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Paths to Downstream Innovation

Janet Freilich

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All innovation is "downstream innovation" — research that builds on prior discoveries. Patent law has an outsized influence on downstream innovation because such innovation often falls within the scope of an in-force upstream patent. In these cases, innovators cannot conduct even the most basic research towards downstream technologies without addressing the upstream patent. Because upstream patents block downstream research, and it is often impractical to license the upstream patent, downstream researchers frequently exploit a group of doctrines that permit research to proceed even in the presence of an otherwise blocking patent.

This Article presents the first systematic review of the paths to downstream research. These paths — avenues by which downstream research can proceed without permission of the upstream patentee — have accumulated haphazardly over the years, often accidentally through legal doctrines intended to apply to other situations. As a whole, they exert a powerful influence on the direction of downstream innovation by exempting certain projects, people, and institutions from patent infringement. However, they do so in ways that are unplanned and not always beneficial. Paths to downstream research therefore shift the course of scientific development — for example, favoring foreign research over domestic research, computer modelling over physical testing, and research on new methods of using products over research on new methods of making products.

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This Article makes two contributions to patent policy. First, it advocates for fixing incentives for downstream research with a broad research exception. Second, an array of policy efforts are founded on the assumption that upstream patents block downstream research. By arguing that patents do not block downstream research — they shift it — this Article re-sets the baseline for these policies. Beyond policy, this Article provides new theoretical perspectives on the interactions between patents and research, which undergirds much scholarship on innovation in both law and economics.

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INTRODUCTION

All innovation builds on previous discoveries.[1] In acknowledgment of the sequential nature of innovation, the patent system — designed to incentivize innovation — explicitly encourages research that improves on existing inventions, called "downstream" or "follow-on" innovation.[2] But the patent system also presents a fundamental roadblock to downstream innovation: making or using a patented technology is an act of infringement.[3] Patents not only block downstream technology from being sold, they block the research

[1] KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 418-19 (2007) ("[I]nventions in most, if not all, instances rely upon building blocks long since uncovered.").

[2] *See* Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEX. L. REV. 989, 999 (1997).

[3] 35 U.S.C. § 271(a) (2018).

needed to conceive of and prototype downstream innovations.[4] New technologies can therefore only come about through three possibilities: the innovator licenses the upstream patent (often not a viable possibility), infringes the patent (discouraged by patent law), or conducts acts that are not defined as patent infringement.

Prior scholarship has by-and-large ignored these paths outside patent infringement.[5] Yet they are of immense importance because they often provide the only legitimate route by which downstream innovation can occur. Their structure therefore deeply impacts the course of downstream innovation. Here, I provide the first catalogue of these paths and their effects. While existing case law and scholarship assumes either that patents present a near-total block to downstream research[6] or that downstream researchers proceed even if an upstream patent is infringed,[7] this Article emphasizes a third option: that much — perhaps even most — downstream research falls into one or more carve-outs from infringement.[8]

However, many of these paths are accidental, in the sense that the doctrines were created to address other challenges and affect downstream research only incidentally.[9] Patent law therefore unintentionally takes research projects that appear quite similar and treats them in ways that are categorically different, rendering some liable for patent infringement while exempting others completely. This incentivizes research in areas that are exempt from patent infringement. Thus, that limit the reach of patent infringement pull downstream research along haphazard and arbitrary paths. For instance, the structure of patent law favors foreign over domestic research,[10] computer modelling over physical testing,[11] research at state

[4] *See* Madey v. Duke Univ. 307 F.3d 1351, 1361-62 (Fed. Cir. 2002).

[5] *See infra* Part II.B. A great deal has been written about the common law research exception, but it effectively no longer exists in the United States, *see Madey*, 307 F.3d at 1361, and is not among the exceptions discussed in this Article.

[6] *See* Lab'y Corp. of Am. Holdings v. Metabolite Lab'ys, Inc., 548 U.S. 124, 127 (2006) (Breyer, J., dissenting). For further discussion, see *infra* Part I.B.1.

[7] O'Reilly v. Morse, 56 U.S. (15 How.) 62, 113 (1853). For further discussion, see *infra* Part I.B.2.

[8] *See infra* Part II.A.

[9] *See infra* Part III.A.1.

[10] Foreign research is not affected by U.S. patents, advantaging foreign researchers. *See infra* Part II.B.1.

[11] Computer models of an invention are not infringement; physical creation is. *See infra* Part II.B.2.

universities over research at private universities,[12] and research on methods of use over research on methods of making.[13]

The following examples illustrate how patent law favors certain types of downstream research. DuPont researchers created a pesticide-resistant soybean that incorporated patented technology.[14] The project involved research only — DuPont never sold their plant. The research infringed a U.S. patent, and a jury found DuPont liable for $1 billion.[15] Had DuPont conducted its research outside of the United States, it would not have been liable for infringement.[16] Patent law incentivizes foreign over domestic research, pushing companies to move research abroad.

In another example, a researcher invented a device to detect security flaws in patented Radio Frequency Identification ("RFID") chips.[17] He bought patented RFID chips and then copied the chips, possibly an act of patent infringement.[18] The patentee threatened to sue the researcher for infringement if he publicized his research.[19] Had the researcher's device worked in an alternative manner — say, by disassembling, modifying, or using the RFID chip — rather than by copying the chip, he could have escaped liability under the first sale exception.[20] Patentees can block critical studies of their products if the criticism requires making the product, but cannot block such studies if the criticism involves using the product — an arbitrary result.[21]

The unintentional nature of these effects on downstream research highlights a deeper ill in how patent law is conceptualized. Courts, scholars, and policy makers take a bifurcated approach to law making, focusing on the effects of a doctrine on either sales or research, but not

[12] State universities cannot be sued for patent infringement under principles of sovereign immunity. *See infra* Part II.A.3.

[13] Experimentation on new uses of commercially available products is not patent infringement under the first-sale exception. *See infra* Part II.A.1.

[14] Monsanto Co. v. E.I. Du Pont de Nemours & Co., 748 F.3d 1189, 1192 (Fed. Cir. 2014).

[15] *See id.* at 1195.

[16] The patent was filed in the U.S. only. Note, however, that the case also involved a question of contract law, which may have applied irrespective of location.

[17] *See* Brenda M. Simon, *Patent Cover-up*, 47 HOUS. L. REV. 1299, 1304-05 (2011).

[18] *Id.*

[19] *Id.*

[20] The first sale doctrine permits any use of a patented product as long as it has been bought in an authorized purchase. The first sale doctrine does not allow the purchaser to make additional copies of the patented product. Bowman v. Monsanto Co., 569 U.S. 278, 280 (2013).

[21] For example, safety studies of drugs would be permitted but safety studies of manufacturing processes would be blocked. *See infra* Part II.A.1.a.

both.[22] But patent law is unitary: doctrines apply to both sales and research alike.[23] This mean that when a doctrine is intended to affect sales, its impact on research — which may be substantial — is often overlooked.

This Article also clarifies several fuzzy assumptions that appear in case law and literature on downstream innovation. One common assumption is that patents block downstream research.[24] As a matter of legal doctrine, patents quite clearly do block downstream research — any act of making or using the patented technology is infringement.[25] However in practice, downstream research plainly occurs even when a blocking patent exists. For example, 12,331 downstream patents were filed on innovation relating to the drug Lipitor (atorvastatin) while the drug was still protected by an upstream patent.[26] This is partially because many researchers ignore patents. But it also occurs because much of the downstream research is not patent infringement at all. It is therefore more accurate to say that patents shift the course of downstream research, rather than block it entirely.

A second strand of case law and literature takes for granted that downstream innovation occurs without permission of the upstream patentee and models how upstream and downstream innovators split the surplus from an existing downstream innovation.[27] But there is a gap in this literature. It assumes that downstream innovation occurs, but it does not explain *how* it occurs.[28] Given that patents at least facially present a complete block to downstream research, this is not a small omission. This Article shows paths by which downstream research occurs. This adds richness to the literature on upstream/downstream negotiations by clarifying when downstream innovators need *ex ante* permission from the patentee before beginning research and when negotiations can happen *ex post* after an invention has been developed.[29]

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[22] *See infra* Part III.A.3.

[23] *See id.*

[24] *See* Lab'y Corp. of Am. Holdings v. Metabolite Lab'ys, Inc., 548 U.S. 124, 127 (2006) (Breyer, J., dissenting). For further discussion, *see infra* Part I.B.1.

[25] 35 U.S.C. § 271(a) (2018).

[26] And only 670 of these patents were owned by Pfizer, the exclusive licensee of the Lipitor patent. *See* Pfizer Inc. v. Apotex, Inc., 2009 WL 2843288 at *3 (D. Del. Aug. 13, 2009) (calling Pfizer the exclusive licensee). Searching Google Patents for patents with the keyword "atorvastatin" with a priority date between July 21, 1987, and September 24, 2009 (the patent's expiration date, adjusted to account for 1213 days of patent term extension), yielded 12,331 hits, 670 of which were owned by Pfizer.

[27] *E.g.*, O'Reilly v. Morse, 56 U.S. (15 How.) 62, 113 (1853); *see also infra* Part I.B.2.

[28] *See O'Reilly*, 56 U.S. 62 at 113.

[29] *See infra* Part II.

After addressing theoretical and doctrinal questions of downstream research, the Article turns to reform. First, recognizing that many doctrines accidentally create incentives for certain types of downstream research means that these doctrines can be harnessed to deliberately push downstream research towards desired outcomes. Alternatively, some of the ills of the current system could be remedied with a broad research exception that allows any research on a patented invention to proceed without fear of liability.[30]

The Article proceeds as follows. Part I defines downstream innovation, explains how it is both encouraged and deterred by patent law, and summarizes the broad existing literature on downstream innovation. Part II develops a taxonomy of doctrines that permit downstream research without patent infringement, identifying both effects of individual doctrines and patterns of effects. Part III explores the problems with these doctrines in the aggregate and their implications for scholarship and policy.

I. BACKGROUND

A. Incentives and Deterrents of Downstream Research

1. Incentives for Downstream Research

In the patent context, the term "downstream innovation" (sometimes more generally called "follow-on" innovation) refers to innovation that falls within the scope of an existing patent.[31] For example, if a patent covers a particular process, downstream innovation includes projects to improve the yield of the process or on outputs of the process.

Many celebrated inventions are the result of downstream innovation — Thomas Edison's lightbulb, for instance. Edison was sued for patent infringement by the owners of an upstream patent that claimed "incandescing conductor[s] of carbon made from a vegetable fibrous material."[32] The patentees sold lamps made from carbonized paper and wood carbon, but they worked poorly and were not a commercial success.[33] Edison, after much experimentation, determined that

[30] *See infra* Part III.B.3.

[31] *See e.g.*, Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1353 (Fed. Cir. 2010) (discussing how the scope of a patent affects the balance between upstream and downstream innovation).

[32] Consol. Elec. Light Co. v. McKeesport Light Co., 159 U.S. 465, 466 (1895).

[33] *See id.* at 472.

bamboo fibers worked particularly well as filaments in lightbulbs.[34] Bamboo fibers are vegetable fibrous material, thus Edison's invention fell within the scope of the earlier patent (which the Supreme Court ultimately found to be invalid).[35]

Another famous example is sofosbuvir (Sovaldi; Harvoni), the first cure for hepatitis C. Idenix Pharmaceuticals discovered that a group of compounds called ß-D-2'-methyl-ribofuranosyl nucleosides could treat hepatitis C and patented use of the compounds for that purpose.[36] Pharmasset Inc., another company investigating hepatitis C treatments, learned of Idenix's discovery[37] and used that knowledge to develop their own ß-D-2'-methyl-ribofuranosyl nucleoside, a compound they named sofosbuvir.[38] Though Idenix had discovered and patented the class of compounds to which sofosbuvir belonged, Idenix had not synthesized or specifically identified sofosbuvir itself.[39]

Idenix and Pharmasset's work was enormously valuable.[40] In later litigation, a court explained that the medical breakthrough was a combination "of Idenix's groundbreaking discovery" with Pharmasset's "revolutionary refinement of that invention . . . without both parties' contributions, humanity may well have been deprived of a cure for HCV."[41]

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[34] *Id.* at 473.

[35] *See id.* at 476.

[36] U.S. Patent No. 7,608,597 (issued Oct. 27, 2009). The patent was later invalidated for lack of enablement. Idenix Pharms. LLC v. Gilead Scis. Inc., 941 F.3d 1149, 1165 (Fed. Cir. 2019).

[37] Pharmasset may have learned of this discovery through disclosure of confidential information. Susan Decker, Caroline Chen & Christopher Yasiejko, *Gilead's Patent Loss to Merck Started with a Broken Friendship*, BLOOMBERG NEWS (Dec. 16, 2016), https://www.bloomberg.com/news/articles/2016-12-16/gilead-s-patent-loss-to-merck-started-with-a-broken-friendship [https://perma.cc/6VQM-GPXQ].

[38] Idenix Pharms. LLC v. Gilead Scis., Inc., 271 F. Supp. 3d 694, 699 (D. Del. 2017). Note that sofosbuvir is a ß-D-2'-methyl-ribofuranosyl nucleoside under the court's construction of the term, but Pharmasset and Gilead dispute the construction. *Id.*

[39] *Id.* at 703-04. The court emphasizes that Pharmasset's discovery was built on Idenix's earlier work. Internal Pharmasset documents called the Pharmasset compound an "Idenix derivative[]." *Id.* The court's language makes it apparent that it considers this a case of downstream innovation. In finding enhanced damages inappropriate, the court discusses the challenges of balancing upstream and downstream innovation and the need to calibrate the patent system to encourage downstream innovation. *Id.* ("The Court—and, more generally, the patent system—wants to encourage, and not deter, innovation on existing ideas . . . .").

[40] Andrew Pollack, *Hepatitis C, a Silent Killer, Meets Its Match*, N.Y. TIMES (Nov. 4, 2013), https://www.nytimes.com/2013/11/05/health/hepatitis-c-a-silent-killer-meets-its-match.html [https://perma.cc/2DZF-YU69].

[41] *Idenix*, 271 F. Supp. 3d at 704.

The patent system recognizes the importance of downstream innovation and explicitly incentivizes downstream research by granting patents on "new and useful improvement[s]" of earlier inventions.[42] This means that the downstream innovator can receive a patent on their improved technology even when the upstream innovator also has a patent on their earlier version of the technology. This was the case for the discovery of sofosbuvir discussed above — Idenix held a broad upstream patent covering a class of compounds that included sofosbuvir; Pharmasset held a patent on sofosbuvir itself.[43]

The patent system also promotes downstream innovation by giving downstream innovators leverage to negotiate with upstream patent holders to extract value from the invention.[44] In situations where an upstream patent is in-force and a downstream innovator obtains their own patent on an improved version of the technology, the upstream and downstream patents are considered "blocking," because neither patentee can fully practice their invention without permission of the other.[45] The downstream patentee's invention falls within the scope of the upstream patent, thus practicing the invention is infringement.[46] At least part of the upstream patentee's invention falls within the scope of the downstream patent, thus, the upstream patentee may not practice that portion of the invention without permission of the downstream patentee.[47] These mutual restrictions give both the upstream and

[42] 35 U.S.C. § 101 (2018).

[43] *See Idenix*, 271 F. Supp. 3d at 698-99. Pharmasset's discovery was patentable because it was not obvious from Idenix's patent that sofosbuvir would be a useful treatment for hepatitis C. Indeed, Pharmasset scientists went to some effort to ensure that their development was eligible for its own patent. After learning about Idenix's patent, Pharmasset scientists "affirmatively reviewed Idenix's patent . . . [,] determined its compound of interest was not included in the closed list of potential compounds described in the patent, then proceeded to make and test that compound — a compound that Idenix itself was not able to make and test until after it reviewed Pharmasset's application." *Id.* at 699. A Pharmasset executing advised scientists at the company to "look for the holes" in upstream patents, "areas . . . that we might work on and still be able to get an invention." *Id.* at 700. Pharmasset scientists succeeded in finding a compound that was novel and nonobvious even in light of Idenix's discovery and obtained their own patent on sofosbuvir. U.S. Patent No. 8,580,765 (issued Nov. 12, 2013).

[44] *See* Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law*, 5 J. ECON. PERSPS. 29, 30 (1991); Lemley, *supra* note 2, at 992.

[45] Prima Tek II, LLC v. A-Roo Co., 222 F.3d 1372, 1379 (Fed. Cir. 2000).

[46] *See id.*

[47] *See id.*

downstream innovators incentive to reach an agreement to commercialize the fruits of the combined innovation.[48]

The availability of blocking patents reflects the value that patent law places on downstream innovation.[49] As put by the Supreme Court, downstream innovation is "both necessary to invention itself and the very lifeblood of a competitive economy"[50] and patent law reflects a careful balance between the need to promote innovation through patent protection, and the importance of "facilitating . . . refinement through imitation . . . ."[51]

2. Deterrents to Downstream Research

Though the patent system values downstream innovation, it also poses a colossal roadblock: the act of conducting downstream research is an act of patent infringement. Patent infringement is defined as making, using, selling, offering to sell, or importing a patented invention.[52] Most downstream research requires conducting one of those actions. For example, to discover a new use for Teflon, one would have to conduct experiments using Teflon — an act of infringement.[53] To discover a new way of making Teflon, one would have to make Teflon — an act of infringement. To discover a new combination of Teflon and other chemicals, one would have to use (and possibly make) Teflon — an act of infringement. Patent infringement is a strict liability offense, so downstream research by anyone and for any purpose at all is an act of infringement.[54]

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[48] *See* Robert P. Merges, *Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents*, 62 TENN. L. REV. 75, 80 (1994). To illustrate the concept of blocking patents, consider the example of sofosbuvir. Both Idenix and Pharmasset patented their inventions. The Idenix patent and the Pharmasset patent blocked each other. Pharmasset could not sell sofosbuvir without Idenix's permission. Similarly, Idenix could not sell sofosbuvir without Pharmasset's permission. Ultimately, Idenix's patent was found to be invalid, so Pharmasset can now sell sofosbuvir without Idenix's permission. Idenix Pharms. LLC v. Gilead Scis., Inc., 271 F. Supp. 3d 694, 699 (D. Del. 2017).

[49] For a discussion of reasons patent law incentivizes downstream innovation, see Lisa Larrimore Ouellette, *Pierson, Peer Review, and Patent Law*, 69 VAND. L. REV. 1825, 1834 (2016).

[50] Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 146 (1989).

[51] Halo Elecs., Inc. v. Pulse Elecs., Inc., 579 U.S. 93, 109 (2016).

[52] 35 U.S.C. § 271(a) (2018).

[53] The patent on Teflon covers any use of polymerized tetrafluoroethylene (Teflon). U.S. Patent No. 2,230,654, claim 1 (issued Feb. 4, 1941).

[54] A common misconception is that activities that do not generate a profit or that do not involve selling a competing product — such as research — are not patent

Historically, this was not the case. The research exception, a judicially created doctrine, exempted certain acts of research from patent infringement.[55] This permitted downstream researchers to conduct experimentation on patented products in at least some circumstances, although the precise contours of the doctrine were never well defined.[56] However, by late 1900s the doctrine was disfavored[57] and it was essentially eliminated by the Federal Circuit's decision in *Madey v. Duke* in 2002.[58]

In theory, downstream research could be permitted by private licensing: upstream patentees have an incentive to license downstream research and split the resulting profits.[59] But in practice this is not a complete solution. Scholars agree that transaction costs are sufficiently high that licensing will often not occur.[60] Anecdotally, there are many reports of instances where transaction costs have prevented a variety of potentially fruitful licensing agreements for downstream research.[61]

Further, the process of negotiation is itself a deterrent. If the downstream researcher discloses her idea to the patentee to begin negotiation, the patentee can freely appropriate the researcher's idea without recompense, since the researcher has no intellectual property

infringement. For example, after academic scientists were named in a patent infringement lawsuit, journalists recorded surprised reactions from the scientists: "'[patent infringement] is something we don't think about,' he said. Basic scientists who use [patented compounds] 'aren't violating the patent for profit . . . so I can't imagine that they would have any liability.'"). Marcia Barinaga, *Scientists Named in PCR Suit*, 268 SCIENCE 1273, 1274 (1995). But patent law is a strict liability tort. *In re* Seagate Tech., LLC, 497 F.3d 1360, 1368 (Fed. Cir. 2007).

[55] The doctrine was first expounded by Justice Story who wrote that "it could never have been the intention of the legislature to punish a man, who constructed such a [patented] machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects."). Whittemore v. Cutter, 29 F. Cas. 1120, 1121 (C.C.D. Mass. 1813).

[56] *See, e.g.*, Giese v. Pierce Chem. Co., 29 F. Supp. 2d 33, 35 (D. Mass. 1998) (finding academic scientists exempt from patent infringement under certain circumstances).

[57] *See, e.g.*, Embrex, Inc. v. Serv. Eng'g Corp., 216 F.3d 1343, 1349 (Fed. Cir. 2000) (using a narrow application of the experimental use exception); Roche Prods., Inc. v. Bolar Pharm. Co., 733 F.2d 858, 863 (Fed. Cir. 1984) ("[T]he experimental use exception [is] truly narrow . . . [and] broad construction is not justified."); Deuterium Corp. v. United States, 19 Cl. Ct. 624, 634 (1990) (finding that the experimental use exception does not apply to scientific inquiries with potential commercial applications).

[58] Madey v. Duke Univ., 307 F.3d 1351, 1360-61 (Fed. Cir. 2002).

[59] *See* Scotchmer, *supra* note 44, at 32-35.

[60] *Id.*; *see also* Lemley, *supra* note 2, at 990.

[61] *See* Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 BERKELEY TECH. L.J. 813, 832 (2001).

protection over the idea.[62] This problem, known as Arrow's information paradox, is a substantial impediment to licensing.[63] In theory, the downstream innovator can obtain a blocking patent to prevent this from happening. But in practice, in order to get a patent (or indeed to be an innovator) the downstream innovator must conduct some preliminary experiments on the technology, which may well infringe the upstream patent.

Even if transactions could be frictionless, patentees still do not have an incentive to permit all socially beneficial research. Patentees will block downstream research by competitors and by researchers who might criticize the patented technology.[64]

B. (Mis)Understanding Downstream Research

There is abundant case law, scholarship, and policy work on downstream innovation. However, this writing does not completely describe the relationship between upstream patents and downstream innovation. Broadly speaking, previous writing falls into one of two camps, each de-emphasizing a different aspect of the relationship. The first camp characterizes patents as blocks to downstream research and does not discuss ways in which downstream research can occur despite the presence of an upstream patent. The second camp assumes that downstream research happens even when there is an upstream patent, but it does not explain *how* downstream research happens, given that much of that downstream research is patent infringement. The Sections below summarizes the literature and caselaw and expands on the holes in the current framing.

1. Patents Block Downstream Research

The simple view of the relationship between patents and downstream research is that patents block downstream research. This follows from the formal structure of patent law — if any activity that falls within the scope of a patent is infringement, then patentees can use their patent to

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[62] Unless she can get a patent of her own *before* negotiating. Merges, *supra* note 48, at 89. Downstream researchers can only do so in certain circumstances, which is itself a form of distortion. *See* discussion *infra* Part II.

[63] Kenneth J. Arrow, *Economic Welfare and the Allocation of Resources for Invention*, *in* THE RATE AND DIRECTION OF INVENTIVE ACTIVITY: ECONOMIC AND SOCIAL FACTORS 609, 615 (1962).

[64] *See* Simon, *supra* note 17, at 1303; *see also id.* at 1303-14 (exploring how patent infringement rules are used by patentees to cover up or hide problems with patented technology).

block downstream research. This assumption appears in a variety of contexts. It has been espoused by the Supreme Court several times. In *Brenner v. Manson*, the Supreme Court invalidated a patent after worrying that it would "confer power to block off whole areas of scientific development, without compensating benefit to the public."[65] In *Special Equipment Co. v. Coe*, the Court noted that patents could be obtained "for the purpose of blocking the development of machines which might be constructed by others."[66] In *Lab Corp. v. Metabolite Labs*, the Court explained that exclusive rights can "forc[e] researchers to avoid the use of potentially patented ideas."[67]

Scholarly writing about the need for a research exception — a large and prominent literature — also focuses on patents' ability to block downstream research.[68] This writing emphasizes the blocking effects of patents with little explicit attention to doctrinal mechanisms that permit

[65] Brenner v. Manson, 383 U.S. 519, 534 (1966); *see also In re* '318 Pat. Infringement Litig., 583 F.3d 1317, 1324 (Fed. Cir. 2009) (quoting *Brenner*, 383 U.S. at 534); *In re* Fisher, 421 F.3d 1365, 1375-76 (Fed. Cir. 2005) (quoting *Brenner*, 383 U.S. at 534).

[66] Special Equip. Co. v. Coe, 324 U.S. 370, 374 (1945). The dissent elaborated, "It is common practice to make an invention and to secure a patent to block off a competitor's progress . . . as to preclude experimentation which might result in further invention by competitors." *Id.* at 382-83 (Douglas, J., dissenting).

[67] Lab'y Corp. of Am. Holdings v. Metabolite Lab'ys, Inc., 548 U.S. 124, 127 (2006).

[68] *See, e.g.*, Rochelle Dreyfuss, *Protecting the Public Domain of Science: Has the Time for an Experimental Use Defense Arrived?*, 46 ARIZ. L. REV. 457, 458 (2004) [hereinafter *Protecting the Public Domain of Science*] (discussing ways in which patents block downstream innovation); Rochelle Cooper Dreyfuss, *Reconsidering Experimental Use*, 50 AKRON L. REV. 699, 712 (2017) (noting that the research community "must cope with a system that sharply reduces incentives to innovate in an arena where the cost of getting to market can be extremely high, yet the law does nothing to fix the research problem created by the patents that do issue"); Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. Chi. L. Rev. 1017, 1071 (1989) (explaining that a system that requires "a license from the original discoverer" in order for downstream research to proceed "is a less satisfactory means of promoting scientific progress than free access to such discoveries," which suggests that upstream patents block free access to downstream discoveries); Maureen A. O'Rourke, *Toward a Doctrine of Fair Use in Patent Law*, 100 COLUM. L. REV. 1177, 1204 (2000) (arguing that "research, if enjoined [as patent infringement], would frustrate further progress" of science); Katherine J. Strandburg, *What Does the Public Get? Experimental Use and the Patent Bargain*, 2004 WIS. L. REV. 81, 82-85 (2004) (explaining that patents can "slow technical progress if the best follow-on inventors are prevented from building upon the inventive idea during the patent term" and that patents "make it more difficult to build on the inventions of others . . . . [E]ither because an improved invention still falls within the claims of a prior patent . . . [or] because the research and development process for a new invention requires the practice of a prior patent").

downstream innovators to evade those blocks.[69] This emphasis is appropriate given that scholarship on the research exception focuses on the deterrent effects of patents, however, it leaves a gap: scholarship on the effect of patents on research does not comprehensively discuss paths by which patent law *permits* downstream research.

The assumption that patents block downstream research also appears in the law and economics literature. The focus of this literature is on how to best divide the patent incentive between upstream and downstream innovators. Some of this literature operates from the baseline assumption that downstream research in a patented area will not happen unless the downstream researcher obtains a license.[70] Thus, broad patents have the potential to control downstream innovation[71] or,

[69] Some articles discuss one or two exceptions, but do not deal with them comprehensively. *See, e.g.*, Julie E. Cohen & Mark A. Lemley, *Patent Scope and Innovation in the Software Industry*, 89 CALIF. L. REV. 1, 36 (2001) (explaining that the doctrine of patent exhaustion could be applied in such a way as to allow reverse engineering of software); Donna M. Gitter, *International Conflicts over Patenting Human DNA Sequences in the United States and the European Union: An Argument for Compulsory Licensing and a Fair-use Exemption*, 76 N.Y.U. L. REV. 1623, 1691 (2001) (advocating for a broader experimental use exception in order to "promote innovation by protecting from infringement liability public-sector and nonprofit scientists engaged in noncommercial research" but also mentioning that scientists at state universities are protected by sovereign immunity); Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 33 (2001) (criticizing the Federal Circuit's narrowing of the experimental use doctrine to categorically exclude commercial research but noting that some noncommercial research is still permitted (though this may not be true after the Federal Circuit's 2002 decision in *Madey*)); Elizabeth A. Rowe, *The Experimental Use Exception to Patent Infringement: Do Universities Deserve Special Treatment?*, 57 HASTINGS L.J. 921, 925 (2006) (arguing that a broad research exemption is not necessary because research can proceed through the *Bolar* exception expanded by the Supreme Court in *Merck v. Integra* or through the doctrine of sovereign immunity); Pamela Samuelson, *Intellectual Property Arbitrage: How Foreign Rules Can Affect Domestic Protections*, 71 U. CHI. L. REV. 223, 223 (2004) (explaining how firms can move research operations abroad to circumvent US patents); Strandburg, *supra* note 68, at 118 (suggesting that the exhaustion doctrine can serve as a research exemption) ("If the follow-on researcher can obtain the necessary information by using a purchased product, which comes with an implied license to use it, then there is no need for a special [research] exemption.").

[70] *See, e.g.*, Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 700 (1998) (explaining "[A patentee can] leverage its proprietary position in upstream research tools into a broad veto right over downstream research and product development.").

[71] *See, e.g.*, Mark F. Grady & Jay I. Alexander, *Patent Law and Rent Dissipation*, 78 VA. L. REV. 305, 307 (1992) (explaining that broad patents block opportunities for later innovation) ("Consider the invention of Alexander Graham Bell's telephone . . . . [U]nder a grant of broad patent protection, Bell would control all opportunities for developing new communication devices. . . . [N]o one would race to improve on Bell's

in the alternative view, to promote innovation by encouraging later innovators to design around the patent and thereby come up with creative alternative technologies.[72]

The emphasis on the block that patents pose to downstream innovation is not wrong — patents *do* prevent certain downstream activities. However, two complications arise. First, focusing on how patents block research does not fit with facts on the ground: it is quite clear that downstream research occurs even when patentees have not permitted it, and some studies have found that downstream research occurs equally frequently in the presence or absence of a blocking patent.[73] Second, it does not fit with the structure of patent law: patent law is riddled with doctrines that permit downstream research in a wide variety of circumstances.[74] Because this literature focuses on ways in which patent law blocks downstream research, it has given little attention to the very important incentives created by the doctrines that permit downstream research.

2. Patents Do Not Block Downstream Research

A second line of case law, policy, and scholarly literature operates on the premise that patents do not block downstream research. Here, the assumption is that downstream research will occur and that, after creating their innovation, downstream researchers will either negotiate an *ex post* license or be mired in litigation with upstream patentees. In this conception of downstream research, third parties conduct research on patented inventions and can develop improved versions without

device. Instead, aspiring improvers would have to buy the right from Bell."). Some scholars view broad upstream patents as a beneficial mechanism to control downstream research. *See e.g.*, Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J.L. & ECON. 265, 276 (1977) ("No one is likely to make significant investments searching for ways to increase the commercial value of a patent unless he has made previous arrangements with the owner of the patent. This puts the patent owner in a position to coordinate the search for technological and market enhancement[s] . . . .").

[72] Peter Lee, Note, *Patents, Paradigm Shifts, and Progress in Biomedical Science*, 114 YALE L.J. 659, 686-87 (2004) ("Patents on upstream [technologies] . . . provide additional incentives — legal and economic — to theorize outside of a dominant paradigm. . . . [A] scientist is induced to develop alternate ways of conceptualizing and investigating the subject of her research.").

[73] *See, e.g.*, Bhaven Sampat & Heidi L. Williams, *How Do Patents Affect Follow-on Innovation? Evidence from the Human Genome*, 109 AM. ECON. REV. 203, 227 (2019) ("[W]e empirically find no evidence that patents induce economically meaningful reductions in follow-on innovation . . . .").

[74] *See infra* Part II.

permission from the patentee.[75] The downstream research itself is not blocked — it occurs notwithstanding the upstream patent — but the improvement cannot be used or sold without permission of the patentee.[76]

The Supreme Court has also endorsed this view of intra-patent research, explaining that "some future inventor" might discover an improvement to a patented process but "if it covered by this patent the inventor could not use it, nor the public have the benefit of it without the permission of the patentee."[77] This assumes that the future inventor has already conducted their (presumably infringing) research and developed their improvement but is then blocked from using the invention.

This line of literature and case law accurately reflects that third parties conduct research in patented areas. It also correctly describes that, when downstream innovations enter the market and start to be sold, the patentee can respond with a lawsuit for infringement.[78] But this literature does not provide a mechanism for downstream innovation —

[75] *See, e.g.*, Rebecca S. Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 YALE L.J. 178, 219-20 (1987) ("Perhaps the most important function of early disclosure is to facilitate improvement of the patented invention around the patent . . . . Since an insufficient disclosure makes the patent invalid and unenforceable, those who have a use for the patented technology will be motivated to uncover defects in the specification in order to avoid liability to the patentee."); Kitch, *supra* note 71, at 268-69 ("Subsequent inventors of superior automobiles will infringe [a first patent on an automobile] . . . . Anyone else who makes a machine embodying that process, even though much superior due to its improvements, will infringe that claim."); Lemley, *supra* note 2, at 991; Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 909 (1990) ("[Broad patents] created problems because other inventors such as Glen Curtiss, following close on the heels of the Wrights, were blocked for a time from introducing their advances into the fledgling industry."); Arti Kaur Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U. L. REV. 77, 127 (1999) ("Although the follow-on improver can then secure a patent on that improvement, the improvement may nonetheless infringe the original patent."); Scotchmer, *supra* note 44, at 30 ("If broad protection is granted, then a derivative or second generation product will likely infringe the prior patent . . . .").

[76] *Id.*

[77] O'Reilly v. Morse, 56 U.S. (15 How.) 62, 113 (1853).

[78] *See, e.g.*, Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 195 (2005) (detailing a claim brought against a competing researcher for their use of a patented pharmacologically useful peptide); Consol. Elec. Light Co. v. McKeesport Light Co., 159 U.S. 465, 471-72 (1895) (addressing infringement claim brought against competing light manufacture for their marketing of a patented lamp); Idenix Pharms., LLC v. Gilead Scis., 941 F. 3d 1149, 1160 (Fed. Cir. 2019) (finding that a patent for drug treatment of the hepatitis C virus was invalid because it did not meet enablement disclosure requirements).

there is no adequate explanation for how the downstream invention came to be.[79] Some scholars assume that downstream inventions arise through infringement or by accident,[80] but ignore legitimate paths to create downstream inventions without permission of the patentee. The literature therefore misses the incentives created by these authorized paths to downstream innovation.

II. PATHS TO DOWNSTREAM INNOVATION

Downstream research presents a paradox: the research is conducted on a patented product or process — yet making or using a patented product is patent infringement, so why is there so much downstream research that falls within the scope of an upstream patent? Some downstream research is simply patent infringement and occurs when the researcher either does not know about or does not care about the upstream patent. But much downstream research is not patent infringement. Rather, it arises from an activity that falls into one of the many limits to and exceptions from patent infringement. Because a downstream researcher who wishes to avoid infringement must proceed through one of these limits or exceptions, these pathways serve to channel downstream research in particular ways.

Below, I use the term "shift" to indicate when a doctrine moves downstream in a certain direction. The baseline against which shifts are seen is the states where researchers select projects without regard to the potential for upstream patent infringement. Comparing the effect of doctrines against this baseline highlights how doctrines have the potential to affect incentives for downstream innovation. Note that the term 'shift' does not imply either a positive or a negative incentive, but merely denotes an influence.

The Section below catalogues some of the limits and exceptions that shift incentives for downstream research. These are only a sample of the

[79] For example, Merges and Nelson's classic article on cumulative innovation describes a significant number of downstream improvements involved in litigation, but does not grapple with how those improvements came to exist in the first place. Merges & Nelson, *supra* note 76, at 909. Some scholars have discussed mechanisms for downstream innovation in particular industries or circumstances. *See, e.g.*, Jorge L. Contreras, *A Market Reliance Theory for FRAND Commitments and Other Patent Pledges*, 2015 UTAH L. REV. 479, 492 (explaining how patentees license patents on "fair, reasonable and non-discriminatory" ("FRAND") terms); Jorge L. Contreras, *Much Ado About Hold-up*, 2019 U. ILL. L. REV. 875, 877-78 (discussing innovation in the context of industry standards such as Wi-Fi); Jacob S. Sherkow, *The CRISPR Patent Landscape: Past, Present, and Future*, 1 CRISPR J. 5, 5-8 (2018) (exploring follow-on CRISPR innovation).

[80] *See* Scotchmer, *supra* note 44, at 30.

limits and exceptions on infringement — almost every patent doctrine creates some limit on the power of the patentee, so a full list cannot be enumerated here. This Section explores how doctrines favor certain downstream activities over others. As described further, the incentives created by these doctrines do not channel downstream innovation in thoughtful, deliberate directions. Rather, the incentives are often accidental.

Table 1: Summarizing how patent doctrine shift downstream research by treating certain activities as infringement while exempting others

Downstream research that is:	
Not infringement (or not enforceable as infringement in practice)	**Infringement**
New methods of using an existing product	New methods of making an existing product
Research on commercially available products	Research on non-commercially available products
Late-stage life sciences research	Early-stage life sciences research
Research at state universities	Research at private universities
Research outside of the United States	Research in the United States
Thinking about hypotheses	Testing hypotheses
Secret research	Public research
Low-cost research	Expensive research
Research in areas where patents are voluntarily not enforced	Research in areas where patents are voluntarily enforced

For each type of research listed in Table 1, the Section below explains the doctrine underpinning the classification of the research as non-infringing and discusses the consequences of treating the research as non-infringing while treating closely related research as infringing.

A. Exception-Based Effects

Some shifts in incentives for downstream research arise from doctrines that specifically define certain downstream activities as non-infringing.

1. Making versus Using

a. Doctrine

Patent law shifts incentives for downstream research by favoring research on new uses for old technology over research on new methods of making old technologies. This shift arises from the first sale doctrine, also known as the exhaustion doctrine.[81] The first authorized sale of a patented product exhausts the patent right so that the purchaser is subsequently free to use the product for any purpose.[82] This releases downstream researchers from the constraints of patent rights in certain circumstances. A downstream researcher can buy a product from a patentee — for example, a drug from a pharmaceutical company — and conduct experiments on that product and those experiments would not be patent infringement.

For example, Pfizer is the exclusive licensee of U.S. Patent No. 4,681,893, which, before expiration, had covered a class of chemical compounds including Lipitor (atorvastatin), used to lower cholesterol.[83] The patent claimed the compounds without limitation, thus, any use or creation of the compounds was patent infringement.[84] Lipitor is sold commercially by Pfizer, therefore researchers can take advantage of the first use exception to study the drug without fear of patent infringement.[85] Researchers can purchase Lipitor and conduct a clinical trial to test whether the drug treats, for example, Alzheimer's disease — and it is not patent infringement.[86] This exception is particularly beneficial because it prevents Pfizer from blocking

[81] Impression Prods., Inc. v. Lexmark Int'l, Inc., 137 S. Ct. 1523, 1526 (2017).

[82] *See id.* at 1527; *see also* Quanta Comput., Inc. v. LG Elecs., Inc., 553 U.S. 617, 618 (2008); United States v. Univis Lens Co., 316 U.S. 241, 244 (1942).

[83] U.S. Patent No. 4,681,893 (issued July 21, 1987). The patent is currently expired.

[84] Claim 1 covers the genus of compounds itself.

[85] *See supra* notes 83–84 and accompanying text.

[86] *See, e.g.*, Cynthia M. Carlsson, Guofan Xu, Zhifei Wen, Jodi H. Barnet, Hanna M. Blazel, Richard J. Chappell, James H. Stein, Sanjay Asthana, Mark A. Sager, David C. Alsop, Howard A. Rowley, Sean B. Fain & Sterling C. Johnson, *Effects of Atorvastatin on Cerebral Blood Flow in Middle-Aged Adults at Risk for Alzheimer's Disease: A Pilot Study*, 9 CURRENT ALZHEIMER RSCH. 990, 990 (2012) (analyzing effects of atorvastatin (Lipitor) on risk of Alzheimer's Disease).

researchers who are investigating aspects of Lipitor that Pfizer might prefer not to study. For example, a trial comparing Lipitor with Crestor, a competing drug, found that Lipitor was less effective — Pfizer could not prevent this study (which was conducted by competitor AstraZeneca, the manufacturer of Crestor) using its patents because use of Lipitor fell into the first-use exception.[87]

b. Shifting Incentives

The first sale exception shifts incentives for downstream research because it exempts one type of research — experiments on commercially available products — from patent infringement while leaving other types of research as infringement. Researchers who buy Lipitor and test new uses are not infringing. But other types of research on Lipitor, if done before the patent expired, would have been infringing.[88] For example, experiments on new methods of synthesizing Lipitor would have been patent infringement because in conducting the syntheses researchers make Lipitor, an act of infringement.[89] In consequence, Pfizer had the power to block any research on new methods of making Lipitor. New methods of synthesizing drugs lead to more efficient and less expensive methods of manufacture and are important components of reducing drug prices and improving access to medicine.[90]

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[87] Lawrence A. Leiter, Robert S. Rosenson, Evan Stein, John P.D. Reckless, Karl-Ludwig Schulte, Margo Schleman, Paul Miller, Michael Palmer & Froukje Sosef, *Efficacy and Safety of Rosuvastatin 40 mg Versus Atorvastatin 80 mg in High-Risk Patients with Hypercholesterolemia: Results of the POLARIS Study*, 194 ATHEROSCLEROSIS e154, e159-61 (2007). It is possible that this study also falls into the 35 U.S.C. § 271(e)(1) research exception, although post-marketing studies such as this are not always covered by that exception. *See, e.g.*, Koninklijke Philips N.V. v. Zoll Med. Corp., 656 Fed. App'x. 504, 519 (Fed. Cir. 2016) (holding that testing intended to "generate marketing materials and on products already on sale — thus not for the purpose of receiving approval from the [FDA]" was not protected).

[88] Or would have been before the patent expired. Depending on the study, the researchers may be purchasing the drug Lipitor, or they may be purchasing just the active ingredient, atorvastatin. Either purchase would be protected under the first-sale doctrine as long as it was authorized.

[89] Many scientists are interested in new methods of synthesizing Lipitor. *See, e.g.*, Sandeep Goyal, Bhautikkumar Patel, Ratnesh Sharma, Mangilal Chouhan, Kapil Kumar, Mukesh Gangar & Vipin A. Nair, *An Efficient Strategy for the Synthesis of* Syn *1,3-diols via Iterative Acetate Aldol Reactions and Synthesis of Atorvastatin Lactone*, 56 TETRAHEDRON LETTERS 5409, 5409 (2015) (note that the authors are based in India and research done in India would not infringe the U.S. patent).

[90] This is illustrated by the fight over methods of producing erythropoietin (EPO). *See* Andrew Pollack, *Amgen Wins Initial Battle in Legal War Over Patent*, N.Y. TIMES (Apr.

The first sale exception preferences research on using over research on making. This preference is arbitrary — both types of research are important and there is no empirical evidence (nor any theoretical arguments) that the former is more important than the latter. Yet they are treated quite differently by patent law.

The first sale doctrine also shifts incentives for downstream research in other ways. It encourages research on commercially available patented products by exempting their use from patent infringement. Commercially available products can (by definition) be bought commercially, and therefore are subject to the first sale doctrine. By contrast, research on non-commercially available patented products is infringement because the product cannot be bought but must be made by researchers in order to be used in experiments, which is an act of infringement. The patent on Lipitor, for example, covers thousands of variations on the core molecule, most of which are not available commercially.[91] Researchers can freely conduct experiments on the Lipitor molecule itself, but not on molecules that are slight variations, even though both molecules are covered by the same patent. If a researcher wanted to test whether a modified version of the compound — for instance replacing the fluorine atom with a chlorine atom[92] — would more effectively reduce cholesterol, the researcher would infringe the patent.

This shift towards commercially available products and away from non-commercially available products also means that there are some patented technologies that researchers cannot investigate at all. Some patents, like the Lipitor patent, have a commercially available embodiment. Other patents do not — meaning that no aspect of the patented invention is available to the public. The first sale exception allows research on Lipitor but does not allow research on similar patents where the patentee does not sell a product.

Perhaps there are reasons for distinguishing between research on commercially available and unavailable products — law may, for example, value the patentee's autonomy in choosing not to make its product available for research. Conversely, law may want to incentivize research on non-commercially available products because the public knows less about these inventions and there may be more benefit to research thereupon.

27, 2000), https://www.nytimes.com/2000/04/27/business/amgen-wins-initial-battle-in-legal-war-over-patent.html [https://perma.cc/9D27-72WX].

[91] U.S. Patent No. 4,681,893 (issued July 21, 1987).

[92] A molecule with this substitution would fall into the patent claim, which specifically covers a chlorine substitution. *Id.* at col. 2 l. 15-30.

Empirically, it is not clear whether patent doctrine should preferentially incentivize downstream research on commercially available inventions, non-commercially available inventions, or treat both equally. Yet patent law as it is currently applied makes a clear choice to favor of research on commercially available inventions — without a clear rationale for doing so.

2. Late-Stage vs Early-Stage Research

a. Doctrine

Much late-stage life sciences research is exempt from patent infringement under an exception set out in 35 U.S.C. § 271(e)(1) (also called the section 271(e)(1) exception, statutory research exception, and Bolar exception).[93] Under this exception, an act that would otherwise be infringing is not considered infringement if it is done "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."[94] This exception was enacted as part of the Hatch-Waxman Act of 1984, which also created an abbreviated pathway for generic drug approval.[95] Generic companies are permitted to enter the market immediately after the relevant brand name patent expired.[96] However, generic companies have to submit test results to the FDA in order to get approval to enter the market — and the act of conducting this testing was an act of patent infringement.[97] As a result, in practice generic companies could not begin testing until the brand name patent expired, and could therefore not enter the market until sometime later — effectively extending the term of the brand name company's exclusivity.[98] Congress enacted the section 271(e)(1) research exemption in order to avoid the lag in generic entry.[99] Under section 271(e)(1), it is not patent infringement to test and manufacture generic drugs in preparation to submit an application for FDA approval.[100]

[93] 35 U.S.C. § 271(e)(1) (2018).

[94] *Id.*

[95] Erika Lietzan, *The History and Political Economy of the Hatch-Waxman Amendments*, 49 SETON HALL L. REV. 53, 55 (2018).

[96] *Id.* at 84.

[97] Roche Prods., Inc. v. Bolar Pharm. Co., 733 F.2d 858, 863 (Fed. Cir. 1984).

[98] *See* Elizabeth Stotland Weiswasser & Scott D. Danzis, *The Hatch-Waxman Act: History, Structure, and Legacy*, 71 ANTITRUST L.J. 585, 604 (2003).

[99] Lietzan, *supra* note 95, at 55.

[100] *Id.* at 102-03.

The plain language of the statute does not limit section 271(e)(1) to generic drugs, and over time the exception was expanded to other applications.[101] In 2005, the Supreme Court interpreted the scope of the exception in *Merck v. Integra*.[102] The exception in section 271(e)(1) is not limited to the development of generic drugs, nor to preparation of submissions to the FDA.[103] It includes "*all* uses of patented compounds 'reasonably related' to the process of developing information for submission under *any* federal law regulating the manufacture, use, or distribution of drugs."[104]

b. Shifting Incentives

The practical effect of the Supreme Court's decision in *Merck* is that a great deal of applied life sciences research is exempted from patent infringement. The section 271(e)(1) exception covers preclinical studies, including tests of drugs that are never submitted for regulatory approval or that generate information that is left out of regulatory submissions.[105] Generic drugs can enter the market earlier because testing the drugs is no longer patent infringement. Researchers on new drugs neither have to worry about patent infringement nor pay for a license for their research.[106] For example, in *Merck v. Integra*, Integra held a patent on proteins with a particular amino acid sequence of use in binding to the outside of cells.[107] Merck conducted research on how several proteins containing this sequence could be used to inhibit

[101] *See, e.g.*, David J. Bloch, *If It's Regulated Like a Duck… Uncertainties in Implementing the Patent Exceptions of the Drug Price Competition and Patent Term Restoration Act*, 54 FOOD & DRUG L.J. 111, 121-22 (1999) (discussing expansion of infringement protections to include devices and FDA-approved products); Courtenay C. Brinckerhoff, *Can the Safe Harbor of 35 U.S.C. § 271(e)(1) Shelter Pioneer Drug Manufacturers?*, 53 FOOD & DRUG L.J. 643, 648-54 (1998) (noting the expansion of protections to apply to "the collateral use of clinical data developed for submission to FDA" for medical implant devices); Samuel M. Kais, *A Survey of 35 U.S.C. § 271(e)(1) as Interpreted by the Courts: The Infringement Exemption Created by the 1984 Patent Term Restoration Act*, 13 SANTA CLARA HIGH TECH. L.J. 575, 579-83 (1997) (noting that the demonstration or display of an accused product will not constitute an infringing use).

[102] Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 195 (2005).

[103] *Id.* at 206.

[104] *Id.*

[105] *Id.* at 208. As long as there is a "reasonable basis for believing that a patented compound may work . . . to produce a particular physiological effect, and . . . if successful, would be appropriate to include in a submission to the FDA." *Id.* at 207.

[106] There are possible exceptions for patents on research tools, however. *See, e.g.*, Allele Biotechnology & Pharms., Inc. v. Pfizer, Inc., No. 20-CV-01958-H-AGS, 2021 WL 1749903, at *5 (S.D. Cal. May 4, 2021).

[107] *Merck*, 545 U.S. at 197.

angiogenesis (growth of blood vessels) with potential applications in treating a variety of diseases including cancer and arthritis.[108] The Supreme Court suggested that the plaintiff's research could fall into the section 271(e)(1) exception (and thus not be considered patent infringement).[109] The district court had originally found Merck liable for over $6 million in damages for infringement — but under the new interpretation of the exception, Merck's research was lawful.

However, there are also vast swaths of research not covered by the section 271(e)(1) exception, and this shifts incentives for downstream research. The exception does not cover "[b]asic scientific research . . . performed without intent to develop a particular drug."[110] It does not cover research on techniques that do not need FDA approval, for example trials of changes to nutrition or exercise routines.[111] It does not exempt research in fields where regulatory approval is not required.[112]

There are reports that companies choose projects specifically in response to the incentives provided by section 271(e)(1). Lawyers advising scientists on applying the exception recommended that companies screening multiple compounds "should have a clear understanding of the biological properties and physiological action of those compounds prior to testing" in order to make it plausible that the experiments were aimed toward ultimate FDA submission.[113] But companies that follow this advice may avoid screening less well-characterized compounds, possibly preventing drug discovery.

The section 271(e)(1) exception effectively serves as a tax on research that falls outside the bounds of the statute because this research must pay for a license to upstream patents whereas applied life sciences research does not. Applied life sciences research is undoubtedly an extremely important area of innovation, yet many other areas of innovation are also important. Why are they treated differently?

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[108] *Id.*

[109] The case was remanded for further consideration. *Id.* at 208.

[110] *Id.* at 205-06 ("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.").

[111] The exception is limited to use of patented techniques for the generation 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) (2018).

[112] *Id.*

[113] Alicia A. Russo & Jason Johnson, *Research Use Exemptions to Patent Infringement for Drug Discovery and Development in the United States*, 5 COLD SPRING HARBOR PERSP. IN MEDICINE 1, 10 (2015).

3. Sovereign Immunity

a. Doctrine

Under principles of sovereign immunity, states are not liable for patent infringement.[114] The effect of this doctrine is that state universities cannot be sued for infringement.[115] Researchers at state universities can therefore conduct downstream research without fear of patent infringement.

b. Shifting Incentives

This may benefit downstream research — many positive discoveries arise from state university researchers, and immunity from patent lawsuits may encourage this work. However, even if sovereign immunity aids downstream research at state universities, it also impacts the progress of downstream research as a whole. While state researchers can infringe freely, researchers at private non-profit institutions cannot do so.[116] This effectively favors researchers at public institutions over researchers at private institutions.

Yet much valuable research is developed at both public and private universities.[117] There are excellent researchers at both types of institutions. The doctrine takes researchers of similar skill and aptitude and positions them very differently with respect to patent incentives.

To be sure, one can think of rationales for favoring public universities. For instance, it may be desirable for the government to subsidize research at public institutions because they focus their research on issues of particular importance to their home state. But the doctrine of sovereign immunity as applied to patents was not created

[114] Fla. Prepaid Postsecondary Educ. Expense Bd. v. Coll. Sav. Bank, 527 U.S. 627, 630 (1999).

[115] *Compare* Vicki C. Jackson, *Principle and Compromise in Constitutional Adjudication: The Eleventh Amendment and State Sovereign Immunity*, 75 NOTRE DAME L. REV. 953, 953 (2000) (condemning the "Court's Eleventh Amendment and sovereign immunity case law"), *with* Eugene Volokh, *Sovereign Immunity and Intellectual Property*, 73 S. CAL. L. REV. 1161, 1170 (2000) (arguing against critics of sovereign immunity in the context of intellectual property), *and* Ann Woolhandler, *Old Property, New Property, and Sovereign Immunity*, 75 NOTRE DAME L. REV. 919, 920 (2000) (same).

[116] *See supra* notes 114–115.

[117] For instance, CRISPR was developed at both UC Berkeley (a public university) and the Broad Institute (an institute affiliated with MIT and Harvard, both private universities). *See, e.g.*, Samantha Zyontz, Making the Cut: The Rate and Direction of CRISPR Innovation 28-29 (May 3, 2019) (Ph.D. dissertation, MIT), https://dspace.mit.edu/handle/1721.1/123571 [https://perma.cc/2SKQ-244C].

with these arguments in mind[118] and the effects of treating state institutions differently from private universities with respect to patent infringement is an open empirical question.

Similar questions arise when comparing the effect of the doctrine on public universities versus private companies. Researchers at private companies must pay for licenses to upstream patents.[119] Perhaps these researchers are better able to pay for licenses to conduct downstream research, so there could be a basis for holding them liable for patent infringement while exempting researchers at public universities. However, there may be circumstances in which private companies cannot obtain a license from the upstream patentee even when they try, meaning they must either abandon the downstream research or infringe and pay a penalty — when researchers at state universities could have continued the same project.

The penalties for falling on the wrong side of the immunity divide can be large.

In *Embrex Inc. v. Service Eng'g Corp.*, the plaintiff held a patent on a method of injecting vaccines into a particular part of an egg.[120] The defendant conducted experiments to determine if it could create a similar effect by injecting vaccines into a different part of an egg, a technique that would not be covered by the patent.[121] The vaccine leaked into the portion of the egg named in the plaintiff's patent, unintentionally making the experiment patent infringement.[122] The defendant was liable; damages were $2,873,000.[123] If the experiment had been done at a state university, damages would have been $0. The differential treatment caused by the doctrine is substantial — it may discount research conducted at state universities by several million dollars.

B. Non-Exception Based Doctrines

Some shifts in incentives for downstream innovation are not specific carve-outs from patent infringement but are instead a function of how

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[118] The seminal case on the topic does not mention downstream research at all. *Fla. Prepaid Postsecondary Educ. Expense Bd.*, 527 U.S. at 627.

[119] If the exceptions described herein do not apply to them.

[120] Embrex, Inc. v. Serv. Eng'g Corp., 216 F.3d 1343, 1346 (Fed. Cir. 2000).

[121] *Id.*

[122] *Id.* at 1347.

[123] Brief for Defendants-Appellants at 6, Embrex, Inc. v. Serv. Eng'g Corp., 216 F.3d 1343 (2000), 1999 WL 33630790 (Fed. Cir. 1999), at 6.

patent scope is defined, limits on government powers, and limits on patent enforcement.

1. Geographic

a. Doctrine

Patents exclude others from making or using an invention in only one jurisdiction.[124] A United States patent will, therefore, provide rights only in the United States.[125] Researchers outside the United States can freely conduct activities that would be infringement if they occurred inside the United States.[126] Patentees often file patents in multiple jurisdictions, providing wider coverage, but the basic principle remains the same: patent protection is bounded by a geographic area. Further, many countries broadly exempt research activities from patent infringement, while the United States does not.[127] As a result, downstream research on a technology patented in the United States can occur outside the United States but is banned inside the United States.[128]

b. Shifting Incentives

The geographic limitations of patent enforcement shift incentives for downstream research by favoring foreign research over domestic research. If domestic researchers (other than the patentee) are barred from working on improvements to a particular technology while researchers elsewhere can freely conduct their research, foreign scientists have an advantage in developing second generation versions of the technology. Such rules also incentivize local companies to move

[124] For instance, the United States defines patent infringement as "without authority mak[ing], us[ing], offer[ing] to sell, or sell[ing] any patented invention, *within the United States* . . ." 35 U.S.C. § 271(a) (2018) (emphasis added).

[125] Microsoft Corp. v. AT&T Corp., 550 U.S. 437, 441 (2007) ("[N]o infringement occurs when a patented product is made and sold in another country.").

[126] *E.g.*, John F. Duffy, *Harmony and Diversity in Global Patent Law*, 17 BERKELEY TECH. L.J. 685, 694 (2002).

[127] The World Intellectual Property Association compiles information on research exceptions in its member countries. World Intell. Prop. Org., Standing Committee on the Law of Patents, *Reference Document on Research Exceptions*, Doc. SCP/29/3 (Nov. 26. 2018), https://www.wipo.int/edocs/mdocs/scp/en/scp_29/scp_29_3.pdf [https://perma.cc/96F9-TXFV].

[128] *See* Gregory Day & Steven Udick, *Patent Law and the Emigration of Innovation*, 94 WASH. L. REV. 119, 135 (2019) ("Since technology is generally developed in one country, the innovation process exposes the typical inventor to infringement claims only in that country.").

research units abroad, which would allow a domestic company to circumvent patent laws.[129] This incentive may run counter to efforts to encourage domestic research.

The penalty for conducting research in the United States, instead of abroad, is considerable. For example, DuPont scientists created a glyphosate-resistant seed that, a court later found, infringed on a patent owned by Monsanto.[130] The research project took place in the United States and infringed a United States patent.[131] The patent was not filed in any other countries. DuPont was liable for $1 billion for its infringing research (the penalty was for research only — DuPont never sold its seeds).[132] If DuPont had conducted the research in another country, it would not have been patent infringement, and damages would have been $0.[133]

As with the other doctrines discussed, there are good reasons to limit the extraterritorial reach of U.S. patent law. For instance, it may violate accepted principles of territorial sovereignty and, as a practical matter, not be possible to enforce U.S. patents abroad. But despite sound rationales for the doctrine, it does treat U.S. researchers differently from their international counterparts, possibly with the effect of pushing research abroad.

2. Constructive Reduction to Practice

a. Doctrine

Patent law also shifts incentives through rules for granting patents on downstream research. Downstream inventors can obtain patents on their discoveries as long as they have made nonobvious improvements over the upstream research.[134] However, the downstream invention must also meet all other requirements of patentability. One that poses a particular problem for downstream inventions is the requirement that the inventor reduce the invention to practice and have sufficient information about the invention to teach others how to make and use

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[129] Pamela Samuelson, *Intellectual Property Arbitrage: How Foreign Rules Can Affect Domestic Protections*, 71 U. CHI. L. REV. 223, 224 (2004).

[130] Monsanto Co. v. E.I. Du Pont de Nemours & Co., 748 F.3d 1189, 1192 (Fed. Cir. 2014).

[131] U.S. Patent No. RE39,247 (granted Aug. 22, 2006).

[132] *Monsanto*, 748 F.3d at 1192.

[133] Breach of contract may still have been an issue in the case. *Monsanto*, 748 F.3d at 1195.

[134] Merges, *supra* note 48, at 75.

it.[135] This may be a challenge for downstream inventors because experiments are often necessary to discover an invention and develop it sufficiently for patenting; but when an upstream patent is in force, such experiments are patent infringement.

Patent law provides a path around this problem by allowing downstream inventors to get a patent without conducting physical experiments — patenting through a path called constructive reduction to practice.[136] Under the doctrine of constructive reduction to practice, inventors do not have to physically create or test their invention (which could be an act of patent infringement); instead, they can prove patentability by describing how their invention would be created and used.[137] Since merely thinking and writing about a technology is not an act of patent infringement,[138] constructive reduction to practice allows downstream inventors innovating within an area covered by an upstream patent to obtain their own patent without committing an act of infringement.

b. Shifting Incentives

The doctrine of constructive reduction to practice creates specific incentives for downstream innovation by rewarding researchers who conduct thought experiments or computer modelling to generate hypotheses but punishing researchers who conduct physical experiments to test those hypotheses. Researchers who conduct only thought experiments can obtain patents on their hypotheses, which are valuable to provide leverage in negotiating with upstream patentees for permission to conduct further downstream research.[139] Patent law therefore pushes researchers to get downstream patents before conducting physical experiments. This is likely a counterproductive exercise because many thought experiments will be wrong, and therefore many of the patents will be granted to inventors who cannot make the claimed technology — yet as granted patents, they will stand

[135] Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1352 (Fed. Cir. 2010); Falko-Gunter Falkner v. Stephen Inglis, 448 F.3d 1357, 1366 (Fed. Cir. 2006).

[136] *Ariad*, 598 F.3d at 1352; Cooper v. Goldfarb, 154 F.3d 1321, 1327 (Fed. Cir. 1998); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1374 (Fed. Cir. 1986).

[137] *E.g.*, *Ariad*, 598 F.3d at 1352.

[138] Classen Immunotherapies, Inc. v. Biogen IDEC, 659 F.3d 1057, 1072 (Fed. Cir. 2011) ("Classen's view of its claim appears to have been that [the patents] covered 'thinking' about their subject matter. That is, of course, incorrect.").

[139] Lemley, *supra* note 2, at 990.

in the way of further downstream researchers who want to work in the field.[140]

3. Secret Research

a. Doctrine

Secret research is incentivized over public research. Both types of research are equally infringing as a matter of patent law. But in practice, research that can be conducted in secret or with a minimal audience is less likely to be the subject of a patent infringement lawsuit because the patentee will not discover the infringing behavior — a necessary predicate for the lawsuit.[141] Upstream patents may therefore not pose a practical impediment to secret downstream research.

b. Shifting Incentives

This shifts incentives for downstream research because the same research, if done in public, would be patent infringement.[142] As a result, some types of research are systematically deterred by this aspect of patent law. Such research includes work by academics, since publication is the researchers' goal, and development of technology that requires certain types of regulatory approval, since the approval process may involve some public disclosure.[143] Conversely, research on processes that occur outside of public view or products that are placed on the inside of machines are favored by this aspect of patent law.

Yet both research with public aspects and research that can be done entirely privately could be socially valuable, so why does patent law effectively discourage the former? Indeed, the patent system deeply values public disclosure: one of the main purposes of patents is to force disclosure of inventions that would otherwise remain secret.[144] It is

[140] Janet Freilich, *Prophetic Patents*, 53 UC DAVIS L. REV. 663, 691 (2019) (explaining that predicted results are less likely to be accurate and thus that inventions constructively reduced to practice are less likely to work).

[141] *See* Joseph M. Barich, *Pre-Issuance Publication of Pending Patent Applications: Not So Secret Anymore*, 2001 J.L. Tech. & Pol'y 415, 419 (explaining that patent rights cannot be enforced if the patent owner is unaware of the infringement).

[142] *See* J. Jonas Anderson, *Secret Inventions*, 26 BERKELEY TECH. L.J. 918, 955 (2011) (discussing distorting effects of trade secrecy).

[143] For example, when drugs are approved, they must be accompanied by a label with extensive information about the drug including its ingredients. 21 C.F.R. § 201.10 (2021).

[144] Bonito Boats v. Thunder Craft Boats, Inc., 489 U.S. 141, 151 (1989); Kewanee Oil Co. v. Bicron Corp., 416 U.S. 470, 480 (1974) ("In return for the right of exclusion

disquieting that the patent system expends much effort to ensure that upstream inventions are publicly disclosed (in the form of patents themselves) but may have the effect of discouraging public disclosure of downstream research. The structure of patent law may either disincentivize downstream research that must be made public or deter downstream researchers from publicizing details of their work that could identify infringement, for instance, the specific machine used to conduct a test or the results of negative tests.[145] Both effects create problems, the former because valuable research may not be done and the latter because obfuscation of this sort is known to contribute to replicability problems.[146]

C. Private Choices

Some shifts in incentives for downstream research are not imbedded in patent doctrine, but instead arise from private choices around how and when patentees enforce their patents. There are many factors that go into those choices, which this Section broadly divides into private choices to enforce patents on case-by-case bases and private choices to enforce patents in more general patterns.

. . . the patent laws impose upon the inventor a requirement of disclosure."); United States v. Dubilier Condenser Corp., 289 U.S. 178, 187 (1933); *see also* Jeanne C. Fromer, *Dynamic Patent Disclosure*, 69 VAND. L. REV. 1715, 1716 (2016); Timothy R. Holbrook, *Patents, Presumptions, and Public Notice*, 86 IND. L.J. 779, 784 (2011); Lisa Larrimore Ouellette, *Do Patents Disclose Useful Information*, 25 HARV. J.L. & TECH. 532, 550 (2012); Jason Rantanen, *Patent Law's Disclosure Requirement*, 45 LOY. U. CHI. L.J. 369, 370 (2013).

145 For instance, the patentee in one lawsuit looked at the brand of PCR (polymerase chain reaction) technology disclosed by academics in their publications and used this information to prove infringement. Marcia Barinaga, *Scientists Named in PCR Suit*, 268 SCI. 1273, 1274 (1995) ("Roche scanned the literature for publications that mentioned PCR, searched the materials and methods section for the source of the Taq polymerase, and listed authors who named Promega as their source of *Taq*."). Note that the academics in this case were the direct patent infringers but they were not defendants in the lawsuit, which was filed against an indirect infringer. Hoffmann-LaRoche, Inc. v. Promega Corp., C-93-1748 VRW, 1999 WL 1797330 at *1 (N.D. Cal. Dec. 7, 1999).

146 *E.g.*, Monya Baker, *Is There a Reproducibility Crisis?*, 553 NATURE 452, 452 (2016); Janet Freilich, *The Replicability Crisis in Patent Law*, 95 IND. L.J. 431, 439 (2020); Marcus R. Munafo, Brian A. Nosek, Dorothy V. M. Bishop, Katherine S. Button, Christopher D. Chambers, Nathalie Percie du Sert, Uri Simonsohn, Eric-Jan Wagenmakers, Jennifer J. Ware & John P. A. Ioannidis, *A Manifesto for Reproducible Science*, 1 NATURE HUM. BEHAV. 21, 21 (2017).

1. Choices to Enforce in Individual Cases

a. Doctrine

Patentees are likely to sue infringers conducting high-cost downstream research and unlikely to sue infringers conducting low-cost downstream research. Patentees can seek an injunction or damages, the latter consisting of either reasonable royalties or lost profits.[147] Lawsuits are expensive, so patentees will only bring suit if the remedy is greater than the cost of litigation — either situations where the patentee greatly values enjoining the infringing work or situations where damages will be high. There is often little value in enjoining a research project because a patentee may not find out about the research project until it is finished and published and further, patentees may decline to sue academic infringers because of the reputational costs of such a suit. With respect to damages, research projects that are small in scope will often generate only small damage awards.[148]

But there are certain scenarios where patentees will sue. Enjoining research may be valuable, for example, when research is conducted by competitors or if research has the potential to criticize the patentee's work. For damages, while many infringing research projects would generate small damages, other research projects are worth litigating — for example, the cases described above where DuPont's liability was $1 billion; Merck's was $6 million, and Service Engineering Corp.'s was $2 million.[149]

b. Shifting Incentives

These incentives to litigate shift incentives for downstream research by making some research projects *de facto* non-infringing in the sense that, while the projects are legally infringement, it is highly unlikely

[147] 35 U.S.C. § 284 (2018); eBay Inc. v. Mercexchange, LLC, 547 U.S. 388, 390 (2006). This is in contrast to copyright, where statutory damages are available. 17 U.S.C. § 504(c) (2018).

[148] Damages in a case where the infringement was research, rather than sales, can be determined by calculating a reasonable royalty, meaning the price that the infringer would have paid the patentee to license the patent had they reached an agreement to do so before the infringement occurred. *See* 35 U.S.C. § 284; *see also* Integra Lifesciences I, Ltd. v. Merck KGaA, No. 96-CV-1307-B(AJB), 2004 WL 2284001 at *12 (S.D. Cal. Sept. 7, 2004) ("After finding patent infringement, a jury may award the patentee 'damages adequate to compensate for the infringement, but in no event less that a reasonable royalty for the use made of the invention by the infringer.'" (quoting 35 U.S.C. § 284)).

[149] *See supra* Parts II.A.1–3.

that a suit will ever be brought.[150] Downstream research that is low-cost to the upstream patentee (either in dollar terms or for reputational reasons) may be incentivized, while high-cost research may be deterred.

One effect of this dynamic may be to deter criticism of a patented technology. Patentees have used patent laws to muzzle critics.[151] For instance, a security researcher found flaws in certain RFID chips and planned to present his results at a conference.[152] The manufacturer of the RFID chips — who also held a patent on the technology — threatened to sue the researcher for patent infringement if he presented.[153] The researcher modified his presentation and no suit was filed[154] so it is not clear precisely what part of the research was allegedly patent infringement, but the research involved cloning the RFID chip, which might constitute "making" a new chip and could, depending on the claims of the patent, be patent infringement. The structure of patent law incentivizes patentee-friendly projects, and disincentivizes others.

Differential enforcement creates a second set of incentives. If patentees rarely enforce their patents against downstream research because most research is low-cost to the patentee (which is likely the case), lack of enforcement may create a situation where researchers who are comfortable committing an act that they know violates patent law but where enforcement is unlikely will freely infringe. Researchers who attempt to follow patent law will thus be disadvantaged. Low likelihood of enforcement in the research context means that patent law advantages researchers who do not care about infringement while deterring their more cautious counterparts.[155] Further, such a situation benefits those who are ignorant about patents and infringement while punishing researchers who attempt to learn about upstream patents.[156]

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150 *See supra* Part II.C.1.a.

151 *See* Simon, *supra* note 17, at 1300.

152 *Id.* at 1305; *see also* Jennifer Granick, *Patently Bad Move Gags Critics*, WIRED (Feb. 28, 2007), https://www.wired.com/2007/02/patently-bad-move-gags-critics/ [https://perma.cc/2D7N-9P4S]; Paul F. Roberts, *Lawsuits, Patent Claims Silence Talk*, INFOWORLD (Feb. 27, 2007), https://www.infoworld.com/article/2659928/lawsuits—patent-claims-silence-black-hat-talk.html [https://perma.cc/D8LL-SZ3M].

153 Simon, *supra* note 151, at 1305.

154 *Id.*

155 This argument has something of a parallel in scholarship on the morality of efficient breach in contract law. *E.g.*, CHARLES FRIED, CONTRACT AS PROMISE: A THEORY OF CONTRACTUAL OBLIGATION 17 (Harv. Univ. Press, 1981); Randy E. Barnett, *A Consent Theory of Contract*, 86 COLUM. L. REV. 269, 277 (1986); Daniel Friedmann, *The Efficient Breach Fallacy*, 18 J. LEGAL STUD. 1, 1 (1989); Avery Katz, *Virtue Ethics and Efficient Breach*, 45 SUFFOLK U.L. REV. 777, 779 (2012).

156 This is a problem in patent law in other situations. Enhanced patent damages are available in certain circumstances where the infringer had actual knowledge of the

2. Pledges

a. Doctrine

Patentees may publicly pledge not to enforce their patents, creating incentives for downstream research in areas covered by those patents. There are a number of high-profile examples of these pledges not to enforce: many patentees have pledged not to enforce patents on technology related to COVID-19,[157] Tesla promised not to enforce its patents against anyone using its technology in good faith for an activity relating to electric vehicles.[158] Toyota and Ford followed suit.[159] These pledges incentivize research on the companies' technology by promising a field free of patent infringement. Some patentees even specify that non-enforcement is intended to promote downstream research, for instance, Myriad Genetics promised not to use its patents to "impede non-commercial, academic research."[160]

Pledges are not the only example of how private parties can affect the course of downstream research: parties may release their inventions into the public domain or simply make the choice not to patent their discovery, leaving it free for all.[161]

infringed patent, which is thought to discourage scientists from reading patents, in order to avoid actual knowledge. Dmitry Karshtedt, *Enhancing Patent Damages*, 51 UC DAVIS L. REV. 1427, 1469 (2018); Michael Risch, *The Failure of Public Notice in Patent Prosecution*, 21 Harv. J.L. & TECH. 179, 213 (2007); Lisa Larrimore Ouellette, Halo v. Pulse *and the Increased Risks of Reading Patents*, STAN. L. SCH. BLOGS (June 16, 2016), https://law.stanford.edu/2016/06/16/halo-v-pulse-and-the-increased-risks-of-reading-patents/ [https://perma.cc/XT64-5WH2]. However, empirical work suggests that many researchers nonetheless read patents. *See* Lisa Larrimore Ouellette, *Who Reads Patents?*, 35 NATURE BIOTECHNOLOGY 421, 422 (2017).

157 *About Us*, OPEN COVID PLEDGE (2020), http://opencovidpledge.org [https://perma.cc/2V9U-9U49].

158 Elon Musk, *All Our Patent Are Belong to You*, TESLA (June 12, 2014), https://www.tesla.com/blog/all-our-patent-are-belong-you [https://perma.cc/9TBX-CXC2].

159 Jorge L. Contreras, *Patent Pledges*, 47 ARIZ. ST. L.J. 543, 544 (2015).

160 *The Myriad Pledge*, MYRIAD GENETICS, http://myriad.com/myriad-cares-2/the-myriad-pledge [https://perma.cc/4YUV-B8VE].

161 One example is the patent on insulin. Its inventors sold the patent rights to a public university for $1, saying, "Insulin belongs to the world, not to me." David Beran, Stephen Colagiuri, Nathalie Ernoult, Margaret Ewen, Cynthia Fleury, Molly Lepeska, Pauline Londeix, Elizabeth Pfiester, John S. Yudkin & Stéphane Besançon, *Failing to Address Access to Insulin in Its Centenary Year Would Be a Catastrophic Moral Failure*, 9 LANCET DIABETES ENDOCRINOLOGY 194, 195 (2021).

b. Shifting Incentives

Patentees are, of course, entirely free to make choices about enforcement. These choices very deliberately incentivize downstream research in the area covered by the patent; they are designed to shift the path of downstream research by attracting researchers to that space. In this way, private parties can — like the public doctrines mentioned above — create rules that affect the course of downstream research.

D. Second Level Shifts in Incentives

The Sections above have been dedicated to identifying individual doctrines that shift incentives for downstream research. From these individual doctrines, broader patterns emerge, which I term second level shifts.

1. Exemptions from Uncertainty

It is almost impossible to be entirely certain that specific activities do not infringe on a patent.[162] Doing so requires cutting through so-called "patent thickets,"[163] often involving a freedom-to-operate search that in most contexts is too complex and expensive to be practical.[164] Any project must therefore bear the risk that it infringes one or more patents. The uncertainty around possible infringement is thought to discourage potential innovators from some investigations.[165]

Some of the doctrines discussed above eliminate this uncertainty by exempting downstream research from infringement on *any* patent. Other doctrines apply only to one specific patent, thereby leaving the researcher at risk of liability based on infringement of other patents. Yet others apply to many, but not all, patents, leaving some minimal risk of infringement.

For instance, the section 271(e)(1) research exemption provides that projects covered by the statute will not infringe any patent. There is no risk of patent infringement for this research. Similarly, the doctrine of constructive reduction to practice allows researchers to get patents

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[162] Janet Freilich, *Patent Shopping*, 10 U.C. IRVINE L. REV. 619, 630-31 (2020).

[163] Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard Setting*, *in* 1 INNOVATION POLICY AND THE ECONOMY 119 (2001) ("[O]ur patent system is creating a *patent thicket*: an overlapping set of patent rights requiring that those seeking to commercialize new technology obtain licenses from multiple patentees.").

[164] Christina Mulligan & Timothy B. Lee, *Scaling the Patent System*, 68 N.Y.U. ANN. SURV. AM. L. 289, 317 (2012).

[165] Heller & Eisenberg, *supra* note 70, at 698.

based on mere hypotheses, and because "thinking" is not an act of patent infringement, the act of constructive reduction to practice will never infringe any patent.[166]

By contrast, the first-sale doctrine removes liability for use of a patented product bought in an authorized sale, but only as to the particular patentee who authorized the sale.[167] The product might be covered by patents owned by other parties, and the doctrine does nothing to protect researchers from liability for infringement of those patents. Similarly, private pledges relate to one particular patent or to a group of specific patents.[168] Downstream researchers may still run afoul of patents not included in the pledge.

Other doctrines fall between these extremes, protecting from many, but not all, patents. For example, the limited geographic scope of patents means that a researcher in Argentina will not be liable for infringing a U.S. patent — however, some U.S. patentees file the same patent in Argentina (and even if not, the Argentinian research may infringe some separate Argentinian patent) — therefore a researcher in Argentina cannot be sure that she is protected from liability for patent infringement.[169] Low-cost downstream research is likewise protected from many, but not all, patent suits.[170] If a project infringes five patents, it will often be low-cost with respect to each of those five patents (a small research project will, for example, not produce extensive damages for any infringed patent).[171] But the project is not entirely immune. It is possible that one of the patentees will have an idiosyncratic motivation to sue — reputation-related, for instance — and so even small projects are still subject to some risk of infringement liability.

166 *See supra* Part II.B.2.

167 *See supra* Part II.A.1.

168 *See supra* Part II.C.2.

169 However, many countries have a research exemption that does, in many cases, exempt researchers in those countries from infringement altogether. For a discussion of the research exception worldwide, see generally *supra* note 127.

170 *See supra* Part II.C.1.

171 *See id.*

Table 2: Doctrines that Exempt from Uncertainty
Size of shift in incentives

Smaller → Larger

Doctrines that. . .		
Exempt from one patent	**Exempt from some patents**	**Exempt from all patents**
First-sale exception	Geographic	35 U.S.C. §271(e)(1)
Private pledges	Low-cost research	Sovereign immunity
		Constructive reduction to practice
		Secret research

Researchers will be most incentivized to conduct downstream research when they are entirely protected from the risk of patent infringement. Conversely, if protection only extends to one patent, it may not greatly affect researchers' behavior, particularly in situations where downstream research is covered by many patents. Thus, doctrines that provide cover for all patent-related uncertainty will be particularly impactful as they provide a super-charged incentive for downstream research. It is therefore especially important that these doctrines be directed towards situations where downstream research is desirable.

2. Doctrines Affecting Projects and Institutions

Some paths around patent infringement are targeted at specific research projects and others are specific institutions. This means that some research projects can be transferred to another researcher or can bring in a collaborator from a different institution and remain exempt from infringement.[172] Other research projects may lose their exempt status if they do so.[173]

[172] For instance, those exempt from infringement under the first-sale doctrine. *Supra* Part II.A.1.

[173] For instance, those exempt from infringement under the doctrine of sovereign immunity. *Supra* Part II.A.3.

For example, under the doctrine of sovereign immunity, a scientist at a state university could conduct a research project without concern for patent infringement. However, if that scientist got hired by a private university, he would have to get a license from the patentee before continuing with the project (or abandon the project, if licensing proved too difficult).[174] Similarly, the state university scientist might not be able to collaborate with scientists at a private company, even if such a collaboration would be beneficial to advancing the research.[175] Analogously, a U.S. company purchasing rights to a research project begun abroad would not be able to bring that project home without worrying about a license.[176]

By contrast, if the doctrine runs with the research, rather than the researcher, moving the research project is not a concern from the standpoint of patent infringement. If research is conducted under the first-sale exception, that research could be transferred to another institution and continued without disrupting the exception.

Some doctrines are combinations. Low-cost research, in particular, can be ignored by patentees for reasons relating to the research (for example, one with minimal infringement) or for reasons relating to the researcher (research by universities may be less concerning to patentees than research by competitors). Low-cost research can become high-cost with respect to either the project or the institution — projects with minimal infringement can grow; university research can be licensed to competitors.

This second level shift in incentives favors activities subject to doctrines that run with the research, rather than the researcher, because there are more avenues for collaboration.[177] This raises important questions about the goal of research exceptions. Is the purpose of exceptions to invest resources in certain *projects* or is it to invest resources in certain types of *institutions*? This division mirrors a debate in the literature on grants — another method of supporting innovation[178] — about whether grants should fund individuals directly (such as a MacArthur Foundation Genius Grant or Howard Hughes

174 *See supra* Part II.A.3.

175 *Id.*

176 *See supra* Part II.B.1.

177 This assumes, of course, that the collaborator could not easily get a license from the upstream patentee.

178 *See* Pierre Azoulay, Danielle Li, Joshua S. Graff Zivin & Bhaven N. Sampat, *Public R&D Investment and Private-sector Patenting: Evidence from NIH Funding Rules*, 86 REV. ECON. STUD. 117, 117 (2019); *see also* Daniel Hemel & Lisa Larrimore Ouellette, *Beyond the Patents-Prizes Debate*, 92 TEX. L. REV. 303, 320 (2013).

grant) or whether grants should be targeted towards specific projects.[179] Both approaches can be useful, but create different incentives. Scholars contrasting patents with other types of innovation incentives such as grants and taxes have argued that a point of contrast between patents and these other incentives is that patent are unable to target particular individuals or institutions — but doctrines shifting incentives for downstream research may provide a mechanism for patents to do just that.[180]

The most desirable configuration for doctrines affecting downstream research is an empirical question beyond the scope of this paper. However, it is a question that should be addressed to the extent that doctrines are created deliberately — in the current haphazard and often accidental environment for these doctrines, there has been little deep analysis about whether the doctrines should attach to projects or to institutions.

Table 3: Doctrines that run with research projects; doctrines that run with research institutions

Doctrines that…		
Attach to projects	**Are a combination**	**Attach to institutions**
First-sale exception	Low-cost research	Sovereign immunity
35 U.S.C. § 271(e)(1)		Geographic
Constructive reduction to practice		
Secret research		
Private pledges		

[179] W. Nicholson Price II, *Grants*, 34 BERKELEY TECH. L.J. 1, 50-54 (2019); Pierre Azoulay, Joshua S. Graff Zivin & Gustavo Manso, *Incentives and Creativity: Evidence from the Academic Life Sciences*, 42 RAND J. ECON. 527, 527-54 (2011) (studying differences between outcomes of grants that fund institutions and those that fund projects); W. Nicholson Price II, *Grants*, 34 BERKELEY TECH. L.J. 1, 50-54 (2019).

[180] Price, *supra* note 179, at 50.

3. Lifecycle Doctrines

As downstream research moves from start to finish, it may also move in and out of various doctrines. This temporal cycling diminishes the impact of certain doctrines because they will be useful for only part of the research project. Take, for example, a life sciences research project that begins by seeking to understand the function of a certain cellular pathway, but does not have an application in mind at that point. At the conception stage, when the research team is simply brainstorming the idea and setting out plans for lab protocols, the project would not be infringement because thinking about an idea is not infringement. Once the team began the physical steps of research, the project would be patent infringement if it falls within the scope of an upstream patent.[181] As the project develops, the team might discover a clinical endpoint and begin to think about how the research could contribute to developing a treatment for some disease. At this point, the project would cease to be patent infringement because it would fall into section 271(e)(1).

It makes little sense for a project to cycle in and out of infringement. It minimizes the utility of the doctrine(s) that do apply — in the example above, there is no point in having an exception to patent infringement to allow late-stage research if the early-stage research that is a necessary predicate for the late-stage research cannot be done.[182] Thus, the incentives created by partial-lifecycle doctrine will be weaker than their counterparts that apply across the lifecycle of a project.

Some doctrines will protect a project throughout its development. For example, research done outside the United States will never infringe on a United States patent no matter how the research develops.[183] Similarly, many private patentees have pledged that they will not enforce their patents downstream, including once a research project reaches commercialization.[184] Likewise, the first-sale exception has no restrictions, so it protects a research project from the very earliest stages when the researcher buys a commercially available product through to

[181] While some early-stage research might be covered by 35 U.S.C. § 271(e)(1), other early-stage research will not be. The precise contours of the doctrine with respect to early-stage research are not clear, but the Supreme Court has noted that some early-stage research (specifically "[b]asic scientific research on a particular compound, performed without the intent to develop a particular drug . . . ") is "surely not" within the exception. Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 205-06 (2005).

[182] In practice, this early-stage research might be done by academic researchers, even though it infringes, because patentees will often not sue academic researchers. The results might then be used to develop a clinical product.

[183] Assuming importation into the U.S. is not a research stage.

[184] Though some private pledges apply only to academic research.

the end of stages of the product, including, under some circumstances, commercialization.[185]

Other doctrines are more of a middle ground, protecting all stages of certain projects but only portions of others. Some secret research, for example, can only remain secret at early stage, and must be publicized as it develops, at which point it loses protection from infringement.[186] Other secret research can stay secret forever, even after commercialization.[187] This type of secret research will never be subject to infringement liability. Similarly, the end goal for some academic research is publication, in which case the research is protected by the doctrine of sovereign immunity from start to finish. Other academic research is ultimately licensed to private companies for further development, at which point sovereign immunity would cease to apply.

Table 4: Doctrines and Life-Cycle Changes
Size of shift in incentive

Smaller → Larger

Doctrines that. . .		
Are stage-dependent	**Are a combination**	**Last forever**
35 U.S.C. § 271(e)(1)	Low-cost research	Private pledges
Constructive reduction to practice	Sovereign immunity	Geographic
	Secret research	First-sale exception

Generally, doctrines that protect projects over their lifetime will create more impactful incentives, particularly if they include protection for commercial sales.

E. Upstream Shifts in Incentives

This Article has enumerated shifts in incentives to downstream research caused by various patent doctrines. Each incentive for

[185] Some companies are in the business of buying a commercially available patented product, changing it in some way, and re-selling it. This is protected under the first-sale exception. Quanta Comput., Inc. v. LG Elecs., Inc., 553 U.S. 617, 621 (2008).

[186] For instance, early-stage drug development is often confidential, but later-stage clinical trials in humans must be publicly disclosed. 42 C.F.R. § 11.2 (2021).

[187] An internal process used to produce some commercial product, for example.

downstream research, however, creates a corresponding incentive for upstream research. If downstream researchers are not liable for acts that would otherwise infringe patents, the value of the upstream patent is diminished.[188] Where doctrines increase downstream incentives to innovate, they may commensurately decrease upstream incentives to innovate.[189] This Article will not delve deeply into the impact of upstream incentives except to recognize their existence and note that any change to incentives for downstream research must consider its upstream counterpart.

III. EXPANDING THE MODEL: IMPLICATIONS, AND POLICY

A. Implications

1. Accidental Incentives

At its core, the problem with doctrines that shift incentives for downstream research is that they provide the wrong motivations to innovators. Downstream researchers must pay the patentee for the right to conduct experiments in areas covered by the patent and must also grapple with transaction costs including interpreting the patent,[190] finding the patentee,[191] and negotiating a license. Some types of downstream projects can be completely blocked by the patentee.[192] These costs all serve as a tax on downstream innovation.

But there are certain areas of downstream research not subject to this tax — areas where infringement liability does not apply for one reason or another. It is less costly to conduct research in these areas, both in pure dollar terms (because the upstream patentee need not be paid[193])

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188 Unless the upstream patentee desires more research on applications for their invention, in which case it might increase the value of the upstream patent.

189 This has been discussed extensively in the literature on research tool patents. Eisenberg, *supra* note 68, at 698; Natalie M. Derzko, *In Search of a Compromised Solution to the Problem Arising from Patenting Biomedical Research Tools*, 20 SANTA CLARA HIGH TECH. L.J. 347, 362 (2004); Mueller, *supra* note 69, at 33-37; Strandburg, *supra* note 68, at 131.

190 JAMES E. BESSEN & MICHAEL J. MEURER, PATENT FAILURE: HOW JUDGES, BUREAUCRATS, AND LAWYERS PUT INNOVATORS AT RISK 53 (2008).

191 This is often surprisingly difficult. *See* Nathan P. Anderson, *Striking a Balance: The Pursuit of Transparent Patent Ownership*, 30 BERKELEY TECH. L.J. 395, 396 (2015).

192 Simon, *supra* note 17, at 1299.

193 In the context of the first-sale exception, the patentee is still paid — through purchase of a commercially available product. However, the patentee cannot block the downstream research and therefore has no leverage to charge inflated prices for a

and because the uncertainty of facing patent rights is alleviated. Avoiding upstream patent rights is a great advantage to researchers in these exempt areas — perhaps enough of an advantage to incentivize downstream research in exempt areas and commensurately disincentivize downstream research in areas still subject to patent infringement.

Exemptions from patent infringement can therefore direct the progress of downstream research. This is a powerful tool. But under current law it is not used intentionally. Almost every shift catalogued above is accidental.[194] Most doctrines were created by laws that were not intended to affect downstream research. For instance, the first-sale doctrine, which shifts incentives for downstream research towards investigations of new methods of use and away from new methods of making, originates from a Supreme Court decision about the limits of property rights[195] and concerns about servitudes running with personal property.[196] The case first articulating the doctrine, *Bloomer v. McQuewan*, does not discuss the doctrine's impact on downstream research — the effect of downstream research was probably not under consideration in any way.[197] Yet the first-sale doctrine may indeed affect the path of downstream research. Because this impact is accidental, it is also quite arbitrary: there is no particular reason to favor research on methods of use over methods of making, as the doctrine does.

Even doctrines specifically intended to exempt certain areas of downstream research from patent infringement have accidental impacts. The statutory research exception, 35 U.S.C. § 271(e), was deliberately enacted to allow generic companies to conduct research on patented drugs before the patent expired.[198] However, it is not clear that

downstream license, as might happen for products that do not fall into the first-sale exception.

194 This is not the only way in which incentives for innovation are accidental. For a different type of accidental innovation incentive involving healthcare policy choices, see Rachel E. Sachs, *The Accidental Innovation Policymakers*, (forthcoming) (on file with author).

195 Bloomer v. McQuewan, 55 U.S. (14 How.) 539, 549 (1852) ("[W]hen the machine passes to the hands of the purchaser, it is no longer within the limits of the monopoly . . . . The implement or machine becomes [the buyer's] private, individual property, not protected by the laws of the United States.").

196 Keeler v. Standard Folding-Bed Co., 157 U.S. 659, 667 (1895) ("The inconvenience and annoyance to the public [of restrictions attached to the sale of patented goods] are too obvious to require illustration."); Andrew T. Dufresne, *The Exhaustion Doctrine Revived? Assessing the Scope and Possible Effects of the Supreme Court's* Quanta *Decision*, 24 BERKELEY TECH. L.J. 11, 14-15 (2009).

197 *Bloomer*, 55 U.S. (14 How.) 539.

198 Weiswasser & Danzis, *supra* note 98, at 604-06.

the statutory provision was originally intended to apply to any life sciences research that supports regulatory approval, which is how the standard is currently interpreted.[199] And the statute was almost certainly not intended to *punish* researchers conducting basic life sciences experiments directed towards general knowledge, but not a specific application subject to regulatory approval. Yet the statute's effect is to tax this basic research while discounting the price of applied research.

Other shifts in incentives for downstream research are deliberate in the sense that they are a known and understood effect of creating a patent law, but accidental in the sense that the shift was not a desired outcome of the law. This applies to the geographic scope of patent law, for example. If a U.S. patent exists, downstream research conducted in the U.S. will infringe, while research conducted outside the U.S. will not. It is no accident that patent infringement follows sovereign borders, and the opportunities for arbitrage have long been understood.[200] But it is still important to recognize that researchers in different countries are subject to different rules with respect to patent infringement.

2. Compounding Incentives

The doctrines described above apply not only to downstream research, but also to how downstream patents are allocated. As explained below, these doctrines favor research by certain entities, who can then get their own patents and use them to perpetuate shifts in incentives. In other words, shifts in incentives compound.

Take, for example, a patent on a widget. A state university researcher and a private university researcher are both interested in improving the patented widget. The state university researcher goes ahead with her researcher without considering the upstream patent because she is immune from infringement.[201] The private university researcher attempts to negotiate a license with the patentee. The patentee agrees to the license, but the negotiations take three months and the researcher must then apply for a grant to cover the cost of the license, further delaying the research. Just as the private university researcher begins his project, the state university researcher — who has gotten a head start on her work — succeeds in making a second-generation widget and files for a patent on her invention. The private university researcher thinks his improvement is better than the one patented by the state university researcher, but also realizes that it falls into the scope of her

199 *See supra* Part II.A.2.a.

200 Samuelson, *supra* note 69, at 223-26.

201 *See supra* Part II.A.3.a.

patent. He therefore needs to negotiate a license with her before he can proceed.

The generalizable point is that research projects that are not subject to infringement have an advantage in getting the second generation of intellectual property rights. This amplifies the effect of the doctrine exempting them from infringement because research projects that are on the wrong side of the doctrine must now address two patents. It also lengthens the doctrine's effect because the effect does not end with the first patent's term but instead effectively extends to the end of the second patent's term.

The scenario with the researchers above may not happen often in practice because university researchers are rarely sued for patent infringement.[202] But it can and does occur with shifts in incentives for downstream research arising from the doctrine of constructive reduction to practice. Downstream researchers who merely think about an improvement to an upstream invention do not infringe an upstream patent, whereas downstream researchers who physically create an improved invention do infringe upstream patents.[203] However, untested hypotheses are enough to support a downstream patent.[204] This means that downstream researchers who think hard about potential applications of an upstream technology can get a series of patents on those applications and then block other downstream researchers who want to test their own ideas for improvements.

For example, Nathan Myhrvold, the founder of Intellectual Ventures, one of the largest patent assertion entities ("PAE", known pejoratively as a patent troll) is in the business of getting patents and asserting them when they are infringed.[205] Myhrvold is listed as an inventor on many patents that claim inventions that have not been physically created — but rather have been constructively reduced to practice.[206] Myhrvold

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[202] *E.g.*, John P. Walsh, Ashish Arora & Wesley M. Cohen, *Working Through the Patent Problem*, 299 SCIENCE 1021, 1021 (2003) ("[I]ndustrial [patentees] agreed that the small prospective gains from a lawsuit were not worth the legal fees, the risk of the patented being narrowed or invalidated, and the bad publicity from suing a university.").

[203] *See supra* Part II.B.2.a.

[204] Freilich, *supra* note 140, at 672-74.

[205] Nathan Myhrvold, *The Big Idea: Funding Eureka!*, HARV. BUS. REV. (Mar. 2010), https://hbr.org/2010/03/the-big-idea-funding-eureka [https://perma.cc/Z8XZ-HD7K].

[206] For example, the experiments in the following patents are labeled as "prophetic," meaning that they are hypothetical, not physical, experiments. U.S. Patent No. 8,724,251 (granted May 13, 2014); U.S. Patent No. 8,167,871 (granted May 1, 2012); U.S. Patent No. 8,815,163 (granted Aug. 26, 2014); U.S. Patent No. 10,311,293 (granted June 4, 2019); U.S. Patent No. 9,286,615 (granted March 15, 2016); U.S. Patent No.

himself need not fear suit for patent infringement because he has not actually used any of the inventions his patents build on — his experiments are only hypothetical. But he is able to construct his own patent portfolio and assert it against others who fall on the other side of the downstream research incentive.

This asymmetry, where some entities are able to obtain patents without infringement but other entities working in the same field do infringe, is a dynamic that will be familiar to scholars of PAEs.[207] Traditionally, companies held patents to protect their own products and to assert against competitors.[208] These competitors might infringe patents, but the owners of the infringed patents might infringe patents themselves.[209] Reciprocal threats of infringement prevented suits. PAEs destabilized this dynamic because they do not produce their own products but are instead solely in the business of asserting patents.[210] This means that they are generally not infringing on patents themselves, and need not worry about a countersuit.[211] A similar asymmetry is created by doctrines affecting incentives for downstream research: some entities can obtain their own patents but need not fear infringing others' patents.

3. Patent Law Is Unitary, Not Bifurcated

Studying shifts in incentives for downstream innovation reveals a larger problem in patent policy and scholarship. Policy and scholarship are bifurcated into two separate areas of focus. One area addresses how patent law affects research — for example, discussions of how broad patents affect research or analysis of whether the demise of the research exemption would affect downstream research.[212] The second area of

8,721,618 (granted May 13, 2014); U.S. Patent Application No. 20160245880 (filed Feb. 2, 2015); U.S. Patent Application No. 20130046235 (filed Aug. 16, 2011).

[207] *See* Mark A. Lemley & A. Douglas Melamed, *Missing the Forest for the Trolls*, 113 COLUM. L. REV. 2117, 2129 (2015); *see also* Gideon Parchomovsky & R. Polk Wagner, *Patent Portfolios*, 154 U. PA. L. REV. 1, 26-27 (2005).

[208] Freilich, *supra* note 162, at 625-26.

[209] John R. Allison, Mark A. Lemley, Kimberly A. Moore & R. Derek Trunkey, *Valuable Patents*, 92 GEO. L.J. 435, 469 (2004); Colleen V. Chien, *Of Trolls, Davids, Goliaths, and Kings: Narratives and Evidence in the Litigation of High-tech Patents*, 87 N.C. L. REV. 1571, 1582 (2009) ("If you build up your patent portfolio, I build up mine—nukes pointing at each other . . . . That has exactly the right outcome. We sit here and exchange patents with each other." (quoting a Sun Microsystems executive)).

[210] Colleen V. Chien, *From Arms Race to Marketplace: The Complex Patent Ecosystem and Its Implications for the Patent System*, 62 Hastings L.J. 297, 300 (2010).

[211] *Id.*

[212] *See supra* notes 65–69 (discussing how patent law affects downstream research).

focus addresses how patent law affects product availability and prices — for example, how patents impact access to affordable medicines or the impact of patent law on standard setting organizations.[213] Each area of focus has produced plentiful policy proposals. However, these policy proposals are typically analyzed only in terms of how they will affect the particular area of focus: research *or* sales, but not both.[214] Assessment of the effects of patent policy is therefore segregated by area of focus.

Policy analysis is split, but patent law is unitary. A law passed to address product availability will also address research. Holes carved into the patent right are available for sales and research alike. In consequence, a policy targeted at sales will also impact research. The first-sale exception, for example, is typically discussed in the context of its effect on sales.[215] But it also has an effect on research.[216]

Similarly, patches that apply only to sales will leave problems remaining for research. For example, patents on methods or processes can be circumvented by conducting the method outside of the United States and importing the finished product into the United States.[217] To resolve this problem, Congress passed 35 U.S.C. § 271(g), which made it an act of infringement to import into the United States "a product

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[213] *E.g.*, Jorge L. Contreras, *Fixing FRAND: A Pseudo-pool Approach to Standards-based Patent Licensing*, 79 ANTITRUST L.J. 47, 48 (2013); Cynthia M. Ho, *Global Access to Medicine: The Influence of Competing Patent Perspectives*, 35 FORDHAM INT'L L.J. 1, 78 (2016); A. Douglas Melamed & Carl Shapiro, *How Antitrust Law Can Make FRAND Commitments More Effective*, 127 YALE L.J. 2110, 2111 (2018); David W. Opderbeck, *Patents, Essential Medicines, and the Innovation Game*, 58 VAND. L. REV. 501, 502 (2005); F.M. Scherer, *The Pharmaceutical Industry and World Intellectual Property Standards*, 53 VAND. L. REV. 2245, 2247 (2000).

[214] *See supra* notes 74–83, 213 (discussion the implications of patent law on downstream research and how they affect sales.).

[215] *E.g.*, Impression Prods. v. Lexmark Int'l, Inc., 137 S. Ct. 1523, 1525 (2017) (discussing whether a seller of toner cartridges can restrict buyers' ability to resell the cartridge); Quanta Comput., Inc. v. LG Elecs., Inc., 553 U.S. 617, 624 (2008) (deciding whether a seller could prevent a buyer from combining the sold products with others and reselling).

[216] *See supra* Part II.A.1.

[217] For example, a patent claiming "a method of making widgets by combining part A and part B" would not be infringed if a third party shipped parts A and B to a manufacturer in Nepal who then combined the parts (an action which would be infringing if it occurred in the United States) and sent the product back to the United States. *E.g.*, Deepsouth Packing Co. v. Laitram Corp., 406 U.S. 518, 519 (1972) (Company A held two combination patents for machinery used for deveining shrimp. Company B, which was enjoined from making or selling the deveining machines throughout the United States, sought actions to sell the parts outside of the U.S.).

which is made by a process patented in United States."[218] This prevents sales in the United States of a product made abroad by a process patented in the United States.[219] However, 35 U.S.C. § 271(g) does not solve the same loophole for research. There is no prohibition on conducting research abroad using a technique patented in the United States and then importing the results of that research back into the United States. In *Bayer v. Housey*, Housey owned U.S. patents on a method of screening for substances that might be useful as drugs.[220] Bayer used Housey's method outside of the United States to discover certain compounds with potential as pharmaceutical treatments.[221] Bayer then imported those products into the United States.[222] The Federal Circuit held that section 271(g) did not apply — that Bayer had not infringed Housey's patents — because the patented process had been used to generate information, not to manufacture a product.[223] The loophole patched by section 271(g) was therefore closed only with respect to sales, but not with respect to research.

The effect of bifurcated thinking about patent policy creates blind spots for scholars. It is obvious that a change to a research exception (such as the Federal Circuit's decision in *Madey*[224] to essentially eliminate the general research exception) will affect research — and there is much scholarship to that effect.[225] But it is less obvious that

[218] 35 U.S.C. § 271(g) (2018) ("Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, offer to sell, sale, or use of the product occurs during the term of such process patent.").

[219] The House report explained that the rationale for the new law was to fix the problem that allowing sales of imported products created according to patented processes "ignores the reality that the offending act is the importation of a product made through the use of a protected patent or its subsequent sale within the United States." H.R. REP. NO. 99-807, at 2 (1986).

[220] Bayer AG v. Housey Pharms., Inc., 340 F.3d 1367, 1369 (Fed. Cir. 2003).

[221] *Id.* at 1370.

[222] *Id.*

[223] *Id.*

[224] Madey v. Duke University, 307 F.3d 1351 (Fed. Cir. 2002).

[225] The Federal Circuit's decision in *Madey* was criticized on these grounds. *See* Rebecca S. Eisenberg, *Patent Swords and Shields*, 299 SCI. 1018, 1018 (2003) ("[The *Madey* decision was] an alarming wake-up call to the academic community."); David Malakoff, *Academia Gets No Help from U.S. in Patent Case*, 300 SCI. 1635, 1635 (2003) ("[T]he case stunned many university administrators, who predict that it will slow academic research and increase costs."); Jennifer Miller, *Sealing the Coffin on the Experimental Use Exception*, 2 DUKE L. & TECH. REV. 1, 6 (2003) ("[R]esearch institutions . . . will be at the mercy of patent holders."); Janice M. Mueller, *The Evanescent Experimental Use Exemption from United States Patent Infringement Liability:*

when a research exception is taken away (as in *Madey*), a number of doctrines intended to affect sales would then affect research, as research was no longer exempted from patent infringement.

4. Crystalizing the Impact of Patents on Downstream Research

As noted above, there is an extensive literature on downstream research, but it makes certain simplifying assumptions about the relationship between upstream and downstream innovation. This Article adds complexity to our understanding of upstream patents and downstream research and thereby helps clarify various arguments in the existing literature.

First, much writing begins with the premise that patents block downstream research.[226] This Article demonstrates that while patents may indeed hamper downstream research, they do not block it completely — patents *shift* downstream research by blocking some forms of downstream research but not others. Second, another stream of literature on downstream innovation notes that downstream innovation exists but does not provide a mechanism for how it happens even when an upstream patent is present.[227] This Article emphasizes that while some downstream innovation may happen after licensing or infringement, there is a third path: downstream innovation can happen quite permissibly without a license as long as it follows one of the paths that avoids infringement.

However, while exceptions permit downstream innovation along certain paths, upstream patents can still dampen incentives for downstream innovation, even in areas covered by exceptions. The

Implications for University and Nonprofit Research and Development, 56 BAYLOR L. REV. 917, 920 (2004) (arguing that the Federal Circuit's unfriendliness towards the research exemption will cause research "to be shifted offshore to legally hospitable forums"); David G. Sewell, *Rescuing Science from the Courts: An Appeal for Amending the Patent Code to Protect Academic Research in the Wake of* Madey v. Duke University, 93 GEO. L.J. 759, 759 (2005) ("[T]he legal edifice on which modern academic research is based began to crumble."); Cristina Weschler, *The Informal Experimental Use Exception: University Research After* Madey v. Duke University, 79 N.Y.U. L. REV. 1536, 1537 (2004) ("[It will be] difficult, if not impossible, for university researchers to rely on [the experimental use defense] in patent infringement suits."); Brief for Ass'n of American Medical Colleges et al., as Amici Curiae in Support of Petitioner at 14, Duke Univ. v. Madey, 123 S. Ct. 2639 (2003) (No. 02-1007) (expressing "grave concerns" that narrowing the research exception would "encourage patent holders to assert claims in a manner that will altogether frustrate university scientists' ability to make further basic advances in critical areas of biotechnology and biomedicine").

226 *See supra* Part I.B.1.

227 *See supra* Part I.B.2.

doctrines discussed in this Article apply to *research*. They do not apply to *sales*. Someone other than the upstream patentee can conduct research and develop an improved technology without infringement. But this entity cannot sell the fruit of their research without the patentee's permission.[228] This constraint on later sales might reduce incentives for earlier research, although the incentives created by blocking downstream sales will affect research at for-profit companies much more than research at non-profit entities.[229]

a. Reinterpreting Empirical Studies

More precisely explaining incentives for downstream innovation is important because it allows improved interpretation of empirical studies of the downstream effects of patents.[230] This is in turn important because these empirical studies are deeply influential that have played a vital role in policy debates.[231] Yet their use in policy debates results from imprecise interpretation of the studies.[232]

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[228] Sales are generally infringement. Some of the exceptions listed above do apply to sales in certain ways — for example, a foreign company could research and sell a downstream innovation abroad, but could not sell it in the US. Similarly, an innovator could buy a patented item and incorporate that item into another product and then sell that product — this innovator would be protected under the first sale doctrine. *See* Quanta Comput., Inc. v. LG Elecs., Inc. 553 U.S. 617, 621 (2008).

[229] Acorda Therapeutics, Inc. v. Roxane Labs., Inc., 903 F.3d 1310, 1337 (Fed. Cir. 2018) ("The existence of such a blocking patent may deter non-owners and non-licensees from investing the resources needed to make, develop, and market such a later, 'blocked' invention, because of the risk of infringement liability.").

[230] *See* Jonathan H. Ashtor, *Does Patented Information Promote the Progress of Technology?*, 113 NW. U. L. REV. 943, 948 (2018); Alberto Galasso & Mark Schankerman, *Patents and Cumulative Innovation: Causal Evidence from the Courts*, 130 Q.J. ECON. 317, 317 (2014); Kenneth G. Huang & Fiona E. Murray, *Does Patent Strategy Shape the Long-Run Supply of Public Knowledge? Evidence from Human Genetics*, 52 ACAD. MANAGEMENT J. 1193, 1196 (2009); Fiona Murray & Scott Stern, *Do Formal Intellectual Property Rights Hinder the Free Flow of Scientific Knowledge? An Empirical Test of the Anti-Commons Hypothesis*, 63 J. ECON. BEHAV. & ORG. 648, 648 (2007); Sampat & Williams, *supra* note 73, at 203; Heidi L. Williams, *Intellectual Property Rights and Innovation: Evidence from the Human Genome*, 121 J. POL. ECON. 1, 1 (2013).

[231] For instance, Bhaven Sampat's and Heidi L. Williams' article, *How Do Patents Affect Follow-on Innovation? Evidence from the Human Genome*, Sampat & Williams, *supra* note 73, was cited in recent hearings before the Senate Judiciary Committee. *Subcommittee Hearing on "The State of Patent Eligibility in America, Part II"*, 116th Cong. (2019) (testimony of Hans Sauer, Ph.D., Deputy General Counsel and Vice President for Intellectual Property, Biotechnology Innovation Organization ("BIO")), https://www.judiciary.senate.gov/imo/media/doc/Sauer%20Testimony.pdf [https://perma.cc/38MG-QATL].

[232] *See* Janet Freilich & Sepehr Shahshahani, *Measuring Follow-on Innovation* (draft on file with author).

The general challenge with these empirical studies is that they attempt to measure how much innovation occurs in an area covered by a patent and compare that to innovation in comparable scenarios not covered by the patent. But many studies assume that downstream innovation covered by an existing patent always constitutes patent infringement. That is not entirely accurate. Patents shift incentives innovation in a field, allowing some activities but not others. Some measures of downstream innovation in these studies are therefore not actually patent infringement. The studies still provide valuable information about the impact of patents on downstream innovation, but the interpretation of the results should be somewhat different.

b. Guiding Patent Doctrine

Understanding precisely how and when downstream research occurs also informs an important question of patent doctrine. The Federal Circuit is split on (and the Supreme Court has so far declined to resolve[233]) the question of how the presence of an upstream patent impacts evidence on the obviousness of a downstream invention.[234] Courts are often asked to determine whether a patented invention is obvious, and, in consequence, whether the patent should be invalidated.[235] This inquiry is challenging because it occurs many years after the invention was first conceived, and what looks obvious in hindsight may not have been obvious at all years earlier.[236]

To reduce the risk of hindsight bias, courts employ "objective indicia of non-obviousness" (also called "secondary considerations of non-obviousness"[237]).[238] These are, as the name suggests, objective

[233] Allergan, Inc. v. Teva Pharms. USA, Inc., 742 F. App'x 511 at *1 (Fed. Cir. 2018), *cert. denied*, 139 S. Ct. 2674 (2019); *Acorda*, 903 F.3d at 1342, *cert denied*, 140 S. Ct. 111 (2019); Merck & Co. v. Teva Pharms. USA, Inc., 395 F.3d 1364, 1377 (Fed. Cir. 2005), *cert. denied*, 546 U.S. 972 (2005).

[234] *Compare* Galderma Lab'ys., L.P. v. Tolmar, Inc., 737 F.3d 731, 740 (2013) (holding that certain objective indicia of nonobviousness are not relevant in the presence of a blocking patent), *with* Merck Sharp & Dohme Corp. v. Hospira, Inc., 874 F.3d 724, 730 (2017) (holding that objective indicia "should not [be] discounted" because of a blocking patent because such a patent does not block all downstream research and development).

[235] 35 U.S.C. § 103 (2018).

[236] Gregory N. Mandel, *Patently Non-obvious: Empirical Demonstration That the Hindsight Bias Renders Patent Decisions Irrational*, 67 OHIO ST. L.J. 1391, 1393 (2006).

[237] *See generally* Dmitry Karshtedt, *Nonobviousness: Before and After*, 106 IOWA L. REV. 1609, 1638 (2021) (discussing the alternate terminology).

[238] Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 17-18 (1966).

indicators that an invention was not obvious at the time it was made.[239] For example, if there was a long-felt need for an invention, but nobody had made it, the inference is that creating the invention was no obvious task.[240] If others tried to create the invention but failed to so, the invention is probably not obvious.[241] Similarly, if the invention was a commercial success, it is less likely to be obvious, since others would presumably have taken the opportunity to succeed commercially if it were obvious to do so.[242]

However, objective indicia of non-obviousness play out quite differently in the presence of an upstream patent. For example, imagine that company A owns a patent on widgets and company B licenses the patent and makes a certain widget improvement. The widget improvement is a wild success — lauded by industry experts as the solution to a long-standing problem and sold to millions of consumers. But is this success evidence that the invention was not obvious? Perhaps not. If company A declined to license its patent to anyone other than company B, others could not have solved the long-standing problem, even if the solution was obvious. Similarly, others could not have experienced commercial success. And finally, others may have tried and failed to make the widget improvement not because it was nonobvious but because they were trying to design around company A's patent. Thus, the presence of an upstream patent may complicate interpretation of objective indicia of nonobviousness.

In recent years, the Federal Circuit has decided a series of cases that find that, a blocking patent "can discount the significance" of objective indicia of nonobviousness.[243] This has the effect of making it easier for a challenger to argue that a patent is obvious, because the objective

239 *See id.*

240 *E.g.*, Goodyear Tire & Rubber Co. v. Ray-O-Vac Co., 321 U.S. 275, 279 (1944) ("During a period of half a century, in which the use of flashlight batteries increased enormously, and the manufacturers of flash light cells were conscious of the defects in them, no one devised a method of curing such defects.").

241 *E.g.*, Expanded Metal Co. v. Bradford, 214 U.S. 366, 381 (1909) ("It may be safely said that if those skilled in the mechanical arts are working in a given field, and have failed, after repeated efforts, to discover a certain new and useful improvement, that he who first makes the discovery has done more than make the obvious . . . .").

242 Merck & Co., Inc. v. Teva Pharms. USA, Inc. 395 F.3d 1364, 1376 (2005) ("[T]he law presumes an idea would successfully have been brought to market sooner, in response to market forces, had the idea been obvious to persons skilled in the art.").

243 *Id.* at 1377; Acorda Therapeutics, Inc. v. Roxane Lab'ys., Inc., 903 F.3d 1310, 1339 (2018); Merck Sharp & Dohme Corp. v. Hospira, Inc., 874 F.3d 724, 730-31 (2017); Galderman Lab'ys., L.P. v. Tolmar, Inc., 737 F.3d 731, 741 (2013); Allergan, Inc. v. Teva Pharms. USA, Inc., No. 15-cv-1455, 2017 WL 4803941, at *48 (E.D. Tex. Oct. 16, 2017).

indicia of nonobviousness tend to support the patentee's contention of validity. In several briefs to the Supreme Court in support of petitions for certiorari, various parties argued that this was a substantial hit to the patent incentive because, since almost all inventions build on previous knowledge, many inventions occur in the shadow of a blocking patent and thus would be affected by this doctrine.[244]

The parties all appear to agree that, if an upstream patent entirely prevents others from working in a particular area, it would indeed be relevant to the objective indicia of nonobviousness. However, there is dispute about how much a particular upstream patent blocks the downstream research in question. Does the upstream patent block all downstream research so that competitors could not develop their own solutions no matter how obvious?[245] Or does the upstream patent allow some downstream research — through, say, the 271(e)(1) exception or by companies located oversees?[246] If some downstream research is permitted, how likely is it to allow the sorts of developments relevant to the objective indicia inquiry?

This question comes up frequently,[247] but there are vast disagreements about when downstream research can occur in the presence of an upstream blocking patent.[248] These disagreements may occur in part because there is no clear catalogue setting out when downstream research can proceed and when it is blocked. This Article provides such a catalogue. Because each case is intensely fact-specific, understanding when downstream research is permitted does not

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[244] *E.g.*, Brief of Biotechnology Innovation Org. as Amicus Curiae in Support of Petitioner at 7, Acorda Therapeutics, Inc. v. Roxane Lab'ys., Inc., No. 18-1280 (Fed. Cir. 2019); Brief of Boston Patent Law Ass'n as Amicus Curiae in Support of Neither Party at 11, Acorda Therapeutics, Inc. v. Roxane Lab'ys., Inc., No. 18-1280 (Fed. Cir. 2019).

[245] *See Acorda*, 903 F.3d at 1338 ("[One relevant question is] whether such improvements will be entirely covered by the blocking patent.").

[246] *See id.* at 1338-39.

[247] *See, e.g.*, Allergan, Inc. v. Teva Pharms. USA, Inc., No. 15-cv-1455, 2017 WL 4803941, at *49 (E.D. Tex. Oct. 16, 2017), *aff'd*, 742 Fed. App'x 511 (Fed. Cir. 2018); Warner Chilcott Co., LLC v. Teva Pharms. USA, Inc., 37 F. Supp. 3d 731, 739 (D. Del.), *aff'd*, 594 F. App'x 630 (Fed. Cir. 2014); Senju Pharm. Co. Ltd. v. Apotex Inc., 717 F. Supp. 2d 404, 426 (D. Del. 2010), *aff'd*, 485 F. App'x 433 (Fed. Cir. 2012); Proctor & Gamble Co. v. Teva Pharms. USA, Inc., 536 F. Supp. 2d 476, 496 (D. Del. 2008), *aff'd*, 566 F.3d 989 (Fed. Cir. 2009); Sanofi-Synthelabo v. Apotex Inc., 492 F. Supp. 2d 353, 392 (S.D.N.Y. 2007), *aff'd*, 550 F.3d 1075 (Fed. Cir. 2008); Aventis Pharma Deutschland GmbH v. Lupin Ltd., No. 05CV421, 2006 WL 2008962, at *44 (E.D. Va. July 17, 2006), *rev'd on other grounds*, 499 F.3d 1293 (2007).

[248] As evidenced by the several petitions for certiorari. *See* petitions cited at *supra* note 233.

provide a blanket answer in each case, but it does provide a framework from which to begin the discussion and a deeper understanding to motivate a court's conclusions.

5. Incentive Shifts and Under-Enforcement

Some empirical work finds that university researchers by-and-large ignore patents and that patentees are reluctant to sue academic researchers for infringement.[249] Scholars have suggested that even outside of academia, many companies simply ignore the possibility of patent infringement when making decisions.[250] In this sort of climate, do doctrines affecting incentives for downstream research still matter?

Yes. First, there is significant empirical evidence that patents *do* deter downstream innovation.[251] This suggests either that patentees are enforcing their patents or that downstream researchers are preemptively skirting areas covered by patents in an attempt to follow the rules and avoid infringement.[252] Second, though underenforcement might blunt the effect of certain doctrines, the doctrines are still available and can be used by patentees. By relying on underenforcement as a mechanism to avoid the ill effects of accidental incentives for downstream innovation, rather than a policy change to remove those incentives, the power to exploit incentives for downstream innovation is shifted from public control to private control.[253]

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[249] *See* Sampat & Williams, *supra* note 73, at 203 (finding that gene patents have no effect on downstream research). Several studies have found that university researchers simply ignore patents when conducting downstream research. *See* John P. Walsh, Ashish Arora & Wesley M. Cohen, *Effects of Research Tool Patents and Licensing on Biomedical Innovations*, *in* PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285 (Wesley M. Cohen & Stephen A. Merrill eds., 2003); Rebecca S. Eisenberg, *Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research*, 45 HOUS. L. REV. 1059, 1063-75 (2008); Zhen Lei, Rakhi Juneja & Brian D. Wright, *Patents Versus Patenting: Implications of Intellectual Property Protection for Biological Research*, 27 NATURE BIOTECHNOLOGY 36, 37 (2009); John P. Walsh, Wesley M. Cohen & Charlene Cho, *Where Excludability Matters: Material Versus Intellectual Property in Academic Biomedical Research*, 36 RSCH. POL'Y 1184, 1191 (2007); John P. Walsh, Ashish Arora & Wesley M. Cohen, *Working Through the Patent Problem*, 299 SCI. 1021, 1021 (2003) [hereinafter *Patent Problem*].

[250] Mark A. Lemley, *Ignoring Patents*, 2008 MICH. ST. L. REV. 19, 21.

[251] *E.g.*, Galasso & Schankerman, *supra* note 230, at 317; Murray & Stern, *supra* note 230, at 648 (finding that citations to knowledge covered by a patent declines by ten to twenty percent after the patent is granted); Williams, *supra* note 230, at 2.

[252] *See supra* Part II.C.b.

[253] There are many examples of patentees choosing to enforce patents in situations where the infringer expected their infringement to be ignored. For example, DuPont use patents on its oncomouse technology to demand licenses from academic

In addition, some researchers are sensitive to the possibility of infringement liability, even if unlikely, and behave accordingly. This fear was enhanced in the wake of the billion-dollar verdict in *Monsanto v. DuPont*.[254] After the DuPont verdict, a law firm advised its clients to

> review the [section 271(e)(1)] exemption to ensure that their research either falls within those bounds or to ensure that all necessary licenses are in order. Simply because an infringing use would not involve selling, offering to sell, or importing a patented invention, it cannot be assumed that damages would be minimal.[255]

Further, interviews with research scientists report that some use "going offshore" as a strategy to avoid patent infringement — evidence that patent law indeed shifts the course of downstream research.[256]

Another example of how patent doctrine plays a role in shaping downstream research is the history of the section 271(e)(1) exception.[257] Patentees were systematically blocking generic drug companies from conducting research, a situation that was so problematic that Congress passed a bill to fix the situation.[258] This is evidence that even in an environment where patents are often underenforced, there are pockets where downstream research is heavily impacted by patent enforcement.

Finally, the argument that incentives for downstream innovation do not matter because patents are under-enforced relies on patentees who care about reputational costs and who do not file suits in low-damage

researchers, who were surprised and outraged to be subject to patent-related threats. Fiona Murray, *The Oncomouse that Roared: Hybrid Exchange Strategies as a Source of Distinction at the Boundary of Overlapping Institutions*, 116 AM. J. SOCIO. 341, 346 (2010). The Wisconsin Alumni Research Foundation similarly created an outcry when it attempted to control creation and distribution of embryonic stem cells. John M. Golden, *WARF's Stem Cell Patents and Tensions Between Public and Private Sector Approaches to Research*, J.L. MED. & ETHICS 314, 314 (2010).

[254] Monsanto Co. v. E.I. Du Pont de Nemours & Co., 748 F.3d 1189, 1192 (Fed. Cir. 2014).

[255] *Damages for Research and Development*, NUTTER (Sept. 18, 2012), https://www.nutter.com/ip-law-bulletin/damages-for-research-and-development [https://perma.cc/3GHJ-GRUA].

[256] *See* Gregory Day & Steven Udick, *Patent Law and the Emigration of Innovation*, 94 WASH. L. REV. 119, 133 (2019); John P. Walsh, Ashish Arora & Wesley M. Cohen, *Working Through the Patent Problem*, 299 SCIENCE 1021, 1021 (2003).

[257] *See supra* Part II.A.2.a.

[258] *Id.*

cases.[259] But patent assertion entities (patent trolls), who make up a substantial percentage of plaintiffs in patent suits, are notoriously not sensitive to reputational costs.[260]

These patentees are also not deterred by low-damage cases. In one example a patentee sought $1,000 in damages from each alleged infringer for their use of a scan-to-email technology.[261] It is quite plausible that a PAE will send (or perhaps has already sent) demand letters to academic laboratories conducting downstream research on patented technology. If this happens often enough, these academic labs might shift to non-infringing research. In short, even in an environment where most patents are not enforced and most researchers ignore patents, incentives matter.

B. Policy

At present, doctrines that shift incentives for downstream research are by-and-large unintended consequences of doctrines designed to address some other legal problem. This creates some negative effects and suggests that patent law may not be using these doctrines in an optimal way. There are three basic options for reform: (1) eliminate all exceptions to patent infringement; (2) target exceptions to create desirable effects; or (3) implement a universal research exception. Each is explored in turn. Although all approaches have some advantages, a universal research exception is the best solution to the problem of suboptimal incentives for downstream research.

1. No Exceptions

If doctrines shifting incentives for downstream research create predominantly negative effects, they could be minimized by removing

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[259] *See* Jacob H. Rooksby, *When Tigers Bare Teeth: A Qualitative Study of University Patent Enforcement*, 46 AKRON L. REV. 171, 174 (2013).

[260] Shawn P. Miller, Ashwin Aravind, Bethany Bengfort, Clarisse De La Cerda, Matteo Dragoni, Kevin Gibson, Amit Itai, Charles Johnson, Deepa Kannappan, Emily Kehoe, Hyosang Kim, Katherine Mladinich, Roberto Pinho, John Polansky & Brian Weissenberg, *Who's Suing Us? Decoding Patent Plaintiffs Since 2000 with the Stanford NPE Litigation Dataset*, 21 STAN. TECH. L. REV. 235, 254 (2018); Although PAEs are generally discussed in the context of software, they also target other industries. Robin Feldman & Nicholson Price W. II, *Patent Trolling: Why Bio & Pharmaceuticals Are at Risk*, 17 STAN. TECH. L. REV. 773, 773 (2014).

[261] Joe Mullin, *Meet the Nice-Guy Lawyers Who Want $1,000 per Worker for Using Scanners*, Ars Technica (Apr. 7, 2013), https://arstechnica.com/tech-policy/2013/04/meet-the-nice-guy-lawyers-who-want-1000-per-worker-for-using-scanners/ [https://perma.cc/2VMA-5DY6].

all exceptions to patent infringement. For example, if there were no first-use exception, downstream research would not be shifted towards methods of using and away from methods of making patented products. However, even if all exceptions were eliminated, some incentive shifts would remain. Most notably, downstream innovation would be channeled towards goals supported by the upstream patentee, who would have absolute power to permit or deny downstream research.[262] This would effectively substitute incentives created by public bodies (Congress and courts) for incentives created by private bodies (patentees). Further, the structure of patent law itself creates incentives in a way that cannot be prevented, even if formal exceptions were removed — for one, domestic law cannot control research in other countries.[263] Finally, because these incentives arise from doctrines intended to affect other areas of law, eliminating the doctrines would have substantial effects on those other areas.

The goal, therefore, should not be to remove incentives for certain types of downstream research but rather to channel the research towards socially desirable and productive outcomes.

2. Targeted Exceptions

Current patterns of incentives for downstream research are generally accidental. One implication of this Article is that exceptions to patent infringement can be exploited to create desired incentives.

To some extent, the current system already has targeted incentives. Section 271(e)(1), for example, was designed to speed access to generic drugs, and there is an exception for medical procedures intended to avoid reduced availability of such procedures.[264] However, the status quo could be improved in two ways. First, although some approaches are targeted to particular goals, others are accidental — the effects of these approaches would be more coherent if all were deliberately targeted. Second, although some existing doctrines are directed at particular goals, they do not consider what other goals might be *disincentivized* by the doctrines. While it is surely desirable to incentivize development of new medicines, is it in the public interest to

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[262] At least to the extent that they could enjoin research work (rather than receive damages). *See* eBay Inc. v. MercExchange, LLC, 547 U.S. 388, 391 (2006); John M. Golden, *Principles for Patent Remedies*, 88 TEX. L. REV. 505, 506-07 (2010).

[263] The U.S. Patent Act limits patent infringement to acts with some relationship to the United States. 35 U.S.C. § 271(a) (2018).

[264] 35 U.S.C. § 287(c) (2018); American Medical Association, Council on Ethical and Judicial Affairs, *Ethical Issues in the Patenting of Medical Procedures*, 53 FOOD DRUG L.J. 341, 341 (1998).

incentivize such research over the basic science that underlies later work towards new medicines? The impact of targeted incentives should be analyzed reciprocally, considering both incentives and disincentives.

Targeted doctrines have several advantages over alternative policies. One is that, by targeting specific activities and omitting others, they reduce the penalty to upstream patent holders as compared to a broad research exception. Any exception from patent infringement removes some of the benefit that would otherwise accrue to the upstream patentee. Such a patentee might charge $5 for a license to conduct research on their widgets; if widget-research is exempt from patent infringement, the patentee effectively loses $5 for each researcher.[265] Shrinking the upstream patentee's reward reduces some of the incentive for that upstream innovation, and so should be done with caution. Doctrines that target specific areas as exceptions to infringement take a smaller bite out of the upstream patent than a broader exception. Targeted downstream incentives therefore permit reciprocally targeted upstream effects.

Additionally, targeted doctrines allow a more fine-grained division between public and private control of downstream research. In the absence of doctrines omitting any downstream research from patent infringement, all downstream research is under private control. Private patentees can choose to permit all research or restrict some research. With a broad research exception, all downstream research is under public control and patents play no role. Targeted doctrines permit policy makers to assign some types of downstream research to private control and others to public control, as appropriate for each type of research.

Targeted doctrines would be better than the status quo because incentives would be less haphazard and would be created with emphasis on socially beneficial research paths. In practice, however, tailoring would be difficult to manage. It is hard to foresee all consequences of shifts to incentives for downstream research and challenging to agree on what types of innovation are most desirable. Further, when the need for downstream innovation arises unexpectedly and urgently, Congress is not always able to act quickly to respond to an urgent need for innovation.[266]

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[265] This is an overly simplistic analysis. It is possible than a research exception for widgets would incentivize more downstream research on widgets, which would lead to more sales of widget-containing devices, which in turn would generate licensing revenue for the original patentee.

[266] *See* Barton H. Thompson Jr., *The Continuing Innovations of Citizen Enforcement*, 2000 U. ILL. L. REV 185, 211 (2000).

3. Broad Research Exception

The best way to avoid the negative effects of incentives that favor certain types of downstream innovation over others is to enact a broad research exception. This has been proposed many times by many scholars.[267] This Article, however, provides a new justification for the policy. Traditionally the case for the research exception was founded on the premise that downstream research will be blocked in the absence of such an exception.[268] However, as shown above, downstream research is not blocked — it is shifted. Shifts can be just as harmful as blockages, perhaps more, if they prevent research in areas that are desirable and direct research towards paths that are harmful. Shifts in incentives for downstream innovation reinforce the case for a broad research exception because they reveal a new ill arising from the exception's lack: a systematic push towards certain types of downstream innovation and away from others.

While a broad research exception is easy to articulate at a general level — all research should be exempt from patent infringement — the devil is, of course, in the details. In particular, it is important that a broad research exception be limited to research *on* a patented technology, and not extend to research *with* a patented technology.[269] If research with a particular technology is not patent infringement, then there is no incentive to develop upstream technologies that are used solely as research tools.[270] Distinguishing research with a patented technology from research on a patented technology adds some complexity to a research exception, but it is still feasible. Many countries have a research exception that incorporates this concept.[271] Beyond the research on/research with distinction, scholars have proposed a variety of detailed schemes to implement a broad research exceptions.[272] Any of those schemes would work to prevent the ills described above.

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267 *E.g.*, Dreyfuss, *Protecting the Public Domain of Science*, *supra* note 68, at 458; Eisenberg, *supra* note 249, at 1071; Strandburg, *supra* note 68, at 85.

268 *See supra* Part I.B.1.

269 *See* Strandburg, *supra* note 68, at 85.

270 This problem is extensively discussed in the literature. *See, e.g.*, Joshua D. Sarnoff & Christopher M. Holman, *Recent Developments Affecting the Enforcement, Procurement, and Licensing of Research Tool Patents*, 23 BERKELEY TECH. L.J. 1299, 1301 (2008) ("[U]ses of patented research tools in almost all contexts, even for university-based basic research, must for now be considered an actionable infringement of exclusive patent rights.").

271 *See* Jordan Paradise & Christopher Janson, *Decoding the Research Exemption*, 7 NATURE REVS. GENETICS 148, 148 (2006).

272 *E.g.*, Eisenberg, *supra* note 249, at 1071; Dreyfuss, *Protecting the Public Domain of Science*, *supra* note 68, at 458; Strandburg, *supra* note 68, at 85.

In the context of shifting incentives for downstream research, the biggest advantage of a broad research exception is its neutrality. Since all research is allowed, there is no incentive for one over another. A broad research exception even prevents incentives that arise from inevitable structural constraints of patent law. For example, international researchers would no longer have an advantage over domestic researchers because domestic researchers are equally able to conduct experiments. A broad research exception removes the ability of individual patentees to incentivize research towards paths in their own private interest.[273] It does not favor research on methods of making over research on methods of using, because both are equally permissible. It avoids the worst distortions caused by the doctrine of constructive reduction to practice by rendering it possible for researchers to conduct experiments before seeking a patent, if they wish to do so. There is less incentive to keep research results secret because disclosing results will not subject the researcher to infringement liability.

A broad research exception is also one sure to apply to socially beneficial projects, since it applies to all projects. It leaves no concerns that certain types of research are incentivized over others. Legislators need not worry that an unforeseen circumstance will create the need for a particular category of research that is excluded from current exceptions because the exception will cover all types of research.

I do not mean to minimize the challenges of implementing a broad research exception. There will certainly be complexities and ambiguities that must be resolved by courts — for one, what is research? But the status quo is also complex and ambiguous. Determining if a particular action infringes a patent is notoriously difficult.[274] The current system taxes innovators in some fields and some circumstances with sorting through this morass of ambiguity while exempting others. A broad research exception may allow researchers (who are usually not patent attorneys) to avoid entangling themselves in patent law. This analysis can be deferred until the research is ready to be sold, at which point it may be supported by an infrastructure better able to deal with legal complexities.

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[273] This of course can be viewed as a negative aspect of a broad research exception, since one aspect of the patent right is the ability to block others' use of the invention for undesired purposes — and this is valuable to some patentees.

[274] *See* JAMES BESSEN & MICHAEL MEURER, PATENT FAILURE: HOW JUDGES, BUREAUCRATS, AND LAWYERS PUT INNOVATORS AT RISK 46 (2008).

A final important benefit of a broad research exception is that it removes minimal rights from patentees.[275] Any exception to infringement reduces the scope of the upstream patent somewhat, and therefore diminishes its value. Policy proposals that change the breadth of current research exceptions must account for an impact on upstream innovators and avoid exceptions so broad that there is insufficient incentive for upstream innovation. A broad research exception does reduce licensing revenue for patentees, and does so more than a series of narrow targeted exceptions. However, it maintains patentees' right to block downstream sales of any product arising from downstream research, meaning that patentees retain the bulk of their patent's profitability.

There are, however, several situations where patent owners will feel deprived of important rights by a research exception. Patent owners will not be able to use their patents to block downstream research when the research will reveal something damaging about the upstream technology, allow a competitor to enter the market sooner after the patent expires than would otherwise be possible, or facilitate a competitor's development of a more appealing version of the technology. Reducing patent rights to prevent this blocking ability is a real loss to the patentee, who may suffer from allowing this downstream research.

However, the situations enumerated above are also areas where society benefits significantly from the downstream research. It is desirable to encourage research that reveals information about flaws in patented technology and patentees should not be able to muzzle speech about dangers to their product. Equally, patentees should not be able to extend the effective term of their patent by preventing research by competitors preparing to enter the market as soon as the patent expires. Finally, it is important to incentivize development of improved versions of technology, even if they do not originate from the patentee. In short, the situations where the patentee will lose key rights from a broad research exception are those where society benefits from downstream research and therefore precisely where a research exemption is most needed.

For all these reasons, a broad research exception is the best way to remedy the ills of distorted incentives for downstream research.

[275] As explained above, this assumes that the exception applies only to research on a patented technology, not research with a patented technology.

CONCLUSION

Prior literature models the relationship between upstream and downstream innovation as either one where the former entirely blocks the latter, or one where downstream research is permitted, and allocation of rights is negotiated *ex post*. This Article presents a new model. Upstream patents provide a broad barrier to downstream research that has been — generally accidentally over the course of many years of doctrinal development — pierced in multiple places by channels along which downstream research can flow. These channels shelter downstream researchers from the costs and uncertainties of the patent system, and thereby provide an enticing path for downstream research. But the safety of these channels pulls downstream research away from other paths that, while more fraught from the perspective of the researcher, may ultimately have more social value.

In this way, such doctrines shift the course of downstream research in ways that are unstructured and not oriented towards planned goals. This outcome is not inevitable. A broad research exception would open all paths to downstream research, avoiding harmful incentives and further the Constitutional purpose of patent law, to "promote the Progress of Science."[276]

[276] U.S. CONST. art I, § 8, cl. 8.