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I. INTRODUCTION

The fundamental protection of intellectual property in the pharmaceutical and biotechnological industries is the patent. The ease of reverse-engineering a drug makes trade secret protection inapposite, leaving the inventor of a new drug with the limited monopoly of a patent. The twenty-year life of a patent from the time of application is a very short window within which a drug-maker may recoup its research and development costs, when preclinical and clinical testing are taken into account. In fact, the approval process by the Food and Drug Administration ("FDA") for a new drug can take so long that Congress saw fit to grant an extension to the affected patent's term.\(^1\) Even with the extension, some estimate that pharmaceutical companies on average have three to seven years of exclusivity under the patent before the entry of low-cost generic equivalents.\(^2\)

Federal law grants the owner of a patent the right to sue for infringement any party who practices the patented invention without the owner's approval. Yet several exceptions exist, in federal statutory law and the common law, that permit infringers to proceed without compensating the patentee. In 1984, Congress passed the Drug Price Competition and Patent Term Restoration Act ("Hatch-Waxman Act"),\(^3\) which has two major provisions. The first extends the term of the patent to allow for the length of time needed for FDA approval.\(^4\) The second provision assists in the

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preparation and development of low-cost generic drugs, which Congress recognized as having significant public value. Specifically, Congress passed 35 U.S.C. § 271(e)(1), which states:

It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention . . . 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. . . .

Although Congress may have intended for § 271(e)(1) to make the development of generic drugs easier, the statute is devoid of any limitation to such drugs. In fact, the nonspecific phrases “a patented invention” and “a Federal law” have allowed a significant expansion of the infringement exemption beyond what Congress may have intended. Recently, the Supreme Court ruled that Congress’s intent does not supplant the actual words of the statute even if the broad language employed may have detrimental consequences to patent holders in the United States.

As more cases are handed down in light of the Supreme Court’s interpretation of § 271(e)(1), it has become increasingly clear that biotechnological and pharmaceutical patents involved in drug discovery are at risk of becoming unenforceable. Congress’s use of broad language has allowed drug researchers to avoid paying patentees for the use of their patents involved in drug research, and it may not be long before infringement without penalty begins to threaten innovation within the industry.

Part II of this comment traces the development of case law leading up to § 271(e)(1) and the passage of § 271(e)(1). Part III delineates the major cases of the Court of Appeals for the Federal Circuit (“CAFC”) and the Supreme Court that interpret the breadth and applicability of § 271(e)(1). Part IV discusses the

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7. See H.R. REP. NO. 98-857, pt. II at 8 reprinted in 1984 U.S.C.C.A.N. 2686 (intending safe harbor for “a limited amount of testing so that generic manufacturers can establish the bioequivalency of a generic substitute.”).


typical drug discovery process and the holding in *Merck KGaA v. Integra Lifesciences I, Ltd.*,\(^{10}\) concerning when the § 271(e)(1) infringement exemption begins.\(^{11}\) Part IV also explores the questions left unanswered by recent Supreme Court rulings and drug researchers' possible reactions to the changes. Finally, the Conclusion in Part V contemplates the future of the pharmaceutical and biotechnological industries in the absence of Congressional action to address the current challenges it faces regarding the § 271(e)(1) safe harbor.

II. *ROCHE V. BOLAR AND THE CREATION OF § 271(e)(1)*

Since the early days of the judicial development of the patent system in the United States, exemptions to the patentee’s “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” have existed.\(^{12}\) The CAFC artificially extended the effective patent term of protection in *Roche Products, Inc. v. Bolar Pharmaceutical Co.*\(^{13}\) The issue in *Roche v. Bolar* involved the development of a generic version of a patented drug prior to the expiration of the patent term.\(^{14}\) Roche was the assignee of U.S. Patent No. 3,299,053 (“053 patent”),\(^{15}\) which taught flurazepam hydrochloride (“flurazepam HCl”), a benzodiazepine that constituted the active ingredient in Roche's highly successful sleeping pill, Dalmane.\(^{16}\) Bolar Pharmaceuticals wanted to enter the market with a generic form of Dalmane before its competitors, but was concerned with the length of time required to obtain approval from the FDA.\(^{17}\) Under the approval scheme for a generic drug at that time, a generic drug company must submit a New Drug Application (“NDA”). The NDA required submission of safety information, such as “stability data, dissolution rates, bioequivalency studies, and blood serum studies,” and

11. Id. at 202.
13. 733 F.2d 858 (Fed. Cir. 1984).
14. See id. at 860.
17. Id.
took approximately two years to achieve FDA approval.\textsuperscript{18} About six months prior to the '053 patent's expiration date,\textsuperscript{19} Bolar obtained the active ingredient flurazepam HCl from "a foreign manufacturer not subject to United States patent law"\textsuperscript{20} and began conducting the required experimentation to develop a generic version of the drug.\textsuperscript{21}

Bolar contended that due to the length of time required for generic drug approval, forbidding generic drug development prior to patent expiration, even for "limited pre-expiration preparation for post-expiration entry into the market," amounted to a de facto patent monopoly extension. Thus, Bolar attempted to circumvent Roche's Dalmane patent.\textsuperscript{22} The district court agreed with Bolar, holding that its use of flurazepam HCl was de minimus and "the law does not concern itself with small matters."\textsuperscript{23} And Bolar's use was not "an experiment with a patented article for the sole purpose of gratifying a philosophical taste, or curiosity, or for mere amusement."\textsuperscript{24} Instead, the court found that Bolar's activities represented merely "a violation of the principle of [Roche's] monopoly" and failed to cause any substantial harm to Roche prior to the expiration of the '053 patent.\textsuperscript{25}

The CAFC reversed the case on appeal, holding that Roche had the right to exclude a competitor from using its patented drug in efforts to supply information for an NDA to the FDA.\textsuperscript{26} The CAFC explained that the experimental use defense\textsuperscript{27} could not be extended so far as to allow competitors to use the patented invention for applications with an underlying commercial motive.\textsuperscript{28}

\begin{itemize}
\item \textsuperscript{18} \emph{Id.}
\item \textsuperscript{19} The '053 patent expired January 17, 1984. \emph{Id.}
\item \textsuperscript{21} \emph{Roche v. Bolar}, 733 F.2d at 860.
\item \textsuperscript{22} \emph{Roche v. Bolar}, 572 F. Supp. at 257.
\item \textsuperscript{23} \emph{Id.} at 258.
\item \textsuperscript{24} Poppenhusen v. Falke, 19 F. Cas. 1048, 1049 (C.C. S.D.N.Y. 1861) (No. 11,279).
\item \textsuperscript{25} \emph{Roche v. Bolar}, 572 F. Supp. at 258.
\item \textsuperscript{26} \emph{See Roche v. Bolar}, 733 F.2d at 863, 867 ("[U]nlicensed experiments conducted with a view to the adaption of the patented invention to the experimenter's business is a violation of the rights of the patentee to exclude others from using his patented invention.").
\item \textsuperscript{27} The experimental use defense is a common law defense against infringement for non-commercial use. For a full description of the experimental use defense and its recent changes, see \emph{Madey v. Duke University}, 307 F.3d 1351, 1360–63 (Fed. Cir. 2002).
\item \textsuperscript{28} \emph{Roche v. Bolar}, 733 F.2d at 863 ("We cannot construe the experimental use rule so broadly as to allow a violation of the patent laws in the guise of 'scientific inquiry,' when
though a de facto extension of a patent's term would result in limiting such a use, the statutes regarding patent infringement and NDA submissions to the FDA did not provide any flexibility for the length of time required for generic drug approval. In light of this obvious discrepancy, the CAFC invited Congress to act in order to address the problems highlighted in this case with the development of generic drugs, and opted not to "rewrite the patent laws here." 29

The Drug Price Competition and Patent Term Restoration Act of 1984, 30 also known as the Hatch-Waxman Act, was Congress's attempt to alleviate the problems highlighted in Roche v. Bolar, namely, "two distortions to the normal 'patent term produced by the requirement that certain products must receive premarket regulatory approval.'" 31 First, the Hatch-Waxman Act created a patent term adjustment for the length of time that a patentee of a drug is barred from commercially marketing the drug prior to FDA approval. 32 This was deemed warranted in light of the typical seven to thirteen year approval time required to bring a drug candidate to market. 33 Second, the Hatch-Waxman Act tried to facilitate the development of generic versions of prescription drugs by granting generic drug companies the right to use patented drugs in order to bring generic versions to market as soon as possible after the expiration of the drug patent. 34

The imprecise language Congress used to embody its intent to convey generic drug companies an exemption for the infringement of drug patents in pursuit of FDA approval of generic drugs provides the basis for all of the cases and commentary to follow. Congress specifically stated in the legislative history of the

that inquiry has definite, cognizable, and not insubstantial commercial purposes.")

29. Id. at 865. The CAFC concluded by restating the oft used phrase from Sony v. Universal Studios, 464 U.S. 417, 456 (1984), "it is not our job to apply laws that have not yet been written."


Hatch-Waxman Act that it wanted to provide "a limited amount of testing so that generic manufacturers can establish the bio-equivalency of a generic substitute."\textsuperscript{35} However, the statute's language granting the exemption, as written, is sweepingly broad in scope:

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 . . . ) 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.\textsuperscript{36}

The question of whether the statutory language or legislative history controls the interpretation of the statute was decided in two recent Supreme Court cases, but questions still remain as to how expansive the exemption of § 271(e)(1) actually is.

III. JUDICIAL EXPANSION OF THE § 271(e)(1) SAFE HARBOR

A. Eli Lilly v. Medtronic

The specific issue concerning the breadth of the "safe harbor" exemption of § 271(e)(1) arose in \textit{Eli Lilly & Co. v. Medtronic Inc.}\textsuperscript{37} Dr. Michael Mirowski held two patents on the development of an internally implanted cardiac defibrillator capable of discharging electric shocks, which could be used to treat two types of cardiac arrhythmias, ventricular tachycardia or ventricular fibrillation.\textsuperscript{38} Medtronic, one of the leading manufacturers of cardiac pacemakers, was originally assigned Mirowski's patents, but declined to commercially develop the implantable defibrillator.\textsuperscript{39} Mirowski then exclusively assigned his patents to Eli Lilly, who

\textsuperscript{35} Id. pt. II, at 8, \textit{reprinted in} 1984 U.S.C.C.A.N. 2686, 2692; \textit{see also} Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860, 865 (Fed. Cir. 2003).


\textsuperscript{37} 496 U.S. 661, 663–64 (1990).


\textsuperscript{39} \textit{Eli Lilly v. Medtronic}, 7 U.S.P.Q.2d (BNA) at 1440.
obtained FDA approval for the medical device described in Mirowski’s patents. Medtronic later decided to enter the implantable defibrillator market and unsuccessfullly attempted to acquire the rights to Mirowski’s patent. After a failed attempt to invalidate Eli Lilly’s patents through reexamination in the United States Patent and Trademark Office (“PTO”), Medtronic developed an improved implantable device, combining the defibrillator with a conventional pacemaker, creating a single unit capable of treating fibrillation, tachycardia, and bradycardia. Medtronic built several of the improved models and installed them in patients in Canada prior to Eli Lilly’s patent infringement suit.

At trial in the United States District Court for the Eastern District of Pennsylvania, Medtronic made a motion for summary judgment, alleging its activity infringing upon Eli Lilly’s patent was exempted by 35 U.S.C. § 271(e)(1) because it was “reasonably related to the development and submission of information” to the FDA under the Federal Food, Drug, and Cosmetic Act (“FDCA”) for medical devices. Finding § 271(e)(1) inapplicable to medical devices, the court noted that the language of the statute covered “Federal law which regulates . . . drugs,” despite Medtronic’s objection that the language “describes the type of law, not the type of patented invention.” With both parties admitting this was a case of first impression for any court in the country, the court found the legislative history most persuasive, holding that the § 271(e)(1) exemption only applied to drugs, denying the motion for summary judgment. The jury subsequently found that Medtronic had willfully infringed upon Eli Lilly’s patents for defibrillators, and the court issued an injunction preventing Medtronic from leveraging “its current strength in the pacemaker industry

40. Id.
41. Id.
42. See id. Bradycardia means “relatively slow heart action.” MERRIAM-WEBSTER, supra note 38, at 137.
43. Eli Lilly v. Medtronic, 7 U.S.P.Q.2d (BNA) at 1440.
46. See id. at 1761–62.
47. Id. at 1762 (quoting 35 U.S.C. § 271(e)(1) (2000) (emphasis added)).
49. See Eli Lilly v. Medtronic, 5 U.S.P.Q.2d (BNA) at 1762.
to dominate the market involving devices for treating tachycardia and fibrillation."

Medtronic brought an interlocutory appeal from the permanent injunction to the CAFC, which reversed and remanded the case. In its opinion, the court commented that both parties "put forth equally plausible interpretations of section 271(e)(1), which to [this court] means the language is fraught with ambiguity." The CAFC, however, relied on a different segment of the legislative history where "Congress explicitly stated: 'The provisions of section 202 of the bill [i.e., the amendment of Title 35 adding section 271(e)] have the net effect of reversing the holding of the court in Roche.'" The CAFC reiterated its holding in Roche v. Bolar:

While the claimed matter in Roche was limited to a drug product, the holding of that case was not so limited. The holding provided an interpretation of the scope of 35 U.S.C. § 271(a) without regard to what particular goods might be involved. Specifically, the court decided that the unlicensed use of a patented invention for testing and investigation, even though strictly related to obtaining FDA approval for a substitute, was an infringement under 35 U.S.C. § 271(a).

The CAFC concluded that "section 271(e)(1) allows a party to make, use, or sell any type of 'patented invention' if 'solely' for the restricted uses stated therein."

On certiorari the Supreme Court reiterated that the question before it was whether the terminal language of § 271(e)(1), specifically "a Federal law which regulates the manufacture, use, or sale of drugs," was determinative as to whether the exemption found in § 271(e)(1) applied only to the submission of information to the FDA under an Abbreviated New Drug Application ("ANDA") for generic drugs or if the language could be extended to include information submitted for premarket approval for

51. Eli Lilly v. Medtronic, 872 F.2d at 405.
53. Eli Lilly v. Medtronic, 872 F.2d at 406.
54. Id.
The Court held that because the FDCA regulates both drugs and medical devices, the § 271(e)(1) exemption applies in both instances.\textsuperscript{59}

In the majority opinion, Justice Antonin Scalia focused on the question of whether the language of the § 271(e)(1) exemption strictly limited its application to patented drugs. The majority indicated that none of Eli Lilly, Medtronic, or even the CAFC's references to the legislative history were necessary in light of the entirety of the Hatch-Waxman Act.\textsuperscript{60} The Court reasoned that Congress chose to create a patent term extension to offset the length of time required for premarket approval for products required to be submitted under the FDCA or other Federal law and the § 271(e)(1) exemption to offset this monopoly expansion.\textsuperscript{61} Through this give-and-take, the extension and infringement exclusion should be read in concert.\textsuperscript{62} The Court found especially enlightening the exclusion from the § 271(e)(1) safe harbor "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)."\textsuperscript{63} Since these particular inventions were explicitly excluded from the patent term extension, this suggested to the Court that any invention that would qualify for patent term extension, including medical devices,\textsuperscript{64} food additives,\textsuperscript{65} color additives,\textsuperscript{66} new drugs,\textsuperscript{67} antibiotic drugs,\textsuperscript{68} and human biological products,\textsuperscript{69} would concurrently be eligible for the § 271(e)(1) safe harbor.\textsuperscript{70}

The Court also noted that Congress approached the issue of generic drug development separately from § 271(e)(1). Referring to § 271(e)(2), which relates to the filing of an ANDA, the Court stated that the submission of an ANDA is a specific type of in-
fringement that, by itself, only pertains to these types of drug patent applications.\textsuperscript{71} In order to file the ANDA, a generic drug producer must possess the requisite safety and efficacy information, and although Congress explicitly chose to codify the ANDA filing as a patent infringing act,\textsuperscript{72} it exempted the procurement of biological information from infringement. The Court, however, affirmed the CAFC’s finding that the § 271(e)(1) safe harbor exemption applied to any patented invention\textsuperscript{73} and stated that no statutory interpretation “can transform § 271(e)(1) into an elegant piece of statutory draftsmanship.”\textsuperscript{74}

The dissent, written by Justice Anthony Kennedy and joined by Justice Byron White, focused on the nature of the infringement and argued that the § 271(e)(1) exemption was inapplicable to medical devices.\textsuperscript{75} Justice Kennedy first opined, “When § 271(e)(1) speaks of a law which regulates drugs, I think that it does not refer to particular enactments or implicate the regulation of anything other than drugs.”\textsuperscript{76} The dissent continued by distinguishing the harm to a drug patent holder whose patent is infringed by generic drug makers conducting safety and efficacy experiments from the harm experienced by Eli Lilly in the case at bar.\textsuperscript{77} For an ANDA submission, the de minimus infringement experienced by the drug patentee is strictly noncommercial, with the generic manufacturer generating sales only after expiration of the patent and FDA approval.\textsuperscript{78} In the case of Medtronic’s infringement, the infringing defibrillators were sold to the patients, which financially infringed Eli Lilly’s patent monopoly by depriving it of a sale of its patented product.\textsuperscript{79} However, the dissent did concede that “Congress could have specified [the safe harbor exemption] in a clearer manner.”\textsuperscript{80}

\textsuperscript{71} See id. at 678.
\textsuperscript{72} See id. at 676–78.
\textsuperscript{73} See id. at 669.
\textsuperscript{74} Id. at 679.
\textsuperscript{75} See id. at 679–80 (Kennedy, J., dissenting).
\textsuperscript{76} Id. at 680 (Kennedy, J., dissenting).
\textsuperscript{77} See id. at 682 (Kennedy, J., dissenting).
\textsuperscript{78} See id. at 682 (Kennedy, J., dissenting).
\textsuperscript{79} See id. at 682–83 (Kennedy, J., dissenting).
\textsuperscript{80} Id. at 680 (Kennedy, J., dissenting).
B. Merck v. Integra

The Supreme Court took advantage of the case presented in Merck v. Integra\(^{81}\) to further expand the safe harbor exemption of § 271(e)(1).\(^{82}\) Integra Lifesciences was the assignee of several patents\(^{83}\) pertaining to the use of the “RGD” peptide\(^{84}\) in modulating cell adhesion.\(^{85}\) Specifically, it was known that living mammalian cells were able to stick to one another by a specific interaction between two proteins found on the surface of cells\(^{86}\) in a manner reminiscent of Velcro. The patent inventors, Drs. Ruoslahti and Pierschbacher,\(^{87}\) determined that half of the cell adhesion process was caused by a simple three amino acid peptide sequence found in one of the proteins, namely the RGD peptide.\(^{88}\) By introducing the RGD peptide into a solution of cells adhered to one another, the peptide, by competing with the native cell-surface protein,

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82. See id. at 197; see also Brendan M. O'Malley, Note, Merck v. Integra and Its Aftermath: A Safe Harbor for the Commercial Use of Biotechnology Research Tools?, 23 CARDOZO ARTS & ENT. L.J. 739, 752 (2006) (“If Justice Scalia thrust the Court’s bayonet into the belly of § 271(e)(1) in Lilly, he pulled out its viscera in Merck v. Integra.”).
84. A “peptide” is defined as a chain of amino acids linked together. For short peptides, such as Integra’s RGD tripeptide, the amino acid sequence is denoted by a shorthand code with letters that stand for individual amino acids. For example, “R” stands for Arginine, “G” stands for Glycine, and “D” stands for Aspartic Acid. It should also be clarified that both peptides and proteins are composed of a chains of amino acids, yet the difference between them is based upon the length of the chain. Although the demarcation between peptide and protein has been suggested to be at 50 amino acids, the arbitrary line is very imprecise near this length and depends upon the specific area of research. The terms are frequently interchanged. Suffice it to say that amino acid chains of less than a few dozen amino acids are probably referred to as peptides, and chains of hundreds, thousands, or tens of thousands of amino acids are clearly proteins. Peptides employed biologically are frequently used as messengers, whereas proteins fall into many diverse classes of use, such as receptors, enzymes (proteins that catalyze chemical reactions), and others.
87. The two inventors were researchers at the Burnham Institute at the time of the invention. They licensed their patents to Telios Pharmaceuticals, which they founded in June of 1987. See Brief for Petitioner at 19–20, Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193 (2005) (No. 03-1237), 2005 WL 389070. Telios spent over $150 million attempting to commercially develop the RGD peptide before declaring bankruptcy, see id. at 20, eventually selling the rights to the peptide patents to Integra in April of 1995, see id., Integra Lifesciences I, Ltd. v. Merck KGaA, No. 96CV1307-B(AJB), LEXIS 20725, at *7 (S.D. Cal. Sept. 7, 2004).
would block all of the adhesion sites and cause the cells to stop sticking to one another. The inventors envisioned their discovery of the RGD peptide could be used to trick cells in the body into adhering to things they would not normally stick to, such as artificial joints, by attaching the RGD peptide to the surface of the prosthesis, allowing faster integration into the body.

Dr. David Cheresh of The Scripps Research Institute ("Scripps") was conducting research on fighting cancer by inhibiting the formation of new blood vessels in the body, a process known as angiogenesis. Because it was known that the rapid growth in solid cancerous tumors was supported by the development of new blood vessels to supply nutrients to the tumors, it was postulated that inhibiting the formation of new blood vessels might lead to the starvation and death of the cancerous tumor. Dr. Cheresh was investigating a particular type of receptor, an integrin, known to be involved in the normal process of wound repair, which also includes the development of new blood vessels (angiogenesis) to replace damaged veins, arteries, and capillaries. By using an antibody capable of specifically binding to the $\alpha\beta_3$ integrin, Dr. Cheresh was able to halt angiogenesis in a wound healing simulation. Applying the same antibody to cancerous tumors in the laboratory led to dramatic losses in tumor size and cancer cell death due to inhibition of angiogenesis.

Merck KGaA, who had funded Dr. Cheresh's research since 1988, supplied Cheresh's laboratory with a tetrapeptide,
cRDPV,\textsuperscript{97} where the R and V had been joined together to form a closed loop or "cyclic" tetrapeptide, to test for inhibition of angiogenesis.\textsuperscript{98} This cyclic tetrapeptide was very effective at suppressing tumor growth by cessation of angiogenesis and presented Cheresh, Scripps, and Merck with a viable drug lead. Based on these preliminary results, the three parties penned an agreement wherein Merck agreed to fund Scripps over the next three years to develop a drug suitable for submission to the FDA as an Investigational New Drug ("IND") application.\textsuperscript{99} Per the agreement, Dr. Cheresh was to determine "the histopathology, toxicology, circulation, diffusion, and half-life of the peptides in the bloodstream" in animals.\textsuperscript{100} In 1997, experimentation with derivatives of cRDPV led to the discovery of EMD 121974, a derivative of cRDPV that was deemed to be the best candidate for clinical development due to its superior activity in suppressing angiogenesis and stability during \textit{in vivo} preclinical testing.\textsuperscript{101}

Integra approached Merck to obtain a license for use of the RGD tripeptide segment after learning of Merck’s research and discovering that Merck’s lead compound, cRDPV, was covered by patents that were owned by Integra.\textsuperscript{102} When negotiations ended with Merck refusing to obtain a license, Integra brought suit against Merck, Scripps, and Dr. Cheresh for patent infringement.\textsuperscript{103} At trial, the United States District Court for the Southern District of California ruled the defendant’s actions were not immunized by the § 271(e)(1) safe harbor exemption.\textsuperscript{104} The jury found Cheresh, Scripps, and Merck infringed on Integra’s patents and awarded a reasonable royalty of $15 million.\textsuperscript{105} Following post-trial motions, the suits against Dr. Cheresh and Scripps were dismissed\textsuperscript{106} and Merck appealed.\textsuperscript{107}

\textsuperscript{97} V stands for Valine, an amino acid, and c stands for cyclic, meaning that both ends are attached to one another to form a closed loop.
\textsuperscript{98} See Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 197 (2005).
\textsuperscript{99} See Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860, 863 (Fed. Cir. 2003).
\textsuperscript{100} Id.
\textsuperscript{101} Id.
\textsuperscript{102} See id.
\textsuperscript{103} Id.
\textsuperscript{104} Id.
\textsuperscript{105} Id.
\textsuperscript{106} See Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 201 (2005).
\textsuperscript{107} See Integra v. Merck, 331 F.3d at 864.
A divided panel of judges for the CAFC affirmed in part the decision that Merck's actions did not qualify for the § 271(e)(1) exemption. The majority, Judges Randall Rader and Sharon Prost, held the infringing actions of Scripps and Merck were not for developing information to submit to the FDA, "but instead identified the best drug candidate to subject to future clinical testing under the FDA processes." The majority's decision was contingent upon the use of "solely" in the § 271(e)(1) exemption, and concluded "[t]he FDA has no interest in the hunt for drugs that may or may not later undergo clinical testing for FDA approval." The CAFC held the link between the actions of Scripps, Cheresh, and Merck, specifically the use of a patented drug to assist a competitor to develop a potential drug candidate of their own, was too remote an activity to qualify for the § 271(e)(1) exemption and issued a warning against such an expansion:

[Expansion of § 271(e)(1) to include the Scripps Merck activities would effectively vitiate the exclusive rights of patentees owning biotechnology tool patents. After all, patented tools often facilitate general research to identify candidate drugs, as well as downstream safety-related experiments on those new drugs. Because the downstream clinical testing for FDA approval falls within the safe harbor, these patented tools would only supply some commercial benefit to the inventor when applied to general research. Thus, exaggerating § 271(e)(1) out of context would swallow the whole benefit of the Patent Act for some categories of biotechnological inventions. Needless to say, the 1984 Act was meant to reverse the effects of Roche under limited circumstances, not to deprive entire categories of inventions of patent protection.]

The Supreme Court's unanimous opinion, written by Justice Scalia, holds, "[W]e think it apparent from the statutory text that § 271(e)(1)'s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of any information under the FDCA." The
decision not only follows the holding in *Eli Lilly v. Medtronic*, the safe harbor applies to "any type of 'patented invention,'" but the unanimity of the Court suggests that the language of the statute will be broadly applied to any activity "reasonably related to the development and submission of information under" the FDCA.

The Supreme Court described several situations when the § 271(e)(1) safe harbor exemption would apply. First, the Court wrote that because the FDA is interested in all information critical to determining the safety of a drug candidate, including preclinical studies, the safe harbor exemption would protect activities involving both *in vitro* and *in vivo* studies. Preclinical studies can either be *in vitro*, biochemical assays not in living organisms, or *in vivo*, assays in living organisms, whether occurring in bacteria, yeast, plants, or even animals such as mice or chimpanzees. Second, the Court specifically addressed the use of patented compounds in preclinical studies, finding that their use "is protected under § 271(e)(1) as long as there is a reasonable basis for believing that the experiments will produce 'the types of information that are relevant to an IND or NDA.'" Third, the Court noted the fact that information derived from the use of patented compounds themselves was omitted from the information submitted to the FDA was not significant because its use was reasonably related to the development of a new, albeit competing, drug. Finally, the Court fixed a point along the drug development process where the acts of infringement would specifically be protected under § 271(e)(1), stating:

At least 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."

116. *See Merck v. Integra*, 545 U.S. at 202, n.6 (2005) ("The Court of Appeals recognized that information included in an IND would come within § 271(e)(1)'s safe harbor . . . Because an IND must be filed before clinical trials may begin, such information would necessarily be developed in preclinical studies.").
117. Id. at 208.
118. See id. at 207.
C. Recent Cases

Several recent federal district court decisions were decided in a matter consistent with the view that § 271(e)(1) applies to "all patented inventions." In 2006, the Northern Division of the District of Maryland dismissed, on the grounds of the § 271(e)(1) exemption, two of Classen Immunotherapies's claims of patent infringement. In the first case, Classen sued Biogen, GlaxoSmithKline ("GSK"), and others for infringing its patent involving a method of administering and monitoring experimental vaccines to evaluate their efficacy and safety. Biogen and GSK moved for dismissal on the grounds of § 271(e)(1), arguing that the FDA requires monitoring information to be collected for submission to the FDA. Classen countered that § 271(e)(1) should not apply in that situation because it was intended to cover generic drugs, not vaccines that have already been approved by the FDA and are currently on the market. In granting Biogen and GSK's motion to dismiss, the district court applied Merck v. Integra and found because § 271(e)(1) applies to any information to be submitted to the FDA, including post-approval studies, the infringing activities were legally permissible.

Classen lost a similar case to Elan Pharmaceuticals. Elan conducted additional FDA studies after initial approval determined that Skelaxin was absorbed differently with food than without. Classen sued Elan, arguing that Elan’s experiments infringed its patents on methods to investigate new uses for existing drugs. In granting Elan’s motion to dismiss, the district court reiterated the holding of the Supreme Court, stating that "there is simply no room in the statute for excluding certain information from the exemption on the basis of the phase of re-

122. See id. at 455.
123. See id. at 455–56.
124. See id. at 456.
127. See id. at *4.
IV. DRUG DISCOVERY AND THE IMPACT OF MERCK V. INTEGRA

Despite the ambiguity of the language in § 271(e)(1), the Supreme Court’s holding in Merck v. Integra, as applied to Merck and Dr. Cheresh’s specific drug discovery activities, actually provides a demarcation that clearly indicates the reach of the safe harbor exemption. In order to fully comprehend the holding in Merck v. Integra, it is necessary to understand the general process by which a new drug is discovered, developed, and ultimately submitted to the FDA for approval.

A. Drug Discovery Roadmap

First, defining technical terms properly is critical to understanding how the recent Supreme Court decisions affect drug discovery today. Drug discovery typically begins with basic research into a particular disease in the hope of identifying an underlying cause which may be manipulated by a new drug to ameliorate the targeted disease. This cause might be discovered to be a receptor on a cell or some biochemical pathway whose existence or significance is realized for the first time. At this stage of basic research, no drugs have entered the picture because research of this type only serves as the background for drug discovery by providing the drug target.

128. See id. at *7 (quoting Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 202 (2005)).
130. See Merck v. Integra, 545 U.S. at 202 (2005).
131. Id.
132. There is a lot of confusion about what exactly constitutes basic research. The author chooses to define “basic research” as research into finding a drug target prior to the search for a drug lead. Such a definition may be appropriate within the context of this comment, but the work is hardly basic. In fact, without the challenging, innovative, and essential research undertaken to understand the cause for a disease, find a drug target, or understand a cellular signaling pathway, drug discovery would grind to a halt. The most important thing to remember when working with ambiguous terms like “basic research” and “research tools” is that the terms must be precisely defined in any discussion, since the terms are inherently vague and have meanings that differ between scientific fields or even scientists within a given field. For an example of such confusion, see Justice Scalia’s exchange with the Assistant to the Solicitor General during oral arguments in Merck v.
Basic research culminates in the creation of an assay with which potential drug targets may be screened for efficacy in relieving the disease of interest. Biologists will have created a drug screening assay that involves the drug target, with the assay providing some type of measurable response that correlates to the desired effect in the diseased state. If the target is a receptor, perhaps the assay will be able to demonstrate when the normal operating state of the receptor has been interrupted. In simpler assays, such as assays looking for antibiotics or anticancer agents, the assay would be able to look for the killing of bacteria or cancer cells, respectively, without regard to the manner by which the drugs will achieve the desired response.

Once the screening assay has been developed during basic research, drug discovery moves into the lead discovery phase. The purpose of the lead discovery stage is to apply the screening assay against thousands, or even millions, of potential new drugs within a small-molecule$^{133}$ drug library$^{134}$ to identify compounds that have activity in the assay.$^{135}$


133. “Small molecules” are molecular compounds that are usually composed of a few atoms to several dozen atoms and are generally prepared (or capable of being prepared) by synthetic organic chemists or pharmaceutical chemists. These are contrasted by large molecules, such as proteins, DNA, and complex carbohydrates, which are composed of thousands or millions of atoms.

134. Having a good drug library is critical to the drug discovery process. One might expect that drug discovery companies would have drug libraries numbering in the millions or billions of compounds, but it costs a great deal of money to both make and screen a library of that size. Thus, drug libraries are carefully constructed to insure that the compounds contained in the library will yield the highest probability of succeeding in finding an effective drug lead for the particular drug target. For example, the library should be highly diverse and contain compounds which have many different types of functional groups with a minimum of overlap. Simply having diversity in the library is not enough, since some compounds would never proceed past clinical trials to become a new drug due to toxicity or solubility problems. Other empirical tests, such as Lipinski’s Rule of Five, see Christopher A. Lipinski et al., Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and Development Settings, 46 ADVANCED DRUG DELIVERY REVIEWS 3 (2001), are helpful in predicting what molecules will make good drugs.

135. One of the most important things to realize in drug discovery is that it is called “drug discovery," and not drug design, construction, or engineering, for a reason. With only a handful of exceptions, new drugs have always been discovered either accidentally or via the “kitchen sink" method, which is throwing every available small molecule at a drug target. It is virtually impossible to enter into drug discovery knowing what the best drug will look like.
The typically small number of active drug leads identified during lead discovery rarely go on to become the new drug used in clinical trials, but the compounds identified serve as the starting point for the third phase, lead optimization. Lead optimization invariably is the slowest phase in drug research prior to clinical trials. The lead compounds are analyzed by chemists and biologists in excruciating detail, looking for trends and similarities. Based on this analysis, dozens or even hundreds of new compounds are proposed that could be even more effective than the discovered leads. Because many of these proposed compounds have only been dreamed of for the first time, however, the duty of synthesizing them falls on the shoulders of medicinal chemists. A delicate balance exists at this stage of development, with compounds being scrapped due to cost of synthesis, length of time required, or even the discovery of an existing patent covering the proposed compound that would inhibit the chance of obtaining a patent of its own should the compound prove to be the best drug candidate. Once synthesized, these new compounds are screened to determine if they exhibit improved activity, or activity at all. Even compounds that fail may have some limited utility in this stage because they may indicate what molecular features of the compounds are detrimental to or required for efficacy.

During the process of lead optimization, the most promising compounds are analyzed in other assays to ascertain other properties, such as mechanism of action (if unknown), pharmacokinetics, and pharmacology. These preclinical assays, in addition to efficacy assays, are important in determining whether a drug candidate would be likely to be a safe and effective drug if taken in humans. All of the information is analyzed and additional derivatives of the lead candidates are ordered. Ultimately, a single compound is determined not only to be the most effective compound known at treating the disease, but also to possess all of the desired properties that make it likely to be a successful drug in humans.

The final stage of drug discovery occurs after the best drug candidate is identified and begins with the filing of an IND application. At this point, the IND is filed with the FDA and includes all of the preclinical information obtained by the drug company that demonstrates the candidate is effective at treating the targeted disease and has a strong track record for safety. Once the FDA is convinced of the safety of the drug and its probability of
actually helping treat the targeted disease, the drug enters clinical trials, which is simply when the drug is tested in humans.

Stage I clinical trials involve a very small number of healthy volunteers to determine whether the drug is safe for people to receive at all.\textsuperscript{136} Stage II clinical trials usually involve "testing in a relatively small group of human volunteers with the disease or condition being treated for initial efficacy and for establishing the proper dose for the intended use of a new drug."\textsuperscript{137} Stage III, the largest and most expensive of the stages, employs up to several thousand patients and involves more long-term evaluation of the drug and its effects on patients.\textsuperscript{138} The tests in Stage III are randomized and employ controls.\textsuperscript{139} Side effects are typically identified in this stage. Upon successfully completing Stage III by demonstrating the drug is effective and safe, the FDA approves the use of the drug, allowing the drug company to market and sell the new drug to the consumers. There is also a Stage IV clinical trial, which involves post-marketing studies to monitor product safety.\textsuperscript{140}

It is important to realize that although the \textit{Merck v. Integra} case involved the use of patented drugs by a third party, in general, drugmakers have no interest in research on patented drugs because they are owned by someone else. Using patented or FDA-approved compounds in research has some benefits, namely known methods of manufacture, modes of action, toxicity, pharmacokinetics, or other published properties, and the possibility that known drugs might be useful for treating other conditions. However, these compounds are either owned by someone else under a patent or have entered the public domain by the expiration of a patent, making it difficult for pharmaceutical companies to protect their research and development investment without the possibility of patent protection. Thus, drug discovery is primarily focused on finding compounds unknown in the literature and not described or covered by existing patents.

\textsuperscript{136} See \textit{VOET}, supra note 2, at 47.
\textsuperscript{137} Id.
\textsuperscript{138} See \textit{id}.
\textsuperscript{139} See \textit{id}.
\textsuperscript{140} Id.
An excellent example of this notion can be found in *Bristol-Myers Squibb v. Rhone-Poulenc Rorer*. Rhone-Poulenc owned a patent on derivatives of Taxol, a powerful drug for combating breast cancer. Bristol-Myers Squibb ("BMS") used the patented derivatives in its research to develop its own cancer drugs. Rhone-Poulenc moved for summary judgment against BMS, alleging that BMS's use of the patented compounds constituted infringement. BMS raised § 271(e)(1) as an affirmative defense, arguing the patented compounds were used as positive controls in its research that ultimately led to submission of an NDA. The finding that the safe harbor exemption of § 271(e)(1) exempted BMS's infringing activity was a harbinger for the Supreme Court's decision in *Merck v. Integra*.

B. Impact of Merck v. Integra

The Supreme Court's decisions in *Eli Lilly v. Medtronic* and *Merck v. Integra* clearly indicate the § 271(e)(1) safe harbor exemption will be interpreted as broadly as the language of the statute states. The CAFC was cognizant of the ramifications that such a broad reading would entail and unsuccessfully attempted to place limitations on the exemption. Keeping in mind Congress's intent to assist the development of generic drugs, the CAFC erected a boundary for § 271(e)(1), holding that it only applies to infringing activities that involve compounds determined to be submitted to the FDA for evaluation. Such an interpretation may have proved difficult to enforce without eviscerating the exemption. As the Court noted, the CAFC's interpretation of the exemption would only be applicable when

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142. See id. at *3.
143. See id.
144. See id. at *1.
145. See id. at *4–5.
146. This case was not lost on Merck, who argued BMS several times in its brief to the Supreme Court as persuasive authority that its actions should similarly be covered by § 271(e)(1). See Brief for Petitioner-Appellant at 31, 37, 42–43, Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193 (2005) (No. 03-1237), 2005 WL 389070.
149. See id. at 865.
150. See id. at 867.
the infringer knew the investigated drug would be submitted to
the FDA, which would effectively make the need for any experi-
tementation moot.\textsuperscript{151} After all, if you already know how a drug will
perform, why would you need to test it?

Thus, the Court's decision correctly highlights the uncertainty
associated with drug discovery, as well as science in general, and
appropriately removes such an interpretation.\textsuperscript{152} However, the
Supreme Court's decision in \textit{Merck v. Integra}, coupled with the
"inelegant draftsmanship" of § 271(e)(1)\textsuperscript{153} and the difficulties of
drug discovery, may have unintended consequences that will re-
verberate throughout the world of pharmaceutical and biotech-
ology.

Although the factual focus of \textit{Merck v. Integra} involved the use
of patented drugs in experiments,\textsuperscript{154} the extent of acts of in-
fringement excused by § 271(e)(1) is not so limited.\textsuperscript{155} Along the
drug discovery process, there are many discoveries and inven-
tions that may be patented, not just the final drug candidate, and
in today's research environment, it is virtually impossible for a
researcher to identify a drug candidate without using some pat-
eted invention they do not own. These other patented inventions
include the assay that can identify a drug target, the DNA se-
quence of a critical gene, or even the mechanical equipment (sy-
ringes, microscopes, etc.) used to conduct the experiments.\textsuperscript{156} In
fact, drug discovery within pharmaceutical companies would be
next to impossible without the important contributions of other
biotechnology companies or academic researchers. There are sev-
eral reasonable definitions of "research tools" and many of these
inventions or discoveries can be called "research tools" because

\textsuperscript{151} \textit{See Merck v. Integra}, 545 U.S. at 206 ("One can know at the outset that a partic-
ular compound will be the subject of an eventual application to the FDA only if the active
ingredient in the drug being tested is identical to that in a drug that has already been ap-
proved.").

\textsuperscript{152} \textit{See id.} ("[I]t disregards the reality that, even at late stages in the development of a
new drug, scientific testing is a process of trial and error.").


\textsuperscript{154} \textit{Merck v. Integra}, 545 U.S. at 208 ("We thus agree . . . . that the use of patented
compounds in preclinical studies is protected under § 271(e)(1) . . . .").

\textsuperscript{155} \textit{Id.} at 202 ("[W]e think it apparent from the statutory text that § 271(e)(1)'s ex-
emption from infringement extends to all uses of patented inventions that are reasonably
related to the development and submission of any information under the FDCA.").

\textsuperscript{156} \textit{See Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860, 878 (Fed. Cir. 2003)
(Newman, J., concurring in part and dissenting in part) (describing patented inventions to
be used in research).
they assist scientists in their research. In *Integra v. Merck*, the CAFC concluded its majority opinion by briefly discussing the importance of "research tools," stating:

The value to a licensee of research tools lies, in part, in the point at which those tools are employed in the drug development continuum. A research tool enabling the identification of a drug candidate during high throughput screening, for instance, may supply more value to the ultimate invention than a research tool used to confirm an already recognized drug candidate's safety or efficacy.  

One could construe "research tools" exceedingly broadly to be "something used in performing an operation or necessary in the practice" of "investigation or experimentation aimed at the discovery and interpretation of facts." 

Although some may advocate for a specific protection of so-called "research tools," such protection could defeat the entire purpose of Congress's intent to facilitate the production of generic drugs. For example, in her dissent, Judge Newman chose to narrow the definition of "research tools" to "a product or method whose purpose is use in the conduct of research." In this manner, the RGD peptides, invented for the purpose of being used as a therapeutic, would not qualify as a "research tool," even though they were used to facilitate Dr. Cheresh's research. This is a perfectly appropriate definition, but its application in a legal sense could be very difficult, because the question of who gets to determine the primary function of an invention is left unanswered. Under Judge Newman's view, the intelligent inventor would declare every invention to have a primary purpose as a research tool, even if the only research it could be used for would be for the development of an improvement of the patented inven-

157. *Id.* at 871 (majority opinion).
158. *MERRIAM-WEBSTER, supra* note 38, at 1243 (tool).
159. *Id.* at 995 (research).
161. *See id.* at 863 (majority opinion).
162. *See Kenneth J. Burchfield, Merck KGaA v. Integra: More Answers Than Questions*, 6 J. HIGH TECH. 79, 90 (2005) ("Unlike a microscope, a chemical compound does not have a single, easily defined utility as a 'research tool.' A microscope can be used to study diseases, but not to treat them. A chemical compound, such as a phenolphthalein dye, may be useful both as a pH indicator in laboratory research, and as a therapeutic agent for treatment of constipation.").
tion itself. If this were true, a drugmaker could thwart even the congressionally intended purpose of § 271(e)(1), i.e. to overrule *Roche v. Bolar*,\(^{164}\) by declaring the drugs to be research tools first and therapeutic agents second. Thus, a generic drug company could not use the patented drug without permission from the patent owner, artificially extending the drug's effective patent life, while the patent holder would remain free to market the drug absent generic competition.

The real threat to the biotechnological and pharmaceutical industry posed by § 271(e)(1) is the freedom of a drug researcher to infringe any patented invention, including the assays and methods commonly used to develop information pertinent to submission of an IND to the FDA, not just the right to use patented compounds in research.\(^{165}\) Drugmakers are rarely interested in developing new uses for known compounds because patents cannot protect new uses. Researchers, however, identify new drug candidates using assays that "cause the sort of physiological effect the researcher intends to induce,"\(^{166}\) as well as other assays designed to measure the compound's pharmacological, toxicological, pharmacokinetic, and metabolic properties, all of which generate information relevant to submission of an IND.\(^{167}\) More importantly, most of these assays are likely to be patented by someone other than the drug researcher, which means that in the absence of § 271(e)(1), the researcher must obtain a license to use the patented assay or risk expensive infringement litigation. However, based upon the Supreme Court's repeated holding regarding the safe harbor exemption that it excuses infringement from "all patented inventions,"\(^{168}\) it is critical to identify at what

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165. Although the law indicates that all patented inventions may be used free from infringement, there are many inventions that would not be likely to be infringed by drug researchers. "Even a large multinational drug maker is unlikely to take up the manufacture of centrifuges, DNA sequencers, fluorescently labeled monoclonal antibodies, or any other product that would be more cheaply and easily obtained by simple purchase even at high price points." O'Malley, *supra* note 82, at 756.


167. *See id.* at 203.

168. *See id.* at 202 ("§ 271(e)(1)'s exemption from infringement extends to all uses of patented inventions . . . "); *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."); *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, No. 95 Civ. 8833, 2001 U.S. Dist. LEXIS 19361, at (S.D.N.Y. Nov. 28, 2001) ("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.").
stage the § 271(e)(1) exemption begins. Once exempt, a drug maker should no longer be required to obtain a license to use a patented assay.169

The Supreme Court, in Merck v. Integra, provided a two-prong test indicating when the § 271(e)(1) safe harbor exemption will not apply:

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 surely not "reasonably related to the development and submission of information" to the FDA.170

While this test indicates when the exemption will not apply, it suggests that if either, or both, of the requirements are present, § 271(e)(1) will excuse all acts of infringement. In Merck v. Integra, the test provided the foundation of the holding by merely substituting "a particular compound" with "a patented compound."171 The Court, however, neglected to decide whether § 271(e)(1) would cover acts of infringement by a researcher who has "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," but not both.172

The use of the phrase "at least" defines the ambiguity in the Supreme Court's ruling.173 By employing this expression, the Court suggested that the § 271(e)(1) safe harbor exemption may begin some time before a researcher has a "reasonable basis for believing that a patented compound may work, through a particular biological process, to produce a particular physiological effect" and generates data suitable for FDA submission.174 Based on this definition, it can be strongly argued that the safe harbor line at

169. See Merck v. Integra, 545 U.S. at 202 ("§ 271(e)(1)’s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of any information under the FDCA.").
170. Id. at 205–06.
171. See id. at 206–07 ("At least 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.’" (quoting 35 U.S.C. § 271(e)(1)).
172. Id. at 206.
173. Id. at 207.
174. Id.
least begins at the lead optimization stage, when a drugmaker would have both the intent to make a drug and a reasonable belief that the compounds analyzed would act in the desired manner.\footnote{175}

This conclusion is also supported by the requirement to include "similar compounds" in the preclinical data submitted to the FDA in order to assist the agency in predicting the safety of the drug candidate.\footnote{176} What constitutes "similar" is not defined, but such a definition would be readily interpreted by medicinal chemists to include compounds structurally related. It should be cautioned that establishing a rigid legal rule for what is "similar" would be inadvisable, and each situation should be examined on a case-by-case basis. An analogy can be drawn to the obviousness standard of 35 U.S.C. § 103 in patent law,\footnote{177} which, for chemical species, is determined by reference to whether an expert in the field would have "the motivation to make the [similar] compositions in the expectation that they would have similar properties" to the drug candidate.\footnote{178}

An excellent case that highlights the difference between obviousness and what would constitute the development of "similar compounds" during lead optimization is embodied in \textit{Yamanouchi Pharmaceuticals v. Danbury Pharmaceutical, Inc.}\footnote{179} Danbury attempted to invalidate Yamanouchi's patent for famotidine, marketed by Merck as Pepcid.\footnote{180} Danbury argued that a person having ordinary skill in the art, upon examining two compounds listed in separate Yamanouchi patents, both known to have properties similar to famotidine, would have found it obvious to mix-and-match functional groups from both molecules to arrive at the

\begin{footnotes}
\begin{enumerate}
\item[175.] See Benjamin G. Jackson, Comment, Merck v. Integra: Bailing Water Without Plugging the Hole, 20 BYU J. PUB. L. 579, 592–93 (2006) (discussing the Supreme Court's acceptance of similar compounds investigated during the lead optimization stage).
\item[176.] Brief for the United States as Amicus Curiae Supporting Petitioner at 19, Merck v. Integra, 545 U.S. 193 (No. 03-1237), 2005 WL 429972 (citing 21 C.F.R. 312.23(a)(5)(v) ("[a] description of possible risks and side effects to be anticipated on the basis of prior experience with the drug under investigation or with related drugs.") (alteration in original)).
\item[178.] In re Dillon, 919 F.2d 688, 693 (Fed. Cir. 1990). Although the chemical obviousness standard is listed here as an analogy, the standards set for drug discovery for what qualifies as a "similar compound" should be less stringent than the standards for obviousness. This is because in lead optimization, creativity and ingenuity are highly valued when identifying hypothetical compounds to test for desired activity.
\item[179.] 231 F.3d 1339 (Fed. Cir. 2000).
\item[180.] See id. at 1341–42.
\end{enumerate}
\end{footnotes}
structure of famotidine. The CAFC correctly rejected this argument, stating that it would not have been obvious to the typical chemist in the field to arrive at famotidine's structure based on the rather unrelated structures in the other patents, but instead, would have required a significant amount of hindsight to achieve such a combination. It is not inconceivable, however, that the structure of famotidine could be arrived at during lead optimization, especially using the reasonable (yet nonobvious) rationale proposed by Danbury. Although the structure of famotidine might not have been obvious based on the disclosure found in the prior art at the time of the filing of the patent application, the reference compounds mentioned by Danbury should readily qualify as "similar compounds" to be included in the submission of famotidine to the FDA in an IND.

The holding in Merck v. Integra left two questions unanswered about drug discovery and the § 271(e)(1) safe harbor exemption. The first question is whether a researcher using patented compounds or screens would be exempt from infringement if the researcher has a reasonable belief that the compound will cause the intended effect, but lacks the specific intent to develop a drug. The language of § 271(e)(1) suggests that the safe har-

181. See id. at 1343–44.
182. See id. at 1345 ("Danbury falls far short of satisfying its burden of showing a prima facie case for structural obviousness by clear and convincing evidence. Instead, as the district court aptly concluded, this case 'has all the earmarks of somebody looking at this from hindsight.'" (quoting Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc., 21 F. Supp. 2d 366, 370 (S.D.N.Y. 1998))).
183. See id. at 1343–44.
184. See Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 205–06 (2005) ("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 surely not 'reasonably related to the development and submission of information' to the FDA." (quoting 35 U.S.C. § 271(e)(1) (2000))).
185. Typical researchers falling into this category would include professors at universities investigating the underlying biochemical or cellular mechanisms for a given condition or disease, although the discoveries from this research might ultimately lead to new drug discoveries. Under the common law, this type of academic research would have been protected by the experimental use doctrine, see Katherine J. Strandburg, What Does the Public Get? Experimental Use and the Patent Bargain, 2004 WIS. L. REV. 81, 93–94, first described in the opinion written by Supreme Court Justice Story for Whittemore v. Cutter, 29 F. Cas. 1120, 1121 (C.C.D. Mass. May 1813) (No. 17,600) ("[It] could never have been the intention of the legislature to punish a man, who constructed such a machine merely for philosophical experiments . . . ."). However, the experimental use doctrine was severely restricted in Madey v. Duke University, 307 F.3d 1351 (Fed. Cir. 2002), limiting the doctrine to non-commercial activities solely "for amusement, to satisfy idle curiosity, or for
bor exemption would not be applicable to acts of infringement without the intent to develop a drug simply because the types of experiments that generate information related to submission to the FDA are generally not conducted outside the typical drug discovery process. Perhaps a situation that would qualify for the § 271(e)(1) safe harbor without an intent to develop a drug would occur during the course of development of an assay designed to evaluate preclinical properties of drugs, such as an assay that determines pharmacology or toxicology of drugs. The patented drugs would be used in the assay to validate that the new assay correctly reproduces the pharmacology or toxicology information previously produced in similar assays. In such an example, use of a patented drug in the assay under development would probably not be infringing because its use is “reasonably related to the development and submission of information under Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.”

The more valuable and legally interesting question left unanswered in Merck v. Integra is whether the mere “intent to develop a particular drug” is sufficient to excuse acts of infringement in pursuit of the “submission of information under a Federal law which regulates the manufacture, use, or sale of drugs. . . .” This situation corresponds to the lead discovery stage of the drug discovery process, where a drugmaker has the intent to discover a new drug but lacks the “reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce.” The importance of this question cannot be understated, because if there is a finding that acts of infringement during lead

strictly philosophical inquiry.” Id. at 1362 (quoting Embrex, Inc. v. Service Engineering Corp., 216 F.3d 1343, 1349 (Fed. Cir. 2000)). Even though the interests of the professor are merely for academic, non-profit pursuits, the holding in Madey suggests that the benefits of the research enjoyed by the university employing the professor would exempt acts of infringement from the experimental use doctrine.

186. See Burchfiel, supra note 162, at 84–85 (discussing the fact that some animal models and other assays “have no other utility” outside drug discovery).


188. Merck v. Integra, 545 U.S. at 206.


190. Merck v. Integra, 545 U.S. at 206; see Daniel J. O’Connor & Tamsen Valoir, The Supreme Court Tilts Toward Drug Developers: Drug Discovery After Merck v. Integra, 5 CHI.-KENT J. INTELL. PROP. 124, 138 (2006) (“Drug companies can be relieved that any experiments conducted after ‘lead’ identification appear to be exempt from infringement, so long as they can be shown to be related to the submission of information to the FDA. This includes both clinical and pre-clinical testing.”).
discovery are protected by § 271(e)(1), then every step of the drug discovery process would be protected by the safe harbor exemption, including experiments intended to determine the efficacy, pharmacology, toxicology, and pharmacokinetics of the compounds studied. This would include not only simple in vitro or cell-based assays, but patented animal studies as well. Because so much of drug discovery occurs using patented technologies, drug researchers would no longer be required to compensate scientific innovators who develop the tools required to conduct research.

C. The Debate Rages On . . .

Numerous discussions focus on the question of whether the § 271(e)(1) safe harbor exemption provides a defense for patent infringement at the lead discovery stage. At this stage, drugmakers are searching for a compound that will eventually lead to a new drug but have little or no information as to which compound the new drug will resemble out of the thousands or even millions of compounds initially screened for activity. Until the Supreme Court or the CAFC weigh in on the issue, it will remain unclear whether the safe harbor will be strictly limited to the lead optimization stage delineated in Merck v. Integra or if it will extend to prior arts on the drug discovery roadmap.

There are many opposed to allowing the § 271(e)(1) safe harbor to extend beyond what Congress originally intended. The American Intellectual Property Law Association ("AIPLA") argued in its amicus brief that lead discovery, including automated discovery, so-called high-throughput screening, should not be within the safe harbor exemption. O'Connor and Valoir suggest that the Supreme Court's agreement with the amicus brief for the United States may indicate the Court will later agree with the Government's position that screening is an activity that should also be exempt from infringement. Burchfiel questioned whether intent alone was sufficient to exempt the use "of thousands of patented compounds screened in an assay to discover pharmacologi-
cal activity." 194 Furthermore, at least one major player in the biotech community interpreted the Merck v. Integra ruling to mean that the exemption did not extend to cover so-called "research tools." 195 But this announcement is most likely premature, because the Supreme Court’s declaration of having no opinion on research tools is far from a ruling in favor of protecting such tools. The CAFC eloquently noted, however, some protection for patents critical to research will be required to protect the biotech industry's intellectual property at all stages of drug discovery. 196

Although the decision to exempt acts of infringement under § 271(e)(1) during the lead discovery phase of drug development remains a close legal question, infringing activities during lead discovery may not fall under the safe harbor exemption because, as a whole, they are not "reasonably related to the development and submission of information" to the FDA. 197 The Court appropriately defined the limits of the exemption when it stated, "Properly construed, § 271(e)(1) leaves adequate space for experimentation and failure on the road to regulatory approval." 198 During lead discovery, a million compounds could be screened for their ability to induce "the sort of physiological effect the researcher intends to induce," 199 yet out of those million compounds, only a few dozen compounds are likely to show any such activity. As the Supreme Court stated in Merck v. Integra, "There is simply no room in the statute for excluding certain information from the exemption on the basis of the phase of research in which it is developed or the particular submission in which it could be included." 200

The Supreme Court did not "quibble" with the CAFC’s conclusion that the § 271(e)(1) exemption “does not globally embrace all experimental activity that at some point, however attenuated,

194. Burchfiel, supra note 162, at 88.
196. See Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860, 867 (Fed. Cir. 2003) ("Expansion of § 271(e)(1) to include the Scripps Merck activities would effectively vitiate the exclusive rights of patentees owning biotechnology tool patents.").
199. Id. at 206.
200. Id. at 202.
may lead to an FDA approval process." Even if a successful screen identified 100 active compounds, it is difficult to argue that the entire experiment, one that produces an anticipated failure rate of more than 99.9%, is "reasonably related to the development and submission of information" to the FDA. It is true that out of those initial millions of compounds, a few compounds might arise that form the basis for the discovery of the drug candidate forwarded to the FDA. The researchers at the lead discovery stage, however, lack sufficient information to form a reasonable or rational basis to expect that any of the compounds in a library will demonstrate activity. Furthermore, even if it can be argued that the handful of compounds identified by the screen to possess activity are protected by §271(e)(1) because they are reasonably related to the drug ultimately submitted to the FDA, the researcher will still have almost a million acts of infringing a patented assay that are not protected by the safe harbor.

Such an argument, however, is subject to the same criticisms of the CAFC opinion that attempted to judicially create a limit to §271(e)(1), when one arguably does not exist within the statute. The CAFC, recognizing the far reaching effects a broad interpretation of §271(e)(1) will carry, attempted to limit the exemption to only compounds that will be submitted to the FDA for analysis. While the CAFC may have been correct to apply Congressional intent, the Supreme Court chose instead to rely

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201. Id. at 205 (quoting Integra v. Merck, 331 F.3d at 867).
203. This argument is very similar to that proffered by the CAFC in rejecting §271(e)(1) protection for Dr. Cheresh's acts of infringement upon Integra's patents. However, in that situation, the RGD peptides were a known starting point for activity from which Merck optimized to find analogs that were simultaneously more active and not claimed by Integra's patents. Every one of the compounds tested by Merck had some activity in the angiogenesis assay and had the potential to be a drug. During lead discovery, a researcher does not have such a starting point or frame of reference. This situation is more aptly described by the words of the CAFC when it wrote that the "experiments did not supply information for submission to the [FDA], but instead identified the best drug candidate to subject to future clinical testing under the FDA processes." Integra v. Merck, 331 F.3d at 865.
204. See Merck v. Integra, 545 U.S. at 206 ("Thus, to construe § 271(e)(1), as the Court of Appeals did, not to protect research conducted on patented compounds for which an IND is not ultimately filed is effectively to limit assurance of exemption to the activities necessary to seek approval of a generic drug . . . ").
205. See id.
upon the language of the statute to define the boundaries of the exemption.\textsuperscript{207}

Until the Supreme Court or the CAFC weigh in on the issue, it will remain unclear whether the safe harbor will be strictly limited to the lead optimization stage delineated in \textit{Merck v. Integra} or if it will extend to prior acts on the drug discovery roadmap. If the courts adhere to the Supreme Court's broad interpretation of § 271(e)(1),\textsuperscript{208} the exemption could be extended to all levels of drug research if the activities conducted are necessary to develop a drug candidate. Such an interpretation would come at a great cost to the industry, and a judicial or legislative clarification is direly needed.

\textbf{D. Do We Care if Lead Discovery is Protected by § 271(e)(1)?}

In its amicus brief, the Government warned that until the scope of infringement protection under § 271(e)(1) is decided, drug researchers will be fearful of infringing any patents, and instead will be inclined to enter into licensing agreements with patentees to avoid a potentially costly adverse finding of infringement.\textsuperscript{209} The decision in \textit{Merck v. Integra}, however, indicates that the safe harbor protects acts of infringement at the lead optimization stage, and the only real question is whether it extends to the lead discovery stage. Based on the CAFC decision in \textit{Bayer A.G. v. Housey Pharmaceuticals, Inc.},\textsuperscript{210} a drugmaker will probably be justified in infringing patents at the lead discovery stage if the predicted revenues of the drug candidate, identified by the act of infringement, greatly exceed the cost of infringing the assay patent.

\textsuperscript{207} As the Court noted in \textit{Eli Lilly & Co. v. Medtronic, Inc.}, 496 U.S. 661, 679 (1990), "[n]o interpretation we have been able to imagine can transform § 271(e)(1) into an elegant piece of statutory draftsmanship."

\textsuperscript{208} \textit{See Merck v. Integra,} 545 U.S. at 202 ("§ 271(e)(1)'s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of \textit{any} information under the FDCA.").

\textsuperscript{209} Brief for the United States as Amicus Curiae Supporting Petitioner at 22, \textit{Merck v. Integra,} 545 U.S. 193 (No. 03-1237) 2005 WL 929972 ("In particular, the exemption cannot be limited to studies that, \textit{in retrospect}, appear to have been strictly 'necessary' to obtain FDA approval . . . . Especially in light of the \textit{in terrorem} effect of potential treble damages awards, that approach would unacceptably chill new drug development by preventing researchers from ascertaining in advance whether their activities were protected by the exemption." (citations omitted)).

\textsuperscript{210} 340 F.3d 1367 (Fed. Cir. 2003).
Recently, patentees in the biotech industry adopted the legal stance that if a drug was identified using patented methods, processes, or other tools, the patentees of the utilized inventions were entitled to a portion of the profits of the drug under a "reach-through" royalty scheme. The foundation for reach-through licensing stemmed from the legal position that information derived from patented processes, such as identifying a drug lead target from a patented assay, was a product of the patented process, subject to injunctive relief and royalties against the product of infringement, namely the identity of the drug target and its subsequent sales revenue. Such a position gave the developers of tools necessary to the drug discovery process leverage in discouraging infringement of such patents, especially in light of the hundreds of millions, or even billions, of revenue dollars at stake in modern pharmaceuticals and the threat of triple damage awards for a finding of willful infringement.

The playing field was leveled in Bayer v. Housey. The CAFC's decision strongly suggested that such "reach-through" royalties are not a component of the monopoly enjoyed by a patentee. Housey owned several patents on a "Method of Screening for Protein Inhibitors and Activators." Bayer allegedly infringed the patents by using the patented methods on foreign soil to uncover a new drug candidate and importing the information—which was embodied by an identified drug target and obtained by utilizing the patented method. Housey sued for infringement under § 271(g), which prohibits the importation, sale, or use of a product made in another country "by a process patented in the United States," and alleged it was entitled to reach-through royalties. The district court found that § 271(g) applied only to prod-

213. See Bayer v. Housey, 340 F.3d at 1378 ("A drug product, the characteristics of which were studied using the claimed research processes, therefore, is not a not a product 'made by' those claimed processes.").
215. See Bayer v. Housey, 340 F.3d at 1370.
217. See Bayer v. Housey, 340 F.3d at 1370.
ucts of patented manufacturing processes, not information derived using patented methods, and dismissed Housey's claim. On appeal, the CAFC affirmed the district court's holding that § 271(g) is inapplicable to information gathered under a patented process or method. The CAFC held that production of the drug by Bayer did not infringe Housey's patent because the patent had no relation to the manufacturing of the drug. The CAFC noted that "[a] drug product, the characteristics of which were studied using the claimed research processes, therefore, is not a product 'made by' those claimed processes."

The ruling in *Bayer v. Housey* sent a strong message to the biotech community that "reach-through" royalties are almost certainly not enforceable. If the information derived from the assay, namely, the most effective drug candidate, is not a product of the patented method used to identify it, then the patent will have no legal authority over the manufacturing and sales of the approved drug. This decision, however, does not leave the patentee of a research tool without the power to sue for infringement. It simply limits the liability of the infringing acts of the drug researcher to the infringement of the methods, processes, or tools under § 271(a). Furthermore, it seems clear that if the infringing drug research occurred upon foreign soil, the patentee is left with nothing, because § 271(a) does not apply to infringing acts that are not "within the United States," and § 271(g) does not prevent importation of information derived from infringement.

218. See Bayer AG v. Housey Pharms., Inc., 169 F. Supp. 2d. 328, 330 (D. Del. 2001) ("Upon a plain reading of the statute, the court finds that Section 271(g) addresses only products derived from patented manufacturing processes, i.e., methods of actually making or creating a product as opposed to methods of gathering information about, or identifying, a substance worthy of further development." (aff'd, 340 F.3d 1367 (Fed. Cir. 2003)).


220. *Id.* at 1377-78 (referring to 35 U.S.C. § 271(g), which states, "[w]hoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer . . . ." 35 U.S.C. § 271(g) (2000) (emphasis added)).

221. See id. at 1378.

222. "[P]rocesses of identification and generation of data are not steps in the manufacture of a final drug product." *Id.* at 1377 (quoting *Bayer v. Housey*, 169 F. Supp. 2d at 331).

223. 35 U.S.C. § 271(a) (2000) ("[W]hoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States, or imports into the United States any patented invention during the term of the patent therefor[e], infringes the patent.").

224. *Id.*
of the patented method conducted on foreign soil. As one major law firm suggested, patentees of research tools may have to think twice if they believe their patents will give them a piece of the multibillion dollar pot of gold at the end of the drug discovery process, or the right to an injunction to stop production of the drug—"such actions are not part of the ongoing manufacture of the drug."

Without the threat of reach-through royalties, the decision in Bayer v. Housey creates a balancing test for drug researchers faced with the decision to either license a patented invention required to identify the next drug candidate or infringe the patents in the hope that § 271(e)(1) will protect them from litigation. When faced with the question of whether the § 271(e)(1) safe harbor will cover the use of another's patented assay, process, or other invention, the prudent researcher will likely proceed with infringement. Under the best possible scenario, the exemption will indemnify the infringement because the actions are "reasonably related to the development and submission of information under a Federal law." The researcher, therefore, will not be liable for any compensation to the patentee. Under the worst possible scenario, the exemption will not apply, and researchers would be open to infringement liabilities equal to the value of the assay infringed, at most. Even if in the millions of dollars, this would be paltry next to the potentially billions of dollars in revenue generated by the next blockbuster drug if the research was successful.

V. CONCLUSION

The current literature indicates the failure of the legislature and judiciary to adequately define significant terms regarding the § 271(e)(1) safe harbor exemption has resulted in a governmen-
tally fashioned state of confusion. Within the arena of drug discovery and biotechnology there is no precise determination of where infringement stops and exemption begins. With a fundamental understanding of the general process of drug discovery and development, however, the holdings in both Merck v. Integra and Eli Lilly v. Medtronic indicate pharmaceutical companies can infringe upon any patent they wish, once they reach the required stage of drug recovery, without the need to enter licensing agreements or fear infringement litigation. Although it is clear that § 271(e)(1) excuses infringement during lead optimization, it remains to be seen whether the initial steps of lead discovery will enjoy similar protection. The decision in Bayer v. Housey suggests that the liability faced by a researcher for a finding of infringement may be relatively minor with respect to the possibility of billions of dollars in profit generated by a successful new drug.228

A solution to the current problem is not as difficult as some have suggested.229 Many of the ambiguities present in the language of § 271(e)(1) can simply be corrected by making the exemption specific only to the development of generic drugs as Congress intended.230 For example, excising the words “a Federal law which regulates the manufacture, use, or sale of drugs” from § 271(e)(1)231 and substituting the “Abbreviated New Drug Application” under 21 U.S.C. § 355(j).232 This change would bring § 271(e)(1) in line with § 271(e)(2), which explicitly names the ANDA statute.233 In addition, the change would eliminate the confusion created by Merck v. Integra, limit the exemption to generic drugs as Congress originally planned, and restore the rights

228. See Bayer v. Housey, 340 F.3d at 1378.
229. Many different theories for correcting § 271(e)(1) have been posited. Judge Pauline Newman has suggested creating an exception to the exemption for patents nebulously defined as “research tools.” Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860, 877–78 (Fed. Cir. 2003) (Newman, J., concurring in part, dissenting in part). Brendon O’Malley suggests against reliance on “appropriate pricing of research tools for initial purchase . . . help[ing] research toolmakers to compensate for lost licensing revenues,” since some technologies are more easily pirated than others. O’Malley, supra note 82, at 756–58. Instead, he advocates changes such as “a patented invention itself under study for future regulatory approval” or “as part of a clinical trial reasonably related.” Id.
230. See Integra v. Merck, 331 F.3d at 865. (“The House Committee . . . described the pre-market approval activity as ‘a limited amount of testing so that generic manufacturers can establish the bioequivalency of a generic substitute.’” (citing H.R. REP. No. 98–857, pt. II., at 8, (1984), reprinted in 1984 U.S.C.C.A.N. 2686, 2692)).
of patent owners for methods, processes, and tools involved in drug research.

Infringers would still be able to conduct the patented inventions on foreign soil without fear of litigation under § 271(g) as interpreted by Bayer v. Housey.\textsuperscript{234} A law that limits the importation of information into the country, or an amendment to § 271(g) in a similar fashion, would have to be carefully constructed and most likely would produce endless litigation over what constitutes "information" derived from using methods or assays in foreign countries patented within the United States.\textsuperscript{235} The simplest solution would be for inventors to patent their inventions in foreign countries as well as the United States to discourage foreign infringement, a strategy more companies are choosing due to the globalization of scientific research.\textsuperscript{236} Although the prosecution of patents all over the globe may prove too costly for some inventors, such measures may simply be the cost of scientific development in today's world.

The recent interpretations of § 271(e)(1) represent a significant challenge to pharmaceutical, biotechnological, and even academic research fields. The foundation of drug discovery rests upon the identification of new drug targets, methods to identify active compounds, and ways to establish the efficacy and safety of the drugs of tomorrow. While the § 271(e)(1) safe harbor was created with the greatest of intentions, its applicability has greatly expanded beyond Congress's intent to facilitate the development of generic drugs. In the absence of a congressional resolution, the broad language will continue to erode the enforceability and value of tools in the field.\textsuperscript{237} This could lead to a decrease in the venture

\textsuperscript{234} Bayer AG v. Housey Pharms., Inc., 340 F.3d 1367, 1378 (Fed. Cir. 2003) ("A drug product, the characteristics of which were studied using the claimed research processes, therefore, is not a product 'made by' those claimed processes.").

\textsuperscript{235} See id. at 1376 ("The importation of information in the abstract . . . cannot be easily controlled. As Bayer points out, a person possessing the allegedly infringing information could, under Housey's interpretation, possibly infringe by merely entering the country.").

\textsuperscript{236} The CAFC has ruled that the existence of the right to foreign patents has no bearing upon its construction of the right of domestic patentees. See AT&T Corp. v. Microsoft Corp., 414 F.3d 1366, 1370 n.2 (Fed. Cir. 2005) ("Obtaining foreign patents would surely alleviate some avoidance of American law, but we must construe our statutes irrespective of the existence or nonexistence of foreign patents.").

\textsuperscript{237} O'Malley suggests a parallel between the loss of enforceability in biotech patents and the challenge faced by the music and movie industries due to rampant copying and other unauthorized use. See O'Malley, supra note 82, at 757.
capital needed to fund the myriad of startup biotech companies whose only assets are the intellectual property embodied in the same patents drug makers may infringe without fear. Without the development of new tools, the entire pharmaceutical industry may face a dearth of new developments that could ultimately lead to its collapse. Congress should act as soon as possible before the damage to the drug discovery infrastructure becomes irreparable.

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