ABSTRACT

The use of research tools is critical for pharmaceutical companies to conduct timely and efficient research in the development of new drugs. Traditionally, the use of any patented inventions during drug development that is reasonably related to submission of information to the Food and Drug Administration for regulatory review has been protected under the section 271(e)(1) safe harbor provision. Recently, the Federal Circuit narrowed the scope of the safe harbor provision excluding the use of certain patented research tools. The effect of this decision on research tools may negatively impact the public by raising the cost of pharmaceutical companies' research and development programs, ultimately raising the cost of drugs available to the public. Legislation specifically including the use of research tools within the safe harbor, or alternatively, judicially supplementing this modern test for safe harbor would resolve the uncertainty faced by pharmaceutical companies.
PROVERIS SCIENTIFIC CORP. V. INNOVASYSTEMS, INC.  SINKS SAFE HARBOR PROTECTION FOR RESEARCH TOOLS

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INTRODUCTION

Historically, pharmaceutical companies have relied upon the protection accorded by the section 271(e)(1) safe harbor provision to protect certain infringing activities that facilitate the research and development of new drugs. An alleged infringer must satisfy a two-prong test for a court to grant the alleged infringer safe harbor protection. First, the alleged infringer must make, use, offer to sell, or sell a "patented invention." Second, the alleged infringer's use of the "patented invention" must be reasonably related to submissions to the Food and Drug Administration ("FDA") for regulatory approval.

The safe harbor provision represents a balance between two very important and competing public interests. The first interest is stimulating innovation through the

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1 Brief for the Pharmaceutical Research and Manufacturers of America as Amicus Curiae in Support of Petitioner at 1–2, Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193 (2005) (No. 03-1237) [hereinafter Brief for PRMA, 2005 WL 429973, at *1–2.


3 It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products. 35 U.S.C. § 271(e)(1).

4 Id.

5 Mylan Pharm., Inc. v. Thompson, 268 F.3d 1323, 1326 (Fed. Cir. 2001) (“These provisions of the Hatch-Waxman Amendments ‘emerged from Congress’ efforts to balance two conflicting policy objectives: to induce name brand pharmaceutical firms to make the investments necessary to research and develop new drug products, while simultaneously enabling competitors to bring cheaper, generic copies of those drugs to market.’” (quoting Abbott Labs. v. Young, 920 F.2d 984, 991 (D.D.C. 1990) (Edwards, J., dissenting on other grounds))); H.R. REP. No. 98-857, pt. 2, at 30 (1984) (“[T]he committee has merely done what the Congress has traditionally done in the area of

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The precarious state of research tools means that parties must expend resources to develop new technologies. The second interest is to allow rapid entry of low-cost drugs to the market.

The research-intensive pharmaceutical and biotechnology industries play a vital role for these competing interests because they are responsible for significant medical advances through the development of new drugs and biomedical discoveries. In turn, research and development programs are dependent on access and use of patented research tools.

Research tools comprise the technology used by pharmaceutical companies to identify potential drug candidates, component parts in drug products, or drug products to treat patients. Research tools include the full range of resources used in intellectual property law: balance the need to stimulate innovation against the goal of furthering the public interest.

7 Id. at 29 (discussing that the section 271(e)(1) safe harbor provision allows generic drugs to enter the market faster, substantially benefiting the government and assisting in the reduction of health care costs).
8 Brief of Amicus Curiae, Biotechnology Industry Organization, in Support of Neither Petitioner Nor Respondent at 1 n.2, Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193 (2005) (No. 03-1237), 2005 WL 435887, at *1 n.2 ("The biotechnology industry has been one of the most research-intensive industries in history.").
9 Raj Bawa et al., Nanopharmaceuticals: Patenting Issues and FDA Regulatory Challenges, SCITECH LAW., Fall 2008, at 10 (reporting that between 1975 and 2008, pharmaceutical research and development investment increased forty-fold from $1 billion to $40 billion).
10 Brief of Amici Curiae Genentech, Inc. and Biogen Idec, Inc. in Support of Petitioner at 1–3, 22 n.10, Merck, 545 U.S. 193 (No. 03-1237), 2005 WL 435893, at *1–3, *22 n.10 (reporting that amici have developed breakthrough drugs and therapies for serious and life-threatening diseases including asthma, multiple sclerosis, cancer, hepatitis B, and psoriasis having both used patented research tools and invented, developed and patented new research tools); Brief for PRMA, supra note 1, at 1 (reporting that the members of Pharmaceutical Research and Manufacturers of America are responsible for almost all of the innovative medicines in the United States and is a "[v]oluntary, nonprofit association representing the nation's leading research-based pharmaceutical and biotechnology companies.").
12 FEDERAL TRADE COMMISSION, THE PRECARIOUS STATE OF RESEARCH TOOLS (2009) [hereinafter FTC Report], available at http://www.ftc.gov/os/2003/10/innovationrpt.pdf (discussing a narrow definition of research tools as "a technology that is used by pharmaceutical and biotechnology companies to find, refine, or otherwise design and identify a potential product or properties of a potential drug product.").
in the laboratory such as: "cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones and cloning tools (such as PCR), methods, laboratory equipment and machines."  

It is unclear whether patented research tools used in drug development may be protected under the safe harbor provision. Uncertainty about whether the safe harbor provision extended to research tools generated inconsistency in early case law and interest among academics.  

Recently, however, in Proveris Scientific Corp. v. Innovasystems, Inc. the United States Court of Appeals for the Federal Circuit modified the first prong of the safe harbor test. The first prong of the Proveris test restricts the scope of "patented inventions" protected under the

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1. Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, 64 Fed. Reg. 72,090, 72,092 n.1 (final notice Dec. 23, 1999); see e.g., Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860, 872 n.4 (Fed. Cir. 2003), vacated, 545 U.S. 193 (2005) (hereinafter Integra I) (discussing the National Institute of Health's definition of research tools).

2. See, e.g., Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 205 n.7 (2005) ("We therefore need not— and do not— express a view about whether, or to what extent, § 271(e)(1) exempts from infringement the use of 'research tools' in the development of information for the regulatory process.").

3. Classen Immunotherapies, Inc. v. King Pharm., Inc., 466 F. Supp. 2d 621, 625 n.2 (D. Md. 2006) (finding that the "extension of the safe harbor to cover the use of these [research] tools is warranted by the language of Merck and a plain reading of the statute."); Genentech, Inc. v. Insmed, Inc., 436 F. Supp. 2d 1080, 1082, 1094-95 (N.D. Cal. 2006) (holding that research using a binding protein was protected under the section 271(e)(1) safe harbor provision); Classen Immunotherapies, Inc. v. Biogen Idec, 381 F. Supp. 2d 452, 454, 456 (D. Md. 2005) (adopting a broad interpretation of the section 271(e)(1) safe harbor provision to immunize a research tool for evaluating the safety of vaccine administration schedules); Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., No. 95-CV-8833 (RPP), 2001 WL 1512597, at *3-4, *7-8 (S.D.N.Y. Nov. 28, 2001) (applying a broad interpretation of section 271(e)(1) to include research tools when it held that patented intermediates used in early-stage drug discovery were exempt from infringement). But see Infigen, Inc. v. Advanced Cell Tech., Inc., 65 F. Supp. 2d 967, 980-81 (W.D. Wisc. 1999) (holding that alleged infringers of cloning patents did not come within the scope of the section 271(e)(1) safe harbor provision because the research tools patents did not cover "products" as specified under section 156(f).

4. Henrik Holzapfel & Joshua D. Sarnoff, A Cross-Atlantic Dialog On Experimental Use and Research Tools, 48 IDEA 123, 141 (2008) ("One district court has held that research tools should be included within the scope of § 271(e)(1).... However, various commentators have argued that the language of § 271(e)(1) is limited to patented inventions that are... potentially subject to regulatory approval...."); Wolfram Prinz zu Waldeck und Pyrmont, Research Tool Patents After Integra v. Merck—Have They Reached a Safe Harbor? 14 MICH. TELECOMM. & TECH. L. REV. 367, 409-11 (2008) (opining that the application of section 271(e)(1) to the use of patented research tools is unclear and noting that some commentators have interpreted section 271(e)(1) narrowly and some have interpreted it broadly to include the exemption of research tools); Xiao, supra note 12, at 54 (noting that research tool developers will be unsure about whether their innovations will be protected by the patent system or under the section 271(e)(1) safe harbor provision of the Hatch-Waxman Act).


6. Compare id. at 1256-66 (holding that the phrase "patented invention" in the section 271(e)(1) safe harbor provision includes only inventions that fall within the meaning of the section 156(f) patent term extension provision), with Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 611, 665 (1990) (articulating that the phrase "patented invention" in the section 271(e)(1) safe harbor provision includes all inventions).
provision. It specifically excludes from protection under the section 271(e)(1) safe harbor provision those patented research tools that are not "products" as defined in the section 156(d) patent term extension provision. As a result of the Proveris decision, many pharmaceutical and biotechnology companies may face liability for their use of patented research tools during the research and development of new drugs.

This comment shows that the Proveris decision departed from broad interpretations of the safe harbor provision. Part I discusses the patent term extension provision and safe harbor provision, which were enacted to remedy unintended effects of the FDA regulatory review process. Part I also provides information about the judiciary's traditionally broad interpretation of the safe harbor provision, and its shift to a narrow interpretation. Part II analyzes the current state of the law regarding the safe harbor provision, and the implications of the Proveris decision. Part III advocates that legislation is necessary to include certain research tool patents among the exempted "products" under the first prong of the safe harbor test, or alternatively that the Proveris test be judicially supplemented to immunize the use of research tools that are inherent to the development of patented products.

I. BACKGROUND

The United States Constitution grants Congress broad power to enact legislation to "promote the Progress of Science and useful Arts . . . ". The patent system promotes this progress by offering inventors exclusive rights for a limited period of time as incentive for their innovative efforts. The limited period of time is known as the patent term. The patent term grants a patentee the right to exclude others from "[m]aking, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States" for twenty years.

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act, also known as the Hatch-Waxman Act. The Hatch-Waxman Act includes the section 156 patent term extension provision and the section 271(e)(1) safe harbor provision. The following section of this comment discusses the safe harbor

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19 Proveris, 536 F.3d at 1265–66.

20 See 35 U.S.C. § 271(a) (2006) (mandating that unauthorized activities such as making, using, offering to sell, or selling a patented invention during the term of the patent constitutes infringement).

21 U.S. Const. art. I, § 1 ("All legislative Powers herein granted shall be vested in a Congress of the United States, which shall consist of a Senate and House of Representatives."). Id. § 8, cl. 8 ("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.").

22 Id. § 8, cl. 8; 35 U.S.C. § 154(a) (granting a twenty year term to the "patentee, his heirs or assigns, the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States . . . ").


24 Id.


26 Id. at §§ 201–02.
provision, the judiciary’s broad interpretation of this provision, and the shift to a narrow interpretation.

A. Congress Enacts the Safe Harbor Provision

The FDA requires that certain drugs and products undergo regulatory approval before market entry. Two patent term distortions developed from the regulatory approval process: (1) a loss of financial benefit in the early years of the patent term and (2) a continuation of the patentee’s exclusive rights beyond the statutory twenty-year patent term. Congress enacted two provisions in the Hatch-Waxman Act to remedy these distortions. The patent term extension provision addresses the first distortion and the safe harbor provision addresses the second distortion.

1. Congress Establishes Patent Term Extension to Remedy the First Distortion of the FDA Regulatory Approval Process

The first distortion of the FDA regulatory approval process is a loss of financial benefit in the early years of the patent term. Regulatory review by the FDA requires extensive investigation of new drugs and products to ensure their safety and efficacy before approval. Most of the testing required for FDA approval is initiated after a patent is issued, and the process may take seven to ten years. As a result of the prolonged approval process, the twenty-year patent term may be shortened by seven to ten years. The FDA review period and the de facto shortened term leads to a potential loss of financial revenue. For example, if it takes Company X ten years to receive regulatory approval for its patented drug, only ten years of the twenty-year patent term remain when the drug enters the market. This ten-year loss of market exclusivity reduces Company X’s ability to derive profit from its innovation prior to regulatory approval.

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31 Eli Lilly, 496 U.S. at 669.
32 See 21 U.S.C. § 355(b), (g) (requiring approval of all new drugs pursuant to application filing contents such as full reports of investigations to show whether or not a drug candidate is safe for use and is effective in use).
33 Eli Lilly, 496 U.S. at 669–70.
35 Id.
36 Eli Lilly, 496 U.S. at 669–70.
Congress enacted the section 156 patent term extension provision as part of the Hatch-Waxman Act to remedy this first distortion.\textsuperscript{37} When certain products are patented before the regulatory review period is initiated, this provision adds up to five additional years to the patent term.\textsuperscript{38} The length of the extension is determined based upon the time necessary for FDA regulatory review.\textsuperscript{39} The products eligible for patent term extension include: drug products, medical devices, food additives, or color additives subject to regulation under the Food, Drug, and Cosmetic Act (“FDCA”).\textsuperscript{40}

2. Congress Establishes the Safe Harbor Provision to Remedy the Second Distortion of the FDA Regulatory Approval Process

The second distortion of the FDA regulatory approval process is a continuation of the patentee’s exclusive rights beyond the statutory twenty-year patent term.\textsuperscript{41} During the twenty-year patent term, the patentee has the exclusive right to manufacture, use, or sell the patented invention.\textsuperscript{42} Competitors are prohibited from making, using, or selling the patented invention until the patent term expires.\textsuperscript{43} This allows competitors such as pharmaceutical companies to benefit from the expired patent to manufacture, use, or sell their own new or generic drugs. Pharmaceutical companies, in order to market or sell new or generic drugs, however, must conduct rigorous testing and must comply with FDA regulations.\textsuperscript{44} The testing and FDA regulatory review period can last many years, and thereby creates a de facto continuation of the patentee’s exclusive rights beyond the twenty-year term.\textsuperscript{45}

Congress included the section 271(e)(1) safe harbor provision in the Hatch-Waxman Act to remedy this second distortion.\textsuperscript{46} The provision confers immunity to researchers to initiate testing and FDA regulatory review of products that use the patented invention prior to patent expiration.\textsuperscript{47} This provision gives competitors the ability to enter the market upon patent expiration.\textsuperscript{48}

Although provisions of the Hatch-Waxman Act addressed the dual distortions,\textsuperscript{49} the Act failed to specifically address research tools. Research tools are neither expressly included nor excluded as products under the section 156(f) patent term extension provision.\textsuperscript{50} Additionally, the language of the section 271(e)(1) safe harbor

\begin{itemize}
\item \textsuperscript{37} Id. at 670; H.R. REP. NO. 98-857, pt. 2, at 5–6, 21 (1984) (proposing the addition of section 156 to Title 35 to extend the patent term).
\item \textsuperscript{38} Eli Lilly, 496 U.S. at 671; see also 35 U.S.C. § 156 (2006).
\item \textsuperscript{39} 35 U.S.C. § 156(c).
\item \textsuperscript{40} 35 U.S.C. § 156(f).
\item \textsuperscript{41} Eli Lilly, 496 U.S. at 670.
\item \textsuperscript{42} 35 U.S.C. § 154(a)(1)–(2).
\item \textsuperscript{43} 35 U.S.C. § 271(a).
\item \textsuperscript{44} 21 U.S.C. § 355(a)–(b), (g) (2006).
\item \textsuperscript{45} Eli Lilly, 496 U.S. at 670.
\item \textsuperscript{46} Id. at 671; H.R. REP. NO. 98-857, pt. 2, at 26 (1984) (proposing a new subsection (e) to section 35 U.S.C. § 271).
\item \textsuperscript{47} 35 U.S.C. § 271(e)(1); Eli Lilly, 496 U.S. at 671.
\item \textsuperscript{48} See Eli Lilly, 496 U.S. at 671.
\item \textsuperscript{49} Id. at 670–71; H.R. REP. NO. 98-857, pt. 2, at 5–6, 21, 26–27, 29–30.
\item \textsuperscript{50} See 35 U.S.C. § 156(f).
\end{itemize}
provision is ambiguous as to whether research tools qualify for immunity. Due to the ambiguous nature of the statute, judicial challenges to the scope of the safe harbor provision reached the Supreme Court for interpretation.

B. The Supreme Court Broadly Interprets Section 271(e)(1) to Include Medical Devices & Preclinical Research

The Supreme Court has addressed the section 271(e)(1) safe harbor provision on two occasions. The Supreme Court broadly interpreted the safe harbor provision in *Eli Lilly & Co. v. Medtronic, Inc.* and *Merck KGaA v. Integra Lifesciences I, Ltd.* In *Eli Lilly*, the Court included medical devices within the scope of the safe harbor provision. In *Merck*, the Court extended the protection under this provision to preclinical research activities.

1. The Supreme Court Grants Safe Harbor to Medical Devices in *Eli Lilly & Co. v. Medtronic, Inc.*

The Supreme Court first addressed the section 271(e)(1) safe harbor provision in *Eli Lilly*. *Eli Lilly* filed suit against Medtronic to enjoin Medtronic from testing and marketing its alleged infringing medical device. Medtronic argued that its activities were exempt from infringement under the safe harbor provision. To qualify for protection under the section 271(e)(1) safe harbor provision, (1) a plaintiff’s product must qualify as a “patented invention;” and (2) the defendant’s alleged infringing use of that product must be “reasonably related to the development and submission of information” for regulatory review. Therefore, to obtain safe harbor protection, Medtronic asserted that its medical device was a “patented invention,” and its use of the device was for regulatory review.

The Supreme Court determined that the phrase “patented invention” in the provision included all inventions unless otherwise specified. Accordingly, the Court

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51 See 35 U.S.C. § 271(e)(1); *Eli Lilly*, 496 U.S. at 679 (“No interpretation we have been able to imagine can transform § 271(e)(1) into an elegant piece of statutory draftsmanship.”).

52 See *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 195 (2005); *Eli Lilly*, 496 U.S. at 663-64.

53 *Merck*, 545 U.S. at 195; *Eli Lilly*, 496 U.S. at 663-64.


56 *Eli Lilly*, 496 U.S. at 664-65, 679.

57 *Merck*, 545 U.S. at 208.

58 See *Eli Lilly*, 496 U.S. at 664-65. (granting certiorari to determine whether the section 271(e)(1) safe harbor provision “exempts from infringement the use of patented inventions to develop and submit information for marketing approval of medical devices under the FDCA.”).

59 Id. at 664.

60 Id.


62 See *Eli Lilly*, 496 U.S. at 664.

63 *Eli Lilly*, 496 U.S. at 665 (“The phrase ‘patented invention’ in § 271(e)(1) is defined to include all inventions, not drug-related inventions alone.” (citing 35 U.S.C. § 100(a))). Section 100(a) states,
found that a medical device was a "patented invention" even though the safe harbor provision does not expressly mention medical devices. Therefore, the Court found that Medtronic's activities must be granted safe harbor protection if its use of the medical device was reasonably related to the development and submission of information for regulatory approval.

Additionally, the Court, in dicta, noted that the section 271(e)(1) safe harbor provision and the section 156(f) patent term extension provision of the Hatch-Waxman Act were meant to be complimentary. It found that all of the products eligible for patent term extension under section 156(f) were protected under section 271(e)(1), creating a "perfect product fit" between the sections. This argument was later used by the Federal Circuit to narrow the scope of the safe harbor provision.

The Court ultimately broadened the scope of the safe harbor provision by including any invention within the definition of a "patented invention" and not limiting it solely to drug inventions. Therefore, the Supreme Court's broad interpretation of the section 271(e)(1) safe harbor provision provided the basis for the argument that research tools are "patented inventions" that fall within the scope of the statute. After Eli Lilly, the Supreme Court did not address the section 271(e)(1) issue again for 15 years until its decision Merck KGaA v. Integra Lifesciences I, Ltd.

2. The Supreme Court Grants Safe Harbor to Preclinical Research Activities in Merck KGaA v. Integra Lifesciences I, Ltd.

The Supreme Court addressed the scope of the section 271(e)(1) safe harbor provision for a second time in Merck.

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"When used in this title unless the context otherwise indicates-(a) [t]he term 'invention' means invention or discovery." 35 U.S.C. § 100(a).

64 See Eli Lilly, 496 U.S. at 664, 673.
66 Eli Lilly, 496 U.S. at 664, 679.
67 Id. at 672-74.
68 Id. at 673-74 (discussing that the products eligible for patent term extension under section 156(f) are subject to exemption under the safe harbor provision because they are subject to pre-market approval under various provisions of the Food, Drug, and Cosmetic Act). Medical devices, food additives, color additives, new drugs, and human biological products are eligible for patent term extension under section 156(f). Id. at 674. Medical devices are subject to pre-market approval under 21 U.S.C. § 360e. 21 U.S.C. § 360e (2006). Food additives are subject to pre-market approval under section 348. 21 U.S.C. § 348. Color additives are subject to pre-market approval under section 379a. 21 U.S.C. § 379a. New drugs are subject to pre-market approval under section 355. 21 U.S.C. § 355. Human biological products are subject to pre-market approval under 42 U.S.C. § 262. 42 U.S.C. § 262 (2006).
70 Eli Lilly, 496 U.S. at 665.
71 See Proveris, 536 F.3d at 1264 ("Innova contends that both Lilly and Merck support its position and that the safe harbor provision should not be limited so as to exclude research tools—assuming its OSA device is viewed as such.").
73 See id. at 195.
preclinical research, early stage research conducted prior to human testing, satisfied the second prong of the safe harbor test.\textsuperscript{74}

Integra owned biotechnology patents on a short tri-peptide sequence ("RGD peptides").\textsuperscript{75} Integra alleged patent infringement against Merck.\textsuperscript{76} Merck claimed that its preclinical studies using Integra's RGD patents were protected under the safe harbor provision.\textsuperscript{77} At trial, the jury did not grant Merck safe harbor protection, and found Merck liable for patent infringement.\textsuperscript{78}

In a split decision, the Federal Circuit affirmed the district court decision that Merck's infringing activities were not protected under the safe harbor provision.\textsuperscript{79} The Federal Circuit held that the preclinical activities were general biomedical research used to identify new pharmaceutical compounds and were not reasonably related to regulatory approval.\textsuperscript{80} In finding that the preclinical activities infringed Integra's patents, the court characterized these patents as research tools.\textsuperscript{81} It merely cautioned that a broad interpretation of this provision to protect the use of patented research tools in preclinical activities would "effectively vitiate the exclusive rights of patentees owning biotechnology tool patents."\textsuperscript{82} Judge Newman, dissenting, identified the RGD technology as "new compositions having certain biological properties" rather than as a research tool.\textsuperscript{83} Judge Newman argued that "discovery-based research" activities should be granted safe harbor.\textsuperscript{84}

Upon review, the Supreme Court vacated the Federal Circuit's decision.\textsuperscript{85} The Court broadened the scope of the safe harbor provision for a second time by including preclinical studies of patented compounds within the definition of the phrase "reasonably related."\textsuperscript{86} The Court determined that the use of a patented invention in experiments that were not included in a submission of information to the FDA was not a categorically infringing use and did not exclude their use from safe harbor.\textsuperscript{87} The Court remanded the case to the Federal Circuit to determine whether the preclinical activities were "reasonably related" to the regulatory approval process.\textsuperscript{88}

\textsuperscript{74} Id. at 202–03.
\textsuperscript{75} Id. at 197 (stating that Integra's five patents related to the tripeptide (amino acid) sequence Arg-Gly-Asp, which is referred to as the "RGD peptide").
\textsuperscript{76} Id. at 200.
\textsuperscript{77} Id.
\textsuperscript{78} Id. at 201.
\textsuperscript{79} Integra I, 331 F.3d 860, 868 (Fed. Cir. 2003), vacated, 545 U.S. 193 (2005).
\textsuperscript{80} Id. at 866.
\textsuperscript{81} Id. at 871–72.
\textsuperscript{82} Id. at 867. Under a broad interpretation of the section 271(e)(1) safe harbor provision, the use of research tools in clinical testing for FDA approval would fall within the safe harbor, leaving the only commercial value of research tools in general research. \textit{Id.} The majority asserted that including preclinical research within the scope of the section 271(e)(1) safe harbor provision would "swallow the whole benefit of the Patent Act for some categories of biotechnological inventions." \textit{Id.}
\textsuperscript{83} Id. at 878 (Newman, J., concurring-in-part, dissenting-in-part).
\textsuperscript{84} See id. at 873 (Newman, J., concurring-in-part, dissenting-in-part).
\textsuperscript{85} Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 208 (2005).
\textsuperscript{86} Id. at 206–08. The section 271(e)(1) safe harbor provision allows researchers to experiment and to fail during development of drugs for regulatory approval when there is a reasonable basis for believing that a patented compound may be appropriate to include in a submission to the FDA. \textit{Id.} at 207.
\textsuperscript{87} Id.
\textsuperscript{88} Id. at 208.
Furthermore, the Court specifically declined to address the issue of whether research tools fall within the protected scope of the safe harbor provision.\(^8\)

On remand, the Federal Circuit held that the preclinical research activities were exempt under the safe harbor provision because the experiments were “reasonably related” to regulatory review.\(^9\) Again, the majority expressly declined to determine whether the safe harbor extends to the use of research tools.\(^9\) In dissent, however, Judge Rader addressed research tools and warned that the majority opinion would have a “devastating impact on research tool inventions” because it implicitly grants these tools immunity under the safe harbor provision.\(^9\) Without explicitly addressing research tools, the Supreme Court’s decision in *Merck* broadened the safe harbor provision.\(^9\) The analysis below shows that after this decision, several district courts applied the safe harbor provision to research tools.

**B. Several District Courts Found that Research Tools Fall Within the Safe Harbor Provision**

Without definitive guidance on whether research tools fall within the scope of the safe harbor provision, several district courts applied it to research tools.\(^9\) For example, in *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*,\(^9\) the United States District Court for the Southern District of New York granted safe harbor protection to research tools.\(^9\) Rhone-Poulenc Rorer (“RPR”) filed suit against Bristol-Myers Squibb Company’s (“Bristol”) for use of RPR’s patented chemical intermediates in Bristol’s research and development program.\(^9\) The court determined that Bristol’s use of RPR’s patented intermediates in drug discovery was exempt from infringement under the safe harbor provision.\(^9\)

Additionally, in *Classen Immunotherapies, Inc. v. King Pharmaceuticals, Inc.*,\(^9\) the United States District Court for the District of Maryland conferred safe harbor to research tools.\(^9\) Classen Immunotherapies, Inc. (“Classen”) developed a new research tool and patented it as a “method[] for identifying and commercializing new uses for existing drugs.”\(^9\) Classen brought suit against Elan for patent

\(^8\) *Id.* at 205 n.7.
\(^9\) *Integra Lifesciences I, Ltd. v. Merck KGaA*, 496 F.3d 1334, 1348 (Fed. Cir 2007) [hereinafter *Integra I*].
\(^9\) *Id.* at 1348.
\(^9\) See *id.* at 1350. (Rader, J. dissenting in part and concurring in part).
\(^9\) *Merck*, 545 U.S. at 207 n.7, 208 (declining to address the issue of research tools and holding that preclinical research may fall within the scope of the section 271(e)(1) safe harbor provision).
\(^9\) See *id.* at *8.
\(^9\) *Id.* at *8.
\(^9\) See *id.* at 623.
infringement. Classen alleged that Elan infringed its patented research tools when Elan: (1) studied the effect of food on the drug Skelaxin (a muscle relaxant); (2) used the study to identify new uses for Skelaxin; and (3) filed a new drug application for regulatory review with the FDA in order to commercialize its new use. The district court determined these activities were protected under the safe harbor provision.

As noted above, the Bristol-Myers and Classen courts found that research tools fall under the scope of the safe harbor provision. In 2008, however, the Federal Circuit determined that research tools do not fall under the safe harbor provision.

C. The Federal Circuit Narrows the Scope of the Section 271(e)(1) Safe Harbor Provision

The scope of the safe harbor provision was recently narrowed in Proveris Scientific Corp. v. Innovasystems, Inc. Proveris alleged patent infringement against Innovasystems, Inc. ("Innova") for making and selling a device known as the Optical Spray Analyzer ("OSA"). The alleged infringing OSA device was not subject to regulatory review by the FDA, but was only sold to the FDA and pharmaceutical companies. The device was used exclusively as a research tool to conduct experiments for FDA regulatory submissions. Innova asserted that its activities were exempt from liability by the safe harbor provision because it satisfied the Eli Lilly two-prong test: (1) Proveris' patent is a "patented invention;" and (2) Innova's alleged infringing device was only used for regulatory submissions.

The Federal Circuit did not grant Innova safe harbor protection. The court first questioned whether all patented inventions should qualify for safe harbor under the first prong of the Eli Lilly test. It stated that the first prong of the Eli Lilly test does not apply to all patented inventions. The court referred back to the narrow approach articulated in Eli Lilly that interpreted the section 271(e)(1) safe

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102 Id. at 623.
103 Id. at 624.
104 Id. at 625.
105 Id. at 625 n.2: Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., No. 95-CV-8833 (RPP), 2001 WL 1512597, at *8 (S.D.N.Y. Nov. 28, 2001).
106 See Proveris Scientific Corp. v. Innovasystems, Inc., 536 F.3d 1256, 1265-66 (Fed. Cir. 2008) (holding that the safe harbor provision does not protect the OSA device from infringement).
107 Id. at 1263-66.
108 Id. at 1259.
109 Id.
110 Id. at 1264.
111 See id. at 1259 (stating that the OSA device "measures the physical parameters of aerosol sprays used in nasal spray drug delivery devices."). Inhaler-based drug delivery devices require FDA regulatory approval. Id. at 1258.
112 Id. at 1259-60.
113 Id. at 1266.
114 See id. at 1261-63.
115 See id. at 1265-66 (finding that the Supreme Court interpreted the section 271(e)(1) safe harbor provision to include at least "all inventions" within the section 156 patent term extension provision based upon the Supreme Court's symmetry analysis between sections 271(e)(1) and 156(f), and the roughly offsetting patent distortions these sections were designed to eliminate).
harbor provision and the section 156(f) patent term extension provision as complimentary provisions of the Hatch-Waxman Act.\textsuperscript{116}

The section 156(f) patent term extension provision was enacted to remedy the first distortion—the adverse affect caused by lengthy regulatory review.\textsuperscript{117} The patent term extension provision applies to “products” that have been subject to regulatory review.\textsuperscript{118} In \textit{Proveris}, the court stated that the patented device was not subject to FDA regulatory review, and was therefore not a “product” under the patent term extension provision.\textsuperscript{119} The court also noted that the alleged infringing OSA device was not subject to FDA regulatory review, and was therefore not adversely affected by the second distortion—the regulatory barriers that extend the patent term.\textsuperscript{120} As a result, the court stated, “we do not think Congress could have intended that the safe harbor of section 271(e)(1) apply to it.”\textsuperscript{121} Accordingly, the court determined that the first prong of the safe harbor provision test only applies to patented inventions that are “products” as defined in the patent term extension provision.\textsuperscript{122}

This determination narrowed the scope of the section 271(e)(1) safe harbor provision.\textsuperscript{123} It modified the first prong of the \textit{Eli Lilly} test from “all patented inventions” to only “products” defined in the patent term extension.\textsuperscript{124} The \textit{Proveris} decision set forth the modern test to determine whether an invention is a “product,” and therefore subject to safe harbor protection. The analysis section of this comment will focus on the implications of \textit{Proveris} on research tools.

\section*{II. Analysis}

The Federal Circuit’s decision in \textit{Proveris} narrowed the scope of section 271(e)(1) safe harbor protection.\textsuperscript{125} After \textit{Proveris}, to qualify for safe harbor protection, (1) the patented invention, itself, must be subject to FDA regulatory review as a “product” defined in the patent term extension provision, and (2) the use of the patented invention must be “reasonably related” to regulatory review.\textsuperscript{126} The following section of this comment first focuses on how this test applies to research tools. Next, this section examines the distinction between the research tools that qualify for safe harbor under the \textit{Proveris} test and those that do not. Finally, this section addresses the inconsistency in the application of the \textit{Proveris} test to research tools.

\footnotesize
\begin{enumerate}
\item \textsuperscript{116} Id. at 1262–63.
\item \textsuperscript{118} 35 U.S.C. § 156(f) (2006).
\item \textsuperscript{119} \textit{Proveris}. 536 F.3d at 1265–66.
\item \textsuperscript{120} Id.
\item \textsuperscript{121} Id. at 1265.
\item \textsuperscript{122} See \textsuperscript{123} id. at 1265–66.
\item \textsuperscript{123} See \textsuperscript{124} id. at 1263–66 (narrowing the safe harbor provision despite its previously broad application of section 271(e)(1)).
\item \textsuperscript{124} Id.
\item \textsuperscript{125} Id.
\item \textsuperscript{126} Id. at 1265–66.
\end{enumerate}
A. Proveris Narrows the "Patented Inventions" that Qualify for Safe Harbor

The Supreme Court's broad interpretation of the section 271(e)(1) safe harbor provision in *Eli Lilly* and *Merck* suggested that the use of patented research tools for FDA regulatory review can be used as an affirmative defense to patent infringement. In *Proveris*, however, the Federal Circuit narrowed the scope of the safe harbor provision, effectively precluding research tools from immunity.

After *Proveris*, the first prong of the safe harbor test mandates that the patented invention be subject to FDA regulatory approval, and must be a "product" as the term is defined in the section 156(f) patent term extension provision. The four products that qualify for patent term extension are: (1) drug products, (2) medical devices, (3) food additives, and (4) color additives. Therefore, in order for a patented research tool to qualify for safe harbor, it must qualify as one of these four products under the patent term extension provision, and its use must be reasonably related to regulatory review. The analysis below gives examples of research tools that are eliminated from safe harbor protection, and research tools that may qualify for safe harbor under the first prong of the *Proveris* test.

1. No Safe Harbor for Research Tools That Are Used to Identify and Design Potential Drug Products

The first prong of the *Proveris* test for "patented inventions" categorically eliminates safe harbor protection for research tool patents that are used to identify and design potential drug products such as: cloning techniques, databases, computer software, and laboratory equipment such as microscopes, analytical balances, and computers. These tools do not satisfy the *Proveris* test because they are not

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127 See *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 202 (2005) (reaffirming the *Eli Lilly* holding that defined "patented invention" to include "all uses of patented inventions that are reasonably related to the development and submission of any information under the FDCA."); *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 665 (1990) ("The phrase 'patented invention' in § 271(e)(1) is defined to include all inventions, not drug-related inventions alone.").

128 See *Proveris*, 536 F.3d at 1263-66 (defining the phrase "patented invention" to mean all inventions within section 156(f) and holding that the safe harbor provision does not protect the OSA device from infringement).

129 *Proveris*, 536 F.3d at 1265-66.

130 35 U.S.C. § 156(f) (2006). A "drug product" is the active ingredient of "a new drug, antibiotic drug, or human biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act) . . . ." 35 U.S.C. § 156(f)(2). A "biological product" is "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings." 42 U.S.C. § 262(a) (2006). A "medical device" within the meaning of section 156(f) is a class III device. 21 U.S.C. § 360e (2006). A class III device is a device that is "purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or presents a potential unreasonable risk of illness or injury . . . ." 21 U.S.C. § 360e(a)(1)(C)(ii)(I)-(II).

131 See *Proveris*, 536 F.3d at 1265-66.

132 See *id.* (determining that the phrase "patented invention" for the purposes of the section 271(e)(1) safe harbor provision is limited to inventions stated in the section 156(f) patent term
products that require FDA regulatory approval and thus do not meet the first prong of the *Eli Lilly* test.\textsuperscript{133} Eliminating these types of research tools from protection under the safe harbor provision is consistent with the policy considerations leading to the enactment of the Hatch-Waxman Act.\textsuperscript{134} Indeed, for these tools, the *Proveris* test prevents a patentee from invoking safe harbor protections when his invention is not subject to regulatory restrictions that reduce the patent term prior to market entry.\textsuperscript{135}

2. No Safe Harbor for Research Tools That are Incorporated Into Qualifying Drug Products and are Analogous to “Products” Under the Patent Term Extension

The first prong of the *Proveris* test for “patented inventions” eliminates safe harbor protection for certain research tools incorporated into drug products that are subject to FDA regulatory approval.\textsuperscript{136} According to *Proveris* these inventions do not satisfy the first prong of the *Eli Lilly* test for “patented inventions” because they are not “products” within the definition of the patent term extension provision, and are therefore not subject to FDA regulatory review.\textsuperscript{137} For example, the use of patented chemical precursors in the research and development of new drugs that require FDA regulatory approval would not be granted safe harbor protection.

*Bristol-Myers*, decided before *Proveris*, illustrates this point. In *Bristol-Myers*, Bristol embarked on a research and development program to discover a new, more active anticancer drug.\textsuperscript{138} It wanted to replace the drug Taxol, the leading anticancer drug, before its patent on Taxol expired.\textsuperscript{139} Bristol used patented chemical intermediates as research tools in testing and screening to develop a new and more effective drug to replace Taxol.\textsuperscript{140} Taxol’s replacement drug would be subject to FDA regulatory approval.\textsuperscript{141}

The district court determined that Bristol’s unauthorized use of the patented intermediates was protected by the safe harbor provision because it met the first and second prong of the *Eli Lilly* test.\textsuperscript{142} Specifically, the court determined that a

\textsuperscript{133} See *Proveris*, 536 F.3d at 1265–66.

\textsuperscript{134} See *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 669 (1990) (stating that the Hatch-Waxman Act was “designed to respond to two unintended distortions of the 17-year patent term produced by the requirement that certain products must receive premarket regulatory approval.”); H.R. REP. NO. 98-857, pt. 1, at 15 (1984) (“The purpose of Title II of the Bill is to create a new incentive for increased expenditures for research and development of certain products which are subject to premarket government approval.”).

\textsuperscript{135} See *Proveris*, 536 F.3d at 1265–66.

\textsuperscript{136} See id.

\textsuperscript{137} See id.

\textsuperscript{138} *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95-CV-8833 (RPP), 2001 WL 1512597, at *4 (S.D.N.Y. Nov. 28, 2001).

\textsuperscript{139} Id.

\textsuperscript{140} Id.

\textsuperscript{141} Id. at *5.

\textsuperscript{142} See id. at *2, *6 (concluding that the phrase “patented invention” applies to all inventions and holding that Bristol’s experiments with the patented chemical intermediates were protected by
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3. Safe Harbor for Research Tools That Qualify as “Products” Under the Patent Term Extension

The facts of Merck, decided before Proveris, illustrate how the use of a patented research tool may be granted safe harbor protection under the first prong of the Proveris test. In Merck, scientists conducted preclinical experiments to evaluate the patented research tool falls under the broad scope of “all patented inventions” and is protected by the safe harbor provision. Under the Proveris standard, however, the use of patented chemical intermediates is not protected under the first prong of the safe harbor provision because these intermediates are not “products” within the meaning of the patent term extension provision.

The final drug product that incorporates a research tool, such as the chemical intermediates in Bristol-Myers, is a “product” under the patent term extension provision, and therefore is subject to FDA regulatory approval. Even though the chemical intermediates are not “products” under the patent term extension provision, these research tools should be considered “products” because they become an inseparable component of a drug product that is subject to FDA regulation. These research tools, however, do not qualify for safe harbor under the first prong of the Proveris test because they are not explicitly listed as “products” in the patent term extension provision.

3. Safe Harbor for Research Tools That Qualify as “Products” Under the Patent Term Extension

The facts of Merck, decided before Proveris, illustrate how the use of a patented research tool may be granted safe harbor protection under the first prong of the Proveris test. In Merck, scientists conducted preclinical experiments to evaluate the

the safe harbor provision because those experiments were “reasonably related” to regulatory review).

See id. at *2. Nothing in the text of Section 271(e)(1) indicates that Congress intended to restrict the scope of the term “patented invention” to those products covered by Section 156. As the U.S. Supreme Court noted, the term patented invention is 271(e)(1) is defined to include all inventions, not drug-related inventions alone. See 35 U.S.C. § 100(a) (when used in this title unless the context otherwise indicates...the term “invention” means invention or discovery.

Id. (quoting Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 66, 665 (1990)). In its determination that the phrase “patented invention” means “all patented inventions,” the district court relied upon two Federal Circuit decisions that applied a broad interpretation of the safe harbor provision and granted immunity to alleged infringing patented inventions that are not “products” within the section 156(f) patent term extension provision. Id. In Abtox, the Federal Circuit held that the safe harbor provision applied even though the alleged infringing Class II device was not eligible for patent extension under section 156(f). Abtox, Inc. v. Extron Corp., 122 F.3d 1019, 1028-30 (Fed. Cir. 1997), amended by 131 F.3d 1009 (Fed. Cir. 1997). Furthermore, in Chartex, the Federal Circuit stated, “[a]lthough section 156 and section 271(e)(1) of title 35 passed Congress....this Court declines to read possible limitations from one section into another.” Chartex Int’l PLC v. M.D. Pers. Prod. Corp., No. 92-1556, 1993 WL 306169, at *5 n.2 (Fed. Cir. Aug. 12, 1993) (reported in table at 5 F.3d 1505).


See id.


See id.: cf. Bristol-Meyers, 2001 WL 1512597, at *5 (discussing the creation of a second generation drug product by incorporating structural changes through chemical modification).
suitability of RGD peptides as potential drug candidates. The experiments “measured the efficacy, specificity, and toxicity” of the potential drug candidates to determine which drugs were effective and safe enough to warrant testing in humans. One of the RGD peptides was chosen to undergo regulatory review as the active ingredient in the drug product. Under the Proveris test, these activities may be protected under the safe harbor provision because the RGD peptides are biological products within the meaning of the patent term extension provision. These products qualify for safe harbor under the first prong of the Proveris test.

B. Inconsistencies Between the Proveris Test as applied to Merck and Bristol-Myers

There is an inconsistency in the applicability of the safe harbor provision when the first prong of the Proveris test is applied to the facts of Bristol-Myers and Merck. Although the use of the patented RGD peptides in Merck and the chemical precursors in Bristol-Myers are analogous, the Proveris test creates a distinction between the two uses. Both the RGD peptides and the chemical precursors played a dual role as research tools to: (1) screen, identify, and develop new drugs, and (2) potentially become components of the final drug products. The final drug products are subject to FDA regulatory approval.

Under the first prong of the Proveris test, the RGD peptides in Merck are “products” under the patent term extension provision and may qualify for safe harbor protection. The chemical precursors in Bristol-Myers, however, are not “products”

149 Id. at 198–99.
150 See id.
151 See 35 U.S.C. § 156(d) (defining drug product to include biological products); Proveris Scientific Corp. v. Innovasystems, Inc., 536 F.3d 1256, 1265–66 (Fed. Cir. 2008).
152 See 35 U.S.C. § 156(d) (defining drug product to include biological products); Proveris, 536 F.3d at 1265–66.
153 Compare Merck, 545 U.S. at 198–99 (discussing the testing and evaluating of RGD peptides to identify a potential drug candidate), with Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., No. 95-CV-8833 (RPP), 2001 WL 1512597, at *4 (S.D.N.Y. Nov. 28, 2001) (discussing experimentation with patented intermediates to identify a potential drug candidate).
154 See Proveris, 536 F.3d at 1265–66 (eliminating safe harbor protection for “all patented inventions” and requiring that “patented inventions” are “products” within the patent term extension provision).
155 See Merck, 545 U.S. at 198–99 (discussing the screening, testing, and evaluating of RGD peptides to identify a potential drug candidate and initiating “a formal project to guide one of its RGD peptides through the regulatory approval process in the United States and Europe.”); Bristol-Myers, 2001 WL 1512597, at *4–5 (experimenting with patented intermediates to identify a potential drug candidate and preparing derivatives of Taxol by chemical modification to develop a new drug).
157 35 U.S.C. § 156(d) (including biological products within the definition of a “drug product”); 42 U.S.C. § 265(i) (2006) (defining “biological product” as “a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsenic compound, applicable to the prevention, treatment, or cure of a disease or condition of human beings.”); see Proveris, 536 F.3d at 1265–66 (defining the phrase “patented invention” within the safe harbor provision to include only “products” stated in the patent term extension provision).
under the patent term extension provision and do not qualify for safe harbor protection. Thus, when a patented research tool is a component of a drug product, the first prong of the Proveris test does not provide consistency between analogous uses. The first prong of the Proveris test requires that the research tool qualify as a "product" under the patent term extension provision regardless of whether the ultimate drug product undergoes FDA regulatory approval.

Additionally, this distinction is contrary to the policy considerations leading to the enactment of the safe harbor provision in the Hatch-Waxman Act because the final drug product that incorporates these research tools is subject regulatory review. These regulatory restrictions reduce the patent term prior to market entry.

This subsection identified the inconsistencies created by Proveris. The next subsection addresses the effect of this decision on research tool patent holders and pharmaceutical companies.

C. Uncertainty and Consequences for Pharmaceutical Companies After a Narrow Interpretation of the Section 271(e)(1) Safe Harbor Provision Effectively Excludes Research Tools

After Proveris, pharmaceutical companies may face increased research and development costs and the uncertainty of litigation because research tool patent holders can enforce their rights against companies that use the research tool patents to obtain FDA regulatory approval. While the effects of Proveris remain to be seen, the analysis below shows that the shift in the Federal Circuit's construction of the section 271(e)(1) safe harbor provision has tipped the balance between the public

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158 35 U.S.C. § 156(f) (including drug products, medical devices, food additives, and color additives that undergo regulatory review among the "products" within the patent term extension); see Proveris, 536 F.3d at 1265–66 (defining the phrase "patented invention" within the safe harbor provision to include only "products" stated in the patent term extension provision).

159 See Proveris, 536 F.3d at 1265–66 (defining the phrase "patented invention" within the safe harbor provision to include only "products" stated in the patent term extension provision).


162 See Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc., 548 U.S. 124, 127 (2006) (Breyer J., dissenting) (per curiam) (asserting that patents can "discourage research by impeding the free exchange of information ... by forcing researchers to avoid the use of potentially patented ideas, by leading them to conduct costly and time-consuming searches of existing or pending patents, by requiring complex licensing arrangements, and by raising the costs of using the patented information ... ."); Brief for PRMA, supra note 1, at 14 (stating that the safe harbor provision affects the cost of new drugs because "[a]s the development process becomes more protracted, therefore, the overall cost of drug development is increased."); Mireles, supra note 10, at 152 (stating that exclusive patent rights allow patent holders to "increase a patented invention's price beyond the competitive market price . . . .").
interest in the rapid entry of low-cost drugs and the rights of research tool patent holders in favor of patentees.

1. Pharmaceutical Companies that Utilize Research Tools for FDA Regulatory Testing Face Uncertainty and Increased Costs

The Federal Circuit's narrow construction of the first prong of safe harbor provision may increase costs and cause more uncertainty for pharmaceutical companies because the use of research tools for FDA regulatory approval may not be given safe harbor. After Proveris, pharmaceutical companies that use patented research tools have four options: (1) make, use, and sell a non-infringing product; (2) disregard the patent and risk a finding of patent infringement in subsequent litigation; (3) obtain a license from the patent holder; or (4) obtain a license and subsequently challenge the validity of the patent through a declaratory judgment suit.

Each of these four options increases overhead for pharmaceutical companies. Time, money, and resources will have to be allocated to producing non-infringing research tools. Additionally, without a proper license, pharmaceutical companies risk costly litigation and the imposition of monetary damages for infringement of patented research tools. Alternatively obtaining licenses for patented research tools will also lead to increased overhead.

163 See Lab. Corp., 548 U.S. at 127 (Breyer J., dissenting) (per curiam) (stating that patents can "discourage research by impeding the free exchange of information . . . by forcing researchers to avoid the use of potentially patented ideas, by leading them to conduct costly and time-consuming searches of existing or pending patents, by requiring complex licensing arrangements, and by raising the costs of using the patented information . . ."); Brief for PRMA, supra note 1, at 14 (stating that the section 271(e)(1) safe harbor provision affects the cost of new drugs because "[a]s the development process becomes more protracted, therefore, the overall cost of drug development is increased."); Mireles, supra note 10, at 152 (stating that exclusive patent rights allow patent holders to "increase a patented invention's price beyond the competitive market price . . .").

164 See Panduit Corp. v. Stahlin Bros. Fibre Works, Inc., 575 F.2d 1152, 1158-59 (6th Cir. 1978) (identifying a competitor's options when a patent has been issued).

165 See Micro Chem., Inc. v. Lextron Inc., 318 F.3d 1119, 1123 (Fed. Cir. 2003) (discussing that the defendant in a patent infringement suit took over four months to produce a non-infringing product, hired consultants to "consider the impact and effectiveness of the new designs," hired a firm to "consider alternative designs," and retained a Ph.D in the field of the invention.).

166 See 35 U.S.C. § 284 (2006) (providing the court with the ability to award damages of lost profits or reasonable royalty fees to compensate for infringement); In re Seagate Tech., LLC, 497 F.3d 1360, 1371 (Fed. Cir. 2007) (en banc) ("To establish willful infringement, a patentee must show by clear and convincing evidence that the infringer acted despite an objectively high likelihood that its actions constituted infringement of a valid patent."); Christopher A. Harkins, Tesla, Marconi, and the Great Radio Controversy: Awarding Patent Damages Without Chilling a Defendant's Incentive to Innovate, 78 Mo. L. Rev. 745, 766-67 (2008) (discussing the "substantial cost of litigation" and the risk of patent litigation).

167 See 35 U.S.C. § 154(a) (providing that a patentee has the right to exclude others from making, using, offering to sell, or selling the invention in the United States); Combined Petition for Panel Rehearing and Rehearing En Banc of Defendant-Appellant Merck KGaA at 1-3, Integra Lifesciences I, Ltd. v. Merck KGaA, Nos. 02-1052, 02-1065, 2003 U.S. App. LEXIS 26547 (Fed. Cir. Dec. 3, 2003) [hereinafter Combined Petition] (asserting that limiting the scope of the section 271(e)(1) safe harbor provision "will increase the number of licenses needed and create additional
The options faced by pharmaceutical companies after Proveris will raise the costs of research and development programs for new drugs. Pharmaceutical companies will likely pass the increased costs associated with litigation and licensing to consumers. This is contrary to the two-fold purpose of the Hatch-Waxman Act: (1) to encourage research and development of safe and effective drugs and (2) to provide for the expedited introduction of low-cost drugs into the market place.

The Proveris test weakened the rights of pharmaceutical companies that use patented research tools for regulatory review, and strengthened the rights of research tool patent holders.

2. Proveris Strengthens Research Tool Patent Holder Rights

Elimination of research tools from protection under the safe harbor provision provides strong patent protection for research tool technology and encourages innovation. Inventive efforts are stimulated through financial incentives, such as litigation risks and uncertainties.

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168 Brief for PRMA, supra note 1, at 14 (arguing that the safe harbor provision directly impacts the cost of drug development because "[a]s the development process becomes more protracted, the overall cost of drug development is increased").

169 See id. (arguing that the safe harbor provision directly impacts the cost of drug development because "[a]s the development process becomes more protracted, the overall cost of drug development is increased"); Stephen R. Lantham, Pharmaceutical Costs: An Overview and Analysis of Legal and Policy Responses by the States, 24 J. LEGAL MED. 141, 173 (2003) (discussing that drug-cost inflation is driven by advances in technology and that Americans will have to choose between paying to provide incentives for the development of new and more costly drugs or deciding that access to current technologies is sufficient); Mireles, supra note 10, at 152 (stating that exclusive patent rights allows the patent holder to "increase a patented invention's price beyond the competitive market price . . .").


171 See Proveris Scientific Corp. v. Innovasystems, Inc., 536 F.3d 1256, 1265-66 (Fed. Cir. 2008) (eliminating safe harbor protection for alleged infringers using "patented inventions" that do not qualify as "products" under the patent term extension provision).

172 Brief of Amici Curiae Wisconsin Alumni Research Foundation, et al. in Support of Respondents at 2, Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193 (2005) (No. 03-1237), 2005 WL 682088, at *2 ("Given the normal expectation that innovation follows invention, the corresponding erosion of patent rights that would necessarily accompany an undue expansion of the safe harbor would also bring with it a lag in innovation."). But see Rebecca S. Eisenberg, Patents and the Progress of Science: Exclusive Rights and Experimental Use, 56 U. CHI. L. REV. 1017, 1031 (1989) ("[T]echnological change has been an extremely important source of economic growth over time, and that levels of invention are responsive to economic stimuli. But it does not necessarily follow that patent protection is necessary to preserve adequate economic incentives for invention and innovation.").
licensing, to encourage companies to invest in the development of new research tools.\textsuperscript{173} Thus, the next generation of research tools could lead to faster research and development of new drugs.\textsuperscript{174} Prior to Proveris, the Federal Circuit expressed concerns that if research tool patents were immunized under the safe harbor provision, those patent holders’ rights would be destroyed.\textsuperscript{175}

Biomedical research, however, is cumulative in nature and requires the use of increasing numbers of patented research tools to develop publicly beneficial drugs.\textsuperscript{176} As a result, a research tool “patent thicket”\textsuperscript{177} could arise to restrict access to broadly useful tools that may stifle pharmaceutical companies’ research and development programs or raise the costs of the drug products that make it to market.\textsuperscript{178} For example, researchers may be forced to obtain expensive licenses for research tool patents and may encounter difficulty because patent holders have the right to refuse licenses on any terms, even if they are not practicing the invention.\textsuperscript{179} Therefore,

\begin{itemize}
\item \textsuperscript{173} Katherine J. Strandburg, \textit{Users As Innovators: Implications for Patent Doctrine}, 79 U. COLO. L. REV. 467, 474 (2008) (“Up until now patent discourse has been relatively unanimous in assuming that inventors of new technology need to recoup their inventive investments through commercial sales of embodiments of the invention or by licensing the technology to others.”).
\item \textsuperscript{174} FTC Report, supra note 11, at ch. 3, p. 19-20 (noting that research tools can considerably reduce the costs and time required for the drug development process); Mireles, supra note 10, at 149 (“Research tools are critical to the efficient development of commercial applications, especially pharmaceutical drugs.”).
\item \textsuperscript{175} Integra I. 331 F.3d 860, 867 (Fed. Cir. 2003) (“[E]xpansion of § 271(e)(1) to include the Scripps Merck activities would effectively vitiate the exclusive rights of patentees owning biotechnology tool patents.”).
\item \textsuperscript{176} Mireles, supra note 10, at 148 (asserting that access to a multitude of research tools is necessary for the development of products that will have a direct impact on public health); Pyrmont supra note 16, at 386 (“Due to the scientific complexity of biotechnology research, investigators need access to a higher number of research tools than in other industries.”).
\item \textsuperscript{177} ROBERT PATRICK MERGES & JOHN FITZGERALD DUFFY, PATENT LAW AND POLICY: CASES AND MATERIALS 943 (4th ed. 2007) (defining the term “patent thicket” to describe as “areas of technology crowded with existing patents.”).
\item \textsuperscript{178} See Lab. Corp. of Am. Holdings v. Metabolite Labs., Inc. 548 U.S. 124, 127 (2006) (Breyer J., dissenting) (per curiam) (stating that patents can “discourage research by impeding the free exchange of information... by forcing researchers to avoid the use of potentially patented ideas, by leading them to conduct costly and time-consuming searches of existing or pending patents, by requiring complex licensing arrangements, and by raising the costs of using the patented information...”); see also Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, 64 Fed. Reg. 72,090, 72,092 (final notice Dec. 23, 1999) (“[I]ntellectual property restrictions can stifle the broad dissemination of new discoveries and limit future avenues of research and product development.”); Damien Geradin, Anne Layne-Farrar, & A. Jorge Padilla, \textit{The Complements Problem Within Standard Setting: Assessing the Evidence on Royalty Stacking}, 14 B.U. J. SCI. & TECH. L. 144, 151 (2008) (citing Thomas D. Kiley, \textit{Patents on Random Complementary DNA Fragments}, 257 SCIENCE 915 (1992)) (“[B]ecause every step along the way draws another patent application, the path toward public possession of real benefit is increasingly obscured by dense thickets of intersecting, overlapping, and cross-blocking patents... . . . The cumulative of royalty obligations threatens to have [a stunting] effect in biotechnology.”); Mireles, supra note 10, at 148 (noting that increasing numbers of patented research tools could “retard innovation and the subsequent development of publicly beneficial commercial applications.”); Mueller, supra note 12, at 5-7 (reporting that the increased patenting activity in biotechnology has increased the difficulty of access and dissemination of patented research tools).
\item \textsuperscript{179} 35 U.S.C. § 271(d)(4) (2006) (providing instruction to the courts not to withhold infringement remedies because a patentee has refused to license or use any rights to the patent);
even though the rights of research patent holders are strengthened, the public may ultimately pay the price because of the high transactional costs of obtaining licenses during the research and development of new drugs.

This section addressed the ramifications of the Proveris court's shift to a narrow construction of the section 271(e)(1) safe harbor provision on research tools. The proposal section of this comment advocates that legislation should be enacted to modify the safe harbor provision to immunize the use of patented research tools in FDA regulatory testing. In the alternative, this comment suggests that any patented invention that is used to develop a product within the scope of the section 156 patent term extension provision should be protected under the section 271(e)(1) safe harbor provision.

III. PROPOSAL

The public interest in low-cost drug prices is in direct conflict with the public interest in maintaining incentives for creating new research tool technologies. Commentators have proposed solutions to balance these public interest tensions through broadening the scope of the experimental use exception to patent infringement, establishing compulsory licensing of research tool patents,
establishing a “reach-through” royalty, or establishing research tool patent pools. While these suggestions indicate that there is a problem, generally, with how biomedical research tools fit in the patent system, this comment focuses specifically on patented research tools with regard to the scope of the section 271(e)(1) safe harbor provision.

A. Public Policy Favors Legislation Exempting Research Tools Under the Section 271(e)(1) Safe Harbor Provision

The Proveris decision departs from Merck’s broad construction of the section 271(e)(1) safe harbor provision, and seemingly tips the balance against low-cost drugs in the face of the increasing needs of an aging community. One solution to reconcile the inconsistency between Merck and Proveris is congressional modification of the section 271(e)(1) safe harbor provision to clearly define the meaning of the phrase “patented invention.” As discussed in the analysis section above, public policy favors a broad statutory construction of this phrase that is not synonymous with the narrower phrase “patented product” within the section 156(f) patent term extension provision.

Defining the phrase “patented invention” of the safe harbor provision to include all patented inventions would encompass patented research tools. Alternatively, Congress could expressly indicate that research tools are patented inventions within the meaning of the safe harbor provision.

Legislation establishing that patented research tools fall within the scope of the safe harbor provision will reduce the transactional costs associated with experimental research exception should be broadened because the increased patenting activity in biotechnology has increased the difficulty of access and dissemination of patented research tools.

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185 Mueller, supra note 12, at 9-10 (proposing a “liability rule” that compensates a patent holder by using “reach-through” royalties).

186 Mireles, supra note 10, at 224-25 (proposing the government facilitate the use of research tool patent pools to overcome the “Tragedy of the Anticommons” involved in accumulating the numerous intellectual property rights necessary to create a commercial product).

187 Compare Proveris Scientific Corp. v. Innovasystems, Inc., 536 F.3d 1256, 1265 (Fed. Cir. 2008) (holding that only “patented invention” within the meaning of the section 156(f) patent term extension provision will qualify for immunization under the section 271(e)(1) safe harbor provision), with Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 202 (2005) (holding that the section 271(e)(1) provision applies to “all uses of patented inventions”).

188 Compare Brief for PRVA, supra note 1, at 14 (stating that the section 271(e)(1) safe harbor provision affects the cost of new drugs because as the development process becomes more protracted, the overall cost of drug development is increased), with Lantham, supra note 169, at 146-47 (“If the drug manufacturers charged only the marginal cost of drug production—the cost of making each new pill—then they would never recover their research costs.... Manufacturers need to recover their R&D costs by allocating some of those costs to the price of each pill sold.”).

189 H.R. REP. NO. 98-857, pt. 2, at 29 (1984) (identifying that the section 271(e)(1) safe harbor provision provides substantial benefits to the government and the general public because it allows faster market entry of generic drugs that will assist in the reduction of health care costs).
pharmaceutical research and development programs. This legislation would ultimately benefit the public through the availability of lower-cost drugs.

The safe harbor provision is a limited exemption. Therefore, this legislation would not frustrate the purpose of the patent system for research tools patent holders. Research tool patent holders would still be able to enforce their rights against alleged infringers under the second prong of the safe harbor analysis. Even if an alleged infringer satisfies the first prong of the Proveris test, the second prong of the test requires that the activities be “solely for uses reasonably related to the development and submission of information” to the FDA.

The safe harbor provision does not protect an alleged infringing pharmaceutical company from all activities with patented research tools. For example, the safe harbor provision does not protect basic scientific research performed without the intent to use the invention for development and submission of information to the FDA.

In addition to the restriction found within the language of the section 271(e)(1) safe harbor provision, there are several situations where a research tool patent holder is not negatively impacted by this exemption. First, if a research tool is encompassed into the final drug product, the safe harbor provision only applies until approval is obtained. Second, pharmaceutical companies will continue to purchase...

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190 See Mireles, supra note 10, at 152 (noting the costs associated with patent rights in discoveries).

191 See id. ("The potential monopoly power that a patent provides allows the patentee to increase a patented invention's price beyond the competitive market price, thus reducing the supply of the patented invention.").


193 Integra II, 496 F.3d 1334, 1348-49 (Fed. Cir. 2007) (Rader, J. dissenting-in-part and concurring-in-part) (asserting that the majority decision "poses a danger to the entire research tool industry" because the court expanded the scope of the section 271(e)(1) safe harbor provision); Integra I, 331 F.3d 860, 867 (Fed. Cir. 2003) (stating that expanding the section 271(e)(1) safe harbor provision would destroy the proprietary rights of research tool patent holders).

194 35 U.S.C. § 271(e)(1): Brief of Patients Not Patents, Inc., as Amicus Curiae in Support of Neither Party at 8, Proveris Scientific Corp. v. Innovasystems, Inc., 536 F.3d 1256 (Fed. Cir. 2008) (No. 07-1428), 2007 WL 3308248, at *8 ("The safe harbor is already limited by the language of the statute to acts 'solely for uses reasonably related to the development and submission of information' to the FDA.").

195 Brief of Amici Curiae Genentech, Inc. and Biogen Idec, Inc. in Support of Petitioner at 22, Merck, 545 U.S. 193 (No. 03-1237), 2005 WL 435893, at *22 (noting that even if research tools fall under the scope of the safe harbor provision, research tool patent holders would be able to enforce their patents when activities with the patented tools are not "reasonably related" to FDA regulatory approval).

196 Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 205-06 (2005) (articulating that "basic scientific research" is not "reasonably related" to the FDA regulatory approval process unless it is performed with "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 ... ").

197 See Stephen B. Maebius & Harold C. Wegner, Merck v. Integra: The Impact of a Broader "Safe Harbor" Exemption on Nanobiotechnology, 2 NANO TECH. L. & BUS. 254, 257 (2005) (noting that when a drug is developed that encompasses the claims of a research tool patent, infringement is actionable after FDA approval is granted).
complicated research tools that cannot be easily duplicated in-house. Third, pharmaceutical companies will continue to obtain licenses from research tool patent holders. One example is when researchers purchase test kits and obtain implied licenses that cover many research tool patents, including methods. Under these types of situations, research tool patent holders will continue to receive a commercial benefit from their inventions.

Legislation that includes patented research tools within the scope of the section 271(e)(1) safe harbor provision provides an acceptable balance between the public interest in low-cost drugs and the need to provide incentives to encourage the continued development of research tools. An alternative to address concerns regarding the scope of the section 271(e)(1) safe harbor provision is a judicial remedy.

B. Extension of the Proveris Test to Include Products that are Inherent to the Development of Patented Products Within the Meaning of the Section 156(f) Patent Term Extension Provision

Another solution to reconcile the Proveris decision with Merck, may be to judicially supplement the first prong of the Proveris test for "patented inventions" to include all patented inventions that are inherent to the development of "products" as that term is defined in the section 156(f) patent term extension provision. This modified test provides broader protection under the safe harbor provision for the use of patented research tools during research and development of new drugs. This modified inherency test is in line with the Supreme Court's determination in Merck and furthers the public interest in obtaining low-cost drugs.

This inherency test would include the use of some research tools under the safe harbor provision. For instance, research tools that are encompassed into an end drug product would be protected products under the safe harbor provision because they are necessary components to reach the final drug product. In contrast, research tools that are not necessary to develop a drug would be protected under this standard. In contrast,
research tools used merely to test or confirm the activity of a potential drug product, such as safety profiling assays, would not qualify as drug products under this test.¹⁰⁶

Supplementing the first prong of the Proveris test to include an inherency standard would not completely eliminate the uncertainty of licensing agreements or potential litigation between pharmaceutical companies and research tool patent holders, but it would provide immunization for the use of research tools that are necessary components of drug development under the safe harbor provision.²⁰⁷ Thus, the public interest in low-cost drugs would be protected to some extent in comparison to the current test that eliminates research tools from protection under the safe harbor provision.

CONCLUSION

The Proveris decision narrowed the scope of the section 271(e)(1) safe harbor provision, and excludes the use of certain patented research tools that are necessary for pharmaceutical companies to conduct timely and efficient research and development of new drugs.²⁰⁸ This decision’s effect on research tools may negatively impact the public by raising the cost of pharmaceutical companies’ research and development programs and may ultimately raise the costs of drugs available to the public.²⁰⁹ Congress should balance the conflict between the public interest in low-cost drugs and the public interest in maintaining incentives that will encourage the innovation of new research tool technologies. This comment proposes that legislation is necessary to include research tools within the scope of the safe harbor provision. In the alternative, this comment proposes that the Proveris test be judicially supplemented to include an inherency component protecting the use of patented research tools that are necessary for drug development.

²⁰⁶ Id. (‘Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.’). This inherency standard comports with the Supreme Court’s statement that basic scientific research “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 surely not ‘reasonably related to the development and submission of information’ to the FDA.” Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 205-06 (2005).

²⁰⁷ See supra note 206 and accompanying text.

²⁰⁸ Proveris Scientific Corp. v. Innovasystems, Inc., 536 F.3d 1256, 1263-66 (Fed. Cir. 2008) (narrowing the safe harbor provision despite its previously broad application of section 271(e)(1)); FTC Report, supra note 11, at ch. 3, p. 19-20 (noting that research tools can considerably reduce the costs and time required for the drug development process).

²⁰⁹ Brief for PRMA, supra note 1, at 14 (arguing that the safe harbor provision directly impacts the cost of drug development because “[a]s the development process becomes more protracted, the overall cost of drug development is increased”); Lantham, supra note 169, at 173 (discussing that drug-cost inflation is driven by advances in technology and that Americans will have to choose between paying to provide incentives for the development of new and more costly drugs or deciding that access to current technologies is sufficient); Mireles, supra note 10, at 152 (stating that exclusive patent rights allows the patent holder to “increase a patented invention’s price beyond the competitive market price . . . ”).