2008).

84. See Mark D. Adams, et al., *supra* note 83, at 1651; Human Genome Organization (HUGO), *Statement on the Patenting of DNA Sequences*, HUGO EUROPE GENOME DIGEST, Apr. 1995, at 6–9.

85. See, for example, the discussion spurred by the application submitted by Craig Venter for the National Institutes of Health (NIH), which was later abandoned. It was directed to numerous ESTs without known function and published January 7, 1991 as WO9300353. For details on the NIH application with detailed analysis of the different views within NIH and internationally, see, JOSEPH STRAUS, GENPATENTE [Gene Patents] 43–45 (1997), Rebecca S. Eisenberg, *Genes, Patents, and Product Development*, 257 SCI. 903 (1992), Rainer Muffang, *Patentierung menschlicher Gene, Zellen und Körperteile?* [Patenting of Human Genes, Cells, and Body Parts?] GRUR INT. 1993, 439, 441–43. See also KEVIN DAVIES, CRACKING THE GENOME 61–64 (2001).

86. Cf., e.g. Lopez-Beverage, *supra* note 2, at 73. The utility requirement is one of the patentability requirements of 35 U.S.C. § 101 provides: “Whoever invents or discovers any new and *useful* process, machine, manufacture, or composition of matter, or any new and *useful* improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.” (emphasis added). Furthermore, § 112(1) provides: “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

invalidated such claims for lack of utility and enablement, and should have alleviated at least part of these concerns.⁸⁷

The classification from a user's perspective is less controversial for biological discoveries, such as (partial) gene sequences, promoters, ligands and receptors controlling pathological symptoms, and methods for their identification or manufacture. Nevertheless, even this group of compounds and methods, often referred to as "upstream discoveries,"⁸⁸ may be the result of considerable research. Even if only their manufacturer viewed such upstream tools as final products, the public may also start viewing such tools as end products where further research shows that a research tool may ultimately be used for a diagnostic or therapeutic purpose.⁸⁹ For example, a gene sequence originally used only for research purposes may turn out to be useful as a diagnostic marker or for gene therapy. These additional uses widely broaden the potential market of such products, expanding it from the market for laboratories to the often much more valuable market for consumer applications.⁹⁰

IV. BLOCKING PATENTS

The problem of blocking patents in biomedical research was first perceived in the context of the patenting of genes. Gene patenting developed mostly unnoticed and, initially, did not generate much public

art to which it pertains, or with which it is most nearly connected, to make and use the same. . . ." (emphasis added). See also Tanya Wei, *Patenting Genomic Technology—2001 Utility Examination Guidelines: An Incomplete Remedy in Need of Prompt Reform*, 44 SANTA CLARA L. REV. 307 (2003).

87. *In re Fisher*, 421 F.3d 1365, 1379 (Fed. Cir. 2005). In this case, the claims were directed to ESTs isolated from the maize genome. The disclosed utilities included identification of polymorphisms, use as a probe or use as source for a primer. Relying on *Brenner v. Manson*, the Court determined that the patent application failed to meet the threshold of substantial and specific utility because no function of the underlying genes was known and thus the ESTs had to be considered mere research intermediates for conducting further research on the maize genome. *Id.* at 1370–75 (citing *Brenner v. Manson*, 383 U.S. 519 (1966)). The disclosed functions were deemed unspecific and without real world use because they would be performed by any EST. Indeed, the applicant was unable to show that any of the ESTs had actually been used to identify a single polymorphism or promoter, or that a polymorphism or promoter so identified would have a substantial and specific use. *Id.* at 1373–74. Cf. Revised Utility Examination Guidelines, 66 Fed. Reg. 1092–99 (Jan. 8, 2001).

88. *Derzko*, *supra* note 3, at 351.

89. NIH, RESEARCH TOOLS, *supra* note 71, at 13.

90. That products may be marketed only to research laboratories does not imply a different appraisal per se, as they are serving the needs of a market in its own right. Numerous biotechnological firms serve this market and are specialized in the production of such research tools as Invitrogen, Incyte, Human Genome Science or Celera Genomics. See Straus, *supra* note 49, at 922.

controversy,⁹¹ unlike the patenting of the first living organisms,⁹² or the expansion of patentable subject matter to software⁹³ and business methods.⁹⁴ The issue reached the public conscience for the first time with the beginning of the Human Genome Project. In 1991, Craig Venter, then working at the National Institutes of Health (NIH), submitted an application for a patent covering numerous ESTs with unknown functions.⁹⁵ Early on, patents were granted for genes coding for known and sought after proteins, a practice that was not perceived as being very different from drug patenting.⁹⁶ However, when the first patent applications were submitted for DNA sequences with unknown functions far removed from a final pharmaceutical product, the perception changed considerably and such applications were compared to the attempt to patent scientific information.⁹⁷ It was feared that the patenting of important parts of scientific knowledge—knowledge that would previously have been made available to the general public without proprietary restrictions—would lead to a privatization of the scientific commons which would adversely influence the future progress of science and technological progress.⁹⁸

91. Peter F. Corless, *Recombinant DNA Inventions after Fiers*, 16 HOUS. J. INT'L L. 503 (1994). A primary reason may have been that the patents for genes closely corresponded to foreseeable commercial products such as the diagnostic test for specific genes or useful proteins. Rebecca S. Eisenberg, *Reaching Through the Genome*, in PERSPECTIVES ON THE PROPERTIES OF THE HUMAN GENOME PROJECT, 209–10 (F. Scott Kieff ed., 2003).

92. *Diamond v. Chakrabarty*, 447 U.S. 303, 305 (1980) (upholding a patent of oil eating bacteria). It was, as the court noted, not the first patent containing claims to a living micro-organism; however it was the first time the Supreme Court addressed the issue. *Id.* at 314 n.9. For the patenting of the first animal, see *Ex parte Allen*, 2 U.S.P.Q. (BNA) 1424 (B.P.A.I. 1987) (allowing a patent on a transgenic mouse).

93. *Diamond v. Diehr*, 450 U.S. 175, 177 (1981).

94. *State St. Bank & Trust v. Signature Fin. Group*, 149 F.3d. 1368, 1370 (Fed. Cir. 1998).

95. The application, which was later abandoned, was published on January 7, 1991 as WO9300353. For more details especially on the NIH application with detailed analysis of the different view within NIH and internationally, see STRAUS, *supra* note 85, at 43–45, Eisenberg, *supra* note 85, and Moufang, *supra* note 85, at 441–43. The Intellectual Property Committee of the Human Genome Organization commented that ESTs should be understood as research tools and that a patenting of short sequences of randomly isolated portions of genes and transcripts encoding proteins of uncertain functions should not be allowed. Furthermore, the committee expressed its opinion that “DNA molecules and their sequences, be they full-length, genomic or cDNA, ESTs, SNPs or even whole genomes of pathogenic organisms, if of *unknown function or utility*, as a matter of policy, in principle, should be viewed as pre-competitive information.” HUGO INTELLECTUAL PROPERTY COMMITTEE, STATEMENT ON THE PATENTING OF DNA SEQUENCES, in PARTICULAR RESPONSE TO THE EUROPEAN BIOTECHNOLOGY DIRECTIVE (2000), <http://www.hugo-international.org/PDFs/Statement%20on%20Patenting%20of%20DNA%20Sequences%202000.pdf> (emphasis added).

96. Eisenberg, *supra* note 91, at 210–11.

97. *Id.*

98. Nelson, *supra* note 2, at 464–66. However, Nelson remains pessimistic in how far patent law will be able to address the problem as lines between research outputs that provide

The problem of access to research tools is perceived as more acute and is better documented in biotechnology than in any other scientific field.⁹⁹ This may be partly due to the high intensity of research being undertaken in the biotechnology industry,¹⁰⁰ and partly due to the perceived restrictions on the developments of new methods of treatment for common diseases. Commentators have voiced their concern that patent owners of research tools restrict the necessary access to research tools for fundamental and basic research by not licensing their proprietary technology or by charging premium prices.¹⁰¹ Due to the scientific complexity of biotechnology research, investigators need access to a higher number of research tools than in other industries.¹⁰² The number of proprietary rights needed to conduct research respectively for the exploitation of a final product may render certain research projects financially infeasible and thus lead to a situation Heller and Eisenberg termed as the “tragedy of the anticommons.”¹⁰³ They feared that “[a] proliferation of intellectual property rights upstream may be stifling life-saving innovations further downstream in the course of research and product development.”¹⁰⁴

tools for advancing a technology and final processes or products per se will remain blurred. *Id.* at 466.

99. Mueller contrasts the field of biotechnological research with the development of software where no difficulties with the access to proprietary research tools have been documented. Mueller, *supra* note 1, at 11. This has not changed in the years after the publication of her article—access to research tools is still discussed only as a problem in the area of biomedical research.

100. The biotechnological industry spent close to \$20 billion on research in 2005. BIO, INDUSTRY GUIDE, *supra* note 26, at 4.

101. See, e.g., Rai & Eisenberg, *supra* note 48, at 295–96.

102. Garde, *supra* note 27, at 251; Mueller, *supra* note 1, at 12 (referring to DNA chip technology making use of up to 40,000 gene sequences which would need to be licensed). See also ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT (OECD), GENETIC INVENTIONS, INTELLECTUAL PROPERTY RIGHTS AND LICENSING PRACTICES 7 (2002), available at <http://www.oecd.org/dataoecd/42/21/2491084.pdf> (“Biotechnology is a fast-moving field in which new products and services are developed from an increasingly complex and cumulative set of underlying technologies.”); NIH, RESEARCH TOOLS, *supra* note 71 (“Biomedical researchers increasingly chose to collaborate with entrepreneurial companies that understood and valued basic science . . .”).

103. Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698 (1998). Heller coined the term “Tragedy of the Anticommons” describing a situation of underuse of assets as a result of too many owners having the right to exclude each other from the use of a scarce resource without anyone having an affirmative right to use. Michael A. Heller, *The Tragedy of the Anticommons: Property in the Transition from Marx to Markets*, 111 HARV. L. REV. 621, 660 (1998).

104. Heller & Eisenberg, *supra* note 103, at 698. Heller and Eisenberg define “upstream” as pre-market (research), as opposed to downstream, which they define as products for diagnostic or therapeutic treatment. *Id.* However, “downstream” and “upstream” is always a relative term depending on the perspective of the user. Even the adjective “pre-market” can be misleading because there is a market for the products of so called “upstream” research, namely the market for research tools. In contrast, under the situation of a “Tragedy of the

Early data seemed to confirm these fears. A survey conducted in 1998 by the NIH Working Group on Research Tools found researchers in all areas of the biotechnology industry in agreement that “the stacking of intellectual property obligations as successive tools are used in the course of an extended research project has the potential to impede or even preclude the development of new and better diagnostic and therapeutic products.”¹⁰⁵ They further reported a widespread belief among interviewed firms that restricted access to research tools impedes the rapid advance of research and that the situation is constantly aggravating.¹⁰⁶ Whereas the study conducted by Walsh and Cohen reported only anecdotal evidence of an existence of anticommons,¹⁰⁷ and a study of the American Association for the Advancement of Science found a slightly higher but still small negative impact,¹⁰⁸ two further studies seem to

Commons” described by Hardin 30 years earlier, numerous people have the right to use a common resource without anyone having the right to exclude the other from such use, which leads to an overuse, and, eventually, to the depletion of a common good. Garret Hardin, *The Tragedy of the Commons*, 162 *Sci.* 1243, 1244 (1968).

105. NIH, RESEARCH TOOLS, *supra* note 71. Based on this report, Mueller described the anticommons theory as “far from a merely academic construct.” Mueller, *supra* note 1, at 7.

106. NIH, RESEARCH TOOLS, *supra* note 71.

107. JOHN P. WALSH ET AL., FINAL REPORT TO THE NATIONAL ACADEMY OF SCIENCES’ COMMITTEE INTELLECTUAL PROPERTY RIGHTS IN GENOMIC AND PROTEIN-RELATED INVENTIONS: PATENTS, MATERIAL TRANSFERS AND ACCESS TO RESEARCH INPUTS IN BIOMEDICAL RESEARCH 37–40 (2005). The study reports that none of the researchers actually discontinued a research project and only a small percentage changed their research approach or experienced a delay of more than one month. It suggests that industry and academia have arrived at working solutions. *Id.* See also Timothy Caulfield, et al., *Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies*, 24 *NATURE BIOTECHNOLOGY* 1091, 1092 (2006) (finding that “the effects predicted by the anticommons problem are not borne out in the available data” and that a statistically significant effect can be found only with respect to gene patents covering diagnostic tests); Richard A. Epstein & Bruce N. Kuhlik, *Is There a Biomedical Anticommons?*, *REG.*, Summer 2004, at 54 (stating that Heller and Eisenberg “have overstated the case against patent protection at both the theoretical and empirical levels.”). *But see* Paul A. David, *The Economic Logic of “Open Science” and the Balance Between Private Property Rights and the Public Domain in Scientific Data and Information: A Primer* 13–16 (Stanford Inst. for Econ. Pol’y Res., SIEPR Discussion Paper No. 02-30, 2003), available at <http://siepr.stanford.edu/papers/pdf/02-30.pdf>. David criticizes the value of such studies (his comments relate to the earlier Walsh/Cohen study of 2002, though) as it will be hard to prove the absence of a “tragedy of anticommons” because the research is aimed at proving a counterfactual issue. Rational researchers are not likely to report abandoned projects that they would otherwise have undertaken had the law not changed. *Id.* at 16.

108. STEPHEN HANSEN, ET AL., THE EFFECTS OF PATENTING IN THE AAAS SCIENTIFIC COMMUNITY 7 (2006), available at http://sippi.aaas.org/survey/AAAS_IP_Survey_Report.pdf. The study found that 35% of academic researchers in biotechnology had difficulties in procuring the necessary licenses to relevant IP rights in a five-year period. The number was even higher for industry respondents, 76% of which reported that their studies had been affected by difficulties in obtaining patented technologies. *Id.* However, as only 30% of the academic respondents and 53% of industry respondents attempted to procure a license, the percentages drop to 11% (for academia) and 40% (for industry). *Id.* at 14, 21. Using the industry-unspecific percentages categorizing the delay, only 6% of the projects were delayed (23

support the finding of a statistically relevant blocking effect (Murray & Stern and Sampat).¹⁰⁹ However, Sampat describes the negative effect on subsequent research as being confined to gene sequences rather than other genomic technologies which are described as easier to invent around and thus are more likely to be licensed liberally.¹¹⁰ Furthermore, the impact on the overall public welfare is not immediately clear because the patent incentive may be necessary to induce a firm to invest in the development of genomic technology even if it reduces scientific research later down the road.¹¹¹ Additionally, where specific research projects are blocked by patents, the impact on the overall welfare depends on which alternative project the researcher pursues with the time and resources available to him. In other words, it depends on the “productivity of the ‘next best’ scientific trajectory.”¹¹²

V. THE COMMON LAW EXEMPTION

This section begins with an analysis of U.S. law on the common law experimental use exemption (A) and contrasts it with the European approach (B). Subsequently, it will be argued why the European approach better reflects the rationale of the patent system (C).

respondents), 5% of the projects needed to be changed (20 respondents), and 2% of the projects had to be abandoned (10 respondents). *Id.* at 22.

109. Fiona Murray & Scott Stern, *Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge? An Empirical Test of the Anti-Commons Hypothesis 5* (Nat'l Bureau of Econ. Res., Working Paper No. 11465, 2005), available at <http://www.nber.org/papers/w11465.pdf> (finding a modest anticommmons effect based on decline of the citation rate after the patent grant between nine and seventeen percent); Bhaven N. Sampat, *Genomic Patenting by Academic Researchers: Bad for Science?* (2004) (on file with author) (surveying the impact of genomic patenting on academic research).

110. Sampat, *supra* note 109, at 26–28; see also E. Jonathan Soderstrom, President-Elect, Ass'n of Univ. Tech. Managers, Statement Before the House Committee on the Judiciary on “Stifling of Stimulating—The Role of Gene Patents in Research and Genetic Testing,” 2–3, 5 (Oct. 30, 2007) available at <http://judiciary.house.gov/media/pdfs/Soderstrom071030.pdf> (testifying that only anecdotal evidence of an anticommmons effect has been found and that gene patents do not have a significant effect on academic research, also partly due to the nuanced approach to patenting and licensing taken by universities, especially concerning research tools).

111. Sampat, *supra* note 110, at 29.

112. *Id.* (citing evidence which shows that there is an excess correlation of scientists' research portfolios in that numerous scientists pursue the same research targets). The necessity of pursuing a different research trajectory could also result in a positive effect on net welfare as it may help to prevent a wasteful duplication of research effort on the same project. *Id.* at n.18; Caulfield, et al., *supra* note 107, at 1093. This would correspond to Kitch's prospect theory that patents help to avoid a wasteful duplication of resources in reserving the further exploitation of the patented technology to the patentee. *Cf.* Kitch, *supra* note 17, at 276–77.

A. *The Unfortunate, Yet Clear, State of Current Law*

The common law experimental use exemption was first promulgated in *Whittemore v. Cutter*¹¹³ as a balance between a patent's exclusive right to exclude and the rights of others to construe the patented invention. Justice Story saw its applicability "merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its desired effects."¹¹⁴ Subsequent decisions have interpreted this defense to infringement narrowly and courts have been very cautious to apply the exemption in cases where a commercial benefit was derived from the use of the invention.¹¹⁵

In reversing the lower court in *Roche v. Bolar*, the Federal Circuit narrowly interpreted the common law research exemption.¹¹⁶ The district court had determined that Bolar's use of the patented drug solely for undertaking the regulatory steps required for marketing an equivalent drug after the expiration of the patent was *de minimis* and experimental, and thus did not infringe Roche's patent.¹¹⁷ The Federal Circuit emphasized that Bolar's "intended 'experimental' use was solely for business reasons and not for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry" and thus not exempted from patent infringement.¹¹⁸ The court further held that even though public policy may warrant an exception in favor of generic drug producers, it was the role of Congress to maximize public welfare through legislation.¹¹⁹ In the following year, Congress passed legislation that was under consideration at the time of

113. *Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (No. 17,600) (opinion by Justice Story while serving on the circuit in Massachusetts). For history and development of the experimental use exemption, see, for example, Ronald D. Hantman, *Experimental Use as an Exception to Patent Infringement*, 67 J. PAT. & TRADEMARK OFF. SOC'Y 617 (1985), Tanuja V. Garde, *The Effect of Disparate Treatment of the Experimental Use Exemption on the Balancing Act of 35 U.S.C. § 104*, 35 IIC 241, 242-47 (2004) and Mueller, *supra* note 1, at 17-41.

114. *Whittemore*, 29 F. Cas. at 1121.

115. *Cf. Spray Refrigeration Co. v. Sea Spray Fishing, Inc.*, 322 F.2d 34, 35 (9th Cir. 1963) (testing patented system for refrigerating fish on vessel that engages in commercial fishing operation constituted infringement); *Radio Corp. of Am. v. Andrea*, 90 F.2d 612, 615 (2d Cir. 1937) (infringing assembly of components to test marketability of the device is commercial use not covered by experimental use exemption). *But see Pitcairn v. United States*, 547 F.2d 1106, 1125-26 (Ct. Cl. 1976) (rejecting the defense that the patented helicopters were purchased only for testing and experimental purposes because "experiments of such nature are intended uses of the infringing aircraft manufactured for the defendant and are in keeping with the legitimate business of the using agency"); *Pfizer, Inc. v. Int'l Rectifier Corp.*, 1982 U.S. Dist. LEXIS 17411, 15 (C.D. Cal. July 20, 1982) (experimental use doctrine applicable only when there is "no intended commercial use of the patented article, none whatsoever").

116. *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858, 861 (Fed. Cir. 1984).

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

118. *Roche*, 733 F.2d at 863.

119. *Id.* at 865.

the Federal Circuit's decision. This piece of legislation, commonly known as the Hatch-Waxman Act, provided for faster marketing approval for drugs that are bioequivalent to approved drugs and a patent term extension equivalent to the time lost during mandatory regulatory approval process, and effectively superseded *Roche v. Bolar*.¹²⁰

However, the new legislation was not intended as a complete substitute for the common law research exemption, but rather, only partly to overrule *Roche v. Bolar*.¹²¹ Consequently, the exemption continued its (narrow) existence.¹²² In *Embrex v. Service Engineering*, the Federal Circuit followed its prior practice of not extending the experimental use exemption to acts committed by an enterprise in furtherance of its commercial activity.¹²³ Uses do not benefit from the experimental use defense when undertaken only in the "guise of scientific inquiry" but with "definite, cognizable, and not insubstantial commercial purposes."¹²⁴

120. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984). The proposal of § 202 of the Hatch-Waxman Act, which became 35 U.S.C. § 271(e), was undoubtedly prompted by the decision in *Roche. Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 670 n.3 (1990); Gerald J. Mossinghoff, *Overview of the Hatch-Waxman Act and its Impact on the Drug Development Process*, 54 FOOD & DRUG L.J. 187, 190 (1999) ("The famous case of *Roche Products v. Bolar Pharmaceuticals* was reversed specifically in Section 291(e)(1) of title of the *United States Code*."). For the scope of § 271(e), see *infra* Part VI.A.

121. The Federal Circuit continued to cite *Roche v. Bolar* as precedent for the narrow interpretation of the common law experimental use exemption and deems it superseded on other grounds only. See, e.g., *Embrex, Inc. v. Service Eng'g Corp.*, 216 F.3d 1343, 1349 (Fed. Cir. 2000) ("This court has construed both the experimental use and *de minimis* exceptions very narrowly."). See also *Roche*, 733 F.2d at 863 (holding that courts should not "construe the experimental use rule so broadly as to allow a violation of the patent laws in the guise of 'scientific inquiry,' when that inquiry has definite, cognizable, and not insubstantial commercial purposes").

122. Cf. Mueller, *supra* note 1, at 28–33 (however, addressing the state of law before *Madey v. Duke*).

123. *Embrex*, 216 F.3d at 1349. Embrex's patent claimed methods for the inoculation of birds against diseases by injecting vaccines in specified regions of the egg before hatching, thus immunizing the birds while they were still in the egg. Service Engineering built a prototype of an in-ovo inoculation device and hired two scientists to design around the patented technology by injecting vaccine into parts of the egg not mentioned in the claims of the patent; however, their tests showed that the device predominantly injected into amnion/yolk-sac, which is an area covered by the patent. When Service Engineering started marketing their device, Embrex sued for infringement. The district court found that the chief commercial purpose of the testing was to demonstrate to its customers the usefulness of the methods of its own in-ovo inoculation device and thus rejected Service Engineering's arguments that the tests were done for the purpose of scientific inquiry. The Federal Circuit affirmed and denied the safe harbor of the experimental use exemption. *Id.*

124. *Id.* (quoting *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858, 863 (Fed. Cir. 1984)). The concurring opinion by Judge Rader was even more restrictive and views the experimental use exemption routed in the law of a *de minimis* excuse, and thus not applicable where any commercial application is envisioned. *Id.* at 1352–53 (Rader, J., concurring) ("Of course, even if the experimental use excuse retains some lingering vitality, the slightest com-

In *Madey v. Duke*, the Federal Circuit again considerably narrowed the common law experimental use exemption.¹²⁵ Professor Madey directed the Free Electron Laser Laboratory at Duke University and held two patents practiced in his lab. The University continued to operate the patented laboratory equipment after Madey had left the University; Madey sued, *inter alia*, for infringement of his two patents. The district court qualified Duke's use of the invention as experimental use and denied infringement.¹²⁶

Revisiting its prior case law, the Federal Circuit reversed and held that its precedents do "not immunize any conduct that is in keeping with the alleged infringer's legitimate business, regardless of commercial implications."¹²⁷ The non-profit status of the researching entity or the purpose of a particular research project (non-commercial basic research) is not sufficient to qualify for the safe harbor when the use is "in keeping with the alleged infringer's legitimate business interests."¹²⁸ Even research projects conducted by major research universities like Duke that are non-commercial were deemed ineligible for the application of the common law research exemption, as such research activities "unmistakably further the institution's legitimate business objectives, including educating and enlightening students and faculty participating in these projects" and serve, *inter alia*, to "increase the status of the institution and lure attractive research grants, students and faculty."¹²⁹ It was the first decision of the Federal Circuit or its predecessor courts addressing a non-profit institution's (in-)ability to rely on the experimental use exemption.¹³⁰

mercial implication will render the 'philosophical inquiry/experimental use' doctrine inapplicable, as occurs in the court's resolution today.").

125. *Madey v. Duke Univ.*, 307 F.3d 1351, 1361–63 (Fed. Cir. 2002).

126. *Madey v. Duke Univ.*, 266 F. Supp. 2d 420, 431 (2001).

127. *Madey*, 307 F.3d at 1362.

128. *Id.*

129. *Id.* In a note, the court referred to Duke University's Policy on Inventions, Patents and Technology Transfer and pointed out that the university "is not shy in pursuing an aggressive patent licensing program from which it derives a not insubstantial revenue stream," which—although not explicitly acknowledged—may have influenced the court's sweeping dictum of "infringer's legitimate business interests." *Id.* at 1363 n.7. See also Rebecca S. Eisenberg, *Patent Swords and Shields*, 299 Sci. 1018 (2003) (regretting that the court did not elaborate on how far Duke's aggressive patent policy was a factor for the decision).

130. *Cai*, *supra* note 48, at 177–78. The only reported decision addressing the question is *Ruth v. Stearns-Roger Mfg. Co.*, 13 F. Supp. 637 (D. Col. 1935). The District Court of Colorado qualified the experimental use of the patented machines in the university's School of Mines's laboratory as non-infringing and thus did not take it into account when calculating the damages for contributory infringement by the supplier of replacement part for the machines. *Id.* at 703.

As neither the Federal Circuit¹³¹ nor the Supreme Court¹³² in *Integra v. Merck* opined on the common law experimental use exemption, *Madey v. Duke*—for the time being—states the current rule of the law, enunciating an extremely narrow scope of the common law exception.¹³³ Under this interpretation, hardly any scenario is conceivable in which a commercial enterprise or a university can engage in research that qualifies under the exemption.¹³⁴ The decision has provoked critical comments both within the legal community and from non-profit institutions voicing their concern that a narrow interpretation of the common law research exemption would hinder scientific progress, especially in the biomedical

131. The Federal Circuit's majority opinion deemed the common law experimental use defense not raised on appeal and thus did not address it. *Integra Lifesciences I, Ltd. v. Merck KGaA (Merck I)*, 331 F.3d 860, 863 n.2 (2003). In her dissenting opinion, Judge Newman considered the issue sufficiently raised and briefed and set forth how the common law experimental use exception should be applied to this case, also stating her disagreement with "the sweeping dictum" in *Madey v. Duke. Id.* at 874–77, 878 n.10, (Newman J., dissenting). However, writing for the majority on remand, she clarified that the common law research exemption was not argued on appeal before the Federal Circuit or the Supreme Court and thus was not at issue. *Integra Lifesciences Inc., Ltd. v. Merck KGaA (Merck II)*, 496 F.3d 1334, 1337 (Fed. Cir. 2007).

132. *Merck KGaA v. Integra Lifesciences Inc., Ltd.*, 545 U.S. 193 (2005). It was not briefed by the parties and thus the court addressed only the scope of § 271(e). The experimental use defense was only argued in an amicus brief. See Brief for Consumer Project on Technology, et al. as Amici Curiae Supporting Petitioners at 12–21, *Merck*, 545 U.S. 193 (No. 03-1237), 2005 WL 435894.

133. The scope of the exception is comparable to the prior scope of permissible experimental use under § 6 German Patent Act 1968. The old German patent laws did not contain a codified experimental use exception. However, the case law had exempted from the effects of the patent experiments with a protected substance only to a very narrow extent, namely in connection with experiments to determine the formation and characteristics of the substance and whether it was sufficiently pure and stable. Additionally, any use had to be of a non-commercial nature, a criterion only met if the invention was used solely for personal or domestic purposes. See *Klinische Versuche II (Clinical Trials II)*, R.P.C. 423, 438 (Bundesgerichtshof [BGH] [Federal Court of Justice] 1998); Thomas Hieber, *Die Zulässigkeit von Versuchen an patentierten Erfindungen nach § 11 Nr. 2 PatG 1981* [The Admissibility of Experiments on Patented Inventions under § 11 No. 2 German Patent Act 1981], GRUR 1996, 439, 440.

134. See, e.g., Cai, *supra* note 48, at 192 ("In *Madey*, the Federal Circuit has essentially destroyed any practical meaning to the experimental use defense. The decision has also shattered the long-held myth about research exemption."); Eisenberg, *supra* note 129, at 1028 ("Although the *Madey* decision did not extinguish the experimental use defense entirely, it eviscerated it to the point that it is essentially useless to research universities."); Garde, *supra* note 113, at 246 ("This holding severely limited, to the point of near elimination, the common law experimental use defense."); Mueller, *supra* note 3, at 918 ("...for all practical purposes, the doctrine has become a nullity."). See also the subsequent application of lower courts, for example, *Applera Corp. v. MJ Research, Inc.*, 311 F. Supp. 2d 293, 297 (D. Conn. 2004). Cf. Suzanne T. Michel, *The Experimental Use Exception to Infringement Applied to Federally Funded Inventions*, 7 HIGH TECH. L.J. 269 (1992) (reaching the same conclusion based on an analysis of the pre-*Madey* jurisprudence).

field.¹³⁵ Even though the empirical study conducted by Cohen and Walsh two years after *Madey v. Duke* suggests that its impact on the way universities perform their research is rather negligible,¹³⁶ numerous legal and economic scholars have advocated a broadened experimental use exemption.¹³⁷ Since it has been repeatedly suggested that the Federal Circuit should look to the approach to experimental use in other jurisdictions, the European approach will be analyzed in the following subsection.¹³⁸

B. *The European Approach to Experimental Use*

A discussion of the “European” approach to the experimental use exemption should be prefaced by saying that there is no truly uniform European approach to patent infringement as a matter of law. A patent issued under the European Patent Convention (EPC) is not a uniform European patent but merely a “bundle” of national patents issued in a unified granting procedure. Article 64(3) of the EPC stipulates that an infringement suit under an EPC patent must be brought in national court under the patent law of the relevant member state.¹³⁹ By the same token, experimental use—as a defense to infringement—is an issue of national law. Thus, a plaintiff enforcing a patent in more than one member state may need to bring multiple parallel law suits with potentially differing outcomes, depending on the relevant member state’s body of law governing infringement and the scope of the experimental use exemption.¹⁴⁰

135. See, e.g., Brief for Association of American Medical Colleges et al. as Amici Curiae at 4–5, *Madey v. Duke Univ.*, 307 F.3d 1351 (Fed. Cir. 2002) (No. 02-1007); Eisenberg, *supra* note 129, at 1018 (calling the decision unsurprising for legal community but “an alarming wake-up call to the academic community”); Mueller, *supra* note 3, at 940 (viewing the decision as excessively restricting experimental use exemption for basic research).

136. John P. Walsh et al., *View from the Bench: Patents and Material Transfers*, 309 Sci. 2002, 2002 (2005) (finding that only two percent of university researchers “have begun checking for patents in the 2 years since *Madey v. Duke*,” and only five percent have been made aware of existing IP rights by notification letters, up from three percent before *Madey v. Duke*). Cf. Cai, *supra* note 48, at 191 (concluding that the decision is not likely to have a great impact on university research in view of rational forbearance of the patent owners).

137. See, e.g., Mueller, *supra* note 3, at 919 n.8 (providing a detailed overview of the scholarship). Mueller considers an experimental use exemption as the international norm. *Id.* at 969. See also Garde, *supra* note 113, at 254–60; Nelson, *supra* note 2, at 466.

138. See, e.g., Mueller, *supra* note 3, at 969. See also *Integra Lifesciences Inc., Ltd. v. Merck KGaA (Merck II)*, 496 F.3d 1334, 1337 (Fed. Cir. 2007) (Rader J., dissenting-in-part and concurring-in-part) (suggesting a look at the German distinction in the context of interpreting 35 U.S.C. § 271(e)(1)).

139. Convention on the Grant of European Patents, Oct. 5, 1973, 1065 U.N.T.S. 199, 274, available at <http://www.epo.org/patents/law/legal-texts/epc.html> (click “PDF version” link in the download box for the full text). Article 64(3) EPC provides: “Any infringement of a European patent shall be dealt with by national law.”

140. The classical case study is the famous “Epilady-saga,” a multi-jurisdictional infringement litigation between Improver and Remington, where different national courts applied Article 69 EPC to determine whether the same device infringed the same patent and

Having said this, there is some uniformity among the approaches the member states have chosen. Most European countries have codified one or more different types of experimental use exemptions. For example, certain provisions exempt from liability scientific experimentation on a patented invention, which will be referred to as the “experimental use exemption.” Others resemble a *Bolar*-style exemption, exempting from liability experiments required for drug approval purposes, which will be referred to as the “clinical trials exception.”¹⁴¹

1. The Experimental Use Exemption

Article 31(b) of the Community Patent Convention (CPC) 1975 exempts from liability for infringement “acts done for experimental purposes relating to the subject-matter of the patented invention.”¹⁴² Even though the CPC has never entered into force¹⁴³ and thus has no binding legal effect, most, if not all member states have codified a similar provision in their national patent laws.¹⁴⁴ For example, § 11 No. 2 German

came to differing results. *See* *Improver Corp. v. Remington Consumer Prods. Ltd.*, R.P.C 69 [U.K. Court of Appeal] (1989) (finding infringement in interlocutory proceedings and granting an injunction) and F.S.R 181 [U.K. Patents Court] (finding non-infringement); Düsseldorf Court of Appeals [OLG Düsseldorf], 24 IIC 838 (1993) (F.R.G.) (finding infringement under the doctrine of equivalents); *Gerechthof* [Court of Appeal], 24 IIC 832 (1993) (Neth.) (finding infringement under the doctrine of equivalents); *Oberlandesgericht Wien* [Vienna Court of Appeals], 23 IIC 391 (1992) (Austria) (rejecting the grant of an injunction in interlocutory proceedings); *Tribunale di Milano*, GRUR INT. 1993, 249 (determining in interlocutory proceedings that the defendant’s device constituted a dependent invention and finding direct infringement).

141. *Cf.*, e.g., Patentgesetz [PatG] [German Patent Act], Dec. 16, 1980 § 11(2) (experimental use exemption) and § 11(3) (clinical trials exemption). Most laws contain a further provision exempting “acts done privately and for non-commercial purposes.” *Id.* at § 11(1).

142. Convention for the European Patent for the common market signed at Luxembourg on December 15, 1975, is commonly referred to as the Community Patent Convention (CPC 1975). An identical provision is contained in Article 27(b) CPC 1989. The provision has been codified without any reference to existing national provisions and has to be interpreted autonomously. *Cf.* PETER CHROCZIEL, *DIE BENUTZUNG PATENTIERTER ERFINDUNGEN ZU VERSUCHS- UND FORSCHUNGSZWECKEN* [The Use of Patented Inventions for Experimental and Research Purposes] 163, 166 (1986) [hereinafter CHROCZIEL, *USE OF INVENTIONS*]; Hieber, *supra* note 133, at 443.

143. Both approaches have failed due to unresolved translation issues and disputes about the constitution of courts responsible for patent infringement suits. *See* Albrecht Krieger et al., *Die dritte Luxemburger Konferenz über Gemeinschaftspatent vom 11. bis 15. Dezember 1989—Bericht der deutschen Delegation*, [Third Luxemburg Conference on the Community Patent, December 11 to 15, 1989—Report of the German Delegation] GRUR INT. 1990, 173. A new attempt to create a uniform Community Patent was initiated by the European Union in 2000. Article 9(b) of the proposed regulation contains an identical provision. *Cf.* Council Proposal for a Regulation on the Community Patent, COM 412 final, OFFICIAL J. EUR. COMMUNITIES C 337, 278, 280 (2000).

144. William Cornish, *Experimental Use of Patented Inventions in European Community States*, 29 IIC 735, 736 (1998) (with reference to the similar or identical national provisions in note 2 and diverging Dutch and Portuguese provisions in note 3).

Patent Act (GPA) uses identical language and provides: “The effects of a patent shall not extend to . . . acts done for experimental purposes relating to the subject matter of the patented invention.”¹⁴⁵

The provenance of the German and other national exemption provisions from Article 31(b) of the CPC is important as European courts favor adopting a common approach to the interpretation of national provisions that are derived from a common European source like the CPC (or the EPC).¹⁴⁶ Article 31(b) of the CPC and the corresponding provisions in the European patent laws exempt from infringement actions under two cumulative requirements: (1) the actions have to be experiments, and (2) they must relate to the patented subject matter.¹⁴⁷ Whereas an experiment is broadly defined as a procedure for obtaining information, such as presupposing existing uncertainties, the requirement that the experiment must relate to the patented subject matter of the invention considerably limits the exception.¹⁴⁸

The German Federal Court of Justice held in its first *Clinical Trials* decision that § 11 No. 2 GPA “in principle exempts all experimental acts as long as they serve to gain information and thus to carry out scientific research into the subject-matter of the invention, including its use.”¹⁴⁹ The disclosure requirement under patent law warrants that third parties can test the invention during the patent term and, based on the informa-

145. Patentgesetz [PatG] [German Patent Act], Dec. 16, 1980 § 11(2).

146. Cornish, *supra* note 144, at 737. *See also* Monsanto Co. v. Stauffer Chem. Co. et al., [1985] R.P.C. 515, 536 (Ct. App.) (U.K.) (referring to § 130(7) U.K. Patent Act, which provides for giving corresponding provisions “as nearly as practical, the same effect in the United Kingdom as the corresponding provisions of . . . the Community Patent Convention”); Bundesgerichtshof [BGH] [Federal Court of Justice], July 11, 1995—*Clinical Trials I*, 28 IIC 838 (1997); [1997] R.P.C. 623, 640 (F.R.G.) [hereinafter *Clinical Trials I*] (principles of interpretation derived from national law cannot be directly applied to provisions which have been adapted to uniform European Law). *Cf.* Peter Ruess, *Accepting Exceptions?: A Comparative Approach to Experimental Use in U.S. and German Patent Law*, 10 MARQ. INTELL. PROP. L. REV. 81, 95–101 (2006) (analyzing the case-law before and after the adoption of § 11 No. 2 GPA).

147. *Cf. Clinical Trials I*, *supra* note 147, at 638; Cornish, *supra* note 144, at 736.

148. *Clinical Trials I*, *supra* note 147, at 638 (requiring a “finality between the act for a particular experimental purpose and the subject-matter of the invention”).

149. *Id.* at 639. *See also, Clinical Trials II*, *supra* note 134, at 438 (stating that an activity is more likely to fall in the experimental use exemption when it is “is oriented towards clearing up uncertainties with regard to the object of the patented invention or bringing out new discoveries about said object, provided these activities with research purposes relate to the object of the patented invention.”). The extension of the exception from experiments merely on the subject matter of the invention to inquiries into its possible uses has been generally adopted in European legal scholarship. *See* Alfred Keukenschrijver, in PATENTGESETZ [Patent Act] (Rudolf Busse ed., 2003) § 11 marginal note 17; Kühnen, in PATENTGESETZ MIT EUROPÄISCHEM PATENTÜBEREINKOMMEN [Patent Act and European Patent Convention], (Rainer Schulte ed., 2005) § 11 marginal note 12. *See also* Wolfgang von Meibom & Johann Pitz, *Experimental Use and Compulsory License Under German Patent Law*, PAT. WORLD, June–July 1997 at 27, 27 (1997).

tion obtained through the permissible trials, further develop the technology.¹⁵⁰ Additionally, the court clarified that ultimate commercial purpose is irrelevant, when it stated: “[I]t cannot matter whether the experiments are used only to check the statements made in the patent or else to obtain further research results and whether they are employed for wider purposes, such as commercial interests.”¹⁵¹ Since the ultimate commercial or non-commercial purpose is irrelevant, research performed by universities or non-profit institutions is subject to the same standards and does not enjoy a broader privilege than research focused on commercial applications.¹⁵² Nevertheless, the courts have clarified that experiments can no longer benefit from the experimental use exemption if they exceed a certain scale.¹⁵³

2. Application to Research Tools

Although no court decision explicitly addressed exempted uses of patented research tools, the rationale underlying those cases establishes a clear line of demarcation. Under § 11 No. 2 GPA, experiments on research tools are exempted from infringement.¹⁵⁴ Therefore, any experiment directed at obtaining new information on a patented research

150. See *Clinical Trials I*, *supra* note 147, at 639; German Federal Court of Justice, June 2, 1984—*Erythronolid*, GRUR, 1985 734. See also von Meibom & Pitz, *supra* note 149, at 28.

151. *Clinical Trials I*, *supra* note 147, at 639. See also *Clinical Trials II*, *supra* note 134, at 431 (the mere fact that the results obtained by the experiments are not solely used for research purposes but “above all” serve commercial purposes as well does not render an experiment infringing); *Monsanto v. Stauffer* [1985] R.P.C. 515, 538 (rejecting a “hard and fast” line that would render experiments that are ultimately directed to commercial exploitation infringing and allowing limited experiments to determine whether a quality product could be manufactured commercially according to the specification of the patent). Cf. von Meibom & Pitz, *supra* note 149, at 30.

152. HENRIK HOLZAPFEL, DAS VERSUCHSPRIVILEG IM PATENTRECHT UND DER SCHUTZ BIOTECHNOLOGISCHER FORSCHUNGSWERKZEUGE [Patent Law’s Experimental Use Privilege and the Protection of Biotechnological Research Tools] 205–07 (2004) [hereinafter HOLZAPFEL, EXPERIMENTAL USE]; Krasser, *supra* note 11, at 813–15.; Kühnen, *supra* note 149; Scharen, in PATENTGESETZ, GEBRAUCHSMUSTERGESETZ, *supra* note 22, § 11 marginal note 7; Wolfgang von Meibom & Johann Pitz, *Klinische Versuche—eine transatlantische Betrachtung vor dem Hintergrund der Entscheidung des BGH “Klinische Versuche II”* [Clinical Trials—A Transatlantic Review in Regard to the Federal Court of Justice’s decision “Clinical Trials II”] [hereinafter Meibom & Pitz, *Clinical Trials*], MITT. 1998, 244, 249.

153. *Monsanto v. Stauffer*, [1985] R.P.C. 515, 543 (exemption did not extend to series of field experiments where potential customers could observe the results); *Applied Research Sys. Holding N.V. v. Organon et al.*, Gerechtshof [Hof] [Court of Appeals], 3 Feb. 1994, NJ 463 (Neth.), 28 IIC 558 (1997) (clinical trials and testing of a generic version of a human follicle-stimulating hormone at hospitals, laboratories and research stations in ten European states too extensive to qualify as experimental use).

154. See, e.g., Henrik Holzapfel, *Die patentrechtliche Zulässigkeit der Benutzung von Forschungswerkzeugen* [The Admissibility of the Use of Biotechnological Research tools under Patent Law], in GRUR INT. 2006, 10, 13 (2006) [hereinafter Holzapfel, *Research Tools*].

tool is exempted from liability, for example, to determine its suitability to be used for a new purpose or to find out properties of modifications. Under the European approach, the experiments conducted by Scribbs and Merck would have been exempted from infringing the product claims for the RGD-peptide even if, *arguendo*, the RGD-peptides were research tools because the experiments were directed at obtaining information about the peptide and its potential uses.¹⁵⁵ Furthermore, as § 11 No. 2 GPA also exempts clinical trials required for the approval of new indications,¹⁵⁶ the trials conducted by Merck would also have been exempted as they were directed at collecting data necessary for obtaining market approval for a new (the first) indication.

However, as the German Federal Court of Justice explicitly stated in *Clinical Trials I*, the experimental use exemption does not extend to uses “which make the invention the *means* for experimental acts.”¹⁵⁷ Consequently, the use of a biotechnology research tool according to its patented purpose, for example to identify useful compounds or their properties, does not fall under the experimental use exemption.¹⁵⁸ The prohibition applies equally to their use in basic research performed by universities and non-commercial enterprises.¹⁵⁹

Although German appellate courts have yet to decide a case on experimental use involving the use of a research tool, the principles set forth in the *Clinical Trials* decisions are clear and have been applied

155. See *Integra Lifesciences I, Ltd. v. Merck KGaA (Merck I)*, 331 F.3d 860, 862 (2003). See facts *infra* Part VI.A.1.

156. *Clinical Trials I*, *supra* note 147, at 628 (experimentation to find new uses for a patented invention are experiments on patented subject matter). See also *Kirin Amgen v. Boehringer Mannheim, Gerichtshof [Hof] [Court of Appeals]*, 3 Feb. 1994, NJ 462 (Neth.) (experiments on erythropoietin to find new medical indications permissible even when product is already marketed for other indication). Cf. *Cornish*, *supra* note 144, at 753 (expecting the other European countries to follow the approach of the German Federal Court of Justice in the *Clinical Trials* decisions.) In its later decision, the court extended the experimental use exemption to clinical trials on the patented compound even if they were not conducted for approval of a new indication as long as the experiments are directed to eliminating “an existing insecurity.” The defendant had conducted clinical trials to determine in which form his human erythropoietin drug is best administered; the court held that it made no difference whether the indication of the agent’s composition is already well known. See *Clinical Trials II*, *supra* note 134, at 433–36. See also *Keukenschrijver*, *supra* note 149, § 11 marginal note 18.

157. *Clinical Trials I*, *supra* note 147, at 641–42 (emphasis added).

158. Cf. Peter Chrocziel, *Benutzung zu Versuchszwecken als Einwand gegenüber einem Anspruch wegen Patentverletzung (Q 105)* [Use for Experimental Purposes as Defense Against a Claim of Infringement (Q105)], GRUR INT. 1992, 203, 205 [hereinafter Chrocziel, *Experimental Use*]; Joseph Straus, *Zur Zulässigkeit klinischer Untersuchungen am Gegenstand abhängiger Verbesserungserfindungen* [The Admissibility of Clinical Trials on Dependent Improvement Inventions], GRUR INT. 1993, 308, 311; von Meibom & Pitz, *Clinical Trials*, *supra* note 152, at 247.

159. Chrocziel, *Experimental Use*, *supra* note 158, at 205; CHROCZIEL, *USE OF INVENTIONS*, *supra* note 142, *passim*; Holzapfel, *Research Tools*, *supra* note 154, at 13; Scharen, *supra* note 22, § 11 marginal note 7.

accordingly by a trial court in 2003 when it was faced with such a situation.¹⁶⁰ In the German part of the infringement proceedings between Bayer and Housey with respect to the use of their patented screening process, the District Court Düsseldorf rejected Bayer's argument that their use of the invention was exempted under § 11 No. 2 GPA.¹⁶¹ Having determined that the patented screening process had been practiced according to its technical teaching, the court had to address the defense of experimental use.¹⁶² The defendant argued that it used the process to determine whether certain compounds can be used for activating or inhibiting soluble Guanylatcyclase (sGC) and that the experiments were solely directed at establishing a cell line; however, the court determined that the experiments had the (additional) purpose of analyzing the characteristics of certain activators of sGC which were known only from cell-free systems.¹⁶³ The court rather summarily rejected Bayer's arguments and found infringement as Bayer had not restricted itself to create a cell-line but had used the patented method as a means of their screening process, thus in accordance with the patented purpose.¹⁶⁴

C. *Why the European Approach Better Reflects the Rationale of the Patent System*

Admittedly, the distinction between "experimentation on a patented invention" and "experimentation using a patented invention" does not have any judicial precedent in U.S. patent law.¹⁶⁵ Nevertheless, the distinction has been widely accepted by commentators as an important, if

160. Landgericht Düsseldorf [LG] [District Court Düsseldorf], Oct. 28, 2003, 4a O 362/02, available at http://cip.bravo771.server4you.de/www/ddorf_entsch/?q=node/395.

161. *Id.* The screening process involved several steps: First, a modified cell line is created, which expresses the protein of interest and exhibits a phenotypic response to the protein. The modified cell line has a lower level of expression and a lesser degree of phenotypic response compared to the original cell line. Agents are applied to both cell lines; based on a comparison of their phenotypic responses it can be determined whether the agent is an inhibitor or activator of the protein. For details on the invention and on the parallel proceedings in the U.S., see *Bayer AG v. Housey Pharms., Inc.*, 340 F.3d 1367 (Fed. Cir. 2003).

162. District Court Düsseldorf, 4a O 362/02, at II.

163. *Id.*

164. *Id.* (the decision was appealed)

165. But see the failed attempt to codify an experimental use exemption which used the distinction, H.R. REP. NO. 100-888 at 51 (1988). Furthermore, in both *Integra v. Merck* decisions of the Federal Circuit, the dissenting judges voiced the appropriateness of such differentiation. See *Merck I*, 331 F.3d 860, 873, 877-878 (Newman, J., dissenting) (distinguishing in her discussion of the common law exemption between research into the science and technology disclosed in patents, and the use in research of patented products or methods, the so-called "research tools": "Use of an existing tool in one's research is quite different from study of the tool itself."); *Merck II*, 496 F.3d 1334, 1351 (Rader, J., dissenting-in-part and concurring-in-part) (referring for guidance to opinions of foreign courts distinguishing between research on and use in research).

not decisive, factor for the determination of whether an experiment should be allowed to benefit from the common law research exemption or not.¹⁶⁶ Distinguishing between research on and research with a patented invention corresponds to the rationale of the patent system that inventive activity should be stimulated by granting exclusive rights without simultaneously imposing undue restrictions on the technological development.¹⁶⁷ Innovation is a cumulative process with innovators building on existing knowledge, colorfully described with the metaphor of “standing on the shoulders of giants.”¹⁶⁸ Exempting research on a patented invention facilitates this cumulative process as it provides for an effective use of the information disseminated through the publication of patent specifications, and thus aids the creation of new technical knowledge.¹⁶⁹ The dissemination of knowledge is an important function of the patent system¹⁷⁰ and would be impaired until after the patent term if no experiments on the patented invention would be allowed.¹⁷¹

166. Mueller, *supra* note 3, at 957–58. See also Eisenberg, *supra* note 3, at 1078 (suggesting that the experimental use exemption should allow experiments directed to testing whether the patent specification sufficiently discloses the patented invention, but not extending to circumstances where the researcher uses the invention like an ordinary consumer). See NIH, RESEARCH TOOLS, *supra* note 71, stating:

Foreign patent systems that recognize a research exemption typically distinguish between experimenting on a patented invention—i.e. using a patented invention to study the underlying technology or perhaps to invent around the patent, which is what the exemption covers—and experimenting with a patented invention to study something else, which the exemption does not cover. So construed, the exemption would not be available for researchers who make use of patented research tools in the course of investigating something else, as opposed to those who are studying the research tools themselves. This is a sensible distinction. It is difficult to imagine how a broader research exemption could be formulated without effectively eviscerating the value of patents on research tools. Researchers are ordinary consumers of patented research tools, and if these consumers were exempt from infringement liability, the patent holder would have nowhere else to turn to collect patent royalties. An excessively broad research exemption could eliminate incentives for private firms to develop and disseminate new research tools, which could on balance do more harm than good to the research enterprise.

167. *Clinical Trials I*, *supra* note 147, at 642; *Merck I*, 331 F.3d at 875 (Newman, J., dissenting) (“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. Prohibition of research into such knowledge cannot be squared with the framework of the patent law.”). See also Krasser, *supra* note 11, at 812.

168. Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law*, 5 J. ECON. PERSP. 29, 29 (1991) (citing Sir Isaac Newton’s acknowledgement “If I have seen far, it is by standing on the shoulders of giants.”).

169. *Clinical Trials I*, *supra* note 147, at 642.

170. Cf. *supra* Part I.D.

171. See, e.g., *Integra Lifesciences I, Ltd. v. Merck KGaA (Merck I)*, 331 F.3d 860, 873 (2003) (Newman, J., dissenting) (“The purpose of the patent system is . . . to add to the body of published scientific/technologic knowledge. . . . The right to conduct research to achieve such knowledge need not, and should not, await expiration of the patent.”). See also *Clinical Trials I*, *supra* note 147, at 642 (“unlimited protection by the patent is unjustified where further technical development is impeded”).

Furthermore, the possibility to experiment on the patented subject matter allows third parties to assess the validity of the patented invention and will help to weed out invalid patents.¹⁷² Consequently, it would serve as an additional corrective element and increase the quality of the patent system.

There are other arguments that suggest that experiments on the patented subject matter should be allowed. The legislature contemplated the patenting of improvements,¹⁷³ which typically involves and requires studying and experimenting on the patented invention.¹⁷⁴ Unless third parties are allowed to experiment on patented subject matter, the patentees will have near-exclusivity for developing improvements and can shield inventions from competition beyond reasonable measure.¹⁷⁵

Negative effects for the patentee as a result of an experimental use exemption are limited. In general, the patentee will benefit from new insights relating to his invention, whereas the commercial value of the invention is only affected to a very limited extent by the experiments. When a third party applies for a patent on an improvement or a new indication as a result of the information obtained by the exempted experiments, he will have to obtain a license for the original patent, therefore increasing its value.¹⁷⁶ However, experiments on the patented invention should be permitted even if they are directed at obtaining information that facilitates designing around the patent and could

172. *Merck I*, 331 F.3d at 875 (Newman, J., dissenting); Rebecca S. Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 *YALE L.J.* 177, 219–22 (1987); Holzapfel, *Research Tools*, *supra* note 154, at 12. *See also* *Whittemore v. Cutter*, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813) (No. 17,600) (allowing the construction of a machine “for the purpose of ascertaining the sufficiency of the machine to produce its described effects”).

173. *See* 35 U.S.C. § 101 (2000) (including “new and useful improvement” of the listed categories as potentially patentable subject matter).

174. *Mueller*, *supra* note 3, at 976.

175. *See Merck I*, 331 F.3d at 875 (Newman, J., dissenting). *But see* MARTIN J. ADELMAN, *PATENT LAW PERSPECTIVES* § 3.6[2] at 3-78.2(59) (2d ed. 2006), who describes the possible situation where the owner of a patent on a species, which has been discovered using the patented technology of the dominating (genus) patent, waits for the expiry of the patent before commencing with the exploitation. Arguably, this would deprive the owner of the dominant genus patent of his share in the benefits of the species patent, as was the case in *Merck I*. *Id.* However, under the assumption of rational economic behavior, neither party would renounce the potential profits obtainable by exploiting the species invention under the term of both genus and species patent, and a license agreement would be concluded. There will be presumably only very few genus-species cases in which strategic considerations will override rational economic behavior (Adelman points to *Merck v. Integra* as one example). *Id.* However, the negative effects of these few cases will be outweighed by the stimulation of research activities resulting from a broadened exemption, as they are likely to arise only where potential profits are small, for example, due to the approaching expiry of the genus patent’s term.

176. *Clinical Trials I*, *supra* note 147, at 644; *Merck I*, 331 F.3d at 875 (Newman, J., dissenting). *See also* Holzapfel, *Research Tools*, *supra* note 154, at 12.

ultimately diminish the value of the patent.¹⁷⁷ That products and processes may become obsolete over time and will be replaced by new innovative technologies reflects the very nature of the technological progress the patent system is meant to stimulate.

The proposed distinction has also been adopted in a resolution of the International Association for the Protection of Intellectual Property (AIPPI), determining that:

Experimental use includes any use of the patented invention to an extent appropriate to experimentation (as opposed to commercial use) which is for the purpose of improving the invention or making an advance over the invention or finding an alternative to the invention, but not the commercial exploitation of the subject of any improvement or advance.¹⁷⁸

Finally, the patentee should not be deprived of the experimental use exemption merely because the experiments on the patented invention were ultimately motivated by further commercial interests.¹⁷⁹ In *Madey*, the Federal Circuit pointed out correctly that even academic research can also be viewed as motivated by monetary incentives.¹⁸⁰ However, as the fair use exemption in the U.S. Copyright Act demonstrates, finding potential commercial use of intellectual property does not inevitably require the finding of infringement.¹⁸¹ Rather, the copyright statute provides that the “purpose and the character of the use, *including* whether such use is of a commercial nature or is for nonprofit educational purposes” is only one of four decisive factors.¹⁸² In other words, another piece of U.S. intellectual property legislation, based on the same constitutional

177. Mueller notes that the distinction between “experimented on” and “experimented with” in such situation “may be an exercise in semantics.” Mueller, *supra* note 1, at 40 n.202.

178. See *Experimental Use as a Defence to a Claim of Patent Infringement*, Association Internationale pour la Protection de la Propriété Industrielle Annuaire, 1992/III [AIPPI Ann.], at 282–83 ¶ 3.3. Cf. World Intellectual Property Organization [WIPO], *Draft Treaty Supplementing the Paris Convention for the Protection of Industrial Property as Far as Patents are Concerned (Patent Law Treaty)*, Art. 19 Alternative B ¶ 3(a)(iii), WIPO Doc. SCP/4/3 (Oct. 2, 2000) (not adopted), available at http://www.wipo.int/edocs/mdocs/scp/en/scp_4/scp_4_3.doc (proposing to exempt acts from infringement “where the act consists of making or using exclusively for the purpose of experiments that relate to the subject matter of the patented invention [or for the purpose of seeking regulatory approval for marketing]”) (alteration in the original).

179. This is generally accepted under the European approach, see *supra* notes 151–153 and accompanying text.

180. *Madey v. Duke Univ.*, 307 F.3d 1351, 1362 (Fed. Cir. 2002). Cf. *supra* notes 125–130 and accompanying text.

181. See generally Maureen A. O’Rourke, *Toward a Doctrine of Fair Use in Patent Law*, 100 COLUM. L. REV. 1177 (2000).

182. See 17 U.S.C. § 107 (2000). See also Mueller, *supra* note 1, at 42–45.

grant of power as the patent act,¹⁸³ recognizes the principle that the commercial nature of use alone is not determinative of infringement.

To conclude, the EU approach is better because it better reflects the patent systems rationale¹⁸⁴ of incentivizing inventive activity by ensuring adequate and sufficient patent protection for inventors without creating unwarranted disincentives by imposing undue restrictions on further technological development.

VI. THE SAFE HARBOR OF SECTION 271(E)(I)

A. *The Uncertain State of Current Law*

In 1984, Congress adopted the Hatch-Waxman Act in order to facilitate a faster introduction of readily available, cheaper generic drugs as a response to an aging population.¹⁸⁵ It, *inter alia*, extends the term of patents on new drugs to make up for the loss of effective patent duration in the FDA approval process¹⁸⁶ and for an abbreviated drug approval process for generic drugs by allowing manufacturers of generic drugs to file an Abbreviated New Drug Application (ANDA) with the FDA.¹⁸⁷ An ANDA application allows researchers to bypass many clinical and pre-clinical experiments, but requires generic manufacturers to demonstrate bioequivalence of the new drug with a listed drug.¹⁸⁸ Except in cases

183. See U.S. CONST. art. I, § 8, cl.8 (“The Congress shall have the power . . . to promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.”).

184. Apart from the rationale of the patent system, macro-economic considerations support an expansion of the experimental use doctrine: without an expansion of the experimental use doctrine, U.S. industry will be likely to move research abroad to benefit from a broader experimental use exemption, thus creating jobs and targeting investment outside of, rather than inside, the United States. Garde, *Disparate Treatment*, *supra* note 113, at 265; Harold C. Wegener & Stephen Maebius, *The Looming Crisis Over the Research Use Exception To Patent Infringement: What Madey Taught Duke University* (2003), http://www.foley.com/publications/pub_detail.aspx?pubid=1250. Incidentally, that was one of the reasons why the EC adopted a *Bolar*-type provision permitting clinical trials by means of a European directive, *cf. infra* Part VI.B.

185. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 1984 Stat. 1538 (codified as amended in scattered sections of 21 and 35 U.S.C.). See generally Mossinghoff, *supra* note 120.

186. Codified as amended in 35 U.S.C. § 156 (2003).

187. Codified as amended in 21 U.S.C. § 355(j) (2003)

188. Codified as amended in 21 U.S.C. § 355(j)(2)(A)(iv). (Furthermore, the ANDA must show that the proposed label instructions have been approved for the original drug, that the active ingredients are identical to the original drug, the dosage, route of administration, and strength are identical, and that the labeling will be identical with the original drugs’ label except for the changes reflecting the different manufacturer. Naturally, the application must include information required for an original drug application, i.e., information regarding the complete listing of its components, its composition, description of methods, facilities and

where the generic company can submit a so-called “paper-NDA” and show bioequivalence by reference to scientific publications, bioequivalence must be established through a series of experiments.¹⁸⁹

Since such experiments would infringe the original drug’s patent under *Roche v. Bolar*, the generic drug industry successfully lobbied Congress to provide a safe harbor provision. The industry argued that the current situation *de facto* prolonged the patent term because the data necessary for the submission of an ANDA could only be compiled after the expiration of the patent.¹⁹⁰ As part of the Hatch-Waxman Act, Congress provided a safe harbor for uses of a patented invention in connection with the drug approval process in § 271(e)(1), which reads in its relevant part:

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 . . . *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.¹⁹¹ (emphasis added)

The provision has been subject to repeated judicial interpretation.¹⁹² In *Eli Lilly v. Medtronic*, the Supreme Court gave it a broad meaning to comprise the testing to develop and submit information for marketing approval of medical devices.¹⁹³ Following cases interpreted the reach of the wording “solely for uses reasonably related” first very narrowly¹⁹⁴ and then more broadly.¹⁹⁵ However, after the Federal Circuit’s decision in

controls, as well as samples of the drug (if required) and its labeling. *See* 21 U.S.C. § 355(j)(2)(A)(i)–(vi). *Cf.* H.R. REP. NO. 98-857(I), at 14–18 (1984), *as reprinted in* 1984 U.S.C.C.A.N. 2647, 2647–48.

189. *See* Food, Drug, and Cosmetics Act, § 505(b)(2), 21 U.S.C. § 355(c) (2003).

190. *See* *Eli Lilly & Co. v. Medtronic, Inc.*, 872 F.2d 402, 404–05 (Fed. Cir. 1989), *aff’d*, 496 U.S. 661, 679 (1990).

191. 35 U.S.C. § 271(e) (2003).

192. Justice Scalia, writing for the court, called the § 271(e)(1) “not plainly comprehensible on anyone’s view” and found that it could not be transformed by interpretation “into an elegant piece of statutory draftsmanship.” *Eli Lilly v. Medtronic*, 496 U.S. 661, 669, 679.

193. *Medtronic*, 872 F.2d at 406 (involving Class III medical devices—cardiac defibrillators which are also subject to patent term extension). In a subsequent case, the Federal Circuit confirmed the availability of the safe harbor for medical devices which are subject to FDA approval but are not eligible for patent term extension. *Abtox Inc. v. Exitron Corp.*, 122 F.3d 1019, 1029–30 (Fed. Cir. 1997).

194. *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379, 1396 (N.D. Cal. 1987), *rev’d in part on other grounds*, 927 F.2d 1565 (Fed. Cir. 1991) (applying the exemption only to activities directly involved in seeking FDA approval).

195. *See, e.g., Exitron*, 122 F.3d at 1029 (activity exempted so long as it is reasonably related to FDA approval, user’s intent or alternative uses irrelevant). Even more broadly, *Nexell Therapeutics, Inc. v. Amcell Corp.*, 199 F. Supp. 2d 197 (D. Del. 2002) (only activities that have no objectively reasonable applications towards FDA approval fall out of the scope of

Integra v. Merck,¹⁹⁶ the Supreme Court's subsequent reversal,¹⁹⁷ and the recently issued opinion on remand,¹⁹⁸ which will be analyzed below, the scope of § 271(e)(1) with respect to the use of research tools remains far from clear.

1. *Integra v. Merck*—Facts

Integra owned several U.S. patents on pharmaceutically useful peptides containing a short tri-peptide segment of fibronectin (the RGD-Peptide)¹⁹⁹ that promotes cell adhesion by interacting with $\alpha_v\beta_3$ receptors on the cell surface proteins (integrins).²⁰⁰ A representative claim 8 of the '525 patent reads:

A substantially pure peptide including as the cell-attachment-promoting constituent the amino acid sequence Arg-Gly-Arg-R wherein R is Ser, Cys, Thr or other amino acid, said peptide having cell-attachment promoting activity, and said peptide not being a naturally occurring peptide.²⁰¹

The invention claimed to improve wound healing and biocompatibility of prosthetic devices and to facilitate the generation of new blood vessels (angiogenesis).²⁰² Dr. Cheresch, working for The Scripps Research Institute (hereinafter: Scripps), discovered that angiogenesis could be inhibited by blocking the $\alpha_v\beta_3$ receptors. He deemed this a promising means of halting tumor growth by starving the dividing tumor cells as

§ 271(e)); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104 (D. Mass. 1998) (safe harbor applies to infringement of a drug patent for purposes which may be related to FDA approval, but may serve additional purposes); *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833, 2001 WL 1512597 at *3 (S.D.N.Y. 2001) (use of patented drug intermediaries in experiments to research drug analogs is exempted from infringement).

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

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

198. *Integra Lifesciences I, Ltd. v. Merck KGaA (Merck II)*, 496 F.3d 1334 (Fed. Cir. 2007).

199. RGD refers to the amino acid sequence arginine-glycine-aspartic acid.

200. *Merck I*, 331 F.3d at 862. Integra asserted that Merck violated four of its patents: U.S. Patents No. 4,988,621 (filed Dec. 10, 1987) (issued Jan. 29, 1991), 4,792,525 (filed Jun. 17, 1985) (issued Dec. 20, 1988), 5,695,997 (filed Jun. 2, 1995) (issued Dec. 9, 1997), 4,879,237 (filed May 24, 1985) (issued Nov. 7, 1989) and 4,789,734 (filed Aug. 6, 1985) (issued Dec. 6, 1988).

201. U.S. Patent No. 4,792,525 (filed June 17, 1985) (issued Dec. 20, 1988). Other patents were directed to processes involving the attachment properties of the RGD-peptides, *see infra* Part VIII.A.

202. *See infra* Part VIII.A. However, as Judge Newman noted in her dissent, the inventors failed to develop a commercially viable product and thus sold them to Integra. *Integra Lifesciences I, Ltd. v. Merck KGaA (Merck I)*, 331 F.3d 860, 873 (Fed. Cir. 2003) (Newman, J., dissenting).

well as a possible means of treating several other diseases.²⁰³ The $\alpha_v\beta_3$ receptors are the receptors stimulated by the RGD-peptides.²⁰⁴

Merck hired Dr. Cheresch and Scripps to identify potential drug candidates which may inhibit angiogenesis.²⁰⁵ After Dr. Cheresch identified the cyclic peptide EMD 66203, Merck entered into a research agreement with Scripps and funded the experiments necessary to satisfy the regulatory requirements for the implementation of clinical trials with the identified peptide or a derivative thereof.²⁰⁶ Scripps identified two additional derivative peptides and conducted several *in vitro* and *in vivo* experiments on the three peptides to determine their specificity, efficacy, and toxicity with respect to various diseases, as well as the best method for therapeutically administering the peptides.²⁰⁷ Eventually, in 1997, the derivative peptide EMD 121974 was chosen for clinical development.²⁰⁸ Scripps also performed basic research on organic mimetics designed to block $\alpha_v\beta_3$ receptors in similar manner and used the RGD-peptides as “positive controls” for efficacy testing.²⁰⁹

When Integra learned of the research agreement between Merck and Scripps, it offered a license to its RGD patents and sued Merck when their lengthy licensing negotiations failed.²¹⁰ Merck contended that the patents were invalid and that their research fell into the safe harbor of

203. *Id.* at 862.

204. *Id.* at 863.

205. *Id.* at 862.

206. *Id.*

207. *Id.*

[The experiments included] modifications in the structure of RGD-containing peptides and investigations of their properties in the Scripps/Merck collaboration, including: receptor binding assays to investigate the efficacy and specificity of structural change; angiogenesis/chick CAM assays for inhibition of blood vessel formation in chick embryos when vessel growth is artificially induced, to study the mechanism of action, pharmacokinetics, and other properties; *in vivo* experiments to investigate inhibition of artificially induced vascularization in mice; cell adhesion assays by spectrophotometric measurement of inhibition of cell attachment to protein, to provide information about mechanisms, efficacy, and other properties; chemotaxis studies to determine the effect of various peptides on cell migration over extracellular matrix fibers; use of chick embryos to obtain pharmacokinetic data; fluorescent-activated cell sorting to study the effect on the receptor-ligand binding reaction, to aid in understanding mechanisms of activity; vascularization of the retina and induced arthritis of the joints, studied with mice and rabbits; chick CAM assays to study angiogenesis associated with tumor transplantation and growth in chick embryos; and tumor growth in SCID-mice or nude mice, including studies of mechanism, pharmacology, and pharmacokinetics.

Id. at 874.

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

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

210. *Merck I*, 331 F.3d at 863.

§ 271(e)(1).²¹¹ After trial, a jury found Merck liable for infringing four of Integra's patents and determined that the safe harbor did not extend to the experiments conducted between 1995 and 1998, i.e. the *in vitro* and *in vivo* experiments to identify suitable RGD peptides and elucidate their properties.²¹²

2. The Federal Circuit's Original Decision

On appeal, the Federal Circuit construed the words "solely for purposes reasonably related to the development and submission of information under a Federal law" very narrowly.²¹³ Analyzing the legislative history, it affirmed the district court's interpretation that the safe harbor of § 271 (e)(1) is confined to "activity that 'would contribute (relatively directly)' to information the FDA considers in approving a drug," i.e. applies only to experiments providing information which is *actually* submitted in FDA approval process.²¹⁴ It qualified part of the experiments conducted by Scripps as general biomedical research to identify new compounds, and, as such, outside of the § 271(e)(1) safe harbor.²¹⁵

The majority opinion explicitly mentioned the problem of applying the § 271(e)(1) safe harbor to research tools and was motivated to a narrow construction by its fear that the inclusion of "the Scripps Merck activities would effectively vitiate the exclusive rights of patentees owning biotechnology tool patents."²¹⁶ Since research tools do not only serve to identify potential drug candidates in upstream research, but are also used in downstream experiments which may fall into the safe harbor of

211. *Id.* at 863.

212. The trial judge instructed the jury as follows:

To prevail on this defense, [petitioner] must prove by a preponderance of the evidence that it would be objectively reasonable for a party in [petitioner's] and Scripps' situation to believe that there was a decent prospect that the accused activities would contribute, relatively directly, to the generation of the kinds of information that are likely to be relevant in the processes by which the FDA would decide whether to approve the product in question.

Merck v. Integra, 545 U.S. at 200–01. The Judge went further in saying that "[Petitioner] does not need to show that the information gathered from a particular activity was actually submitted to the FDA." *Id.*

213. *Merck I*, 331 F.3d at 865.

214. *Integra Lifesciences I, Ltd. v. Merck KGaA (Merck I)*, 331 F.3d 860, 867 (Fed. Cir. 2003) (citing *Intermedics Inc. v. Ventritex Inc.*, 775 F. Supp. 1269, 1280 (N.D. Cal. 1991), *aff'd*, 991 F.2d 808 (Fed. Cir. 1993)). The court stated that "[t]he FDA has no interest in the hunt for drugs that may or may not later undergo clinical testing for FDA approval." *Id.* at 866.

215. *Id.*

216. *Id.* at 867.

§ 271 (e)(1), a broad reading of the provision would greatly diminish the commercial benefit owners of patented research tools could expect.²¹⁷

Dissenting from the majority's construction of § 271(e)(1), Judge Newman opined that all activities conducted by Merck and Scripps should be exempted from infringement either under the common law experimental use exemption or the statutory exemption of § 271(e)(1).²¹⁸ Her dissent addresses in detail the scope of the common law research exemption and why her proposed interpretation would not vitiate the commercial value of biotechnology research tools.²¹⁹ However, Judge Newman is not explicit about the extent to which she would apply the statutory exemption of § 271(e)(1) to the use of research tools for FDA purposes because she ultimately determined that the RGD peptides were not used as research tools.²²⁰ Nevertheless, one can speculate that she would make the same distinction between "research *on*" (exempted) and "research *with*" (not exempted) a patented tool that she suggested as appropriate for the common law research exemption.²²¹

3. The Supreme Court Decision

The Supreme Court reversed the lower court's narrow interpretation of § 271(e)(1) and construed the provision more broadly.²²² It agreed with the Federal Circuit that "basic scientific research on a particular compound, performed without the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce" is no longer "reasonably related" in the meaning of § 271(e)(1).²²³ However, it stated that

[I]t does not follow from this, however, 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. Under

217. *Id.*

218. *Id.* at 874 (Newman J., dissenting) (arguing that there should not be an "intervening kind of limbo" between exploratory research exempted under the common law exemption and research for FDA approval exempted under § 271(e)(1) as it would defeat the purpose of both exemptions).

219. *Id.* at 874-76.

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

221. *Id.* at 876.

222. *Merck KGaA v. Integra Lifesciences, Ltd.*, 545 U.S. 193 (2005). Justice Scalia, writing for a unanimous court, stated that "§ 271(e)(1) provides a wide berth for the use of patented drugs in activities related to the federal regulatory process." *Id.* at 193.

223. *Id.* at 205-06.

certain conditions, we think the exemption is sufficiently broad to protect the use of patented compounds in both situations.²²⁴

Categorically excluding the first category would ignore the realities of the drug development process where no one can predict whether a particular compound will “survive” testing as a potential drug candidate and will eventually be submitted for FDA approval.²²⁵ Similar reasons apply to the second category because not all experiments necessary to determine the suitability of potential drug candidates yield information that is ultimately submitted to the FDA.²²⁶ Finally, the court held that all activities fall into the safe harbor of the statutory exemption where

a drugmaker has a reasonable basis for believing that a patented compound may work, 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.²²⁷

4. The Federal Circuit Decision On Remand

On remand, the Federal Circuit reversed the district court’s finding of infringement and held that all experimental activities under dispute fell under the safe harbor of § 271(e)(1) because they were conducted to determine the *optimal* candidate angiogenesis inhibitor and to comply with requirements of the drug approval process.²²⁸ It determined that the experiments were conducted after the tumor-inhibiting property of the RGD-peptide was discovered and were directed to obtaining information on efficacy, mechanism of action, pharmacology, and pharmacokinetics.²²⁹ Following the Supreme Court’s construction of § 271(e)(1), the Federal Circuit determined that the experiments were exempted from infringement as the information was deemed relevant to the drug approval

224. *Id.* at 206.

225. *Id.* at 207. Additionally, as the court noted, a party is often uncertain, especially at the preclinical stage, what kind of information and in what quantity will be required to receive the FDA’s approval. *Id.* (citing *Intermedics v. Ventritex*, 775 F. Supp. 1269, 1280 (N.D. Cal. 1991)) (“[I]t 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.”).

226. *Id.* at 207–08.

227. *Id.* at 207.

228. *Integra Lifescience I, Ltd. v. Merck KGaA (Merck II)* 496 F.3d 1334, 1340 (Fed. Cir. 2007).

229. *Id.* at 1346–47.

process and did not constitute inquiry into basic science.²³⁰ Finally, the court rejected Integra's contention that only "routine" experiments devoid of any discovery (i.e. experiments to show bioequivalence) could be subject to the exemption under § 271(e)(1); to the contrary, it confirmed that experiments are not deprived of the safe harbor if they yield further information which lead to a better understanding.²³¹

The majority expressly did not opine on whether and how far the safe harbor extends to the use of research tools, finding that the Supreme Court ruled that the case did not raise the issue and taking into consideration that "the parties emphatically confirmed that research tools were not at issue."²³² In his separate opinion, however, Judge Rader considered the issue to be raised when he characterized two of the patents as being directed to research tools and, therefore, criticized the majority's reversal of infringement as an improper extension of the safe harbor to research tools.²³³ It is true that the patents in question were directed to research tools; however, the fear that the majority decision would cast a "large shadow" over patent protection may not materialize to the extent predicted, as will be discussed *infra* VIII. A.²³⁴

5. Analysis

The application of § 271(e)(1) to the various stages of experimentation now seems somewhat clearer: basic experimentation does not benefit from § 271(e)(1), whereas clinical and pre-clinical tests fall under the scope of § 271(e)(1). Nevertheless, the impact of the Supreme Court decision on the use of patented research tools is not clear. Some commentators have interpreted the decision narrowly, only applying § 271(e)(1) to the patent on the listed drug the generic version is meant to substitute;²³⁵ some favor a broader application to any patented invention used during the experiments, thus also exempting the use of research tools;²³⁶

230. *Id.* The court explicitly rejected Integra's argument that only obtaining information on safety could constitute an acceptable purposed under § 271(e)(1).

231. *Id.* at 1346–47.

232. *Id.* at 1348 (stating that the decision "casts no 'large shadow' on the subject of 'research tools'").

233. *Id.* at 1352–53 (Rader J., dissenting-in-part and concurring-in-part); *see also* 3 MARTIN J. ADELMAN, PATENT LAW PERSPECTIVES § 3.6[2] at n.34 (Matthew Bender 2d ed. 2007).

234. *Integra Lifescience I, Ltd. v. Merck KGaA (Merck II)* 496 F.3d 1334, 1348 (Fed. Cir. 2007).

235. *Cf., e.g., Pfaff, supra* note 61, at 267.

236. *See, e.g., Bradley J. Olson, The Supreme Court's Merck KGaA v. Integra Lifesciences I, Ltd. Opinion Extends the Exemption from Infringement under § 271(e)(1) to Biotechnology "Research Tools", 3 J. INT'L BIOTECHNOLOGY L. 16 (2006)* (interpreting the decision as "in essence, a new form of compulsory license"); Tara Stuart, *Has the Supreme Court Incorrectly Expanded § 271(e)(1) to Risk a Regulatory Taking?*, 5 J. MARSHALL REV.

and yet others argue that the decision does not make any statement about research tools at all.²³⁷

The better arguments speak in favor of a neutral interpretation, which is also the view adopted both by the Federal Circuit's majority opinion and Judge Rader's dissent/concurrence on remand.²³⁸ Some may find the Court's extension of the exception to the "use of patented compounds in experiments that are not ultimately submitted to the FDA" as ambiguous and interpret this as holding that the exception relates also to research tools used for the experiments. However, the immediate context, as well as the Court's reasoning, warrant a less inclusive, or at the very least neutral, reading.²³⁹ Throughout the decision, the court refers only to "patented inventions" or "patented compounds" which "are appropriate for submissions to the FDA," giving no reason for implying that the use of research tools is generally exempted under § 271(e)(1).²⁴⁰ Additionally, the "ominous" footnote 7 of the opinion clearly states that the Supreme Court did not opine on the scope of research tool patents.²⁴¹ Finally, considering that the court determined that the RGD peptides were not used as research tools, the principle of judicial restraint sup-

INTELL. PROP. L. 216, 229 (2006) (finding the new scope of § 271(e)(1) extremely broad and including the use of research tools); Li Westerlund, *Blocking Effects? Research Tool Patents and the 'Safe Harbor' Exemption*, 174 PAT. WORLD 16 (2005) (stating that the Supreme Court's decision "effectively diminished the value of research tool patents").

237. See, e.g., Martha M. Rumore, *Safe Harbor or Pirate Cove? Merck v. Integra and its Seeming Impact on International Research Activities*, 3 ABA SCITECH LAW, Winter 2007, at 14 (recalling the fact, that the Supreme Court did not opine on whether research tools are exempted under § 271(e)(1), a disappointment for academia and biotech industry); Jonathan McPherson, *The Impact of the Hatch-Waxman Act's Safe Harbor Provision on Biomedical Research Tools after Merck KGaA v. Integra Lifesciences I, Ltd*, 10 MICH. ST. J. MED. & L. 369, 370 (2006); James Borchardt, Note, *Merck v. Integra: § 271(e)(1) and the Common Law Exemption*, 19 J. CORP. L. 943, 955 (2007).

238. *Merck II*, 496 F.3d 1334. The majority opinion declined to rule on question because it determined that the Supreme Court ruled the issue as not raised by this case. *Id.* at 1348. While Judge Rader stated in his dissent that the Supreme Court did not express any view on the issue of research tools, he nevertheless inferred that the Supreme Court did not expect to extend the exception to the use of research tools. *Id.* at 1350, 1353 (Rader J., dissenting-in-part and concurring-in-part) ("The Supreme Court simply did not intend to even address research tools, let alone, render research tools valueless for their one and only use—to test and ascertain information about candidate compounds. . . . The Supreme Court in *Merck* did not expect such a broad result.").

239. *Merck v. Integra Lifesciences Inc.*, 545 U.S. 193, 206–07 (2005).

240. *Id.* at 207. See also Pfaff, *supra* note 61, at 267.

241. The court cited Judge Newman's distinction of "[u]se of an existing tool in one's research is quite different from study of the tool itself" in the same note. *Merck v. Integra*, 545 U.S. at 206. Nevertheless, it would seem a stretch to interpret the court's citation as "subscribing to her point of view." But see Pfaff, *supra* note 61, at 267 for such interpretation. See also McPherson, *supra* note 237, at 282–83 (interpreting the allusion to Judge Newman's distinction as a hint as to how the court would analyze the issue absent further congressional clarification).

ports the interpretation that the Supreme Court did not address the impact of the statutory experimental use exemption with respect to the use of research tools, and only defined at which level experiments can fall into the safe harbor of § 271(e)(1).²⁴²

Where does that leave us? The Supreme Court has left a virtually blank slate for the Federal Circuit to determine whether the use of patented research tools in experiments that are “reasonably related” falls into the safe harbor of § 271(e)(1). On remand, the Federal Circuit did not state a rule on whether the use of research tools is exempted under § 271(e)(1), and the court declined to opine on the issue as not being before the court.²⁴³ As will be shown in section VIII. A. of this Article, the facts make the case unsuitable for establishing a *general* rule.²⁴⁴

B. The German Exemption for Clinical Trials

It may seem counter-intuitive to look to a European clinical trial exemption for guidance on the interpretation of the safe harbor provision of § 271(e)(1), since the European provisions have been inspired by § 271(e)(1) and are often referred to as the *Roche-Bolar* provision.²⁴⁵ Nevertheless, the European provisions can provide some guidance because the rationale for both provisions is to correct an unintended *de facto* term extension for patented drugs and facilitate an early market debut of cheap generic drugs.²⁴⁶

As discussed above, the distinction between experiments “on” and “with” the patented invention is settled law in the context of the experimental use exemption. However, no case law exists with respect to the clinical trials exemption which was introduced to implement the European Directive 2004/27/EC.²⁴⁷ The German experimental use exemption and corresponding provisions in most European countries have generally been interpreted as not allowing experiments to prove bioequivalence. Such experiments are deemed as not directed at obtaining new

242. See also McPherson, *supra* note 237, at 381 (stating that the Supreme Court followed its “role within the judiciary branch, leaving legislative activities to elected officials”).

243. *Integra Lifescience I, Ltd. v. Merck KGaA (Merck II)* 496 F.3d 1334, 1347-48 (Fed. Cir. 2007).

244. *Infra* at Part VIII.A.

245. Compare the explicit references to the U.S. provision in the legislative proposal, Commission Proposal for a Regulation of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products, at 72-73, 130-31, COM (2001) 404 final, (Nov. 26, 2001).

246. Cf. Pub. L. No. 98-417, *supra* note 185; Council Directive 2004/27/EC, *infra* note 247.

247. Council Directive 2004/27/EC, 2004 O.J. (L 136) 34 (EC) (amending Directive 2001/83/EC on the Community code relating to medicinal products for human use). The directive had to be implemented into national laws by October 30, 2005.

information on the patented compound but merely at confirming that the generic product had the claimed properties.²⁴⁸ This restrictive interpretation stifled competition between original and generic drug manufacturers and forced manufacturers to conduct the required testing for drug approval abroad.

To secure a sufficient supply of inexpensive drugs and allow generic drug producers to conduct the required experiments within its territory, the European Communities amended the *Community code relating to medicinal products for human use* through European Directive 2004/27/EC.²⁴⁹ Besides harmonizing and streamlining the drug approval process for generic drugs in Europe, the directive introduced a new *Bolar*-type provision in amended Article 10(6), which stipulates that studies and trials necessary for generic drug approval and “consequential practical requirements” are not to be regarded as “contrary to patent rights or supplemental protection certificates for medicinal products.”²⁵⁰

The German legislator implemented the exemption in § 11 No. 2b of the German Patent Act, which now exempts from the effects of the patent “[s]tudies and trials and the consequential practical requirements necessary to obtain a permission to market in the European Union or to obtain an authorization in the Member States or in third countries according to the effective pharmaceutical regulations.”²⁵¹

The broad wording of the provision does not expressly limit the exception to experiments *on* the patented subject matter, which could be (mis-)understood as exempting from infringement the use of *any* patented invention, i.e. including the use of research tools if they are used

248. Cornish, *supra* note 144, at 753. Reformulating the requirements set forth in the *Clinical Trials* decisions, academics defined “experiment” as necessarily presupposing the existence of uncertainty. See Rolf Pietzcker, *Patentrechtliche Fragen bei Klinischen Versuchen—eine Erwiderung* [Questions of Patent Law relating to Clinical Trials—A Response], GRUR INT. 1995, 319, 320; Hieber, *supra* note 133, at 441; von Meibom & Pitz, *Clinical Trials*, *supra* note 152, at 248; HIDERO NIIOKA, KLINISCHE VERSUCHE IM PATENTRECHT [CLINICAL TRIALS IN PATENT LAW] 276–78 (2003). See also Andries van der Merwe, *Experimental Use and Submission of Data for Regulatory Approval*, 31 IIC 380, 380 (2000).

249. Council Directive 2004/27/EC, *supra* note 247.

250. Article 10(6) reads: “Conducting the necessary studies and trials with a view to the application of paragraphs 1, 2, 3 and 4 and the consequential practical requirements shall not be regarded as contrary to patent rights or to supplementary protection certificates for medicinal products.” *Id.* at 40. Paragraphs 1, 2, 3 and 4 specify the data which has to be submitted for drug approval process in case of generic drugs. *Id.*

251. The provision has been introduced as part of the 14th Law amending the German Pharmaceuticals Act and entered into force on September 6, 2005. The legislative proposals referred to the provision as a “Roche-Bolar-Rule.” See BTDrucks 15/5656 at 1–3, 75–77; BTDrucks 15/5316, at 1–3, 31–34.

for experiments necessary for the drug approval process.²⁵² However, the better arguments favor a more restrictive interpretation.

1. Legislative History

The legislative history of § 11 No. 2b as well as the legislative history of its European root give no indication that the provision should extend to the use of research tools. Whenever legislators discussed the necessity to exempt generic drug manufacturers during clinical trials, reference was only made to the patent or supplementary protection certificate on the *original product*.²⁵³ Furthermore, the provision needs to be interpreted in systematic context of the experimental use exemption of § 11 No. 2 German Patent Act and thus—absent of any diverging intent of the legislator—needs to be read consistently with the *Clinical Trials* jurisprudence limiting the exception to experiments on the patented subject matter.²⁵⁴ Additionally, as will be argued in the next subsection, an extension to research tools would conflict with higher ranking law.²⁵⁵

2. Constitutional Guarantee of Property Under Article 14 I German Basic Law

Patent rights fall under the constitutional guarantee of property under Article 14(1), 1st sentence German Basic Law.²⁵⁶ However, property rights are not guaranteed without limits and, pursuant to Article 14(1), 2nd sentence of the German Basic Law, the legislator can determine the boundaries of property rights. The Federal Constitutional Court held that the experimental use exemption codified in § 11 No. 2 German Patent Act constitutes a permissible limit on the property rights conveyed by a

252. See Holzapfel, *Research Tools*, *supra* note 154, at 16 (citing Wolfgang von Meibom & Ina vom Feld, *Durchgriffsansprüche (Reach-Through-Ansprüche) bei Patenten für Forschungszwecke* [Reach-Through Claims in Patents on Research Uses], in “Festschrift für Bartenbach” 398 (2005)).

253. Cf. European’s provision the Commission’s proposal, *supra* note 245, COM (2001) 404 final, at 72, 130, 197 (provision allows the testing required “prior to the expiry of the originator product’s period of patent protection”). With respect to the German provision, compare the Legislative Proposals BTDrucks 15/5316, at 31, 48, and BTDrucks 15/5656, at 18, as well as the Final Report of the Committee for Health and Social Security, BTDrucks 15/5728, at 84. Furthermore, the amendment is not found in legislation directed at amending the German patent law, but in a revision of the medicinal laws, which suggests that the legislators were concerned with the patents covering medicinal products and not with any other patent affected during the clinical trials. See Pfaff, *supra* note 61, at 270–71.

254. See Holzapfel, *Research Tools*, *supra* note 154, at 16; Pfaff, *supra* 61, at 271–72.

255. See *infra* Part VII.C.2. See also Holzapfel, *Research Tools*, *supra* note 154, at 16.

256. Bundesverfassungsgericht [BverG] [Federal Constitutional Court], May 10, 2000, 1 [BvR] 1864/95—*Klinische Versuche* [Clinical Trials], GRUR 2001, 43 (hereinafter: *Clinical Trials III*). Article 14 reads: “(1) Property and the right of inheritance shall be guaranteed. Their content and limits shall be defined by the laws.”

patent under Article 14(1), 2nd sentence of the Basic Law.²⁵⁷ Furthermore, the court confirmed that the German Federal Court of Justice's interpretation is constitutional.²⁵⁸ experiments on a patented invention can be exempted even if they are not directed at finding a new medical indication.²⁵⁹ Losses directly incurred by the patentee as a consequence of the clinical trials have to be accepted because those losses will be limited if the clinical trials are actually experimental.²⁶⁰ However, the court noted that disproportional losses could be incurred if the experimental use privilege was abused by actually exploiting the patented compound, and that an extension of the privilege to such cases would violate the constitutional guarantee of property under Article 14(1), 1st sentence of the Basic Law.²⁶¹

Permitting experiments with biotechnological research tools either under the experimental use exemption or the clinical trial exemption under § 11 Nos. 2, 2b German Patent Act would allow for the full exploitation of the patented invention because the research tools would be used for the very purpose that merited the grant of the patent. The research tool owner does not benefit from a successful market approval of the final drug as his patent will regularly not cover the final drug. An extension of the exemptions to some or all uses of pure research tools²⁶² would strip the patent right of its value and violate the institutional guarantee of property under Article 14(1), 1st sentence of the German Basic Law.²⁶³

Accordingly, the use of research tools in experiments would not be exempted under the § 11 No. 2b German Patent Act.

VII. WHY AN EXTENSION OF EITHER EXEMPTION IS INADVISABLE

Neither a broadly understood common law experimental use exemption nor a properly construed § 271(e)(1) should extend the safe harbor

257. *Id.* at 44.

258. *Clinical Trials II*, *supra* note 133 (rejecting to restrict the scope of the exemption only to experiments which are directed to finding a new indication). *Cf. Clinical Trials I*, *supra* note 156.

259. *Clinical Trials III*, *supra*, note 256, at 44–45.

260. *Id.* at 45.

261. *Id.*

262. Philippe Ducor, *Research Tool Patents and the Experimental Use Exemption—A No-Win Situation?*, 17 *NATURE BIOTECHNOLOGY* 1027 (1999); Eisenberg, *supra* note 3, at 1074; Eisenberg, *supra* note 172, at 225.

263. Holzapfel, *Research Tools*, *supra* note 154, at 16; HOLZAPFEL, *EXPERIMENTAL USE*, *supra* note 152, at 330. A different conclusion may be reached for dual purpose research tools, where the final pharmaceutical product would fall into the scope of the research tool patent because the patentee could still stop the use of the pharmaceutical product, meaning that the patent would not yet be stripped of any value. *Id.*

for the use of a patented research tool beyond experiments *on* a patented invention. Under this narrow principle, experiments *on* research tools are exempted from infringement liability by § 271(e)(1) whereas the use of research tools in experiments constitutes patent infringement. As will be shown below, such interpretation is supported by the legislative history, best conforms to the rationale of the patent system, and stays within the limits of higher-ranking law.

A. The Legislative History Warrants a Limited Interpretation of Section 271(e)(1)

An expansion of the safe harbor of § 271(e)(1) to the use of research tools would go beyond the intent of Congress when it adopted this legislation.²⁶⁴ As noted above, § 271(e)(1) was introduced in part to respond to Federal Circuit's narrow application of the common law experimental use exemption in order to allow drug manufacturers to conduct the experiments necessary for the approval of their generic version of a patented drug.²⁶⁵ During the deliberations on § 271 (e)(1), the responsible House Committee characterized the "nature of the interference with the rights of the patent holder" as "de minimis" and not "substantial."²⁶⁶ The provision was intended to exempt only the amount of testing necessary for the drug manufacturers to establish bioequivalence of their generic drug version during the term of the patent, thus rectifying a *de facto* extension of the patent term due to the FDA approval process.²⁶⁷ Since the research tools are not subject to drug approval, there is no distortion of the patent term requiring amelioration.²⁶⁸

Extending the provision to the use of research tools would no longer affect the patentee's rights in the "limited" or "de minimis" way foreseen by Congress because the commercial value of the patent would be

264. See Brief for the United States as Amicus Curiae Supporting Petitioner at *20, *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005) (No. 03-1237), 2005 WL 429972; Pfaff, *supra* note 61, at 266. For an even more limited interpretation of the safe harbor as not extending to testing directed to finding new drugs, see Stuart, *supra* note 236, at 236; Paul Wiegel, *Was the FDA Exemption to Patent Infringement, 35 U.S.C. § 271(e)(1), Intended to Exempt a Pharmaceutical Manufacturer's Activities in the Development of New Drugs*, 2007 B.C. INTELL. PROP. & TECH. FORUM & J. 112901.

265. See *supra* Part VI.A. See also *Scripps Clinic & Research Found. v. Genentech, Inc.*, 666 F. Supp. 1379, 1396 (N.D. Cal. 1987) (interpreting the legislative history to allow only testing for bioequivalence).

266. H.R. REP. NO. 98-857 (II), as reprinted in 1984 U.S.C.C.A.N. at 2686, 2714.

267. *Id.* at 2692.

268. Stuart, *supra* note 236, at 234. Cf. George Fox, Note, *Integra v. Merck: Limiting the Scope of the § 271(e)(1) Exception to Patent Infringement*, 19 BERKELEY TECH. L.J. 193, 197 (2004) (explaining the rationale of Hatch-Waxman with the need to reduce both "front term" and "back term" distortion).

greatly, if not completely, diminished.²⁶⁹ Furthermore, as will be argued in a following section, the extended exception would arise to the level of a regulatory taking, which would violate the express intent of Congress.²⁷⁰

B. Public Policy Demands a Restrictive Interpretation

Although there are different justifications for a broadly understood common law experimental use exemption and the safe harbor provision of § 271(e)(1),²⁷¹ similar considerations of public policy caution against exempting the use of research tools from infringement under either exemption.

1. Common Law Experimental Use Exemption

It is questionable whether an extension of the common law experimental use exemption would provide long-term benefits to technological progress. One might expect that research and development activity increases over the short term, as all *existing* research tools could be freely used by any interested researcher. Also, no project would be affected by a lack of access to a needed research tool, which is arguably in the public interest.²⁷² However, free access to inventions assumes that there are, in fact, inventions to be accessed, and thus can only arise *after* an invention has been conceived.²⁷³ To limit the patent owner's remedies of injunctive or monetary relief could deleteriously take away incentives for the creation of new research tools.²⁷⁴ There are few reasons for a commercial

269. See Ducor, *supra* note 262; Eisenberg, *supra* note 3, at 1074; Eisenberg, *supra* note 172, at 225.

270. H.R. REP. NO. 98-857(II), at 29–30 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2686, 2713–14; Stuart, *supra* note 236, at 231. With regard to regulatory taking, *see infra* Part VII.C.1.

271. Whereas the purpose of the common law exemption is to facilitate technological progress by permitting experiments to obtain new knowledge on the patented invention in all technical fields, the safe harbor merely permits for the rapid introduction of cheap generic drugs. *See supra*, Part VI.A. with regard to § 271(e)(1) and *supra* Part V.C. with regard to the common law experimental use exemption.

272. In any case, empirical studies suggest that intellectual property rights are not of high concern to academic researchers and do not usually stop them from pursuing a research project. Walsh et al., *View from the Bench*, *supra* note 136, at 2002 (Only four out of 32 researchers who were aware of relevant IP rights (of a total of 381 respondents) changed their research approach and 5 delayed experiments for more than a month). *See also infra*, Part VII.B.5.

273. FRIEDRICH-KARL BEIER & JOSEPH STRAUS, *DER SCHUTZ WISSENSCHAFTLICHER FORSCHUNGSERGEBNISSE* [THE PROTECTION OF SCIENTIFIC RESEARCH RESULTS] (1982), marginal note 78; Ducor, *supra* note 262, at 1028; Holzapfel, *Research Tools*, *supra* note 154, at 14.

274. Mueller, *supra* note 1, at 47 n.235 (citing Rebecca S. Eisenberg & Robert P. Merges, *Opinion Letter As To the Patentability of Certain Inventions Associated With the Identification of Partial cDNA Sequences*, 23 AIPLA Q.J. 1, 19 (1995)).

enterprise to invest in the development of a new research tool without a chance to recoup the investment and realize a profit.²⁷⁵ As patents for their developed technologies are often the only asset for biotechnological tool companies, an evisceration of this value could drive these companies out of business.²⁷⁶ Inaccessibility to a particular technology can serve as a powerful stimulant to design around and find alternative means, which may provide a better solution to the problem at hand.²⁷⁷

Consequently, research tools would increasingly have to be developed by non-for-profit research institutions or in-house by the companies needing them, diminishing the highly successful diversification and specialization of the biotechnology industry.²⁷⁸ Presumably, this would lead to a decrease in innovation because it would dry up the contribution of small- and medium-sized companies, who are the most innovative.²⁷⁹

Furthermore, even assuming that the industry giants would succeed in developing the necessary tools themselves, the very nature of research tools—their use in laboratories—makes them a highly suitable candidate for trade secret protection because they are used only in a controlled environment by highly educated personnel. Without a guarantee of exclusivity, a firm would have no reason to disclose the research tool, thus depriving the public of learning of (and studying) the invention.²⁸⁰ The kind of technology transfer between firms, which is facilitated

275. Stuart, *supra* note 236, at 234–35. See also Eisenberg, *supra* note 3, at 1074 (“An experimental use exemption seems most likely to undermine critical patent incentives when the researcher is an ordinary consumer of an invention with a primary or at least significant market among research users. For example, an exemption from infringement liability for research users of a patented laboratory machine would effectively eliminate the benefits of patent protection for the invention.”).

276. See Ducor, *supra* note 262, at 1027; Michel, *supra* note 134, at 369–70; M. Patricia Thayer & Richard A. De Liberty, *The Research Exemption to Patent Infringement: The Time Has Come for Legislation*, 41 J. Biolaw & Bus. 1, 7 (2000); HOLZAPFEL, EXPERIMENTAL USE, *supra* note 152, at 329–31.

277. *State Indus. v. A.O. Smith Corp.*, 751 F.2d 1226, 1236 (Fed. Cir. 1985) (“One of the benefits of a patent system is its so-called ‘negative incentive’ to ‘design around’ a competitor’s products, even when they are patented, thus bringing a steady flow of innovations to the marketplace.”).

278. See Wolfgang von Meibom & Ina vom Feld, *Durchgriffsansprüche (Reach-Through-Ansprüche) bei Patenten für Forschungszwecke* [Reach-Through Claims in Patents on Research Uses], in *FESTSCHRIFT FÜR BARTENBACH* 385 (2005) (referring to the progressing and successful specialization in pharmaceutical research).

279. Cf. Aggarwal et al., *supra* note 30, at 643 (considering small-and medium-sized enterprises as playing a key role as suppliers of knowledge in the biotech sector); HOLGER PATZELT, *BIOENTREPRENEURSHIP IN GERMANY* 19 (2005), http://deposit.d-nb.de/cgi-bin/dokserv?idn=979509874&dok_var=d1&dok_ext=pdf&filename=979509874.pdf (last accessed Jan. 3, 2008) (“Since modern biotechnological methods are most efficiently invented and developed in an academic and entrepreneurial atmosphere, it is difficult for pharma firms to build up these technologies internally.”).

280. Stuart, *supra* note 236, at 234–35 (comparing such extension to a general compulsory licensing of research tools). See also Mireles, *supra* note 2, at 216.

through the publication of the patent specification, will be severely curtailed and result in a wasteful duplication of research and development efforts, as each firm would have to develop the (same) tool itself.

Circling back to the distinction between “research on” and “research with” a patented tool, a further difference between the two categories deserves mentioning. Research “on” a patented tool to further understanding of its technology absolutely cannot be conducted without experimenting on that invention. On the other hand, only a small minority of research projects would seem to absolutely require the use of one particular research tool. Admittedly, there will always be a “best” research tool, and a research project could progress faster or at a lower cost with its use rather than with one that is less effective. However, as discussed above, a decision to change the research trajectory need not have a negative overall welfare effect.²⁸¹ Finally, higher license fees for more effective tools may be the appropriate prize to stimulate the continuous innovation of research tools.

2. Section 271(e)(1)

This same policy consideration, i.e. the preservation of the necessary incentives for research tool manufacturers, counsels against extending the safe harbor to the use of research tools. The rationale of § 271(e)(1) is to facilitate the early introduction of cheap generic drugs and research tools, which can significantly contribute to shaving time and money off the drug development process.²⁸² Of course, if the common law experimental use exemption continues to apply in the narrow form established by the current state of law,²⁸³ the incentive to invest would not be diminished to the same extent because there is still a market for research tools outside the domain of clinical trials for FDA approval. However, even where a market for research tools remains, the incentive provided by the patent grant could be dangerously impaired.²⁸⁴

281. See *supra* notes 110–111 and accompanying text.

282. See, e.g., Malakoff & Service, *supra* note 52, at 1193 (“Aided by new technologies that enable researchers to rapidly screen thousands of genes and their protein products for potentially useful properties, the companies sped from gene identification to product testing in just eight months, shaving at least two years off the typically long and costly drug-discovery process.”).

283. See *supra* Part V.A.

284. Mireles, *supra* note 2, at 214–15. See also Eisenberg, *supra* note 3, at 1074 (“[A]n exemption from infringement liability for research users would deprive patent holders of some of the social value of their inventions, thereby reducing the value of patents and weakening patent incentives. Whether such an exemption is nonetheless desirable in the interest of promoting continuing scientific progress is ultimately an empirical question.”).

3. Why A Liability Rule Should Also Be Rejected

Various proposals have been made for adopting a liability rule for research tool patents.²⁸⁵ Under the liability rule concept, patents no longer confer exclusivity but only give the patentee the right to demand reasonable compensation for the use of the patented invention.²⁸⁶ This concept is based on the argument that patents on (upstream) research tools impede the innovation process, and that unfettered access to research tools best serves the public interest in stimulating the technological and economic progress.²⁸⁷ An exemption distinguishing between basic research and commercial research will be impossible to administer in practice because basic research can often result in highly practicable applications.²⁸⁸ Likewise, research performed in laboratories of commercial enterprises can produce scientific discoveries.²⁸⁹ Finally, the ex-post determination of appropriate compensation for the use of a research tool patent would raise considerable difficulties.²⁹⁰

Even if practical, such models would violate obligations under the TRIPS Agreement (especially Articles 27(1), 28(1) and 30) for the same reasons that an extension of an experimental use exemption to the use of

285. See, e.g., Derzko, *supra* note 3, at 388–408 (proposing a differentiated liability rule for research tool patents depending on the type of entity using the tool (public vs. for-profit) and the intended use (basic science vs. development of commercial product)); Eisenberg, *supra* note 3, at 1078 (proposing the exemption of the use of “an invention in subsequent research in the field of the invention, which could potentially lead to improvements in the patented technology or to the development of alternative means of achieving the same purpose” and with a compensation for the patent owner only in appropriate cases); Mueller, *supra* note 1, at 54–60 (further developing Eisenberg’s proposal and arguing for a liability rule with ex post royalty determined based on the market value of products developed through the use of the patented research tool); Feit, *supra* note 77, at 840 (proposing to allow for the making and using of patented technology for significant improvements, with the sale of resulting products being excused from infringement of the underlying technology). For a detailed analysis of the socio-economic arguments in favor of and against the introduction of a liability rule in general see Mark A. Lemley & Philip J. Weiser, *Should Property or Liability Rules Govern Information?*, 85 TEX. L. REV. 783 (2007); Robert P. Merges, *Contracting into Liability Rules: Intellectual Property Rights and Collective Rights Organizations*, 84 CAL. L. REV. 1293, 1302–07 (1996). Particularly with regard to research tools, see HOLZAPFEL, EXPERIMENTAL USE, *supra* note 152, at 334–36, 344–48.

286. See Merges, *supra* note 285, at 1302 (regarding the general liability rule framework).

287. But see Eisenberg, *supra* note 3, at 1075–76 (stating that a broad exemption may stimulate inventive activity by permitting free access to necessary resources while at the same time depressing the inventive activity by reducing the incentive, and observing the difficulty of assessing the net impact on willingness to conduct research).

288. Eisenberg, *supra* note 172, at 195–96.

289. *Id.*

290. Cf. Mueller, *supra* note 3, at 979 (“Although courts are adept at computing reasonable royalty compensation for past infringements, it is unclear that the same judicial expertise could be applied without significant modification to the case of prospective, ongoing experimental use.”).

research tools would fail to comply with the TRIPS obligations.²⁹¹ Furthermore, a general liability rule could not be justified under the compulsory licensing provision of Article 31 of the TRIPS Agreement.²⁹² Even if all other conditions were satisfied, each of the cases would have to be considered on its individual merits (Article 31(a) of TRIPS) and would be subject to judicial review (Article 31(1) of TRIPS), which would result in markedly different proceedings than those suggested under the liability rule concepts.

4. Complementary Measures to Facilitate Access

As argued above, the distinction under the European approach would preserve the necessary incentives for the creation of research tools. As a consequence of preserving the patentee's exclusive right, some situations may arise where strategic bargaining will prevent access to a particular resource.²⁹³ Nevertheless, complementary measures to facilitate improved access to needed research tools exist which better conform to the principles of a market economy than either the extension of exemptions or a liability rule concept.

a. Facilitating Access to Government Funded Research Tools

The commercial sector spends a very small portion of its funds on early stage R&D and is predominantly focused on evolutionary R&D.²⁹⁴ This suggests that a significant proportion of research tools are developed under government-funded programs, mainly through NIH grants. Access to research tools created through NIH-funded research could be facilitated by including a provision in the grant that requires non-discriminatory licensing of the research tool to any party, similar to the principle of "license of right" in other patent jurisdictions.²⁹⁵ The rationale of the patent system is different for product companies and tool companies: product companies have an incentive to invest/commercialize

291. See *infra* Part VII.C.2.

292. But see Mueller, *supra* note 1, at 58 n.283 (rather summarily stating that her proposal of limiting the exemption to cases "where the research tool is not readily accessible through licensing or purchase in the marketplace is in keeping with the 'failure of private bargaining' restriction on compulsory licensing" under Article 31 of TRIPS).

293. See, e.g., Robert Merges, *Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents*, 62 TENN. L. REV. 75, 78 & nn.6-8 (1994).

294. U.S. DEP'T OF COMMERCE, *ATP Report*, *supra* note 43, at 2. For a detailed analysis, see LEWIS M. BRANSCOMB & PHILIP. E. AUERSWALD, BETWEEN INVENTION AND INNOVATION 42-47 (2002), available at <http://www.belfercenter.org/files/betweeninnovation.pdf> (last visited Jan. 3, 2008).

295. See Garde, *Supporting Innovation*, *supra* note 27, at 276-84 (discussing the concept of license of right in European statutory provisions and suggesting that the NIH includes such provisions in their grants with respect to research tools).

due the expensive development process, whereas tool companies are incentivized to invent, which would need to be balanced with the research grant system to maintain the same rate of invention.²⁹⁶

Alternatively, government agencies could exercise their statutory march-in rights under the Bayh-Dole Act and compel the licensing of invention derived from previously funded research.²⁹⁷ However, the NIH has refrained from ever exercising that right thus far.²⁹⁸

b. Last Resort Compulsory Licensing

It remains a possibility that free market negotiations may fail to facilitate access to research tools for the continuation of a socially useful and desirable research project.²⁹⁹ In such cases, the grant of a compulsory license may be appropriate. A compulsory license would be less intrusive on the patent owner's exclusive rights than a liability rule, which is a general extension of the experimental use extension to the use of research tools.³⁰⁰ Article 31 of TRIPS limits the member states' freedom to grant compulsory licenses.³⁰¹ It sets certain minimum standards that the

296. Cf. Garde, *Supporting Innovation*, *supra* note 27, at 277–78 (arguing that only the incentive to invent has to be balanced where public access to research tools should be facilitated through licenses of right).

297. 35 U.S.C. § 203(a) (2000).

298. Rai & Eisenberg, *supra* note 48, at 294–95 (suggesting that the procedure of exercising the march-in right is too cumbersome). Mireles, who argues in favor of facilitating access through an increase of patent pools, suggests an amendment to the provision that would allow the government to transfer a non-exclusive license to patented research tools developed under government funding to patent pools created by industry participants if the patentee unreasonably opposes the licensing of his research tools to the pool. Mireles, *supra* note 2, at 230–34. For an example of a case in which the NIH denied exercising its right, see Cell-Pro, Inc. March-In Petition (Mar. 3, 1997) and *In Re* Petition of CellPro, Inc. (Aug. 1, 1997), both available at <http://www.nih.gov/icd/od/foia/cellpro>. See also Amy R. Schofield, *The Demise of Bayh-Dole Protections Against the Pharmaceutical Industry's Abuses of Government-Funded Inventions*, 32 J.L. MED. ETHICS 777, 778 (2004) (analyzing the case in detail).

299. The previously described measures—even if applied extensively—could not be used to facilitate access to research tools developed without government funding.

300. Cf. Holzapfel, *Research Tools*, *supra* note 154, at 17; HOLZAPFEL, EXPERIMENTAL USE, *supra* note 152, *passim*; von Meibom & Pitz, *supra* note 149, at 30–33. However, empirical studies identified only isolated cases of abuse of patent rights which could justify the grant of a compulsory license. See NIH, RESEARCH TOOLS, *supra* note 71; Ducor, *supra* note 262, at 1028; OECD, *supra* note 102, at 10, 45–47, 77; John P. Walsh et al., *Working Through the Patent Problem*, 299 SCI. 1021 (2003); JOSEPH STRAUS ET AL., GENETIC INVENTIONS AND PATENT LAW: AN EMPIRICAL SURVEY OF SELECTED GERMAN R & D INSTITUTIONS 20–22 (2004).

301. Article 5A of the Paris Convention imposes additional limitations as it prohibits the grant of a compulsory license for failure to work the invention within a certain period after the date for the patent grant. For an analysis of both provisions and their relationship, see Joseph Straus, *Implications of the TRIPs Agreement in the Field of Patent Law*, in FROM GATT TO TRIPS—THE AGREEMENT ON TRADE-RELATED ASPECTS OF INTELLECTUAL PROPERTY RIGHTS 203–08 (Friedrich-Karl Beier & Gerhard Schrickler, eds. 1996). See generally Sara M.

compulsory licensing provisions of most European countries track closely.³⁰² However, the efficacy of compulsory licensing provisions has always been that their mere existence facilitates contractual license negotiations, and thus few compulsory licenses have actually been granted.³⁰³

As noted at the outset of this article, compulsory licensing provisions are alien to U.S. patent law and are unlikely to be adopted in the near future.³⁰⁴ However, despite the absence of compulsory licensing provisions in the US Patent Act and the almost automatic grant of a permanent injunction upon a finding of patent infringement under previous case law,³⁰⁵ there have been several cases where a court has determined that a patent was infringed but denied injunctive relief on equitable considerations.³⁰⁶ In its recent decision, *eBay v. Mercexchange*, the Supreme

Ford, *Compulsory Licensing Provisions under the TRIPS Agreement: Balancing Pills and Patents*, 15 AM. U. INT'L L. REV. 941 (2000).

302. See Grace K. Avedissian, *Global Implications of a Potential U.S. Policy Shift Toward Compulsory Licensing of Medical Inventions in a New Era of "Super-Terrorism"*, 18 AM. U. INT'L L. REV. 237 (2003) for an overview of U.S. and foreign positions towards compulsory licensing of research tools. On June 11, 2007, the Swiss Council of States approved the proposed amendments to the Swiss Federal Law on Patent for Inventions, which include, *inter alia*, a compulsory licensing provision for biotechnological research tools. See Law of June 22, 2007 available at <http://www.admin.ch/ch/d/ff/2007/4593.pdf> (last accessed Jan. 3, 2008) (amending the Federal Law on Patents for inventions). The new Article 40b provides for a right to a non-exclusive license for the use of patented biotechnological research tools, with the terms of the license to be judicially determined where negotiations fail. See *id.* at Article 40e(1). It seems questionable, however, that a statutory provision codifying the right to a license for a group of inventions observes the requirement of Article 31(a) of TRIPS, namely that the decision on the grant has to be based on individual merits.

303. Even prior to the limitations imposed to TRIPS, compulsory licensing occurred only rarely. See Straus, *supra* note 301, at 208. The frequency of compulsory licenses granted in industrialized countries after the adoption of TRIPS has certainly not increased. In Germany, there had been only 12 applications for a compulsory license between 1961 and 1991, and only one was granted. See von Meibom & Pitz, *supra* note 149, at 30–32. No compulsory licenses have been granted since.

304. See *supra* note 6.

305. In a decision later vacated by the Supreme Court, the Federal Circuit recited its general rule that "that a permanent injunction will issue once infringement and validity have been adjudged", and that "courts have in rare instances exercised their discretion to deny injunctive relief in order to protect the public interest." *Mercexchange, L.L.C. v. eBay Inc.*, 401 F.3d 1323, 1338 (Fed. Cir. 2005), *vacated*, 547 U.S. 388 (2006). See also Mueller, *supra* note 3, at 967–68 (reporting on the repeated rejection of remedies to infringement which would resemble compulsory licensing); Colleen Chien, *Cheap Drugs at What Price to Innovation: Does the Compulsory Licensing of Pharmaceuticals Hurt Innovation?*, 18 BERKELEY TECH. L.J. 853, 880–91 (2003) (analyzing six cases where compulsory licenses to pharmaceutical patents were ordered by the FTC under consent decrees as an antitrust remedy).

306. *Cf., e.g., Hybritech, Inc. v. Abbott Lab.*, 4 U.S.P.Q.2d 1001, 1987 WL 123997 (C.D. Cal. 1987), *aff'd*, 849 F.2d 1446 (Fed. Cir. 1988) (continuing supply of infringer's medical test kits not marketed by patentee required by public interest); *Vitamin Technologists, Inc. v. Wis. Alumni Research Found.*, 146 F.2d 941, 955–56 (9th Cir. 1945) (finding patentee's refusal to allow irradiation of oleomargarine, which would have aided or cured rickets in consumers, to

Court held that even after a finding of infringement, the decision to grant or deny a permanent injunction remains governed by equitable considerations.³⁰⁷ Injunctive relief is to be granted only after the application of a four-factor test. The patentee must show that (1) he has suffered an irreparable injury, (2) that available remedies, such as monetary damages, are insufficient to compensate for that injury, (3) that a remedy in equity is warranted in view of a balance of hardships of patentee and infringer, and (4) that the public interest would not be disserved by a permanent injunction.³⁰⁸

With the Supreme Court's *eBay* decision, a sword of Damocles, similar to the existence of a compulsory licensing provision, hangs over the patentee's head as he can no longer count on obtaining a permanent injunction quasi-automatically when his patent is infringed. A stringent application of this test, especially of the public interest factor, could benefit researchers who are unable to negotiate adequate access to research tools where the use of a specific research tool is crucial for the pursuit of an identified research goal, such as the treatment of a particular disease.

5. Why Differential Treatment for Universities is Inappropriate

Different proposals have been made to treat universities and other non-profit organizations preferentially and to permit their use of research tools.³⁰⁹ However, as will be argued in this subsection, the distinction between permissible research on a patented invention and impermissible

be against the public interest). *See also* Roche Prods., Inc. v. Bolar Pharm. Co., 733 F.2d 858, 865–66 (remanding after a finding of infringement for determination on the grant of injunctive relief).

307. *eBay Inc. v. Mercexchange, L.L.C.*, 547 U.S. 388, 391 (2006).

308. *Id.* at 389. The *eBay* decision seems to make redundant the change to § 283, as originally proposed in § 7 of the Patent Reform Act of 2005, H.R. 2795. The contested proposal—if implemented—would have weakened the strong pre-*eBay* presumption for permanent injunctive relief after a finding of infringement, Christopher M. Holman, *Biotechnology's Prescription for Patent Reform*, 5 J. MARSHALL REV. INTELL. PROP. L. 318, 322 (2006). The Biotechnology Industry Organization (BIO) was adamant about removal of the provision curtailing the grant of permanent injunctions. *See* Statement of Robert Chess, *supra* note 19, at 6. As a matter of fact, the implementation of the proposed language would strengthen the position of the patent owner post-*eBay*, as the infringer would have to affirmatively show that a stay of the injunction would not result in irreparable harm to the patent owner and that the balance of hardships does not favor the owner of the patent. Under *eBay*, the patent owner has the burden of proof that the four factor test is satisfied; additionally, Section 7 of H.R. 2795 would only weaken the presumption in the case of a decision which can be appealed, whereas *eBay* still applies the four-factor test to decisions that can no longer be appealed. The new proposals H.R. 1908 / S. 1145 do not include a proposal to restrict the grant of injunctive relief.

309. *See, e.g.*, Derzko, *supra* note 3 (distinguishing, *inter alia*, based on the profit or non-profit status of the researching entity).

research with a patented invention should apply equally to industrial research and to research by non-profit institutions.³¹⁰

Historically, basic (or upstream) research results were predominantly published without attaining patent protection because the prestige and reputation resulting from the successful completion and publication of a research project was sufficient motivation.³¹¹ This practice led to direct enrichment of the public domain and did not restrict the use of these results for further research.³¹² However, the idea that universities are disinterested temples of knowledge, and thus their accumulation and dissemination of knowledge should be favored by a broader exemption, is no longer apposite in view of the profound changes that the Bayh-Dole Act has brought upon the previously non-commercial and purely research-oriented academic landscape.³¹³ The distinction between upstream non-profit institutions conducting basis research and downstream for-profit companies researching practical applications is reflective of the 1980s, but does not correspond with today's reality.³¹⁴

310. See Cai, *supra* note 48, at 191 which considers a bright-line elimination of the experimental use exception for universities as they aggressively enforce their patent rights to not be unfair, and thus universities should be reciprocally liable to infringement litigation. Furthermore, public universities still have the benefit of sovereign immunity, but this does not extend to private universities. *Id.* The European experimental use exemption does not distinguish at all between research conducted by universities and that conducted by for-profit enterprises, as it is solely focused on the object of the research and ignores further (commercial) motivation. See *supra* notes 149–151 and accompanying text. See also Cornish, *supra* note 144, at 736 (finding that national European courts have moved back from drawing “a strategic distinction between academic research and research in industry,” which reflects the closer assimilation of basic and applied science, especially in the area of biotechnological and biomedical research).

311. See Eisenberg, *supra* note 172, at 181 (“Universities, where much of the research was conducted, encouraged the dissemination of research results through publication and occasionally showed a positive aversion to patenting discoveries.”) Academic researchers are motivated by the professional recognition they receive for original contributions. *Id.* at 183–84.

312. *Id.* at 184.

313. Arti K. Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 Nw. U. L. Rev. 77, 110 (1999) (“[T]he legal developments of the 1980s and 1990s have generated a large variety of academic-industrial relationships [S]ome academic-industrial relationships resemble commercial joint ventures.”). See Eisenberg, *supra* note 129, at 1019 (viewing universities as more vulnerable to patent infringement suits as they have become “increasingly aggressive as patent owners [and thus] have compromised their claim to disinterested stewardship of knowledge in the public interest.”).

314. Cockburn, *supra* note 43, at 388–90; Lynn E. Nimtz et al., *University-Industry Partnerships: Meeting the Challenges with High Tech Partner*, 27 SRA J. 9, 9 (1996) (“Today’s knowledge-based, technological society demands much from higher education and the corporate world—demands that often can be met through effective university—industry partnerships.”); NIH, RESEARCH TOOLS, *supra* note 71 (“Biomedical researchers increasingly chose to collaborate with entrepreneurial companies that understood and valued basic science”). See generally Powell & Owen-Smith, *supra* note 44.

While non-commercial research still makes up the bigger part of their work, university researchers have become more intensively engaged in commercial activities.³¹⁵ The commercial component of their research can hardly be considered insignificant when university-private industry cooperations have added \$41 billion to the U.S. economy and supported 270,000 jobs in 1999.³¹⁶ The distinctions between academic and research institutions and for-profit enterprises have become more and more difficult to ascertain. Close cooperation and overlap between these formerly distinct sectors has increased greatly, partly due to the success of the Bayh-Dole Act.³¹⁷ This change is seen in the increase of corporate-sponsored research in universities, which rose from \$236 million in 1980 to \$1.3 billion in 1992.³¹⁸ Further evidence of closer cooperation is highlighted by increased patenting,³¹⁹ increased licensing activities,³²⁰ and the (sometimes aggressive) enforcement of intellectual property rights by academic and research institutions.³²¹

Equal treatment under law is not unfair where academic and research institutions conduct commercial research and compete with for-profit enterprises. Even when universities and other non-profit organizations are subject to the same rules as commercial entities, they enjoy a *de*

315. Industry funding of university research rose from 2.7% in 1970 to 6.9% in 1990 and remained somewhat stable at the level, accounting for 7% of university research funding in 2001 with declining trend. WALSH ET AL., *supra* note 107, at 11 (citing to data of the National Science Board 2004).

316. Mireles, *supra* note 2, at 156 (citing DAVID M. EPSTEIN, ECKSTROM'S VOL. 2 LICENSING IN FOREIGN AND DOMESTIC OPERATIONS § 11.16 (2003)).

317. See Mueller, *supra* note 1, at 33–38. Nelsen partially attributes the increased interaction of universities with the private sector to the reduction in government funding of research and development as the result of the attempts to balance the federal budget and the decreased spending for military research following the decline of communism, Nelsen, *supra* note 47, at 1460. Cf. Eisenberg, *supra* note 172, at 179 (stating that “[t]he sudden juxtaposition of commercial incentives and scientific norms has been particularly striking in the biomedical sciences, in part because of the strong public interest in health-related research and in part because of the rapid onset and proliferation of university-industry research relationships in biotechnology fields following decades of predominantly public funding”).

318. See U.S. DEP'T OF COMMERCE, ATP REPORT, *supra* note 43, at 6.

319. University patenting has increased from less than 250 in 1980 to more than 3,800 in 2004. See AUTM SURVEY, *supra* note 45, at intro. 2; since 1993, more than 34,500 patents have been granted to institutions participating in the AUTM survey. *Id.* at 2.

320. Between 1991 and 1995, nearly 5,400 licenses were granted by universities; more than 250 companies were founded directly through university licensing in 1996. Nelsen, *supra* note 47, at 1460. Since 1980, more than 4,500 companies have been created based on licenses from universities, hospitals and research organizations, AUTM SURVEY, *supra* note 45, at 3.

321. See, e.g., Univ. Of Rochester v. G.D. Searle & Co., 358 F.3d 916 (Fed. Cir. 2004) (patent infringement suit by university patent holder against drug manufacturer); Marcia Baringa, *Biotech Patents: Genentech, UC Settle Suit for \$200 Million*, 286 SCI. 1655 (1999) (discussing the patent infringement suit between the University of California and Genentech); Eisenberg, *supra* note 129, at 1018 (reporting the patent infringement suit between the University of Minnesota and Glaxo-Wellcome).

facto privilege over industrial research.³²² Patents are still unlikely to be asserted against university researchers even without a meaningful experimental use exemption, and such patent infringement suits are unlikely to become more frequent in the wake of a broadened exemption.³²³ Commercial enterprises are generally reluctant to sue non-profit enterprises, partly because they are concerned with their public image and do not want to be perceived as impairing university research. As an example, when Roche filed its suit against more than 40 American universities and research institutions (including Stanford, Harvard, MIT and The Scripps Research Institute) and more than 200 individual researchers, Roche maintained that it was not concerned with their use of Roche's patented Taq polymerase for "pure research" purposes, but would have to enforce their patent rights if the researchers engaged in "highly practical" research with the potential of making profits.³²⁴ Even DuPont, whose aggressive licensing approach has caused concerns in academic research, offered "free" research licenses to NIH scientists or grantees for non-commercial research to its OncoMouse and Cre-LoxP technologies and only charged a license fee when the respective animals are used in commercial activities, e.g. in drug screening.³²⁵

This "indulgent" attitude by commercial enterprises is mirrored by the predominantly careless, if not ignorant, attitudes of academic researchers who largely ignore patent rights when conducting their research.³²⁶ Furthermore, even when commercial enterprises attempt to

322. Walsh et al., *View from the Bench*, *supra* note 136, at 2002 ("Our research thus suggests that 'law on the books' need not be the same as 'law in action' if the law on the books contravenes a community's norms and interests."). *But see* Rai & Eisenberg, *supra* note 48, at 296 (deeming it "foolhardy for nonprofit researchers to rely on the forbearance of patent holders" in view of individual examples of aggressive licensing approaches).

323. *Cf.* Nelson, *supra* note 2, at 467 (Industry has granted a *de facto* experimental use exemption to universities. However, companies have become more reluctant to do so as they view universities as competitors to their own research efforts for achieving patentable practical results; additionally, as they have to increasingly license patented research results of universities, they feel more comfortable to reciprocate through the experimental use exemption.).

324. Mueller, *supra* note 1, at 3 (citing Bruce Rubenstein, *La Roche and Promega in Tug of War Over Enzyme; DNA-Testing Tool Patent at Issue*, CORP. LEGAL TIMES, Jan. 1996, at 28).

325. *See* Eliot Marshall, *The Mouse That Prompted a Roar*, 277 SCI. 24 (1997) [hereinafter Marshall, *Mouse*]; Eliot Marshall, *Intellectual Property: DuPont Ups Ante on Use of Harvard's OncoMouse*, 296 SCI. 1212 (2002). Even though DuPont offered free licenses for both technologies, academics perceived the license terms as burdensome and restrictive, as the patented mice could only be shared with researchers who had signed the license agreement. *Id.* The president of the U.S. National Academy of Science, Bruce Alberts, characterized the restrictive license terms on the Cre-loxP as a commercial barrier to basic research. Marshall, *Mouse*, *supra*, at 25. Rai & Eisenberg, *supra* note 48, at 296 (finding a general practice of informal prize discrimination for licensing to industry and academia).

326. *See* Eyal H. Barash, *Experimental Use, Patents, and Scientific Progress*, 91 Nw. U. L. REV. 667, 698 (1997) ("University researchers rarely check the patent literature to deter-

impose prohibitive licensing terms, academic research institutions are not defenseless but can muster considerable clout to achieve more permissive licensing terms, e.g. with the help of the NIH.³²⁷

C. Legal Restrictions Bar an Extension

1. Constitutional Restraints—The “Takings Clause”

As shown above, the commercial value of a patented invention that is solely or predominantly used for research purposes would greatly decrease, if not completely disappear, if the use of research tools is exempted for experiments under § 271(e)(1) or the common law exemption.³²⁸ Since patents are recognized as property rights under U.S. law,³²⁹ the permissibility of eviscerating such patents raises constitutional questions under the Fifth Amendment.³³⁰ A regulatory taking occurs when the government takes either the entire property right, or substantially deprives its owner of his rights so that the property is *de facto* taken.³³¹ In 1984, the Supreme Court clarified in *Ruckelshaus v. Monsanto* that the takings clause is applicable to intellectual property.³³² When Congress adopted the limited safe harbor of § 271(e)(1), it considered the restrictions of the takings clause, but determined that the safe harbor did not rise to the level of a taking and thus would not cause constitutional concerns.³³³

However, an extension of the safe harbor to permit any use of research tools needs to be evaluated differently and appears to rise to the

mine whether their proposed research will infringe on any patents.”); Walsh et al., *View from the Bench*, *supra* note 136, at 2002 (surveying the impact of patents on research choices in academia and reporting that even after *Madey*, only 5% of the respondents regularly check for existing patents in their field of research).

327. In the licensing of the *Cre-loxP* mouse technology mentioned *supra* note 325, DuPont initially included reach-through clauses in their license agreements. However, after the NIH threatened to boycott the technology unless academic researchers were granted access on more reasonable terms, DuPont agreed to the license the technology on less restrictive terms. *See, e.g.*, Memorandum of Understanding Between NIH and DuPont (Jul. 1, 1998), available at http://www.ott.nih.gov/policy/policies_and_guidelines.html (last accessed Jan. 3, 2008).

328. *See supra* notes 274–275 and accompanying text.

329. *See, e.g.*, *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 730 (2002).

330. The Fifth Amendment reads: “Private property [shall not] be taken for public use, without just compensation.” U.S. CONST. amend V.

331. *See Penn. Coal Co. v. Mahon*, 260 U.S. 393, 415 (1922).

332. *See Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1003–04 (1984).

333. H.R. REP. NO. 98–857(II), at 27–30 (1984), reprinted in 1984 U.S.C.C.A.N. 2686, 2713–14. However, Congress reached that conclusion after analyzing only the rather limited scope of the exception under debate, i.e. exempting testing on generic drugs to show bio-equivalence with already FDA approved drugs; not for the use for experiments of new innovative drugs or for the use of inventions not intended for FDA approval.

level of a taking under the *Penn Central*³³⁴ balancing test. Under this test, three factors must be taken into consideration: (1) the economic impact of the regulation on the property owner; (2) the character of governmental regulatory action; and (3) the extent the regulation interferes with reasonable “investment-backed expectations.”³³⁵ In her analysis of the Supreme Court’s *Merck* decision and its compatibility with the takings clause, Stuart convincingly concludes that an extension of the safe harbor for pure research tools would constitute a regulatory taking, but considers the situation more ambiguous with respect to patents on research tools which would allow the owner to dominate a final pharmaceutical product.³³⁶ In the latter case—dual purpose research tools—the detrimental effect on the investment-backed expectations caused by the uncompensated use of the research tool may be offset by the fact that an approved drug would fall in the scope of the patent and likely result in the payment of appropriate license fees for the exploitation of the drug.³³⁷

As a consequence, while extending the scope of the safe harbor to the use of research tools may not constitute a regulatory taking in all cases of research tool patents, a taking would presumably occur in a large number of cases. A general rule, meant to replace the case-by-case differentiation required under the *Penn Central* balancing test, must limit the safe harbor to experimentation *on* the patented subject matter and refrain from extending it to the use of research tools *in* experiments in order to eliminate any risk of a regulatory taking³³⁸

2. Restraints Imposed by the TRIPS Agreement

The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) entered into force on January 1, 1995 as part of the agreement establishing the World Trade Organization.³³⁹ The TRIPS Agreement was concluded after intensive negotiations to “reduce distor-

334. *Penn Cent. Transp. Co. v. New York City*, 438 U.S. 104 (1978).

335. *Id.* at 124.

336. Stuart, *supra* note 236, at 231–33.

337. *Cf. id.* at 233 (finding it difficult to determine the extent of encroachment on Telios’ property rights as Merck—even after gaining FDA approval—would not have been allowed to sell the tri-peptide under § 271 (e)(1))

338. *See id.* at 234–35.

339. Article II, Section 2 of the Marrakesh Agreement Establishing the World Trade Organization binds all of its members to the Agreement on Trade-Related Aspects of Intellectual Property Rights (“TRIPS”). Agreement Establishing the World Trade Organization, Apr. 15, 1994, 1867 U.N.T.S. 154, 33 I.L.M. 1144. For an account of the negotiating history, see Daniel Gervais, *The TRIPS Agreement: Drafting History and Analysis* (2d ed. 2003). For the effect of the TRIPS Agreement on the field of patent law, see Straus, *Implications of TRIPS*, *supra* note 301. The legal texts of the TRIPS Agreement and the WTO Agreement, available at http://www.wto.org/english/docs_e/legal_e/legal_e.htm.

tions and impediments to international trade” and set minimum standards for the protection of intellectual property rights.³⁴⁰ Both Germany and the United States are contracting parties to TRIPS and are thus bound by its limitations, which dictate restricting the experimental use exemption to research on the patented invention.

a. Articles 28(1) and 30

Article 28(1) of the TRIPS Agreement enumerates the minimum rights a patent confers on its owner, namely the exclusive right to “prevent third parties not having the owner’s consent from the acts of: making, using, offering for sale, selling, or importing for these purposes that product.”³⁴¹ Whereas any of the stated activities would, in principle, infringe a patent and could be enjoined by the patentee, the member states may introduce exceptions to the right conferred within the limits of Article 30 of TRIPS, which reads:

Members may provide limited exceptions to the exclusive rights conferred by a patent, provided that such exceptions do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.

Article 30 of TRIPS is generally understood as a compromise incorporating the generally accepted principle that actions should not constitute patent infringement if it stifles technological progress.³⁴² While

340. Agreement on Trade-Related Aspects of Intellectual Property Rights, Apr. 15, 1994, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments—Results of the Uruguay Round, 33 I.L.M. 333 (1994) [hereinafter TRIPS Agreement] (preamble).

341. Article 28 of the TRIPS Agreement reads:

Rights Conferred

1. A patent shall confer on its owner the following exclusive rights:
 - (a) where the subject matter of a patent is a product, to prevent third parties not having the owner’s consent from the acts of: making, using, offering for sale, selling, or importing for these purposes that product;
 - (b) where the subject matter of a patent is a process, to prevent third parties not having the owner’s consent from the act of using the process, and from the acts of: using, offering for sale, selling, or importing for these purposes at least the product obtained directly by that process.
2. Patent owners shall also have the right to assign, or transfer by succession, the patent and to conclude licensing contracts.

Id. at Art. 28.

342. See Straus, *supra* note 301, at 202–03.

it allows member states to introduce exceptions to the rights conferred by a patent, Article 30 does impose limits to their legislative freedom.³⁴³

In the WTO dispute settlement proceedings, *Canada—Patent Protection of Pharmaceutical Products*, the panel had the opportunity to interpret the restrictions under Articles 27, 28 and 30 of the TRIPS Agreement.³⁴⁴ At the heart of the proceedings were the regulatory review and the stockpiling exception codified in § 55(2) Canadian Patent Act. The regulatory review exception of § 55(2) No. 1 Canadian Patent Act was similar to 35 U.S.C. § 271(e)(1), as it allowed for the production, use and sale of a patented invention when used solely for the purpose of producing or submitting information required for the approval of the product.³⁴⁵ The stockpiling exception of § 55(2) No. 2 Canadian Patent Act let the third-party produce, use and stockpile patented pharmaceutically-active substances during the last six months of the patent term; the commercial sale of these products was prohibited.³⁴⁶

Canada conceded that these provisions conflicted with Article 28 of the TRIPS Agreement, but maintained that the exceptions were admissible under Article 30.³⁴⁷ It argued that the stockpiling exception permitted only limited actions by third parties and did not threaten the ordinary exploitation of the patent, as commercial competition would not be al-

343. See *infra* text accompanying notes 344–369. See also NUNO PIRES DE CARVALHO, *THE TRIPS REGIME OF PATENT RIGHTS* 304–06 (2005); Straus, *Implications of TRIPS*, *supra* note 301, at 203.

344. Panel Report, *Canada—Patent Protection of Pharmaceutical Products*, WT/DS114/R (Mar. 17, 2000) available at http://www.wto.org/english/tratop_e/dispu_e/cases_e/ds114_e.htm. For general information on dispute settlement proceedings, see Sigrid Dörmer, *Dispute Settlement and New Developments Within the Framework of TRIPS—An Interim Review*, 31 IIC 1 (2000); Sue Ann Mota, *TRIPS—Five Years of Disputes at the WTO*, 17 ARIZ. J. INT’L & COMP. L. 533 (2000).

345. Section 55.(2)(1) of the Canadian Patent Act states:

It is not an infringement of a patent for any person to make, construct, use or sell the patented invention solely for uses reasonably related to the development and submission of information required under any law of Canada, a province or a country other than Canada that regulates the manufacture, construction, use or sale of any product.

Patent Act, R.S.C., ch. P-4, § 55.2(1) (1985).

346. Section 55.2(2) of the Canadian Patent Act stated:

It is not an infringement of a patent for any person who makes, constructs, uses or sells a patented invention in accordance with subsection (1) to make, construct or use the invention, during the applicable period provided for by the regulations, for the manufacture and storage of articles intended for sale after the date on which the term of the patent expires.

Patent Act, R.S.C., ch. P-4, § 55.2(2) (1985) (repealed 2001);

Panel Report, *supra* note 344 at ¶ 2.1.

347. Panel Report, *supra* note 344, at ¶¶ 4.9–21.

lowed to enter the market prior to the end of the patent term.³⁴⁸ Furthermore, the exceptions were warranted in view of the goal of Articles 8(2) and 40 of the TRIPS Agreement to ensure unfettered competition as soon as possible after the expiration of the patent.³⁴⁹ Canada furthermore maintained that Articles 7 and 8(1) of the TRIPS Agreement permit the restriction of the rights and duties of a patentee for the public good and to ensure an affordable health care system.³⁵⁰ Countering these propositions, the EU and the member states argued that the stockpiling exemption violated Article 28(1) and 33 of the TRIPS Agreement because it effectively reduced the patent term for pharmaceuticals to nineteen and a half years.³⁵¹ Furthermore, they maintained that the provision violated the non-discrimination requirement of Article 27(1), because pharmaceutical patents would be treated differently from “ordinary” patents with respect to the effective patent term³⁵² and the permissible uses of the invention during the patent term.³⁵³

The panel found the regulatory review exception permissible under Article 30 of the TRIPS Agreement but determined that the stockpiling exception violated Canada’s obligation under the TRIPS agreement.³⁵⁴ It interpreted Article 30 to incorporate three cumulative limitations, requiring that exceptions (a) must be limited, (b) must not “unreasonably conflict with a normal exploitation of the patent,” and (c) must not “unreasonably prejudice the legitimate interests of the patent owner, taking account of the legitimate interests of third parties.”³⁵⁵

“Limited exception” connotes a narrow exception which makes only a “small diminution of the rights in question.”³⁵⁶ Decisive is the extent the legal rights have been curtailed, not the commercial impact of the limitation or the number of legal rights impaired.³⁵⁷ The stockpiling exception completely removed the patentee’s right to exclude competitors from “making” or “using” the patented invention as it neither restricted the quantity of production nor the market to be served.³⁵⁸ By eliminating the possibility of cutting off the supply of competing goods at the source, the exception abrogated those rights and thus could no longer qualify as

348. *Id.*

349. *Id.* ¶ 4.14.

350. *Id.* ¶¶ 4.11–14, 4.21.

351. *Id.* ¶¶ 3.1.I, 4.1–3.

352. *Id.*

353. *Id.* ¶¶ 3.1.II., 4.4–5.

354. *Id.* ¶ 8.1.

355. *Id.* ¶¶ 7.20–21.

356. *Id.* ¶ 7.30.

357. *Id.* ¶¶ 7.31–35.

358. *Id.* ¶ 7.34.

“limited exception.”³⁵⁹ Neither the limitation to the last six months of the patent term, which was deemed a commercially significant period of time,³⁶⁰ nor its limitation to entities which benefited from the regulatory review exception and to products which required regulatory approval could change the “limited exception” analysis, as the impact on each *affected* patent has to be considered, not the impact on patents as a whole.³⁶¹

However, regarding to the regulatory review exception, the panel concluded that the legal rights of the patent owner were curtailed only to a narrow extent, thus constituting a “limited exception.” It stated that

[a]s long as the exception is confined to conduct *needed* to comply with the requirements of the regulatory approval process, the extent of the acts unauthorized by the right holder that are permitted by it *will be small and narrowly bounded*. Even though regulatory approval processes may require substantial amounts of test production to demonstrate reliable manufacturing, the patent owner’s rights themselves are not impaired any further by the size of such production runs, as long as they are solely for regulatory purposes and *no commercial use* is made of resulting final products.³⁶² (emphasis added)

The panel further defined “normal exploitation” of a patent as the right to “exclude all forms of competition that could detract significantly from the economic returns anticipated from a patent’s grant of market exclusivity” during the patent term.³⁶³ Consequently, as only testing (and not the sale) of the pharmaceutical compounds was allowed, the panel saw no conflict with a normal exploitation of the patent.

Finally, the panel defined “legitimate interests” as being broader than “legal interests”³⁶⁴ and encompassing those interests which “are

359. *Id.* ¶ 7.36.

360. Especially in view of the absence of limitations with regard to quantity and market destination of the products. *Id.* ¶ 7.37.

361. *Id.* ¶ 7.37. The limitation regarding entities benefiting from the regulatory review exception does not exclude any competitors, as anyone intending to market a generic drug would have to undergo the drug approval process and thus would qualify under the exception. That the limitation is only for “products subject to regulatory approval” and did not apply to other products was deemed irrelevant for the analysis under Article 30 TRIPS as the impact on each affected patent has to be considered. *Id.*

362. *Id.* ¶ 7.45.

363. *Id.* ¶ 7.55. Economic returns during an additional period of market exclusivity after the expiration of the patent as a result of delayed competition due to a mandatory regulatory approval process do not fall under the “normal exploitation.” Such exclusivity is not purposely conferred by the patent right but is an unintended consequence of the conjunction of patent law and regulatory laws. *Id.* ¶ 7.57.

364. *Id.* ¶ 7.71.

supported by relevant public policies or other social norms.³⁶⁵ The patentee's interest in market exclusivity after the statutory patent term as "compensation" for the loss of effective patent duration due to regulatory approval processes was not recognized as a "legitimate interest" because such an extension was not a generally accepted legal principle.³⁶⁶ The provision already reflects the objectives and principles of Articles 7 and 8 of the TRIPS Agreement and cannot be interpreted as allowing the countries to *re-negotiate* the careful balance achieved in the TRIPS Agreement.³⁶⁷

Under the panel's interpretation, it seems clear that an extension of a clinical trial exception to the use of research tools would violate Articles 28(1) and 30 of the TRIPS Agreement. The exclusionary right of owners of research tool patents would be significantly curtailed because its use for research purposes (i.e. the primary, if not the sole application of such an invention) would be exempt from the patent right. Consequently, the limitation can hardly be considered limited. Compared to the situation reviewed by the WTO panel, extending the exemption would allow the use of the invention for its original patented purpose and conflict with the normal patent exploitation purpose, if not make it impossible. A judicial or legislative construction of the exception which would eviscerate the patent right would contradict the decision to grant patents for such technologies in the first place.³⁶⁸ The conferral of the patent right makes the patentee's interest in exploiting his invention during the patent term a legitimate interest. Furthermore, as discussed *supra*, the patentee's interest is not outweighed by the public interest in accessing research tools because maintaining the incentives for the creation of research tools is beneficial, if not vital, for a potential user of research tools and for research as such.³⁶⁹

365. *Id.* ¶ 7.69

366. *Id.* ¶¶ 7.68–83. Though several nations (e.g. European Communities, the U.S., Japan, Australia, Switzerland and Israel. Countries) had compensated the patentee by creating a period of market exclusivity or through a restoration of the patent term, other countries (Canada, Poland, Thailand, Argentina and Hungary) had refrained from doing so despite having a regulatory review exception. Consequently, the panel refrained from adjudicating a politically still unresolved policy issue by recognizing this interest as legitimate in the meaning of Article 30(1) of the TRIPS Agreement. *Id.* ¶¶ 7.77–79.

367. *See* Panel report in the dispute settlement proceedings. *Id.* ¶ 7.26.

368. HOLZAPFEL, EXPERIMENTAL USE, *supra* note 152, at 311.

369. *Supra* Part VII.B. *See also* HOLZAPFEL, EXPERIMENTAL USE, *supra* note 152, at 311; Ducor, *supra* note 262, at 1028.

b. Article 27 of the TRIPS Agreement

The impact of Article 27 of the TRIPS Agreement is slightly less clear. Article 27 prohibits, *inter alia*, discrimination in the granting of patents for technology. Article 27(1) reads:

Subject to the provisions of paragraphs 2 and 3, patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application. Subject to paragraph 4 of Article 65, paragraph 8 of Article 70 and paragraph 3 of this Article, patents shall be available and *patent rights enjoyable without discrimination* as to the place of invention, the field of technology and whether products are imported or locally produced.³⁷⁰ (emphasis added).

Articles 65(4) and 70(8) of the TRIPS Agreement, which provide transitional periods for developing countries,³⁷¹ and the exclusions from patentability under Article 27(3) are not relevant to the present issue as

370. Paragraphs 2 and 3, permitting the contracting states to deviate from the general prohibition of discrimination, allow exclusions from patentability only and thus do not impact the scope of rights conferred by a patent. They read:

Article 27(1): . . .

(2): Members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect *ordre public* or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law.

(3): Members may also exclude from patentability:

(a) diagnostic, therapeutic and surgical methods for the treatment of humans or animals.

(b) plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, Members shall provide for the protection of plant varieties either by patents or by an effective *sui generis* system or by any combination thereof. . . .

For the rationale and negotiation history of these provisions, see generally Pires de Carvalho, *supra* note 343, at 205–18, Gervais, *supra* note 339, at 222–25 (marginal notes 2.261–.265), and Charles M. McManis, *Patenting Genetic Products and Processes: A TRIPS Perspective*, in PERSPECTIVES ON THE PROPERTIES OF THE HUMAN GENOME PROJECT 79 (F. Scott Kieff, ed. 2003).

371. The referenced provisions allowed developing countries to delay the introduction of product protection for technical fields where it had not been available under the national law (Art. 65(4)) and establishes the “mail-box” system for pharmaceutical and agricultural chemical products (Art. 70(8)). For the negotiating history, see Pires de Carvalho, *supra* note 343, at 165–68.

they do not allow for an exception to the prohibition of discrimination with regard to the rights conferred by a patent.³⁷² The panel in the dispute settlement proceedings *Canada—Protection of Pharmaceutical Products* did not rule on whether a limitation of the regulatory review exception to pharmaceuticals actually violates the non-discrimination clause because it decided the case based on procedural issues and not on an interpretation of substantive law.³⁷³ The panel has, however, clarified that the prohibition against discrimination based on the field of technology also applies to exceptions under Article 30 of the TRIPS Agreement.³⁷⁴

An extension of the experimental use doctrine to research tools would unduly favor the use of an invention in research over the use of an invention for other purposes and would no longer be technology-neutral.³⁷⁵ Research tool technologies would be considerably disadvantaged compared to other technologies because the patentee would be unable to prevent their normal exploitation by third parties, thus eviscerating their commercial value.³⁷⁶ Such an extension would arguably be contrary to Article 27(1) of the TRIPS Agreement, as patent rights would no longer guarantee an equal opportunity of commercial exploitation across all fields of technology. This discriminatory treatment would be even more pronounced under the § 271(e)(1) safe harbor provision

372. The provisions allow for an exception to non-discrimination with regard to patentable subject matter only. The exclusion of diagnostic methods for the treatment of humans should, in principle, not apply to research tools, as their primary purpose is the use in laboratories to gather information, even if they may be used in diagnostics. For an interpretation of the corresponding EPC provision Article 52(4) (as in effect 1973), see the decision of the Enlarged Board of Appeal, G 1/04—*Diagnostic Methods*, 2006 O.J. Eur. Pat. Off. 331 (allowing patentability if the diagnostic step is not performed on the human body but can be performed in a laboratory). The U.S. Congress did not introduce an exception from patentability for these methods but chose to immunize medical practitioners and health care providers through 35 U.S.C. § 287(c)(1).

373. The panel first distinguished two different possibilities of discrimination: *de jure* discrimination, resulting from explicit different treatment, and *de facto* discrimination, as a result of identical treatment of different circumstances. It rejected the allegation of an *de jure* discrimination, determining that the EU did not present sufficient evidence that the exception was limited to pharmaceuticals because the wording of the statute extended its application to all products subject to market approval requirements. Likewise, it rejected the contention of a *de facto* discrimination because the EU did not present systematic information to substantiate its allegation that the provision “in effect” only applied to pharmaceutical patents despite its broad wording. See WT/DS/114/R, ¶¶ 7.99–102. However, while the panel did not *decide* based on substantive law, some language in the report suggests that it viewed a *de facto* application of the *de jure* broad regulatory review exception only to the field of pharmaceuticals as discriminatory. *Id.* ¶ 7.104 (“So long as the broader application is not a sham, the legislation cannot be considered discriminatory.”).

374. *Id.* ¶ 7.91.

375. HOLZAPFEL, EXPERIMENTAL USE, *supra* note 152, at 331.

376. See *supra* notes 274–275 and accompanying text.

because it is further limited to the group of research tools used in drug development processes.³⁷⁷

VIII. BORDERLINE CASES

Having established the general principle that the use of research tools should not be exempted under (any) experimental use exemption, it is readily apparent that there are some borderline cases that arguably warrant a different evaluation. The general principle stands in the case of research tools that the user cannot or only under great difficulties manufacture herself, can be best obtained from the patentee or his licensee, and—once they have been bought—can be used continuously as a result of exhaustion of the patent rights, e.g., a laboratory microscope or the Free Electron Laser used at Duke University.³⁷⁸ The same must apply where a laboratory commercially exploits a patented method for detecting a specific compound or specific characteristics of a compound.³⁷⁹ However, in some situations it is difficult to ascertain whether the experiment is solely directed at obtaining information about the patented invention or used to gather information about other compounds as well.

A. *Overlapping Inventive Concepts*—Merck v. Integra

Judge Rader correctly qualified two of Integra's asserted patents as being directed to research tools.³⁸⁰ Consequently, applying the same distinction adopted in this Article, he argues that the two patents should have been held to be infringing and appropriate damages should be awarded to the patentee.³⁸¹ Nevertheless, the specific facts of this case could constitute one of the borderline cases where policy considerations warrant an exception permitting the use of the research tools.

Claim 4 of the '237 patent claims:

A method for detaching animal cells from a substrate to which *they are bound in an Arg-Gly-Asp mediated manner*, comprising contacting said bound cells with a solution containing non-naturally occurring peptide *consisting essentially of the amino*

377. HOLZAPFEL, *EXPERIMENTAL USE*, *supra* note 152, at 331. *See generally* Eisenberg, *supra* note 172, at 225 (pointing out that individual areas of technology should not be left without adequate patent protection).

378. *Madey v. Duke Univ.*, 307 F.3d 1351 (Fed. Cir. 2002), cert. denied, 539 U.S. 958 (2003).

379. Holzapfel, *Research Tools*, *supra* note 154, at 14.

380. *Integra Lifesciences I, Ltd. v. Merck KGaA (Merck II)*, 496 F.3d 1334, 1350–52 (Rader, J., concurring-in-part and dissenting-in-part).

381. *Id.* at 1349.

acid sequence Arg-Gly-Asp-Y, wherein Y is any amino acid such that the peptide has cell-detachment activity.³⁸² (emphasis added)

The only claim of the other research tool patent, the '734 patent reads:

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.³⁸³ (emphasis added)

Since the '237 patent claims methods for detaching cells from an animal substrate, and the '734 claims a surface receptor, both inventions are research tools because they can only be used in a laboratory to conduct further research.³⁸⁴ Both patents are directed at compounds or methods that could not possibly be subject to FDA approval. Thus, they cannot benefit from the safe harbor of § 271(e)(1).³⁸⁵ Nonetheless, use of the patented methods should be exempted under § 271(e)(1) if the patented methods *must* be used during experiments on the patented RGD-peptide that are required for FDA-approval processes, lest the purpose of the Hatch-Waxman Act would be defeated.

In the present case, all four patents are directed either at specific types of RGD-peptides or at methods involving specific uses of those RGD-peptides; all four of these inventions are directed at or directly relate to the RGD-peptides' cell adhesion properties.³⁸⁶ Scripps' and Merck's experiments are directed at obtaining the necessary information for the drug approval process of their cyclic RGD-peptide EMD 121974, whose therapeutic value lies in influencing (blocking) the cell adhesion

382. U.S. Patent No. 4,879,237 (filed May 24, 1985).

383. U.S. Patent No. 4,789,734 (filed Aug. 6, 1985).

384. *Merck II*, 486 F.3d at 1350–52 (Rader J., dissenting).

385. *Id.* at 1350–53.

386. *Cf., e.g.*, Claim 1 of 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." (emphasis added); Claim 8 of the '525 patent: "A substantially pure peptide including as *the cell-attachment-promoting constituent* the amino acid sequence Arg-Gly-Arg-R wherein R is Ser, Cys, Thr or other amino acid, said peptide having *cell-attachment-promoting* activity, and said peptide not being a naturally occurring peptide." (emphasis added); Claim 4 of the '237 patent: "A method for detaching animal cells from a substrate to which *they are bound in an Arg-Gly-Asp mediated manner . . .*" (emphasis added); Claim 1 of the '734 patent: "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 . . .*" (emphasis added).

process.³⁸⁷ It would defeat the purpose of the Hatch-Waxman Act if experiments on the RGD-peptides, which are exempted from infringing the '525 and the '997 patents due to the safe harbor of § 271(e)(1), would nevertheless infringe the '237 patent and the '734 patent and could be enjoined by the patentee when they are all directed at the very characteristics that make the compound a (potential) drug candidate. If that were the case, any reasonably skilled patent drafter would be able to prevent generic drug manufacturers from using the safe harbor provision.

Whenever a molecule with potential therapeutic properties is discovered, the inventor will aim to receive a patent covering the molecule as well as potential useful applications (hereinafter referred to as the "molecule patent"; e.g. the '525). To prevent competitors from benefiting from the safe harbor of § 271(e)(1) in the future, an inventor will apply for an additional patent (hereinafter referred to as the "research tool patent") covering methods for conducting laboratory experiments with the molecule; the claims will be directed to methods on the physiological process which confers the therapeutic value to the molecule.³⁸⁸ The claims will be drafted in such way that anyone intending to conduct the experiments for FDA approval would have to make use of the method claimed in the research tool patent (such as, e.g. the '274 patent). In principle, the method patent does not confer any additional protection as compared to the molecule patent when the method is limited to uses of the molecule claimed in the other patent, as in *Integra v. Merck*. However, it could be used to attain a *de facto* extension of the patent term by enjoining clinical testing of the molecule, which would come back full circle to the scenario the Hatch-Waxman Act was intended to rectify. This should apply just the same as when a research tool patent has been filed years after the molecule patent when both patents are owned by the same entity.³⁸⁹ If the safe harbor is extended only to the exception discussed above, this would prevent the circumvention of the Hatch-Waxman Act, while not inappropriately disadvantaging the patentee be-

387. *Integra Lifesciences I, Ltd. v. Merck KGaA (Merck II)*, 496 F.3d 1334, 1344–45 (Fed. Cir. 2007).

388. The drafting of two applications would not conflict with the prohibition of double patenting under § 101 as the claims would be directed to different categories of patentable subject matter. See *Studiengesellschaft Kohle mbH v. N. Petrochemical Co.*, 784 F.2d 351, 355 (Fed. Cir. 1986) (per curiam), *cert. denied*, 478 U.S. 1028 (1986) ("Our predecessor court refused to find double patenting based, variously, on differences in claimed subject matter; on different statutory classes; on the existence of non-infringing uses; on differences in the breadth of the claims; and on the absence of 'cross-reading' (whether the claims of one patent can be infringed without infringing the other).").

389. The author notes that the factual situation would be considerably different where the ownership of the research tool patent and molecule patent diverge and reserves judgment on the best resolution of such situations.

cause no additional commercial value (beyond the value of the patent itself) is conferred to the clinical testers during the patent term.

The proposed resolution of the *Merck v. Integra* facts extends an argument that Holzapfel made with respect to a hypothetical situation where a patent contains claims directed at a molecule and its corresponding gene sequence.³⁹⁰ When the molecule is produced and used in experiments to further research its biological activity and suitability for therapeutic purposes, the experiments are exempted under the general principle—that is, permitting research *on* and prohibiting research *with* a patented invention—as they are directed at obtaining information about the molecule.³⁹¹ Using the DNA sequence for the sole purpose of producing the molecule would, in principle, not be exempted because such uses are not directed at obtaining information on the DNA sequence or on the molecule. However, when such claims are contained in the same patent application, the concept of unity of invention embedded in Article 84 of the EPC, Section 34 GPA requires the claims to be directed to the same invention.³⁹² It is recognized under European and German law that final products, processes for the production, and intermediate products constitute only a single, uniform invention.³⁹³ Consequently, as the claims must relate to the same invention, the experimentation on the subject of any one claim, i.e. the molecule, should be allowed to make use of any process, method, compounds claimed in any other claim of the patent.³⁹⁴

The concept of unity of invention is embedded in the international patent system through Article 3(4)(iii) of the Patent Cooperation Treaty (PCT) and has been adopted by several countries for their domestic proceedings.³⁹⁵ Rule 13.1 of the PCT Regulations defines unity of invention as “a group of inventions so linked as to form a single general inventive concept.”³⁹⁶ Under Rule 13.2, this concept requires a “technical relationship

390. Holzapfel, *Research Tools*, *supra* note 154, at 16 (Scenario 5).

391. *Id.*

392. *Id.*

393. BGH [German Federal Court of Justice], Case X ZB 2/73, GRUR 1974, 774 Alkalidiamidophosphite (June 26, 1974); EPO [European Patent Office] Board of Appeal, T 57/82, GRUR INT. 1982, 747 Copolycarbonates/BAYER (Apr. 29, 1982), <http://legal.european-patent-office.org/dg3/biblio/t820057ep1.htm>; Schulte, *in* Schulte, *supra* note 149, § 34 marginal note 260; Keukenschrijver, *in* Busse, *supra* note 149, § 34 marginal note 124. See Holzapfel, *Research Tools*, *supra* note 154, at 16.

394. Holzapfel, *Research Tools*, *supra* note 154, at 16.

395. Patent Cooperation Treaty, June 19, 1970, 28 U.S.T. 7645, 1160 U.N.T.S. 231, available at <http://www.wipo.int/pct/en/texts/pdf/pct.pdf>. See generally Jay Erstling & Isabelle Boutillon, *The Patent Cooperation Treaty: At the Center of the International Patent System*, 32 WM. MITCHELL L. REV. 1583 (2006).

396. Regulations Under the Patent Cooperation Treaty, Rule 13.1, June 19, 1970, 28 U.N.T. 7645, 1160 U.N.T.S. 231 [hereinafter *PCT Regulations*], available at http://www.wipo.int/pct/en/texts/pdf/pct_regs.pdf.

among those inventions involving one or more of the same or corresponding special technical features,” where the special features must lay in what each of the invention contributes over the prior invention.³⁹⁷ While U.S. patent law follows the restriction practice under § 121 for their domestic proceedings,³⁹⁸ it applies the unity of invention concept when acting in its PCT capacity.³⁹⁹ In that regard, 37 C.F.R. 1.475(b) clarifies that the requirement may also be satisfied where claims are directed to different categories of statutory subject matter.⁴⁰⁰

The *Merck v. Integra* situation differs markedly from Judge Rader’s hypothetical, where a university professor invents a highly useful research tool with the sole purpose of testing the effectiveness of other compounds in fighting cancer.⁴⁰¹ In his hypothetical, the inventor found a research tool with a broad application. Since the invention was not limited to a particular group of compounds (like RGD-peptides), the research tool and the compound undergoing experimentation could not be viewed as a uniform invention or as having a similar relationship. Furthermore, contrary to the situation in *Integra v. Merck*, the patented screening method does not have to be used in FDA mandated experiments. If it were the most effective method, it would indeed be a

397. See *supra* note 396, *PCT Regulations*, at Rule 13.2.

398. 35 U.S.C. § 121 (2002). See also 37 C.F.R. § 1.142. Requirement for restriction: “(a) If two or more independent and distinct inventions are claimed in a single application, the examiner in an Office action will require the applicant in the reply to that action to elect an invention to which the claims will be restricted, this official action being called a requirement for restriction (also known as a requirement for division)”

399. 35 U.S.C. § 372(b)(2) (2000); 37 C.F.R. §§ 1.475–.477, 1.488–.489, 1.499 (2005). See also U.S. Patent & Trademark Office, U.S. Dep’t of Commerce, Manual of Patent Examination Procedure 1850, 1875, 1893.03.d (8th ed. 2001, latest revision Sept. 2007), available at <http://www.uspto.gov/web/offices/pac/mpepl/>.

400. 37 C.F.R. § 1.475(b) provides:

An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

- (1) A product and a process specially adapted for the manufacture of said product; or
- (2) A product and process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) A process and an apparatus or means specifically designed for carrying out the said process; or
- (5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

401. *Integra Lifesciences I, Ltd. v. Merck KGaA (Merck II)*, 496 F.3d 1334, 1352 (Fed. Cir. 2007) (Rader, J., concurring-in-part and dissenting-in-part).

researcher's preferred choice; however, other, albeit less effective, methods will be available for testing so that a *de facto* extension of the patent term will not occur.⁴⁰²

B. Simultaneous Gathering of Information on Tool and Compound

Some biotechnological research tools are used in experiments to gather information on how a certain molecule interacts with another. Experiments *with* a patented research tool on a potential drug candidate will simultaneously produce information on both the compound under experimentation and on the research tool.⁴⁰³ For example, a screening with a receptor will yield information on the molecules binding to the receptor and about the binding characteristics of the receptor itself; similarly, screening with pharmaceutically active compounds for analogues will yield information both on the analogues and on the biologically active regions of the patented molecule. Consequently, it has been argued that the distinction between "research *on*" and "research *with*" no longer allows a distinction in such cases because the experiments will also, at the very least, yield information that relates to the subject matter of the invention—the research tool.⁴⁰⁴ While this argument certainly can be made, it is solely results-based and neglects the purpose of the respective experiments. Where the experiments are directed at obtaining information about another molecule, the research tool is nevertheless used according to its technical teaching, whose commercial exploitation has been allocated to the patentee by virtue of the patent grant.

1. Pure Research Tools

Permitting the use of pure research tools—such as a receptor—for experiments under the safe harbor of § 271(e)(1) would allow third parties to exploit the sole commercial application of the patented technical teaching. Consequently, the patent's value would be destroyed and the patent grant would be rendered a facade. As the application of the patent laws is meant not to eviscerate the incentive and reward function of the patent system, such a practice should not be permitted.⁴⁰⁵

402. As suggested above, allowing access to any research tool would diminish the incentive to design around existing patents and invent innovative new methods. *See supra* note 277 and accompanying text.

403. Holzapfel, *Research Tools*, *supra* note 154, at 14–16.

404. Alan W. White, *Problems of Patents for Research Tools*, 4 *BIOSCIENCE L. REV.* 138 (1998/1999); Bernhard Fischer, *Germany: Reach-through Claims and Experimental Use*, *MANAGING INTELLECTUAL PROPERTY Supplement—IP Strategy Yearbook 2001*, at 10. *But see* HOLZAPFEL, *EXPERIMENTAL USE*, *supra* note 152, at 328–29.

405. *See Merck II*, 496 F.3d, at 1352 (Rader, J., concurring-in-part and dissenting-in-part) (providing a hypothetical); *see supra* notes 401–402 and accompanying text. *Cf.*

2. Dual Purpose Research Tools

When the patented invention is a dual-purpose research tool, the economic impact on the patent owner is considerably different. Consider the situation where the patent is directed at a pharmaceutically active molecule; its use for screening purposes is disclosed but not explicitly claimed.⁴⁰⁶ When the molecule is used for screening purposes, the experiments will produce information on both the molecule and potential receptors. Compared to pure research tools, the commercial value of the patent will not be completely diminished as the screening does not affect the use of the molecule for therapeutic purposes. Nevertheless, the patentee would be deprived of the opportunity to commercialize its use for screening. This approach (hereinafter, the “value impact test”) suggests that the exemption should be extended to situations when the incursion on the patent right would be negligible when compared to the much more lucrative market for therapeutic purposes and justifiable in outweighing public interests.⁴⁰⁷ This should be the case even where the patented molecule is used in screening for analogues which are themselves intended to be submitted for drug approval and marketed as competing drugs.⁴⁰⁸

Only where the pharmaceutically active molecule is used for screening as part of industrially manufactured test kits, e.g. to screen cells to verify the existence of certain receptors, could one no longer faithfully argue that information on the molecule is being collected, and thus, such uses should not be exempted under the experimental use exception.⁴⁰⁹

The value impact test essentially results in a distinction based on the extent of the encroachment on the patent right, i.e., how much would the value of the patent be diminished by allowing the experiments. The test would allow the use of the technical teaching in research where the patent has an additional application so that its value would not be completely eliminated. However, it is not clear how the test would treat

Holzappel, *Research Tools*, *supra* note 154, at 14 (with regard to the use of a receptor for screening).

406. Holzappel, *Research Tools*, *supra* note 154, at 15.

407. *Id.* (Scenario 2) Holzappel recognized that such extension would not be conforming to the European patent law doctrine of absolute product protection; nevertheless, they are to be accepted because that doctrine should be considered in relation to the experimental use exemption. *Id.* at 12–13. Under that doctrine, the scope of a patent for a product extends to all uses of the product, whether they have been disclosed in the patent or not. *See* BGH [German Federal Court of Justice], GRUR 1972, 541—Imidazoline (Mar. 14, 2003); EPO [European Patent Office], Enlarged Board of Appeal, G2/88 Friction Reducing Additive/MOBIL OIL III, 1990 O.J. EPO 093, 110 (Dec. 11, 1989); EPO [European Patent Office], Technical Board of Appeal, T 80/96 L-Carnitin/LONZA, O.J. EPO 2000, 50, 54 (June 16, 1999). *See also* Keukenschrijver, *in* Busse, *supra* note 149, § 9 marginal note 51.

408. Holzappel, *Research Tools*, *supra* note 154, at 15 (Scenario 3).

409. *Id.*

the hypothetical situation when a molecule is used for screening where both the molecule and screening process have been disclosed and claimed in the patent.⁴¹⁰ It would seem that the test would allow the use of a pharmaceutically-active molecule for screening purposes (even though the screening process is claimed) because it would only have a very limited impact on the value of the patent.⁴¹¹ Assuming, *arguendo*, in an extension of the hypothetical, that several years later the claim on the molecule is invalidated and only the claim for the use of the molecule in the screening process remains. At this point, the use permitted just before the invalidation of the claim to the molecule would be prohibited, leading to the untenable result that a narrowing of the scope of a patent would permit the owner to enjoin acts which were theretofore covered under the experimental use exemption. Similar inconsistencies result when considering the opposite situation: the sole application of a patented molecule in research, which should be treated identically to pure research tools, i.e. the scenario with the patented receptor,⁴¹² and thus no use in research should be allowed under this differentiation. Why should the outcome change only because the molecule is later discovered to be useful in therapeutic application, and when an exemption for screening purposes would be only a relatively limited encroachment on the patent's value?

Ultimately, a case-by-case determination based on how far exemptions on the use of the research tool would diminish the economic value of the patent is impractical and would yield inconsistent results. Furthermore, it would contradict patent policy because the patent is granted, not based on the commercial value of the invention, but on the fulfillment of patentability requirements which have no correlation to the commercial value. The general rule must remain that the use of a research tool for research purposes, i.e. according to its technical teaching, should not be exempted even when dual-purpose research tools are used. Where information is simultaneously obtained on both the research tool and the compound under experimentation, the decisive inquiry must not be into the effects the exemption would have on the value of the patent.

410. Holzapfel's first scenario involves screening for possible ligands with a patented receptor, which does not have a second application in therapy (prohibited); his second scenario involves a patent for a pharmaceutically-active compound where its use for screening is disclosed, but not claimed (permitted); his third scenario involves screening with a patented molecule where a therapeutic application has been disclosed (permitted). *Id.* at 14–15.

411. It would be different from the first scenario as the molecule—unlike the receptor in the hypothetical—has a further therapeutic application. The difference with the second scenario is that the patent explicitly claims the screening method—which, in view of the German doctrine of absolute product protection confers protection beyond the claim to the compound itself. *Id.*

412. See *supra* Part VIII.B.1.

Rather, the following question has to be asked and answered: What were the experiments directed at: the gathering of information about the research tool or about another compound?

C. Applying the Distinction

It has not escaped this author's attention that the determination of the purpose requires a subjective inquiry. The proposal for a subjective inquiry may seem untimely when other inquiries into other subjective elements required for the establishment of the first-inventor priority, for determining whether the best mode requirement has been met or the infringer has acted willfully, have been criticized as creating superfluous litigation and have been subject to proposals for reform.⁴¹³ However, the determination of the subjective element is remarkably different in the present scenario, and much easier to administer in court. In these inquiries, it is the defendant who alleges that the patentee did not disclose the best mode, and the patentee who alleges that the infringement was willful. In both cases, the allegations are brought by the opponent of the party whose motivation has to be determined.

In the present case, however, it would be the alleged infringer who would argue that the purpose of his experiments was the obtaining of information on the patented receptor rather than on the other molecule, thus necessitating a subjective inquiry into his own motivation, and not that of the opposing party. As a consequence, an alleged infringer's motivation for conducting the experiments would be easier to determine as he himself would have the burden of proof. Although the Federal Circuit has left open whether the common law experimental use exemption constitutes an exception from the patent scope or a defense against infringement, it clarified in *Madey v. Duke* that the alleged infringer bears the burden of proof when invoking the experimental use exception.⁴¹⁴ Likewise, as an affirmative defense, the alleged infringer bears the burden of establishing the safe harbor of § 271(e)(1).⁴¹⁵

413. The current patent law reform proposal would, *inter alia*, introduce the first-to-file system and eliminate the discovery-laden process to establish the conception date; additionally, requirements for finding of willfulness will be objectified. *See e.g.*, The Patent Reform Act of 2001, H.R. 1908 and S. 1145, 110th Cong. (2007).

414. It was referred to as both a defense and as exception by the Federal Circuit in *Roche v. Bolar*. *Roche Prods., Inc. v. Bolar Pharm. Co.*, 733 F.2d 858, 862 (Fed. Cir. 1984). However, while the Court has rejected the view that it is an affirmative defense which has to be raised in responsive pleading, it has confirmed that the burden of proof for establishing the defense is with the defendant, *Madey v. Duke Univ.*, 307 F.3d 1351, 1361 (Fed. Cir. 2002).

415. As a defense to infringement, the safe harbor of § 271(e)(1) has to be pleaded pursuant to 35 U.S.C. § 282(4). *See Maxon Premix Burner Co. v. Mid-Continent Metal Products Co.*, 279 F. Supp. 164, 190 (N.D. Ill. 1967) (defendant has the burden to prove the essential facts of its affirmative defenses in patent infringement proceedings); *Sinclair Refining Co. v.*

It is to be expected that the alleged infringer will try to argue that his experiments were directed at obtaining information about the research tool to avoid liability for infringement, and it would be in the ambit of the court to develop proper standards where an alleged infringer has discharged his burden of proof and submitted enough evidence to benefit from the common law research exemption or from the safe harbor of § 271(e)(1). Similar to evidence required for corroboration of the conception in interference proceedings,⁴¹⁶ the alleged defender should be required to have detailed laboratory notebooks which clearly specify the purpose of the experiments.

CONCLUSION

The introduction of a broadened experimental use exemption would not alleviate all, but only part of the perceived problems in biomedical research by permitting researchers to conduct experiments on patented subject matter. Access to patented research tools should not be permitted under either common law exemption or § 271(e)(1) in order to maintain the necessary incentives for the development of new research tools. When the distinction between permissible research on an invention and impermissible research with a research tool may not be easily ascertained in borderline cases because information on both compound and research tool is obtained, a subjective inquiry in the motivation for the experiments may be necessary to arrive at an appropriate judicial determination. There is only limited evidence that research tool owners abuse patent rights; such evidence is insufficient to outweigh the removal of incentives for the development of research tools, which would drive out of business highly innovative companies and could ultimately slow down the pace of biomedical research. So far, the economic benefits achieved through widely licensing an invention on reasonable terms seem to prevail. With respect to government-funded research, widespread licensing of research tools can be facilitated through contractual clauses or by the

Globe Oil & Refining Co., 20 F. Supp. 681, 690 (D.C. Del. 1937), *rev'd on other grounds* 103 F.2d 95 (3d Cir. 1939) ("Generally speaking, the defendant must establish its defenses, so from that point of view the burden of proof is on defendant."). *Cf.* Fuji Photo Film Co. v. Int'l Trade Comm'n, 474 F.3d 1281, 1293 (Fed. Cir. 2007) ("Repair is an affirmative defense to a claim of infringement, and Benun, as the party raising the affirmative defense, had the burden of establishing this defense . . .").

416. Corroborating evidence for establishment of conception in interference proceedings can have the form of (a) testimony of a person different from the inventor, who from discussion with the inventor understood the claimed invention at the time it was conceived, or (b) by documents created at the time of conception. *Woodland Trust v. Flowertree Nursery, Inc.*, 148 F.3d 1368, 1371 (Fed. Cir. 1998); *Sturtevant v. Van Remortel*, No. 93 Civ. 3466(JFK), 1995 WL 611320, at *5 (S.D.N.Y. 1995).

exercise of march-in rights, which would be a smaller encroachment on the incentives provided by the patent system.

In individual cases, the strategic behavior of research tool patent owners may prevent researchers from continuing on a specific research trajectory. While that is certainly lamentable, it must be accepted to maintain the incentives of the patent system for research tool owners. Although there is empirical evidence of a statistically significant problem of blocking patents in specific areas, there is no evidence that such blocking patents actually have a negative impact on overall welfare that would warrant a general exemption on the use of research tools. Extreme circumstances are better addressed through individual equity considerations, e.g. when a court has to decide on a preliminary or permanent injunction, than through a general exemption of research tools.

One can hope that the Federal Circuit will clarify that research tools are not exempted under either exemption following the general distinction of “experimenting on” versus “experimenting with.” Although it may be presumptuous to hope that the court will reconsider its application of the common law exemption and deviate from the narrow holding in *Duke v. Madey* to adopt a meaningful experimental use exemption, a meaningful exemption would also allow for a more consistent (and narrow) application of the § 271(e)(1) safe harbor without hindering the development of innovative drugs. As a consequence of the nature of biotechnological research, there will presumably be numerous cases in which the alleged infringer will defend himself by arguing that the experiments were directed at obtaining information on the properties of a research tool. It will be the responsibility of the Federal Circuit to establish stringent rules on what evidence must be produced to sustain such allegation, and for the district courts to apply the subjective inquiry in trial.