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Drug Prices: The Role of Patents and Regulatory Exclusivities

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SUMMARY

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Drug Prices: The Role of Patents and Regulatory Exclusivities

Intellectual property (IP) rights play an important role in the development and pricing of prescription drugs and biologics. To encourage innovation, IP law grants inventors exclusive rights in a particular invention or product, potentially enabling them to charge higher-than-competitive prices. IP rights are typically justified as necessary to allow pharmaceutical manufacturers the ability to recoup substantial costs in research and development, including clinical trials and other tests necessary to obtain regulatory approval from the U.S. Food and Drug Administration (FDA). However, IP rights have been criticized as contributing to high prices for pharmaceutical products in the United States by operating to deter or delay competition from generic drug and biosimilar manufacturers.

Two main types of IP rights may protect pharmaceutical products: patents and regulatory exclusivities. Patents, which are available for a wide range of technologies beyond pharmaceuticals, are granted by the U.S. Patent and Trademark Office. Patents may claim chemical compounds in the pharmaceutical product, a method of using the product, a method of making or administering the product, or a variety of other patentable inventions relating to a drug or biologic. The holder of a valid patent generally has the exclusive right to make, use, sell, and import the invention for a term lasting approximately 20 years. Pharmaceutical patent disputes are subject to certain specialized procedures under the Hatch-Waxman Act and the Biologics Price Competition and Innovation Act, which can affect when generic and biosimilar manufacturers can market their follow-on products.

In addition to patent protection, certain pharmaceuticals, such as innovative products or those that serve particular needs, may qualify for periods of regulatory exclusivity when they are approved or licensed by FDA. Pharmaceutical products may only be sold in the United States after FDA has determined they are safe and effective, based on submitted data, and has approved or licensed them. FDA generally may not accept and/or approve a generic drug or biosimilar if the pharmaceutical product being used as a reference to show the follow-on product is safe and effective is covered by an unexpired regulatory exclusivity. Regulatory exclusivities vary in length from six months to 12 years, depending on the basis for the exclusivity.

Because the exclusivity that IP law provides may enable the rights holder (e.g., a brand-name drug manufacturer) to charge higher-than-competitive prices for a period of time, rights holders may have an incentive to lengthen that time period as much as possible. Some commentators allege that certain brand-name drug manufacturers (brands) have engaged in patenting practices that unduly extend the period of exclusivity. Critics argue that these patenting practices are used to keep drug prices high, without any benefit for consumers or innovation. Such patenting practices include so-called (1) patent "evergreening," (2) "product hopping," (3) "patent thickets," and (4) "pay-for-delay" settlements. Patent "evergreening" is the alleged practice of filing for new patents on secondary features of a pharmaceutical as earlier patents expire, thereby extending effective patent exclusivity past the original 20-year term. "Product hopping" is the alleged practice of a brand manufacturer attempting to switch the market to a new, similar product covered by later-expiring patents before IP rights on an existing product expire. "Patent thickets" refer to portfolios of numerous, overlapping patents on the same pharmaceutical, which allegedly deter competition due to the risk of infringement and the high cost of patent litigation. "Pay-for-delay" or "reverse payment" settlements resolve patent litigation through payments from a brand to a generic or biosimilar manufacturer to delay generic market entry; in some cases, they may be anticompetitive because they allow the brand to continue to charge high prices without risking invalidation of its patent.

Drug manufacturers counter that their patenting practices protect new, innovative inventions as Congress intended when it created the patent system. In their view, the terms for these practices are unfairly pejorative, or, at most, describe outlier behavior by a few companies. Defenders of these patenting practices reject their characterization as anticompetitive and emphasize that strong patent rights encourage innovation and life-saving research and development efforts.

In recent years, some Members of Congress have introduced bills to address these and other IP-related issues that some perceive as contributing to high pharmaceutical prices. (For a detailed discussion of such legislation introduced in the 116th Congress, see CRS Report R46741, *Drug Pricing and Intellectual Property: The Legislative Landscape for the 117th Congress*.)

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The prices consumers pay for prescription drugs have been of significant congressional interest. In the 116th Congress, several House and Senate committees held hearings on drug pricing issues,[1] and Members introduced dozens of bills to address the perceived high costs of prescription drugs and other pharmaceutical products.[2] The U.S. Department of Health and Human Services (HHS) has found that national spending on pharmaceutical products has been rising in recent years, predicting that these expenditures would continue to rise faster than overall health care spending.[3] Many factors contribute to the prices consumers pay for prescription drugs and biologics, including demand, manufacturing costs, research and development (R&D) costs, the terms of private health insurance, and the involvement of a government insurance program such as Medicaid or Medicare.[4]

Pharmaceutical products are often protected by intellectual property (IP) rights,[5] and some studies have suggested that IP rights are among the most important factors driving high drug prices.[6] For

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[1] *See, e.g.*, *Unsustainable Drug Prices: Testimony from the CEOs (Parts I and II): Hearing Before the H. Comm. on Oversight & Reform*, 116th Cong. (2020); *Intellectual Property and the Price of Prescription Drugs: Balancing Innovation and Competition: Hearing Before the S. Comm. on the Judiciary*, 116th Cong. (2019); *Drug Pricing in America: A Prescription for Change (Parts I–III): Hearing Before the S. Comm. on Fin.*, 116th Cong. (2019); *The Cost of Rising Prescription Drug Prices, Hearing Before the H. Ways & Means Comm.*, 116th Cong. (2019); *Examining the Actions of Drug Companies in Raising Prescription Drug Prices: Hearing Before the H. Comm. on Oversight & Reform*, 116th Cong. (2019).

The Trump Administration also issued reports and executive orders addressing rising drug prices during the 116th Congress. *See* Most Favored Nation (MFN) Model, 85 Fed. Reg. 76,180 (Nov. 27, 2020) (interim final rule); Exec. Order No. 13,948, Lowering Drug Prices by Putting America First, 85 Fed. Reg. 59,649 (Sept. 13, 2020); Exec. Order No. 13,947, Lowering Drug Prices by Putting America First, 85 Fed. Reg. 59,171 (July 24, 2020); Exec. Order No. 13,939, Lowering Prices for Patients by Eliminating Kickbacks to Middlemen, 85 Fed. Reg. 45,759 (July 24, 2020); Exec. Order No. 13,938, Increasing Drug Importation to Lower Prices for American Patients, 85 Fed. Reg. 45,757 (July 24, 2020). *See also* U.S. DEP'T OF HEALTH & HUMAN SERVS., AMERICAN PATIENTS FIRST: THE TRUMP ADMINISTRATION BLUEPRINT TO LOWER DRUG PRICES AND REDUCE OUT-OF-POCKET COSTS (2018) [hereinafter AMERICAN PATIENTS FIRST].

[2] For an examination of some of these proposals, see CRS Report R46741, *Drug Pricing and Intellectual Property: The Legislative Landscape for the 117th Congress*, by Kevin J. Hickey, Kevin T. Richards, and Erin H. Ward.

[3] DEP'T OF HEALTH & HUMAN SERVS., OBSERVATIONS ON TRENDS IN PRESCRIPTION DRUG SPENDING 1 (Mar. 8, 2016), https://aspe.hhs.gov/sites/default/files/pdf/187586/Drugspending.pdf; *see also* CRS Report R44832, *Frequently Asked Questions About Prescription Drug Pricing and Policy*, by Suzanne M. Kirchhoff, Judith A. Johnson, and Susan Thaul, at 3–6.

[4] *See generally* Kirchhoff et al., *supra* note 3, at 3–13; Joseph Antos & James C. Capretta, *Prescription Drug Pricing: An Overview of the Legal, Regulatory and Market Environment*, AM. ENTER. INST. 4–12 (2018), https://www.aei.org/wp-content/uploads/2018/07/Prescription-Drug-Pricing.pdf; Aaron S. Kesselheim et al., *The High Cost of Prescription Drugs in the United States: Origins and Prospects for Reform*, 316 JAMA: J. AM. MED. ASS'N 858, 860–63 (2016).

[5] *See, e.g.*, WILLIAM M. LANDES & RICHARD A. POSNER, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 313 (2003) (citing data that new drug manufacturers are unusually "avid in seeking patent protection"); Emily Michiko Morris, *The Myth of Generic Pharmaceutical Competition under the Hatch-Waxman Act*, 22 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 245, 252 (2012) ("[P]harmaceuticals are also widely recognized as one of the industries most dependent on patent protection to recoup its enormous research, development, regulatory, and post-marketing costs."); Adi Gillat, *Compulsory Licensing to Regulated Licensing: Effects on the Conflict Between Innovation and Access in the Pharmaceutical Industry*, 58 FOOD & DRUG L.J. 711, 722 (reviewing data "supporting relatively high dependency of the pharmaceutical industry on patent rights").

[6] *See, e.g.*, Kesselheim et al., *supra* note 4, at 861 ("The most important factor that allows manufacturers to set high drug prices for brand-name drugs is market exclusivity, which arises from 2 forms of legal protection against competition [i.e., regulatory exclusivities and patent rights.]"); *Generic Competition and Drug Prices*, FOOD & DRUG ADMIN. (Nov. 28, 2017), https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm129385.htm (finding association between generic competition and lower drug prices); *see also America's Overspend: How the Pharmaceutical Patent Problem is Fueling High Drug Prices*, I-MAK 1 (Oct. 2017), https://www.i-mak.org/wp-content/uploads/2020/10/Excess-Costs-Briefing-Paper-FINAL-2017-10-24-with-cover-rev.compressed.pdf [hereinafter *America's Overspend*] (finding that patenting strategies caused $55 billion in excess

example, the U.S. Food and Drug Administration (FDA) has found that increased competition from generic drug manufacturers is associated with lower prices for pharmaceuticals.[7] Given that IP rights can deter or delay the market entry of generic drug or biosimilar competition, and thus may allow the rights holder to charge higher-than-competitive prices, some see changing IP rights as a potential way to lower prices for pharmaceutical products.[8] As IP rights play an important role in facilitating development of new pharmaceutical products,[9] however, a key focus of this debate is whether existing IP law properly balances the need for innovation with the costs that IP rights may impose on the public.[10] Understanding the interplay between several complex legal regimes is necessary to understand this debate.

In general, IP law comprises a set of exclusive rights that prevent others from making, copying, or using certain intangible creations of the human mind.[11] Federal law contains several different varieties of IP, depending on the type of intellectual creation at issue.[12] Each form of IP covers a different type of creation, has a different procedure for obtaining rights, and grants the IP owner legal rights that vary in scope and duration.[13]

New pharmaceutical products generally benefit from two primary[14] forms of IP protection: patent rights and regulatory exclusivities.[15] These two sets of exclusive rights are distinct, yet often confused. Patents, which are available to many technologies beyond pharmaceuticals,[16] are

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costs for the American health care system with respect to just three drugs).

[7] *See Generic Competition and Drug Prices*, *supra* note 6.

[8] *See, e.g.*, Robin Feldman & Evan Frondorf, *Drug Wars: A New Generation of Generic Pharmaceutical Delay*, 53 HARV. J. ON LEGIS. 499, 556–61 (2016) (urging "comprehensive overhaul" of pharmaceutical patent laws to curtail strategies used by pharmaceutical companies to avoid competition and maintain monopoly pricing); Kesselheim et al., *supra* note 4, at 864 (proposing limits on secondary patents and increased policing of pay-for-delay patent settlements as possible means to curtail high drug prices).

[9] *See* Henry G. Grabowski et al., *The Roles of Patents and Research and Development Incentives in Biopharmaceutical Innovation*, 34 HEALTH AFFS. 302, 302 (2015) ("Patents and other forms of intellectual property protection are generally thought to play essential roles in encouraging innovation in biopharmaceuticals.").

[10] *See infra* notes 23–31 (discussing economic rationale for IP and the costs and benefits that it may impose on the public).

[11] *Cf. Intellectual Property*, BLACK'S LAW DICTIONARY (10th ed. 2014) ("A category of intangible rights protecting commercially valuable products of the human intellect.").

[12] *See generally* CRS In Focus IF10986, *Intellectual Property Law: A Brief Introduction*, by Kevin J. Hickey.

[13] *See* Hickey, *supra* note 12.

[14] Although patents and regulatory exclusivities are the most important forms of IP rights for pharmaceuticals, drugs and biologics may be subject to other varieties of IP. For example, the brand name of a new drug is typically trademarked, which prevents other manufacturers from using the same (or similar) name in a way that would confuse consumers. *See* 15 U.S.C. § 1114(1).

[15] Although not a traditional form of IP such as a copyright or patent, regulatory exclusivities share many of the features of traditional IP rights and thus are often characterized as a form of IP. *See, e.g.*, John R. Thomas, *The End of "Patent Medicines"? Thoughts on the Rise of Regulatory Exclusivities*, 70 FOOD & DRUG L.J. 39, 43 (2015) (describing regulatory exclusivities as "FDA-administered intellectual property rights"); Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 359 (2007) (describing FDA regulatory exclusivities as "pseudo-patents"). Regulatory exclusivities are analogous to patent rights because they confer a limited monopoly on the exclusivity holder to provide an incentive for drug manufacturers to undertake the investments necessary to complete the FDA regulatory process. *See* Maxwell R. Morgan, *Regulation of Innovation under Follow-on Biologics Legislation: FDA Exclusivity As an Efficient Incentive Mechanism*, 11 COLUM. SCI. & TECH. L. REV. 93, 98 (2010) ("Like patent law, an FDA-administered exclusivity period can effectively confer a monopoly on a market entrant, and thereby act as an incentive mechanism for firms to invest in the generation and clinical development of new medicines, and also in commercializing them.").

[16] In general, a patent may be granted on any "new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." 35 U.S.C. § 101. However, "laws of nature, natural phenomena, and

granted by the U.S. Patent and Trademark Office (PTO) for inventions that are new, useful, nonobvious, and directed at patentable subject matter.[17] The holder of a valid patent generally has the exclusive right to make, use, sell, or import a patented invention within the United States for a period beginning when the PTO issues the patent and ending 20 years after the filing date of the patent application.[18]

Regulatory exclusivities are granted to qualifying pharmaceutical products upon being approved or licensed for marketing by FDA.[19] Only certain pharmaceutical products, such as innovative products (e.g., a new active ingredient or new indication for an existing drug) or those that serve a specific need (e.g., treating rare diseases), receive such exclusivities.[20] Regulatory exclusivities generally prevent FDA from accepting or approving an application for a follow-on product (i.e., a generic or biosimilar version) of a previously approved pharmaceutical that relies on safety and efficacy data submitted by the original manufacturer for a period of time.[21] Depending on the type of pharmaceutical product and other factors, regulatory exclusivities may last anywhere from six months to 12 years.[22] In overlapping ways, both patent rights and regulatory exclusivities can operate to deter or delay the market entry of a generic drug or biosimilar.

Although each of these forms of IP is legally distinct, they broadly share a common motivation: encouraging innovation.[23] Patents, for example, are typically justified by a utilitarian rationale that exclusive rights are necessary to provide incentives to produce new creative works and technological inventions.[24] This rationale maintains that absent legal protections, competitors could freely copy such creations, denying the original creators the ability to recoup their investments in time and effort, thereby reducing the incentive to create in the first place.[25] IP

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abstract ideas are not patentable." Alice Corp. v. CLS Bank Int'l, 573 U.S. 208, 216 (2014) (quoting Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 589 (2013)); *see generally* CRS Report R45918, *Patent-Eligible Subject Matter Reform in the 116th Congress*, by Kevin J. Hickey.

[17] *See* 35 U.S.C. §§ 101-103, 131. Patent applications must also conform to a number of requirements related to the sufficiency of the technical disclosure in the patent itself. *Id.* § 112; *see generally* CRS Report R46525, *Patent Law: A Handbook for Congress*, by Kevin T. Richards, at 8–17 (reviewing patentability requirements).

[18] 35 U.S.C. §§ 154(a)(2), 271(a).

[19] *See infra* "FDA Approval and Licensure of Pharmaceutical Products."

[20] *See infra* "Regulatory Exclusivities"; *see generally* CRS In Focus IF11217, *Drug Pricing and the Law: Regulatory Exclusivities*, by Erin H. Ward.

[21] Ward, *supra* note 20.

[22] *Id.*

[23] An exception is trademark law, which is usually justified by a different rationale: protecting consumers from confusion and lowering product search costs by preventing businesses from misrepresenting the source of goods or services. *See* Qualitex Co. v. Jacobson Prods. Co., 514 U.S. 159, 163–64 (1995). Many alternative rationales for IP rights exist in addition to the incentives-for-creation theory. *See, e.g.*, Justin Hughes, *The Philosophy of Intellectual Property*, 77 GEO. L.J. 287, 296–314 (1988) (articulating justification for intellectual property as natural right deriving from the author's labor); *id.* at 330–39 (articulating justification for intellectual property as rooted in notions of personhood); Colleen V. Chien, *Contextualizing Patent Disclosure*, 69 VAND. L. REV. 1849, 1850–51 (2016) (overviewing justification for patent system as an incentive to encourage innovators to disclose technical information to public).

[24] *See* Sony Corp. of Am. v. Universal City Studios, Inc., 464 U.S. 417, 429 (1984) ("[Copyrights and patents are] intended to motivate the creative activity of authors and inventors by the provision of a special reward, and to allow the public access to the products of their genius after the limited period of exclusive control has expired."); Twentieth Century Music Corp. v. Aiken, 422 U.S. 151, 156 (1975) ("The immediate effect of our copyright law is to secure a fair return for an 'author's' creative labor. But the ultimate aim is, by this incentive, to stimulate artistic creativity for the general public good.").

[25] *See* Kewanee Oil Co. v. Bicron Corp., 416 U.S. 470, 480 (1974) ("The patent laws promote [the progress of the useful arts] by offering a right of exclusion for a limited period as an incentive to inventors to risk the often enormous

incentives are said to be particularly necessary for products, such as pharmaceuticals, that are costly to develop but easily copied once marketed.[26] In the words of the Supreme Court, IP rights are premised on an "economic philosophy" that the "encouragement of individual effort by personal gain is the best way to advance public welfare through the talents of authors and inventors."[27] From this perspective, the fundamental aim of IP law is to find the optimal balance between providing incentives for innovation and the costs that IP rights impose on the public.[28]

By design, IP rights may lead to increased prices for IP-protected goods or services. IP rights are often said to grant a temporary and limited "monopoly" to the rights holder.[29] The existence of a patent on a particular manufacturing process, for example, generally means that only the patent holder (and persons licensed by the patent holder) can use that patented process until the patent expires.[30] In some circumstances, this legal exclusivity may allow the patent holder (or her licensees) to charge higher-than-competitive prices for goods made with the patented process, as a monopolist would, because the patent effectively shields the patent holder from competition.[31]

As a result, a patent holder, such as a drug manufacturer, may have an incentive to prolong the period of exclusivity, such as by filing for additional patents to cover a product.[32] In the pharmaceutical context, critics argue that some brand-name drug and biological product manufacturers (the brands) use patenting strategies to "game[] the patent system" to maximize profits and forestall competition from generic drug or biosimilar manufacturers (the generics).[33]

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costs in terms of time, research, and development.").

[26] *See* Grabowski et al., *supra* note 9, at 302 ("[T]he process of developing a new drug and bringing it to market is long, costly, and risky, and the costs of imitation are low. After a new drug has been approved and is being marketed, its patents protect it from competition from chemically identical entrants (or entrants infringing on other patents) for a period of time."); LANDES & POSNER, *supra* note 5, at 24 ("If the fixed costs of intellectual property—the costs incurred before a single sale is made—are very high and . . . the costs of duplication are slight, then in the absence of intellectual property rights either the intellectual property will not be created or the government will have to finance it . . . ."); *id.* at 317 ("In the case of new drugs . . . the fixed costs of research and development are very high, in part because of stringent regulatory requirements, but the marginal costs [of imitators] are very low.").

[27] Mazer v. Stein, 347 U.S. 201, 219 (1954).

[28] *See Sony*, 464 U.S. at 429 ("[D]efining the scope of [patents and copyrights] involves a difficult balance between the interests of authors and inventors in the control and exploitation of their writings and discoveries on the one hand, and society's competing interest in the free flow of ideas, information, and commerce on the other hand . . . ."); Mark A. Lemley, *Property, Intellectual Property, and Free Riding*, 83 TEX. L. REV. 1031, 1031 (2005) ("[Traditionally,] the proper goal of intellectual property law is to give as little protection as possible consistent with encouraging innovation.").

[29] *See, e.g.*, Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S. 722, 730 (2002) (characterizing patents as a "temporary monopoly"); Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 147 (1989) (characterizing patents as a "limited monopoly"); *Sony*, 464 U.S. at 442 (characterizing copyright as a "statutory monopoly"). Notably, this usage of "monopoly" is somewhat imprecise, because the exclusive rights provided by IP law do not necessarily confer monopolistic market power in the economic sense; for example, there may be noninfringing substitutes for a patented good in the relevant market. *See* LANDES & POSNER, *supra* note 5, at 22 ("[IP] protection creates a monopoly, in the literal sense in which a person has a monopoly in the house he owns but [only] occasionally in a meaningful economic sense as well because there may be no good substitutes for a particular intellectual work.").

[30] 35 U.S.C. §§ 154(b), 271(a).

[31] *See* LANDES & POSNER, *supra* note 5, at 299–300; FTC v. Actavis, Inc., 570 U.S. 136, 147 (2013) ("[Patent rights] may permit the patent owner to charge a higher-than-competitive price for the patented product.").

[32] *See infra* "Pharmaceutical Patenting Practices."

[33] Press Release, Office of Sen. Dick Durbin, Durbin, Cassidy Introduce REMEDY Act To Lower Drug Prices By Curbing Patent Manipulation, Promoting Generic Competition (Apr. 11, 2019), https://www.durbin.senate.gov/newsroom/press-releases/durbin-cassidy-introduce-remedy-act-to-lower-drug-prices-by-curbing-patent-manipulation-promoting-generic-competition ("Americans are facing skyrocketing prescription drug costs in part because brand-name pharma manufacturers have gamed the patent system to extend their monopolies and avoid competition from

Others contend that these practices are a legitimate use of the patent system and are necessary to incentivize the billions of dollars in R&D that lead to new, life-saving drugs.[34] As these pharmaceutical patenting practices may affect drug prices, they have attracted congressional interest. Several legislative proposals seek to curtail these patenting practices by reducing their effectiveness or outlawing them entirely.[35] Proponents see such legislation as a potential way to lower pharmaceutical prices.[36]

This report discusses four alleged patenting practices. First, commentators allege that some pharmaceutical companies obtain new patents to cover a product as older patents expire to extend the period of exclusivity without significant benefits for consumers, a practice referred to as "evergreening."[37] Second, commentators also contend that pharmaceutical manufacturers engage in "product hopping" by attempting to switch or "hop" the market to a slightly different product covered by a later-expiring patent when the patent covering a current product is close to expiration.[38] Third, commentators argue that pharmaceutical companies have allegedly acquired many overlapping patents on a single product, creating so-called "patent thickets."[39] Critics allege these patent "thickets" may deter potential competitors, even if the patents are weak or invalid, due to the time, expense, and uncertainty of challenging many patents.[40] Finally, brand and generic pharmaceutical companies will often settle litigation that results when a generic seeks to compete with a patented branded product.[41] Certain settlement agreements transfer value from the

lower-cost generic drugs.") (quoting Sen. Durbin); Press Release, Office of Sen. John Cornyn, Cornyn, Blumenthal Introduce Bill to Prevent Drug Companies from Abusing Patent System (May 9, 2019), https://www.cornyn.senate.gov/content/news/cornyn-blumenthal-introduce-bill-prevent-drug-companies-abusing-patent-system ("Drug companies have taken advantage of the patent system to maintain their monopoly on certain drugs and prevent generics from coming to market.") (quoting Sen. Cornyn).

[34] *See, e.g.*, *infra* notes 396–411 and accompanying text.

[35] *See* CRS Report R46741, *Drug Pricing and Intellectual Property: The Legislative Landscape for the 117th Congress*, by Kevin J. Hickey, Kevin T. Richards, and Erin H. Ward.

[36] *See, e.g.*, Feldman & Frondorf, *supra* note 8, at 556–61 (urging "comprehensive overhaul" of pharmaceutical patent laws to curtail strategies pharmaceutical companies allegedly use to avoid competition and maintain monopoly pricing); Kesselheim et al., *supra* note 4, at 864 (proposing limits on secondary patents and increased policing of pay-for-delay patent settlements as possible means to curtail high drug prices).

[37] Eisenberg, *supra* note 15, at 354; Julian W. Marrs, *Forever Green? An Examination of Pharmaceutical Patent Extensions*, 18 OR. REV. INT'L L. 81, 83–89 (2016); Michael Enzo Furrow, *Pharmaceutical Patent Life-Cycle Management After* KSR v. Teleflex, 63 FOOD & DRUG L.J. 275, 276 (2008). Although the literature is not entirely consistent regarding the definition of "evergreening," sometimes equating it with other patenting practices, *see, e.g.*, Michael A. Carrier & Steve D. Shadowen, *Product Hopping: A New Framework*, 92 NOTRE DAME L. REV. 167, 171 (2016) (equating evergreening with "product hopping"), this report uses the term to refer to using later-filed patents to extend the length of a product's effective protection.

[38] *See, e.g.*, Carrier & Shadowen, *supra* note 37, at 171–72.

[39] Cynthia Koons, *This Shield of Patents Protects the World's Best-Selling Drug*, BLOOMBERG BUSINESSWEEK (Sept. 7, 2017), https://www.bloomberg.com/news/articles/2017-09-07/this-shield-of-patents-protects-the-world-s-best-selling-drug (using the term "patent thicket" to refer to a large patent portfolio amassed on one product by a single biologics manufacturer); *see also America's Overspend*, *supra* note 6 (using "thicket of patents" to refer to large patent portfolio claiming aspects of a single drug); Robin Feldman, *"One-and-Done" for New Drugs Could Cut Patent Thickets and Boost Generic Competition*, STAT (Feb. 11, 2019), https://www.statnews.com/2019/02/11/drug-patent-protection-one-done/ ("[D]rug companies build massive patent walls around their products, extending the protection over and over again.").

[40] *Failure to Launch: Patent Abuse Blocks Access to Biosimilars for America's Patients*, BIOSIMILARS COUNCIL 8 (June 2019), https://www.biosimilarscouncil.org/wp-content/uploads/2019/06/Biosimilars-Council-White-Paper-Failure-to-Launch-June-2019.pdf [hereinafter *Failure to Launch*] (estimating it would cost $3 million per patent to challenge the patent thicket surrounding the biologic Humira).

[41] Michael A. Carrier, *A Real-World Analysis of Pharmaceutical Settlements: The Missing Dimension of Product Hopping*, 62 FLA. L. REV. 1009, 1014 (2010) (stating the 180-day exclusivity period "has resulted in numerous

brand to the generic in return for the generic delaying its market entry.[42] Some characterize such "pay-for-delay" or "reverse payment" settlements as anticompetitive because they may delay cheaper generic drugs from entering the market, thereby allowing the brand to maintain its exclusivity period on a patent that otherwise may have been invalidated, benefiting the settling companies at the expense of consumers.[43]

The scope and enforcement of IP rights in pharmaceutical products depend upon several underlying legal and regulatory regimes, including FDA law, patent law, and certain specialized patent dispute procedures. FDA regulates pharmaceutical products differently if they derive from biological, as opposed to chemical, sources. In particular, under the Federal Food, Drug, and Cosmetic Act (FD&C Act), FDA must approve nonbiological "drugs" before they can be marketed or sold,[44] whereas "biologics"[45] must be licensed by FDA under the Public Health Service Act (PHSA).[46] This regulatory distinction has patent law consequences because patents on pharmaceutical drugs or biologics are subject to different specialized patent dispute resolution procedures, which can affect a manufacturer's ability to bring a generic drug or biosimilar to market. Provisions of the Drug Price Competition and Patent Term Restoration Act of 1984[47] (the Hatch-Waxman Act) govern FDA approval and patent disputes for generic drugs, whereas the Biologics Price Competition and Innovation Act of 2009[48] (BPCIA) governs FDA licensure and patent disputes for biosimilars.

Given these complexities, a fair amount of legal background is necessary to understand how drug manufacturers obtain and enforce IP rights in pharmaceuticals and how IP rights may impact drug prices. This report provides this background, proceeding in four parts. First, it overviews FDA requirements for obtaining approval to market a drug or biological product, the abbreviated pathways for generic drug approval under the Hatch-Waxman Act and biosimilar licensure under the BPCIA, and different regulatory exclusivities that FDA grants to certain approved pharmaceutical products.[49] Second, it reviews patent law, including the requirements for obtaining a patent, the rights granted to patent holders, and various limitations on those rights.[50] Third, the report describes and compares the different specialized patent dispute procedures for generic drugs and biosimilars under the Hatch-Waxman Act and the BPCIA, respectively.[51] Finally, it identifies several patenting practices used by pharmaceutical companies to enforce their

settlements between brand firms and first-filing generic companies").

[42] Erik Hovenkamp, *Antitrust Law and Settlement Design*, 32 HARV. J.L. & TECH. 417, 434 (2019) ("[T]he brand-name firm agrees to give a 'reverse payment' (conventionally a cash lump sum) to the generic firm. In exchange, the latter agrees to terminate its challenge and delay its entry into the market for some number of years, often until soon before the patent expires." (footnote omitted)).

[43] *See id.*

[44] Under the FD&C Act, a "drug" means, among other things, an article that is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals." 21 U.S.C. § 321(g)(1).

[45] Under the PHSA, a "biological product" or "biologic" is a medical product derived from natural sources (human, animal, microorganism) and applicable to the prevention, treatment, or cure of disease. 42 U.S.C. § 262(i)(1).

[46] *See infra* "FDA Approval and Licensure of Pharmaceutical Products."

[47] Pub. L. No. 98-417, 98 Stat. 1585 (1984).

[48] Pub. L. No. 111-148, tit. VII, 124 Stat. 199, 804–21 (2010).

[49] *See infra* "FDA Approval and Licensure of Pharmaceutical Products."

[50] *See infra* "Patent Law."

[51] *See infra* "Patent Dispute Procedures for Generic Drugs and Biosimilars."

IP rights; describes how the practices operate under current law; and overviews the debate between various stakeholders over such practices.[52]

FDA Approval and Licensure of Pharmaceutical Products

The FD&C Act generally promotes public health by protecting consumers from pharmaceuticals that are adulterated, misbranded, unsafe, or ineffective.[53] To this end, new drugs and biologics cannot be marketed in the United States without FDA approval.[54] But FDA law also balances encouraging advancements in medicine through innovation against the benefits of competition, similar to patent law.[55] To that end, federal law provides certain regulatory exclusivities—generally upon approval—for pharmaceutical products that meet the requisite criteria.[56]

FDA determines which drugs and biologics may be marketed in the United States through similar but distinct approval processes.[57] This section first overviews the approval processes for new and generic drugs, and then discusses the distinct processes for new and follow-on biologics. It also describes the exclusivities Congress has created to encourage research and development of new pharmaceutical products as well as competition from follow-on products.

New and Generic Drug Approval

Drugs are articles—generally chemical compounds—"intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or "intended to affect the structure or any function of the body."[58] New drugs, as the term is used in the FD&C Act, are those drugs that scientific experts do not generally recognize as safe and effective for their intended use.[59] A new drug may contain an active ingredient that FDA has not previously approved, or may contain a previously approved active ingredient but modify another aspect of the drug, such as the indication, patient population, formulation, strength, dosage form, or route of administration. All new drugs require FDA approval before they are marketed.[60]

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[52] *See infra* "Pharmaceutical Patenting Practices."

[53] *See generally* Wallace F. Janssen, *The Story of the Laws Behind the Labels*, FOOD & DRUG ADMIN. (1981), https://www.fda.gov/downloads/aboutfda/history/forgshistory/evolvingpowers/ucm593437.pdf.

[54] 21 U.S.C. § 355(a); 42 U.S.C. § 262(a)(1).

[55] *See, e.g.*, King Drug Co. of Florence, Inc. v. Smithkline Beecham Corp., 791 F.3d 388, 394 (3d Cir. 2015) ("Congress attempted to balance the goal of 'mak[ing] available more low cost generic drugs, H.R. Rep. No. 98-857, pt. 1, at 14–15 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647–48, with the value of patent monopolies in incentivizing beneficial pharmaceutical advancement, *see* H.R. Rep. No. 98-857, pt. 2, at 30 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2686, 2714."); Yaniv Heled, *Patents v. Statutory Exclusivities in Biological Pharmaceuticals—Do We Really Need Both?*, 18 MICH. TELECOMM. & TECH. L. REV. 419, 427–30, 434–36 (2012).

[56] *See infra* "Regulatory Exclusivities."

[57] *See generally* 21 U.S.C. § 355; 42 U.S.C. § 262.

[58] 21 U.S.C. § 321(g).

[59] *Id.* § 321(p).

[60] *Id.* § 355(a).

New Drug Approval

New drugs are approved through the new drug application (NDA) process. To obtain approval for a new drug, a sponsor must conduct "costly and time-consuming studies"[61] demonstrating the drug's safety[62] and effectiveness[63] for humans.[64] Clinical trials, conducted after the company has completed basic research and animal testing, test the safety, efficacy, and effectiveness of the drug in volunteer human subjects under carefully controlled conditions.[65] When the company is ready to begin clinical trials, it submits an investigational new drug (IND) application to FDA.[66] The IND application provides FDA with information about the drug, including what the drug does, the condition(s) and population(s) the drug is intended to treat, and any data from and analysis of animal studies with the drug.[67] It also includes a proposed clinical study design and written approval from an Institutional Review Board, which reviews the study design.[68] FDA has 30 days to review the IND application and object; otherwise, clinical investigations may proceed.[69]

Clinical testing occurs in three phases.[70] Phase I clinical trials generally test the drug in a small number of subjects and focus on evaluating the drug's safety.[71] During Phase I clinical trials, the sponsor evaluates how the drug is processed (metabolized and excreted) in the body, determines the highest tolerable dose and optimal dose of the drug, and identifies any acute adverse side effects of the drug.[72] Phase II and Phase III clinical trials evaluate the drug's efficacy in addition to safety.[73] These trials generally use a larger group of test subjects who have the characteristic, condition, or disease the drug treats.[74]

Once clinical trials are complete, the sponsor submits the results in an NDA to FDA's Center for Drug Evaluation and Research (CDER).[75] The NDA also includes a list of articles used as components of the drug; a statement of the drug's composition; a description of manufacturing

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[61] FTC v. Actavis, 570 U.S. 136, 142 (2013).

[62] "Safety" in the FDA context is measured by the number and seriousness of adverse events and reactions in persons exposed to the drug. *See, e.g.*, 21 C.F.R. § 312.32.

[63] "Efficacy" refers to whether the drug performs better than a placebo under controlled conditions. *See generally* Amit Singal, Peter Higgins & Akbar Waljee, *A Primer on Effectiveness and Efficacy Trials*, 5(1) J. CLINICAL & TRANSLATIONAL GASTROENTEROLOGY e45 (2014), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3912314/. Effectiveness examines how the drug performs under real-world conditions where it may not be prescribed or taken as intended or may interact with other drugs or health conditions. *Id.*

[64] 21 C.F.R. § 314.50(d)(5).

[65] *Id.* § 312.21.

[66] *Id.* § 312.20.

[67] *Id.* § 312.22–312.23.

[68] *Id.* § 312.23.

[69] *Id.* §§ 312.40, 312.42.

[70] *Id.* § 312.21.

[71] *Id.* § 312.21(a).

[72] *Id.*

[73] *Id.* § 312.21(b)–(c).

[74] *Id.*

[75] 21 U.S.C. § 355(b). The FD&C Act provides for two types of NDAs in section 505(b), depending whether the application includes only studies to which the company has a right of reference (under 505(b)(1)) or includes studies to which the company does not have a right of reference (e.g., published literature or FDA's finding of safety and efficacy for a related approved drug) (a so-called "paper NDA" under 505(b)(2)). *Id.*; U.S. FOOD & DRUG ADMIN., DRAFT GUIDANCE FOR INDUSTRY: APPLICATIONS COVERED BY SECTION 505(B)(2) (1999), https://www.fda.gov/downloads/Drugs/Guidances/ucm079345.pdf.

methods, facilities, and controls; specimens of the proposed labeling; any required pediatric assessments; and patient information.[76] In general, an NDA also contains the product description, the indication(s) (i.e., the disease or condition and population for which the drug will be used), information about the manufacturing process, and proposed labeling.[77] The NDA may also include a proposed Risk Evaluation and Mitigation Strategy (REMS) as needed.[78]

FDA reviews the NDA to determine whether there is substantial evidence that the drug is safe and effective for the proposed use, including whether the benefits of the drug outweigh the risks.[79] Sponsors must submit "substantial evidence" to FDA that their products are safe and effective to obtain FDA approval.[80] Section 505(d) of the FD&C Act defines substantial evidence to mean adequately and well-controlled investigations on the basis of which qualified scientific experts could fairly and responsibly conclude the product has the purported effect.[81] FDA assesses both the quality and quantity of the data provided when determining whether a product meets this standard.[82] The agency also reviews the proposed labeling and the manufacturing controls.[83]

After FDA completes its review, it sends a letter to the drug sponsor with the agency's determination.[84] If the NDA meets the requirements for approval, FDA sends an approval letter or, if patent rights or exclusivities bar immediate approval, a tentative approval letter.[85] FDA may impose conditions on its approval of the NDA, such as requiring the company to conduct additional post-market clinical studies, referred to as Phase IV clinical trials.[86] If the NDA does not meet the requirements for approval, FDA sends a "complete response letter" explaining the deficiencies FDA identified in the NDA and how they might be remedied.[87]

Generic Drug Approval

Before the Hatch-Waxman Act was enacted in 1984, every new drug submitted to FDA for preapproval required a complete application under Section 505(b) supported by clinical trial data demonstrating safety and effectiveness.[88] To encourage generic drug entry, the Hatch-Waxman

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[76] *Id.*

[77] 21 C.F.R. § 314.50.

[78] 21 U.S.C. § 355-1(a)(1). "A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the [FDA] can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh the risks." *Risk Evaluation and Mitigation Strategies*, U.S. FOOD & DRUG ADMIN. (Aug. 8, 2019), https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems. REMS aim to prevent, monitor, or manage risks through information and controls. *Id.*

[79] 21 U.S.C. § 355(d).

[80] *Id.*

[81] *Id.*

[82] U.S. FOOD & DRUG ADMIN., DEMONSTRATING SUBSTANTIAL EVIDENCE OF EFFECTIVENESS FOR HUMAN DRUG AND BIOLOGICAL PRODUCTS: DRAFT GUIDANCE FOR INDUSTRY 3 (Dec. 2019), https://www.fda.gov/media/133660/download[83] *Id.* Manufacturing information includes the manufacturer's name and address, manufacturing methods and process controls, and specifications to ensure a product's integrity for both the marketed drug substance and any drug components used to manufacture the drug. 21 C.F.R. § 314.50(d)(1).

[83] *Id.* Manufacturing information includes the manufacturer's name and address, manufacturing methods and process controls, and specifications to ensure a product's integrity for both the marketed drug substance and any drug components used to manufacture the drug. 21 C.F.R. § 314.50(d)(1).

[84] 21 C.F.R. § 314.105.

[85] *Id.*

[86] *Id.*

[87] *Id.* § 314.110.

[88] 21 U.S.C. § 355(b) (1982). FDA did permit applicants to rely on published studies to meet the "full reports of

Act established a pathway for abbreviated new drug applications (ANDAs),[89] which allows generic manufacturers to rely on FDA's prior approval of another drug with the same active ingredient—the reference listed drug (RLD)—to establish that the generic drug is safe and effective.[90] The ANDA pathway allows generic manufacturers to avoid the long, expensive process of conducting their own clinical trials.[91] Instead, the generic manufacturer need only conduct studies with its generic product and samples of the RLD to demonstrate that the generic drug is pharmaceutically equivalent[92] and bioequivalent[93] to the RLD.[94] The ANDA also includes the generic manufacturer's proposed labeling, which must be identical to the RLD's labeling except for manufacturing information and any FDA-approved changes.[95] ANDA filers submit this information, proposed labeling, and any patent certifications[96] to FDA to obtain approval.[97]

Biological Product and Biosimilar Licensure

A biological product is derived from biological material, such as a virus, toxin, blood component, or protein, and used for "the prevention, treatment, or cure of a disease or condition of human beings."[98] Biological products "are generally large, complex molecules" that "may be produced through biotechnology in a living system, such as a microorganism, plant cell, or animal cell."[99] "Inherent variations" between different batches of the same biological product are "normal and expected."[100] According to FDA, the complexity and variability of biological products "can present challenges in characterizing and manufacturing these products that often do not exist in the manufacture of small molecule drugs."[101] FDA's process for approving biological products and generic versions of previously approved products aims to account for these challenges.

Biological Products

To be marketed in the United States, a biological product must be (1) covered by a valid biologics license; and (2) marked with the product's proper name; the manufacturer's name, address, and

investigations" requirement through its Paper NDA policy. *See* Publication of "Paper NDA" Memorandum, 46 Fed. Reg. 27,396, 27,396 (May 19, 1981).

[89] Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, § 101, 98 Stat. 1585 (1984) (referred to as the Hatch-Waxman Act).

[90] 21 C.F.R. §§ 314.92, 314.94.

[91] Actavis v. FTC, 570 U.S. 136, 142 (2013).

[92] Drugs are pharmaceutically equivalent if they have the same active ingredient(s), strength, dosage form, and route of administration. 21 C.F.R. § 314.3. Other elements that do not impact safety or effectiveness, such as the drug's inactive ingredients, may be different. *Id.*

[93] Bioequivalence means the drugs work the same way inside the body; that is, there is no significant difference in the rate at which and extent to which the drug's active ingredient reaches the place in the body where the drug is active, when administered at the same dose and under similar conditions. *Id.* § 320.1(e).

[94] 21 U.S.C. § 355(j)(2)(A); 21 C.F.R. §§ 314.94, 320.21.

[95] 21 U.S.C. § 355(j)(2)(A)(v).

[96] *See infra* "The Hatch-Waxman Act: Patents and Generic Drug Approval."

[97] 21 U.S.C. § 355(j)(2)(A).

[98] 42 U.S.C. § 262(i); 21 C.F.R. § 600.3.

[99] U.S. FOOD & DRUG ADMIN., BIOLOGICAL PRODUCT DEFINITIONS, https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM581282.pdf (last visited Dec. 3, 2020).

[100] *Id.*

[101] *Id.*

applicable license number; and the product's expiration date.[102] A biological product manufacturer may obtain a biologics license by submitting a biologics license application (BLA) to FDA's Center for Biologics Evaluation and Research (CBER) or CDER for approval.[103] The BLA must include, among other things, data from nonclinical and clinical studies, information about the manufacturing methods and locations, proposed labels and containers to be used, and (if applicable) a proposed Medication Guide.[104] FDA must also be able to examine the product and determine that it "complies with the standards established" in the BLA and other requirements, including good manufacturing practices.[105]

To approve a BLA, FDA must determine that the biological product is "safe, pure, and potent" and that the production and distribution process "meets standards designed to assure that the biological product continues to be safe, pure, and potent."[106] As with drug approvals, FDA either issues the license or issues a complete response letter detailing the reasons for denying the license.[107] After approval, BLA holders must notify FDA of any changes to "the product, production process, quality controls, equipment, facilities, responsible personnel, or labeling."[108]

Biosimilar or Interchangeable Products

As with the Hatch-Waxman Act, Congress created an abbreviated approval process for biological products through the BPCIA. Under the abbreviated process, a company can obtain a license to market a biological product if it can demonstrate that the product is biosimilar to, or interchangeable with, an approved biological product, referred to as the "reference product."[109]

Along with its BLA for a biosimilar, the manufacturer must submit data demonstrating that its product is "highly similar to the reference product notwithstanding minor differences in clinically inactive components" with no "clinically meaningful differences" between the two products "in terms of the safety, purity, and potency of the product."[110] "[T]he condition or conditions of use prescribed, recommended, or suggested in the labeling" must have been approved for the

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[102] 42 U.S.C. § 262(a)(1).

[103] 21 C.F.R. § 601.2(a). An intercenter agreement between CBER and CDER governs which center reviews a particular product application and regulates the product if approved. *Intercenter Agreement Between the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research*, FOOD & DRUG ADMIN. (Oct. 25, 1991), https://www.fda.gov/CombinationProducts/JurisdictionalInformation/ucm121179.htm. In 2003, FDA transferred some therapeutic biological products from CBER to CDER. *See Transfer of Therapeutic Biological Products to the Center for Drug Evaluation and Research*, FOOD & DRUG ADMIN. (June 30, 2003), https://www.fda.gov/CombinationProducts/JurisdictionalInformation/ucm136265.htm.

[104] 21 C.F.R. § 601.2(a). FDA requires Medication Guides for products that "pose a serious and significant public health concern," necessitating patient labeling to inform patients of serious adverse risks and ensure safe and effective use of the product. *Id.* § 208.1. Generally, FDA requires Medication Guides for "prescription drug products used on an outpatient basis without direct supervision by a health professional." *Id.*

[105] *Id.* § 601.20.

[106] 42 U.S.C. § 262(a)(2)(C). A product is safe when it is "relative[ly] free[] from harmful effect to the persons affected, directly or indirectly, by a product when prudently administered," accounting for the product's nature and the recipient's condition. 21 C.F.R. § 600.3(p). A pure product is "relative[ly] free[] from extraneous matter in the finished product," regardless of whether the extraneous matter is harmful. *Id.* § 600.3(r). Finally, the potency of the product depends on its "specific ability or capacity . . . to effect a given result," as demonstrated through "appropriate laboratory tests or by adequately controlled clinical data." *Id.* § 600.3(s).

[107] 21 C.F.R. §§ 601.3, 601.4.

[108] *Id.* § 601.12.

[109] 42 U.S.C. § 262(k).

[110] *Id.* § 262(i)(2).

reference product.[111] The biosimilar product must use "the same mechanism or mechanisms of action" to treat any applicable conditions, and have the same route of administration, dosage form, and strength as the reference product.[112] Finally, the biosimilar product license application must demonstrate that the production and distribution facilities meet "standards designed to assure that the biological product continues to be safe, pure, and potent."[113]

Along with a BLA for an interchangeable product, the manufacturer must submit data demonstrating that the product is biosimilar to the reference product and "can be expected to produce the same clinical result as the reference product in any given patient."[114] Additionally, for a biological product administered to an individual more than once, the manufacturer must also show that the product does not create a greater "risk in terms of safety or diminished efficacy" from alternating from or switching between the biosimilar product and reference product than if the reference product was used alone.[115] Interchangeable products "may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product."[116]

Regulatory Exclusivities

To balance increasing competition—which the abbreviated approval pathways aim to facilitate—with the countervailing interest in encouraging innovation, federal law establishes periods of regulatory exclusivity that limit FDA's ability to approve generic drugs and biosimilars under certain circumstances.[117] This right to exclusivity aims to encourage new drug or biologics applicants to incur the expense of generating clinical data and other information needed to support an NDA or BLA.[118] It also encourages follow-on product manufacturers to submit abbreviated applications as soon as permissible.[119]

There are two general categories of regulatory exclusivity: (1) *data exclusivity*, which precludes other applicants from relying on FDA's safety and effectiveness findings for the reference product (based on the NDA or BLA holder's data) to demonstrate a follow-on product's safety and effectiveness; and (2) *marketing exclusivity*, which precludes FDA from approving any other application for the same pharmaceutical product and use, regardless of whether the applicant has generated its own safety and effectiveness data.[120] During a period of data exclusivity, a company could submit an NDA or BLA for the same pharmaceutical product and use if it conducted its

[111] *Id.* § 262(k)(2)(A)(i)(III).

[112] *Id.* § 262(k)(2)(A)(i)(II) & (IV).

[113] *Id.* § 262(k)(2)(A)(i)(V).

[114] *Id.* § 262(k)(4).

[115] *Id.* § 262(k)(4).

[116] *Id.* § 262(i)(3).

[117] *See, e.g.*, King Drug Co. of Florence, Inc. v. Smithkline Beecham Corp., 791 F.3d 388, 394 (3d Cir. 2015) ("[Through Hatch-Waxman, Congress attempted to balance the goal of 'mak[ing] available more low cost generic drugs,' with the value of patent monopolies in incentivizing beneficial pharmaceutical advancement[.]" (internal citations omitted)); Heled, *supra* note 55. For a comparison of regulatory exclusivities and patent exclusivities, see *infra* **Table 2**.

[118] Heled, *supra* note 55, at 427–30, 440.

[119] 21 U.S.C. § 355(j)(5)(B)(iii), (iv); 42 U.S.C. § 262(k)(6); *see also* Actavis v. FTC, 570 U.S. 136, 143–44 (2013); Heled, *supra* note 55, at 428–29.

[120] There is no standard terminology for regulatory exclusivities. Some commentators use terms such as "data protection" and "marketing exclusivity" synonymously with "regulatory exclusivity." This report follows a second approach that ascribes distinct meanings to the terms. *See generally* Heled, *supra* note 55, at 436 n.67.

own clinical trials.[121] Functionally, data exclusivity and marketing exclusivity may generate the same result due to the investment required to generate the necessary data.

New Drugs or Biological Products

Federal law provides regulatory exclusivities for new drug and biological products that differ based on such factors as how innovative the product is or the nature of the treatment population. For new drugs, an NDA filer who obtains approval for a drug that contains a *new chemical entity* (i.e., a new active ingredient) for which no other drug has been approved is eligible for **five years** of data exclusivity running from the time of NDA approval.[122] During that period, no ANDA or 505(b)(2) NDA (i.e., applications that, by definition, would reference the NDA data) containing the same active ingredient as the RLD may be submitted to FDA.[123] One exception is that after **four years**, FDA may accept for review an ANDA or 505(b)(2) application for the same active ingredient if the application contains a paragraph (IV) certification that a listed patent for the RLD is invalid or would not be infringed by the generic drug.[124]

NDA or supplemental NDA (sNDA)[125] sponsors who obtain approval for drugs that contain approved chemical entities, but are sufficiently changed from the approved drug (e.g., a new indication or formulation) to require additional clinical studies to be approved, are eligible for **three years** of data exclusivity running from the time of NDA approval.[126] Unlike the five-year exclusivity for new chemical entities, FDA may *accept* ANDA and 505(b)(2) submissions that reference the changes meriting exclusivity during the three-year time period.[127] The three-year exclusivity relates to when FDA may *approve* such applications.[128] To obtain such three-year exclusivity, the NDA or sNDA must "contain[] reports of new clinical investigations (other than bioavailability studies)" that were "essential to the approval" of the application.[129] In other words, the sponsor must have conducted or sponsored additional clinical trials that were necessary to obtain approval of the new drug in order to benefit from the three-year exclusivity for that new condition. As a result, three-year exclusivity is generally limited to new drugs that are significantly changed from approved drugs, rather than to minor modifications of those products.

For brand-name biological products, the BPCIA establishes two applicable periods of exclusivity. First, for *new biological products* (i.e., reference products), no biosimilar applications can be

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[121] *Id.*

[122] 21 U.S.C. § 355(c)(3)(E)(ii), (j)(5)(F)(ii); 21 C.F.R. § 314.108(b)(2).

[123] This five-year new drug exclusivity, however, would not prevent FDA from accepting and approving a duplicate version of the same drug product if the duplicate version is the subject of its own NDA with its own safety and efficacy data. *See Small Business Assistance: Frequently Asked Questions for New Drug Product Exclusivity*, FOOD & DRUG ADMIN. (Feb. 11, 2016), https://www.fda.gov/drugs/developmentapprovalprocess/smallbusinessassistance/ucm069962.htm.

[124] 21 U.S.C. § 355(c)(3)(E)(ii), (j)(5)(F)(ii); 21 C.F.R. § 314.108(b)(3). For more information on paragraph (IV) certifications, see *infra* "The Hatch-Waxman Act: Patents and Generic Drug Approval."

[125] Under FDA regulations, changes to a drug's label, dosage, strength, or manufacturing methods require an sNDA. 21 C.F.R. § 314.70. sNDAs must include post-market information such as commercial marketing experience and reports in scientific literature, in addition to descriptions and analyses of clinical studies. *Id.* § 314.50(d)(5)(iv). sNDA sponsors are only eligible for three-year exclusivity because sNDAs amend existing NDAs with approved chemical entities. *Id.* § 314.108(b).

[126] 21 U.S.C. § 355(c)(3)(E)(iii)–(iv), (j)(5)(F)(iii)–(iv).

[127] *Compare id., with id.* § 355(c)(3)(E)(ii), (j)(5)(F)(ii).

[128] *Id.* § 355(c)(3)(E)(iii)–(iv), (j)(5)(F)(iii)–(iv).

[129] *Id.*

submitted for **four years** "after the date on which the reference product was first licensed."[130] Second, approval of biosimilar applications cannot become effective until **12 years** "after the date on which the reference product was first licensed."[131] Together, these exclusivity periods mean that for the first four years after a reference biological product is licensed, FDA does not accept any biosimilar applications for review; for the next eight years, FDA accepts biosimilar applications for review, but it cannot approve any biosimilar application until 12 years after the date on which the reference product was first licensed. FDA has not adopted a formal position on whether these exclusivity periods are data or marketing exclusivity periods.[132] Supplemental BLAs, for example to change the "indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength," are not eligible for these 4- and 12-year regulatory exclusivity periods.[133]

Generic Drug and Biosimilar Exclusivities

In addition to providing incentives for innovation, regulatory exclusivities are also used to promote competition by encouraging the entry of follow-on products. When an RLD has one or more patents listed in the *Orange Book*—an FDA publication that catalogs the patents associated with each approved drug[134]—that have not expired, potential ANDA applicants have two choices: (1) wait until all listed patents have expired to apply for approval or (2) file a paragraph (IV) certification[135] asserting that any active patents are invalid or would not be infringed by the generic product.[136] The potential for ensuing patent litigation raises the anticipated costs for the first ANDA filer with a paragraph (IV) certification, as compared to subsequent ANDA filers.[137] Accordingly, to incentivize generic manufacturers to be the first filer and to challenge listed patents purportedly covering an RLD, the Hatch-Waxman Act provides a **180-day** exclusivity to the first ANDA applicant who successfully challenges an unexpired patent listed for the RLD using a paragraph (IV) certification, and obtains a settlement or court ruling finding the patent is invalid.[138] This exclusivity period precludes FDA from approving another ANDA for the same RLD during the 180-day period.

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[130] 42 U.S.C. § 262(k)(7)(B).

[131] *Id.* § 262(k)(7)(A).

[132] This issue has been the subject of discussions between FDA and some lawmakers. *See* Letter from Rep. Anna G. Eshoo et al., to FDA (Dec. 21, 2010), http://patentdocs.typepad.com/files/letter-to-fda.pdf (signed by Reps. Barton, Eshoo, and Inslee); Letter from Sen. Sherrod Brown et al., to Dr. Margaret Hamburg, Comm'r, FDA (Jan. 24, 2011), http://patentdocs.typepad.com/files/senator-letters-exclusivity.pdf (signed by Sens. Brown, Harkin, McCain, and Schumer). If the exclusivity periods are marketing exclusivities, they would more broadly prevent even an application supported by its own, full clinical trial data from being approved during the 12-year period. More recently, FDA issued guidance that describes the exclusivity periods as limiting approval of an application "referencing [the reference] product," which indicates FDA may consider the exclusivity periods to provide only data exclusivity. U.S. FOOD & DRUG ADMIN., INTERPRETATION OF THE "DEEMED TO BE A LICENSE" PROVISION OF THE BIOLOGICS PRICE COMPETITION AND INNOVATION ACT OF 2009: GUIDANCE FOR INDUSTRY 3 (2018), https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm490264.pdf.

[133] 42 U.S.C. § 262(k)(7)(C).

[134] *See infra* notes 286–288 and accompanying text.

[135] ANDA applicants must provide one of four certifications for each listed patent for the RLD. 21 U.S.C. § 355(j)(2)(vii). Paragraph (IV) certifications assert that the listed patent has not expired but is invalid or will not be infringed by the generic product. *Id.* § 355(j)(2)(vii)(IV); *see also infra* "The Hatch-Waxman Act: Patents and Generic Drug Approval."

[136] *See infra* "Patent Dispute Procedures for Generic Drugs and Biosimilars."

[137] *Id.*

[138] 21 U.S.C. § 355(j)(5)(B)(iv), (j)(5)(D)(iii)(II).

The BPCIA similarly awards regulatory exclusivity to the first interchangeable biological product for a particular reference biological product.[139] This exclusivity precludes FDA from making an interchangeability determination for a subsequent biologic relying on the same reference product for any condition of use until such exclusivity expires, the timing of which depends on the status of a relevant patent dispute.[140] Specifically, the exclusivity period ends at the earlier of

- 1 year after the commercial marketing of the first interchangeable product;
- 18 months after a final court decision in a patent infringement action against the first applicant or dismissal of such an action;
- 42 months after approval if the first applicant has been sued and the litigation is still ongoing; or
- 18 months after approval if the first applicant has not been sued.[141]

Other Regulatory Exclusivities

There are also a number of regulatory exclusivities aimed at encouraging entry into markets that serve smaller or underserved populations or have limited competition. For example, Congress passed the Orphan Drug Act in 1983 to encourage development of drugs and biologics to treat rare diseases and conditions, called "orphan drugs."[142] Because these drugs often treat small patient populations, and thus may provide fewer financial incentives for pharmaceutical manufacturers to develop them, the law (among other measures) provides a **seven-year** marketing exclusivity for companies that obtain approval for these drugs.[143] During the seven-year period, FDA cannot approve an NDA or BLA for the same drug or biologic to treat the same disease or condition, even if the second application generates its own safety and efficacy data.[144]

To receive the *orphan-drug exclusivity*, (1) the drug must be intended to treat a "rare disease or condition,"[145] and (2) FDA must not have previously approved the same drug "for the same use or indication."[146] To meet the first condition, a sponsor may request, before submitting an NDA or BLA, that FDA designate its drug as one for a rare disease or condition.[147] To designate an orphan drug, FDA must determine—when the designation is requested—the disease or condition the drug will treat "(A) affects less than 200,000 persons in the United States or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation than the cost of

[139] 42 U.S.C. § 262(k)(6).

[140] *Id.*

[141] *Id.*

[142] Pub. L. No. 97-414, § 1, 96 Stat. 2049 (1983).

[143] 21 U.S.C. § 360cc(a).

[144] *Id.* § 360cc. This exclusivity is subject to two exceptions: (1) if the exclusivity holder "cannot ensure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated"; and (2) if the NDA or BLA holder consents to the approval of another application for the same drug. *Id.* § 360cc(b).

[145] *Id.* §§ 360bb, 360cc.

[146] *Id.* § 360cc; 21 C.F.R. § 316.3(b)(12). However, an NDA or BLA filer may receive exclusivity for an already-approved drug designated for the same rare disease or condition if it can demonstrate clinical superiority. 21 U.S.C. § 360cc(c).

[147] An orphan drug is one that treats a "rare disease or condition" that either (1) "affects less than 200,000 persons in the United States" or (2) "affects more than 200,000 persons in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug." *Id.* § 360bb(a)(2).

developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug."[148] Drugs so designated are entitled to the seven-year exclusivity if they also meet the second condition.

In addition, the FD&C Act provides a **180-day** exclusivity to ANDAs for drugs designated by FDA (pursuant to the ANDA filer's request) as a "competitive generic therapy" (CGT) due to "inadequate generic competition."[149] To receive the exclusivity, the ANDA must be the first filed for the CGT.[150] The ANDA must also have been submitted when there were "no unexpired patents or exclusivities listed in the *Orange Book* for the relevant RLD."[151] Finally, the applicant must commercially market the drug within 75 days of approval.[152]

To encourage manufacturers to evaluate the safety and effectiveness of their pharmaceutical products for children, NDA and BLA filers may obtain a *pediatric exclusivity* if FDA determines the drug or biological product "may produce health benefits" in the pediatric population and the filer completes pediatric studies at FDA's request.[153] Pediatric exclusivity adds **six months** to any existing exclusivity the NDA or BLA filer has obtained.[154] For example, if the NDA filer obtains a five-year exclusivity for a new active ingredient and conducts the requested pediatric studies, it is entitled to five and a half years of exclusivity.[155]

Table 1. Regulatory Exclusivities for Pharmaceutical Products

Type of Exclusivity	Length	Criteria	Effect
Drugs			
New Chemical Entity 21 U.S.C. § 355(c)(3)(E)(ii), (j)(5)(F)(ii), (u)	5 years (4 years if ANDA contains a paragraph (IV) certification)	Application for drug containing an active ingredient that has never been approved; *or* application for a drug that contains as an active ingredient a single enantiomer (each of a pair of molecules that are mirror images of one another) of a previously approved racemic drug (a mixture of both enantiomers) that treats a different therapeutic category and does not rely on the racemic drug's data	FDA cannot accept an abbreviated application for the same active ingredient that relies on the data in the reference drug application
New Clinical Investigation 21 U.S.C. § 355(c)(3)(E)(iii)–(iv), (j)(5)(F)(iii)–(iv)	3 years	Application for a change to an approved drug that contains at least one new clinical investigation that is "essential to the approval" of the application and is conducted or sponsored by the applicant	FDA cannot approve an application that relies on the data in the reference drug application for 3 years

[148] *Id.*

[149] *Id.* § 356h(b).

[150] *Id.* § 355(j)(5)(B)(v).

[151] U.S. FOOD & DRUG ADMIN., COMPETITIVE GENERIC THERAPIES (2019), https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm631401.pdf.

[152] 21 U.S.C. § 355(j)(5)(B)(v), (j)(5)(D)(iv); COMPETITIVE GENERIC THERAPIES, *supra* note 151, at 18.

[153] 21 U.S.C. § 355a(b)–(c); 42 U.S.C. § 262(m).

[154] 21 U.S.C. § 355a(b)–(c); 42 U.S.C. § 262(m).

[155] 21 U.S.C. § 355a(b)–(c).

Type of Exclusivity	Length	Criteria	Effect
First to File Paragraph IV Certification 21 U.S.C. § 355(j)(5)(B)(iv)	180 days	First to file an ANDA with a paragraph IV certification that a patent listed for the reference drug is invalid or not infringed by the generic product	FDA cannot approve an ANDA for the same drug until 180 days after first commercial marketing of first filer
Competitive Generic Therapy 21 U.S.C. §§ 355(j)(5)(B)(v), 356h(b)	180 days	Designation as competitive generic therapy by FDA based on finding of "inadequate generic competition" (only one active approved drug); No unexpired patents or exclusivities for reference product	Once first approved applicant commences commercial marketing, FDA cannot approve an ANDA for the same reference product for 180 days after first commercial marketing
Biologics			
Biologic Reference Product 42 U.S.C. § 262(k)(7)(A), (B)	4 years (application) and 12 years (approval) after date of first licensure	First licensure of a biological product that is: 1. Not a supplemental application; 2. Not a change resulting in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device, or strength; and 3. Not a modification to structure of product that does not result in a change in safety, purity, or potency	FDA cannot accept an abbreviated BLA referencing the product for first 4 years; FDA cannot approve an abbreviated BLA referencing the product for 12 years
Interchangeable Biologic 42 U.S.C. § 262(k)(6)	12–42 months (see Effects column)	First interchangeable biologic approved for a reference product; Interchangeable means the product is biosimilar to the reference product, produces the same clinical result in any given patient, and a patient can switch between the interchangeable and reference products over multiple doses without altering risk	FDA cannot determine another product is interchangeable with the reference product for any condition of use until the earliest of: (1) 1 year after commercial marketing; (2) 18 months after approval if not sued; or (3) if sued, 18 months after decision or 42 months after approval
Other Purposes			
Pediatric Studies 21 U.S.C. § 355a(b), (c) 42 U.S.C. § 242(m)	6 months	FDA requests that applicant conducts pediatric studies and such studies are completed	Extends other exclusivities by 6 months; Delays approval for 6 months after listed patents expire
Orphan Drug 21 U.S.C. § 360cc	7 years	FDA designation as an orphan drug: a drug that treats a disease or condition that affects less than 200,000 people in the United States, or affects more than 200,000 people in the United States but there is no reasonable expectation that the cost of developing and making the drug would be recovered	FDA cannot approve another application for the same drug for the same disease or condition for 7 years, with limited exceptions

Type of Exclusivity	Length	Criteria	Effect
Qualified Infectious Disease Product 21 U.S.C. § 355f	5 years	FDA designation as a qualified infectious disease product (QIDP): an antibacterial or antifungal drug intended to treat serious or life-threatening infections, including those caused by qualifying or resistant pathogens	Extends other exclusivities by 5 years

Source: CRS.

Patent Law

Congress's authority to grant patents derives from the IP Clause of the U.S. Constitution, which grants Congress the power "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to . . . Inventors the exclusive Right to their . . . Discoveries."[156] Congress has exercised this power since the early days of the Republic to make patent protection available to inventors.[157] The currently operative patent statute is the Patent Act of 1952 (the Patent Act),[158] as amended by laws such as the 2011 Leahy-Smith America Invents Act (AIA).[159] This section briefly overviews the requirements for obtaining a patent, the legal rights granted to the holder of a valid patent, common pharmaceutical patent types, and the authority of the federal government to grant compulsory licenses for patents.[160]

Requirements for Obtaining a Patent

Patent rights do not arise automatically. Rather, to obtain a patent, an inventor must file a patent application with the PTO, and a PTO patent examiner must review the application and conclude it meets the statutory requirements before the PTO issues a patent.[161]

Patents are generally available to anyone who "invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof."[162] To obtain a patent, the inventor must formally apply for a patent with the PTO, beginning a process called patent prosecution.[163] During prosecution, a patent examiner at the PTO evaluates the patent application to ensure it meets all applicable legal requirements to merit the grant of a patent.[164] Along with requirements regarding the technical disclosure of the invention,[165] the claimed invention must be (1) directed at patentable subject matter, (2) new, (3) nonobvious, and

[156] U.S. CONST. art. I, § 8, cl. 8.

[157] *See* An Act to Promote the Progress of Useful Arts, Pub. L. No. 1-7, 1 Stat. 109 (1790).

[158] *See* Patent Act of 1952, Pub. L. No. 82-593, 66 Stat. 792 (codified as amended at 35 U.S.C. §§ 1–390).

[159] Pub. L. No. 112-29, 125 Stat. 284 (2011).

[160] For more detailed information on patenting requirements and patent enforcement, see Richards, *supra* note 17.

[161] 35 U.S.C. §§ 111, 131.

[162] *Id.* § 101.

[163] *See General Information Concerning Patents*, U.S. PATENT & TRADEMARK OFF. (Oct. 2015), https://www.uspto.gov/patents-getting-started/general-information-concerning-patents.

[164] 35 U.S.C. § 131.

[165] *See id.* § 112.

(4) useful.[166] If granted, patents typically expire 20 years after the date the initial patent application was filed.[167]

Patentable Subject Matter

The field of patentable inventions is broad, embracing nearly "anything under the sun that is made by man."[168] By statute, patents are available on any new and useful "process, machine, manufacture, or composition of matter, or . . . improvement thereof."[169] Examples of technological areas for patentable inventions include pharmaceuticals, biotechnology, chemistry, computer hardware and software, electrical engineering, mechanical engineering, and manufacturing processes.[170] Although the subject matter of patents is wide-ranging, the Supreme Court has long held that "laws of nature, natural phenomena, and abstract ideas are not patentable."[171] The Court has reasoned that to permit a monopoly on the "'basic tools of scientific and technological work' . . . might tend to impede innovation more than it would tend to promote it."[172]

In a series of cases over the past decade, the Supreme Court has established a two-step test for patentable subject matter, sometimes called the *Alice* test or the *Alice/Mayo* framework.[173] The first step addresses whether the patent claims are "directed to" ineligible subject matter—a law of nature, natural phenomenon, or abstract idea.[174] If not, the invention is patentable. If directed at ineligible subject matter, the invention is not patentable unless the patent claims have an "inventive concept" under the second step of the *Alice*/*Mayo* test. To have an "inventive concept," the patent claims must contain elements "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself," transforming the nature of the claim to a patent-eligible *application* of ineligible subject matter.[175]

Novelty and Nonobviousness

Perhaps the most fundamental requirement for patentability is that the claimed invention must be *new*. The PTO will not issue a patent if "the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the

[166] *See id.* §§ 101–103.

[167] *Id.* § 154(a)(2).

[168] Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980) (quoting S. REP. NO. 1979, 82d Cong., 2d Sess., 5 (1952); H.R. REP. No. 1923, 82d Cong., 2d Sess., 6 (1952)).

[169] 35 U.S.C. § 101.

[170] *See Patent Technology Centers Management*, U.S. PATENT & TRADEMARK OFF., https://www.uspto.gov/patent/contact-patents/patent-technology-centers-management (last visited Nov. 27, 2020) (listing technological divisions for PTO examiners).

[171] Diamond v. Diehr, 450 U.S. 175, 185 (1981); *see generally* Hickey, *supra* note 16, at 10–20 (overviewing development of the law of patent-eligible subject matter).

[172] Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. 66, 71 (2012) (quoting Gottschalk v. Benson, 409 U.S. 63, 67 (1972)).

[173] *See* Alice Corp. v. CLS Bank Int'l, 573 U.S. 208 (2014); Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576 (2013); *Mayo*, 566 U.S. at 66. The PTO recently issued revised guidelines for its patent examiners to determine whether a patent application seeks to claim ineligible subject matter. *See* 2019 Revised Patent Subject Matter Eligibility Guidance, 84 Fed. Reg. 50 (Jan. 7, 2019).

[174] *Alice*, 573 U.S. at 217.

[175] *Id.* (quoting *Mayo*, 566 U.S. at 73).

effective filing date of the claimed invention."[176] In other words, if every element of the claimed invention is already disclosed in the "prior art"—the information available to the public at the time of the patent application—then the alleged inventor "has added nothing to the total stock of knowledge," and no valid patent may issue to her.[177]

Even if a claimed invention is novel in the narrow sense that it is not "identically disclosed" in a prior art reference (such as an earlier patent or publication), the invention must further be *nonobvious* to be patentable.[178] Specifically, an invention cannot be patented if "the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious . . . to a person having ordinary skill" in the relevant technology.[179] When determining obviousness, courts may evaluate considerations such as "commercial success, long felt but unsolved needs, [or] failure of others . . . to give light to the circumstances surrounding the origin of the subject matter sought to be patented."[180] By its nature, obviousness is an "expansive and flexible" inquiry that cannot be reduced to narrow, rigid tests.[181] That said, if an invention merely combines "familiar elements according to known methods," yielding only "predictable results," it is likely to be obvious.[182]

Utility

An invention must also be *useful* to be patentable, which means that it must have a specific and substantial utility.[183] The utility requirement derives from the IP Clause's command that patent laws exist to "promote the Progress of . . . *useful* Arts."[184] The constitutional purpose of patent law thus requires a "benefit derived by the public from an invention with substantial utility," where the "specific benefit exists in currently available form."[185] The bar for utility, however, requires only that the claimed invention have some "significant and presently available benefit to the public" that "is not so vague as to be meaningless."[186]

Disclosure Requirements

Along with substantive requirements relating to the invention, the Patent Act imposes many requirements relating to the form of the patent application. These provisions ensure the patent adequately discloses the invention to the public so that the public can use the invention after the

[176] 35 U.S.C. § 102(a)(1). There are certain exceptions to this requirement when, for example, the prior art disclosure derives from the inventor and the patent application is made within one year of the disclosure. *Id.* § 102(b)(1).

[177] Great Atl. & Pac. Tea Co. v. Supermarket Equip. Corp., 340 U.S. 147, 153 (1950); Graham v. John Deere Co. of Kan. City, 383 U.S. 1, 6 (1966) ("Congress may not authorize the issuance of patents whose effects are to remove existent knowledge from the public domain, or to restrict free access to materials already available.").

[178] 35 U.S.C. § 103.

[179] *Id.* Patent law frequently relies on the concept of a "person having ordinary skill in the art," a "hypothetical person" with a typical level of skill in the relevant technology who is "presumed to be aware of all the pertinent prior art" in the particular field. *See* Standard Oil Co. v. Am. Cyanamid Co., 774 F.2d 448, 454 (Fed. Cir. 1985).

[180] *Graham*, 383 U.S. at 17–18.

[181] KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 415–19 (2007).

[182] *Id.* at 416.

[183] Brenner v. Manson, 383 U.S. 519, 534–35 (1966); *In re* Fisher, 421 F.3d 1365, 1371 (Fed. Cir. 2005).

[184] Stiftung v. Renishaw PLC, 945 F.2d 1173, 1180 (Fed. Cir. 1991) (citing *Brenner*, 383 U.S. at 528–29); *see also Graham*, 383 U.S. at 5–6.

[185] *Brenner*, 383 U.S. at 534–35.

[186] *In re Fisher*, 421 F.3d at 1371–72.

patent term expires.[187] Section 112 of the Patent Act requires that patents must contain a "specification" that includes

> a *written description* of the invention, and of *the manner and process of making and using it*, in such full, clear, concise, and exact terms as to enable any person skilled in the art to . . . make and use the same, and shall set forth *the best mode* contemplated by the inventor or joint inventor of carrying out the invention.[188]

This statutory language yields three basic disclosure requirements for patentability.[189] First, to satisfy the *written description requirement*, the specification must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date" of the patent application.[190] Second, to satisfy the *enablement requirement*, the specification must contain enough information to teach a person skilled in the art how "to make and use the invention without undue experimentation."[191] Finally, to satisfy the *best mode requirement*, the specification must show that the inventor "possessed a best mode for practicing the invention" at the time of the patent application, and disclose that preferred way of practicing the invention.[192]

Patent Claims

If granted, the patent's legal scope is defined by the *patent claims*, words which "particularly point[] out and distinctly claim[] the subject matter which the inventor . . . regards as the invention."[193] In essence, while the specification explains the invention in a *technical* sense, the claims set forth the patent's *legal* effect.[194] Much as a deed may describe the boundaries of a tract of land, the claims define the "metes and bounds" of the patent right.[195] Patent claims must be sufficiently *definite* to be valid—that is, when the claims are read in context, they must "inform, with reasonable certainty, those skilled in the art about the scope of the invention."[196]

Patent Enforcement

Rights of Patent Holders

Once granted, the holder of a valid patent has the exclusive right to make, use, sell, or import the invention in the United States until the patent expires.[197] Any other person who *practices* the invention (i.e., makes, uses, sells, offers to sell, or imports it) without permission from the patent holder infringes the patent and is liable for monetary damages, and possibly injunctive relief, if

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[187] *See* Kewanee Oil Co. v. Bicron Corp., 416 U.S. 470, 480–81 (1974).

[188] 35 U.S.C. § 112(a).

[189] *See* Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 535 U.S. 722, 736 (2002); Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1344 (Fed. Cir. 2010) (en banc).

[190] *Ariad*, 598 F.3d at 1351.

[191] *In re* Wands, 858 F.2d 731, 735 (Fed. Cir. 1988).

[192] Eli Lilly & Co. v. Barr Labs., Inc., 251 F.3d 955, 963 (Fed. Cir. 2001).

[193] 35 U.S.C. § 112(b).

[194] *See Ariad*, 598 F.3d at 1347 (Fed. Cir. 2010); *In re* Vamco Mach. & Tool, Inc., 752 F.2d 1564, 1577 n.5 (Fed. Cir. 1985).

[195] Corning Glass Works v. Sumitomo Elec. U.S.A., Inc., 868 F.2d 1251, 1257 (Fed. Cir. 1989).

[196] Nautilus, Inc. v. Biosig Instruments, Inc., 572 U.S. 898, 901 (2014).

[197] 35 U.S.C. § 271(a).

sued by the patentee.[198] Patents have the attributes of personal property, and the patentee may sell or assign the patent to another person.[199] A patentee may also *license* other persons to practice the invention, granting them permission to make, use, sell, or import the invention, usually in exchange for consideration (such as monetary royalties).[200]

Patents thus provide a *negative* right to exclude another person from practicing the claimed invention. But patents do not grant the patentee any affirmative right to practice the invention.[201] In the pharmaceutical context, this means that even if a manufacturer has a patent on a particular drug (or inventions related to making or using that drug), it still cannot market that drug without FDA approval.[202]

With some exceptions, a patent is generally granted "for a term beginning on the date on which the patent issues and ending 20 years from the date on which the application for the patent was filed."[203] The Patent Act includes provisions that may modify the 20-year term, including to account for excessive delays in patent examination at the PTO,[204] or delays associated with obtaining marketing approval from other federal agencies (including FDA).[205] In the pharmaceutical context, the PTO may extend the term of patents claiming a drug product or medical device (or a method of using or manufacturing the same) for up to five years to account for delays in obtaining regulatory approval, if certain statutory conditions are met.[206]

Patents are not self-enforcing: to obtain relief from infringement, the patentee must sue in court.[207] Patent law is an area of exclusive federal jurisdiction,[208] and the traditional forum for most patent disputes is federal district court.[209] Although patent suits may be filed in any district court across the country with jurisdiction over the defendant and proper venue, all appeals in

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[198] *Id.* §§ 271, 281, 283–85.

[199] *Id.* § 261.

[200] *License*, BLACK'S LAW DICTIONARY (10th ed. 2014); 35 U.S.C. § 271(a).

[201] Leatherman Tool Grp. v. Cooper Indus., Inc., 131 F.3d 1011, 1015 (Fed. Cir. 1997) ("[T]he federal patent laws do not create any affirmative right to make, use, or sell anything.").

[202] *See* discussions *supra* in "New and Generic Drug Approval" and "Biological Product and Biosimilar Licensure."

[203] 35 U.S.C. § 154(a).

[204] *Id.* § 154(b)(1).

[205] *Id.* § 156.

[206] *See* Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661, 670–71 (1990); Merck & Co. v. Hi-Tech Pharmacal Co., 482 F.3d 1317, 1320–21 (Fed. Cir. 2007); *see generally* Stephanie Plamondon Bair, *Adjustments, Extensions, Disclaimers, and Continuations: When Do Patent Term Adjustments Make Sense?*, 41 CAP. U. L. REV. 445 (2013).

[207] 35 U.S.C. § 281.

[208] 28 U.S.C. § 1338.

[209] In 2019, roughly 3,347 patent lawsuits were filed in federal district courts, as compared to 1,322 petitions for administrative review of issued patents before the Patent Trial and Appeal Board (PTAB). *See 2019 Patent Dispute Report: Year in Review*, UNIFIED PATENTS (Jan. 1, 2020), https://www.unifiedpatents.com/insights/2019/12/30/q4-2019-patent-dispute-report [hereinafter *2019 Patent Dispute Year in Review*]. The third main forum for patent disputes is the International Trade Commission (ITC), which has authority to conduct administrative trials (called "section 337 investigations") into whether imported goods violate patent and other IP rights. *See* 19 U.S.C. § 1337. The ITC may issue exclusion orders to stop such goods from entering the United States. *See About Section 337*, U.S. INT'L TRADE COMM., https://www.usitc.gov/intellectual_property/about_section_337.htm (last visited Nov. 27, 2020); *see generally* Sapna Kumar, *The Other Patent Agency: Congressional Regulation of the ITC*, 61 FLA. L. REV. 529, 534–40 (2009) (overviewing ITC procedures). In contrast to the thousands of cases heard by the PTAB and district courts, the ITC typically initiates only several dozen section 337 investigations per year. *See Section 337 Statistics: Number of New, Completed, and Active Investigations by Fiscal Year*, U.S. INT'L TRADE COMM. (Oct. 15. 2020), https://www.usitc.gov/intellectual_property/337_statistics_number_new_completed_and_active.htm (reporting 58 new complaints in Fiscal Year 2019).

patent cases are heard by a single specialized court, the U.S. Court of Appeals for the Federal Circuit (the Federal Circuit).[210]

Defenses to Claims of Patent Infringement

Parties accused of patent infringement may defend on several grounds. First, although patents are subject to a presumption of validity, the accused infringer may assert that the patent is *invalid*.[211] To prove invalidity, the accused infringer must show, by clear and convincing evidence, that the PTO should not have granted the patent because it failed to meet the requirements for patentability.[212] Thus, for example, the accused infringer may argue that the invention lacks novelty, is obvious, or claims nonpatentable subject matter; that the patent fails to enable the invention; or that the patent claims are indefinite.[213] Second, the accused infringer may claim an "absence of liability" based on *noninfringement*.[214] In other words, even presuming the patent is valid, the patentee may fail to prove that the activities of the accused infringer fall within the scope of the patent claims.[215] Finally, the accused infringer may argue the patent is *unenforceable* based on the patent holder's inequitable or illegal activities, such as obtaining the patent through fraud on the PTO.[216]

Remedies for Patent Infringement

If the patentee succeeds in proving infringement, the patent holder may obtain two major forms of judicial relief: monetary damages and injunctive relief.[217] Damages must be "adequate to compensate for the infringement,"[218] and typically take the form of either (1) *lost profits* (the net revenue "lost to the patentee because of the infringement"),[219] or (2) a *reasonable royalty* (the amount the patentee would have received in a "hypothetical negotiation" if the patentee and the infringer had negotiated a good-faith license).[220] Courts may increase these damages "up to three times the amount found or assessed,"[221] but such enhanced damages are "generally reserved for egregious cases of culpable behavior" by the infringer.[222] Finally, courts may award attorneys'

[210] 28 U.S.C. § 1295(a)(1).

[211] 35 U.S.C. § 282(a)–(b).

[212] *Id.* § 282(b)(2)–(3); Microsoft Corp. v. i4i Ltd. P'ship, 564 U.S. 91, 95–96 (2011).

[213] *See supra* "Requirements for Obtaining a Patent."

[214] 35 U.S.C. § 282(b)(1).

[215] To prove direct infringement, the plaintiff must show that each element contained in a patent claim is practiced by the alleged infringer, either literally or by an equivalent. Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 29–30 (1997). Often, whether or not the accused infringer's activities fall within the patent claims depends upon *claim construction*, that is, how the words used in the patent claims are interpreted. *See generally* Markman v. Westview Instruments, Inc., 517 U.S. 370, 372–74 (1996); Phillips v. AWH Corp., 415 F.3d 1303, 1312–19 (Fed. Cir. 2005) (en banc).

[216] Therasense, Inc. v. Becton, Dickinson & Co., 649 F.3d 1276, 1285, 1290–91 (Fed. Cir. 2011) (en banc).

[217] 35 U.S.C. §§ 283–284. A judicial declaration of the parties' rights—known as a declaratory judgment—is another important form of relief in patent suits that is sometimes available to patentees or accused infringers. 28 U.S.C. § 2201; *see also* discussion *infra* note 281.

[218] 35 U.S.C. § 284.

[219] Rite-Hite Corp. v. Kelley Co., 56 F.3d 1538, 1545 (Fed. Cir. 1995) (en banc).

[220] Lucent Techs., Inc. v. Gateway, Inc., 580 F. 3d 1301, 1324 (Fed. Cir. 2009).

[221] 35 U.S.C. § 284.

[222] Halo Elecs., Inc. v. Pulse Elecs., Inc., 136 S. Ct. 1923, 1932 (2016).

fees in "exceptional cases"[223] that "stand[] out from others with respect to the substantive strength of a party's litigating position" or "the unreasonable manner in which the case was litigated."[224]

A patent holder may also ask a court to order various forms of injunctive relief.[225] At the outset of a patent litigation, a patent holder may seek a *preliminary injunction*, a court order that prevents the defendant from committing the allegedly infringing acts while the litigation proceeds.[226] If a patent infringement lawsuit succeeds, the patent holder may seek a *permanent injunction*, a final order prohibiting the defendant from infringing the patent in the future.[227]

The Patent Trial and Appeal Board

Following the passage of the AIA, the PTO's Patent Trial and Appeal Board (PTAB) has become an increasingly important forum for patent disputes.[228] The AIA created several new administrative procedures for challenging patent validity,[229] including (1) *post-grant review* (PGR), which allows petitioners to challenge patent validity based on any of the requirements of patentability if the PGR petition is filed within nine months of the patent's issuance;[230] (2) *inter partes review* (IPR), which allows any person other than the patentee to challenge patent validity on limited grounds (novelty or obviousness based on prior patents or printed publications) at any time after nine months following the patent's issuance;[231] and (3) a transitional program for *covered business method patents* (CBM), a PGR-like process that was limited to certain patents claiming "business methods," which was available only through September 2020.[232] Of these procedures, IPR is by far the most widely used.[233]

Types of Pharmaceutical Patents

If a person is the first to synthesize a particular chemical that she believes to be useful for treating disease, she may file for a patent on that chemical itself, and—presuming the application meets

[223] 35 U.S.C. § 285.

[224] Octane Fitness, LLC v. ICON Health & Fitness, Inc., 572 U.S. 545, 554 (2014).

[225] 35 U.S.C. § 283.

[226] In deciding whether to exercise their discretion to grant a motion for a preliminary injunction, courts weigh four factors: (1) the likelihood that the plaintiff will succeed on the merits of the lawsuit; (2) whether the plaintiff is likely to suffer irreparable harm in the absence of a preliminary injunction; (3) the balance of equities; and (4) whether an injunction is in the public interest. *See* Titan Tire Corp. v. Case New Holland, Inc., 566 F.3d 1372, 1375–76 (Fed. Cir. 2009) (citing Winter v. Natural Res. Def. Council, Inc., 555 U.S. 7, 20 (2008)).

[227] 35 U.S.C. § 283. Courts may grant permanent injunctions to remedy patent infringement as justified by traditional equitable principles, but injunctions are not issued solely because the patent holder succeeds in proving infringement. *See* eBay, Inc. v. MercExchange LLC, 547 U.S. 388, 394 (2006).

[228] *See generally* Rochelle Cooper Dreyfuss, *Giving the Federal Circuit a Run for Its Money: Challenging Patents in the PTAB*, 91 NOTRE DAME L. REV. 235, 249 (2015); Richards, *supra* note 17, at 24–28 (reviewing PTAB proceedings).

[229] Prior to the AIA, the PTO administered two earlier administrative mechanisms to challenge patents. The first, inter partes reexamination, was generally considered to be "underutilized" and has been replaced by IPR. *See* Dreyfuss, *supra* note 228, at 235 n.2; Brian J. Love & Shawn Ambwani, *Inter Partes Review: An Early Look at the Numbers*, 81 U. CHI. L. REV. DIALOGUE 93, 95–96 (2014). The second, ex parte reexamination, which was left unchanged by the AIA, permits the PTO to reopen patent prosecution if a "substantial question of patentability" is presented based on certain prior art cited by a third party to the PTO. 35 U.S.C. §§ 301–307.

[230] 35 U.S.C. §§ 321–329.

[231] *Id.* §§ 311–319.

[232] Pub. L. No. 112-29, § 18, 125 Stat. 284, 329–30 (2011) (not codified in U.S.C.).

[233] *See 2019 Patent Dispute Year in Review*, *supra* note 209, fig. 12.

all requirements for patentability—the PTO will grant the patent.[234] Manufacturers may find patents on a pharmaceutical product's active ingredient particularly valuable because these patents are often difficult, if not impossible, to "invent around" (i.e., develop a competing product that does not infringe the patent).[235] However, manufacturers may obtain many other types of patents relating to the pharmaceutical product, beyond active ingredient patents,[236] and manufacturers of some biological products may not be able to patent some naturally-occurring active ingredients if they are patent-ineligible subject matter.[237]

Pharmaceutical patents may cover many different features of a drug or biologic beyond a claim on the active ingredient itself.[238] Such patents may claim, among other things,

1. formulations of a pharmaceutical (e.g., an administrable form and dosage, or a combination of active and other ingredients);
2. methods of using the pharmaceutical (e.g., an indication or use of the drug for treating a particular disease);
3. technologies and methods used to administer the pharmaceutical (e.g., an inhaler or injector device);
4. technologies and methods for manufacturing the pharmaceutical (e.g., a manufacturing process);
5. other chemicals related to the active ingredient, such as crystalline forms, polymorphs, intermediaries, salts, and metabolites.[239]

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[234] *See supra* "Requirements for Obtaining a Patent"; 35 U.S.C. § 101 (allowing patents on "any new and useful . . . composition of matter").

[235] *See* Margaret K. Kyle, *Competition Law, Intellectual Property, and the Pharmaceutical Sector*, 81 ANTITRUST L.J. 1, 2 (2016) ("[A]t least one type of pharmaceutical patent, the product patent on the molecule itself, is particularly hard to invent around.").

[236] *See* Kyle, *supra* note 235, at 6 ("[T]he primary patent on the molecule is rarely the only one associated with a drug. Typically, the innovator (or others) files additional patent applications [that] may cover methods of manufacturing the chemical or biological substance, purified forms, new salts or esters, new uses of the substance, new combinations, new delivery routes, etc.").

[237] *See generally* Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 580, 589–96 (2013) (discussing "natural phenomena" category of patent-ineligible subject matter and holding that a "naturally occurring DNA segment is a product of nature and not patent eligible"); Priti Deka Phukan, *Patenting Proteins After* Myriad, 23 FED. CIR. B.J. 619, 621 (2014) (analyzing "whether synthetically produced biological compounds," such as therapeutic proteins and hormones, are patentable "when the synthetic compound is indistinguishable from the naturally occurring compound"). Biologics that derive from biological organisms, but are genetically modified or otherwise modified by man into a non-naturally occurring form, are generally patent-eligible. *See* Diamond v. Chakrabarty, 447 U.S. 303, 309–10 (1980) (upholding patent on genetically engineered bacterium).

[238] Studies have found that active ingredient patents are a minority of pharmaceutical patents. *See* Amy Kapczynski et al., *Polymorphs and Prodrugs and Salts (Oh My!): An Empirical Analysis of "Secondary" Pharmaceutical Patents*, 7 PLOS ONE 1, 4–6 (2012) (surveying patents listed in FDA's *Orange Book* for new chemical entities and finding that secondary patents, such as formulations and methods of use, were more common than active ingredient patents); Tahir Amin & Aaron S. Kesselheim, *Secondary Patenting of Branded Pharmaceuticals: A Case Study of How Patents on Two HIV Drugs Could Be Extended for Decades*, 31 HEALTH AFFS. 2286, 2289 (2012) (finding that only about 1% of the 108 patents covering particular HIV drugs claimed the active ingredient, with around 39% claiming formulations and related chemicals, 32% claiming manufacturing processes, 15% claiming methods of treatment, and 13% claiming other aspects).

[239] *See* JOHN R. THOMAS, PHARMACEUTICAL PATENT LAW 46–64 (3d ed. 2015) (overviewing these and other categories of pharmaceutical patent claims).

To be patentable, however, all of these types of inventions must be new, useful, and nonobvious, and sufficiently described in the patent application, like any other invention.[240]

In addition, if a person invents an *improvement* on any of these technologies—for example, a more effective formulation of the drug, a new use, or a different manufacturing process—then the inventor can file for a patent on that improvement, which receives its own patent term.[241] To be patentable, the improvement must be new and nonobvious, that is, "more than the predictable use of prior art elements according to their established functions."[242] Any person wishing to practice the improved form of the invention would need permission from both the patent holder of the original technology and the holder of the improvement patent (who need not be the same entity), if neither patent has yet expired.[243] If the original patent has expired but the improvement patent has not, permission from the improvement patentee is needed to practice the improved version, but as a matter of patent law, any person is free to make and use the original, unimproved version.[244]

Because many different aspects of pharmaceutical products (and improvements thereto) are patentable, dozens of different patents may protect some pharmaceutical products. For example, one study of the top 12 drugs by gross U.S. revenue found that pharmaceutical manufacturers obtained an average of 71 patents on each of these drugs.[245] As discussed below, there is a significant public policy debate over such patent portfolios, particularly over the number, timing, and enforcement of nonactive ingredient patents (sometimes called "secondary" patents).[246]

Compulsory Licensing

As explained above, a patent holder generally has the exclusive right to practice an invention. Thus, any other person who wishes to make, use, sell, or import the invention would ordinarily need a license (i.e., permission) from the patent holder, or else be exposed to legal liability.[247] In certain cases, however, patents may be subject to a "compulsory license," which allows another person to use the invention *without* the patent holder's prior consent.[248] Compulsory licenses are typically authorized by statute and usually require the sanction of a governmental entity and

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[240] *See supra* "Requirements for Obtaining a Patent."

[241] 35 U.S.C. § 101 ("Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, *or any new and useful improvement thereof,* may obtain a patent therefor . . . ." (emphasis added)).

[242] KSR Int'l Co. v. Teleflex, Inc., 550 U.S. 398, 417 (2007); *see also supra* notes 178–182 and accompanying text (discussing the nonobviousness requirement).

[243] *See* Robert Merges, *Intellectual Property Rights and Bargaining Breakdown: The Case of Blocking Patents*, 62 TENN. L. REV. 75, 80–82 (1994) (analyzing "blocking patents" situation where holder of improvement patent and holder of the original patent need each other's permission before either can practice the improved invention).

[244] *Id.* at 91; *see also* Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEX. L. REV. 989, 991, 1010 (1997).

[245] *See Overpatented, Overpriced: How Excessive Pharmaceutical Patenting Is Extending Monopolies and Driving Up Drug Prices*, I-MAK 6–8 (Aug. 2018), https://www.i-mak.org/wp-content/uploads/2018/08/I-MAK-Overpatented-Overpriced-Report.pdf [hereinafter *Overpatented*]. However, the number of patents per product is likely much smaller for less-valuable pharmaceuticals. *See* Lisa Larrimore Ouellette, *How Many Patents Does It Take to Make a Drug? Follow-On Pharmaceutical Patents and University Licensing*, 17 MICH. TELECOMM. & TECH. L. REV. 299, 314 (2010) (finding, on average, 2.97 patents listed per drug in FDA's *Orange Book*); *but see infra* notes 301–302 (discussing the limitations on the types of patents that may be listed in the *Orange Book*).

[246] *See infra* "Pharmaceutical Patenting Practices."

[247] *Id.* § 271.

[248] *Compulsory License,* BLACK'S LAW DICTIONARY (10th ed. 2014) ("A statutorily created license that allows certain people to pay a royalty and use an invention without the patentee's permission.").

payment of compensation to the patent holder.[249] Compulsory licenses differ from ordinary licenses in two important respects: (1) the person seeking to use the invention need not seek advance permission from the patent holder; and (2) the compensation paid to the patentee is generally determined by operation of law, not by private contractual negotiations between the licensee and the patent holder.

Current federal law contains several compulsory license provisions for patents.[250] For example, under 28 U.S.C. § 1498, sometimes described as an "eminent domain" provision for patents,[251] the U.S. government has authority to use any patented invention "without license."[252] The patentee, however, has the right to sue in the U.S. Court of Federal Claims for "reasonable and entire compensation" for the government's use of the patented invention.[253] A court, though, would not issue an injunction against the United States to prevent its use of the invention.[254] In effect, then, section 1498 allows the United States to issue itself a compulsory license to use any patented invention without obtaining the patentee's permission in exchange for the payment of reasonable compensation.[255] This compulsory license may extend to federal contractors, subcontractors, and any person acting "with the authorization and consent of the [U.S.] Government."[256] The federal government relies on section 1498 authority with some frequency,[257] particularly in the defense context.[258] In the pharmaceutical context, however, the United States has not used its eminent domain authority in recent decades.[259]

Compulsory licensing is also available for inventions made with federal funding under the Bayh-Dole Act.[260] In general, the Bayh-Dole Act permits certain government contractors to obtain patents on inventions produced with federal funding.[261] However, the federal government retains

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[249] *See generally* Subhasis Saha, *Patent Law and TRIPS: Compulsory Licensing of Patents and Pharmaceuticals*, 91 J. PAT. & TRADEMARK OFF. SOC'Y 364, 366–67 (2009).

[250] *See generally* Jesse S. Chui, *To What Extent Can Congress Change the Patent Right Without Effecting a Taking?*, 34 HASTINGS CONST. L.Q. 447, 462–66 (2007) (reviewing examples of compulsory licensing provisions in existing law, including 28 U.S.C. § 1498, and provisions of the Clean Air Act, Atomic Energy Act, Invention Secrecy Act, and Plant Variety Protection Act).

[251] *See* Motorola, Inc. v. United States, 729 F.2d 765, 768 (Fed. Cir. 1984); Leesona Corp. v. United States, 599 F.2d 958, 964 (Ct. Cl. 1979).

[252] 28 U.S.C. § 1498(a).

[253] *Id.*

[254] Advanced Software Design Corp. v. Fed. Reserve Bank of St. Louis, 583 F.3d 1371, 1375 (Fed. Cir. 2009) ("[Section 1498] has the effect of removing the threat of injunction . . . ."); *Motorola*, 729 F.2d at 768 n.3.

[255] Amanda Mitchell, *Tamiflu, the Takings Clause, and Compulsory Licenses: An Exploration of the Government's Options for Accessing Medical Patents*, 95 CAL. L. REV. 535, 541–42 (2007) (analogizing section 1498 to a compulsory license).

[256] 28 U.S.C. § 1498(a).

[257] Hannah Brennan et al., *A Prescription for Excessive Drug Pricing: Leveraging Government Patent Use for Health*, 18 YALE J.L. & TECH. 275, 302 (2016) (characterizing the government use of section 1498 as "routine" and citing a number of examples).

[258] *See, e.g.*, FastShip, LLC v. United States, 892 F.3d 1298 (Fed. Cir. 2018); Beacon Adhesives, Inc. v. United States, 134 Fed. Cl. 26 (2017); Ensign-Bickford Aerospace & Def. Co. v. United States, 118 Fed. Cl. 363 (2014).

[259] Brennan et al., *supra* note 257, at 303–07 (describing various uses of section 1498 by the federal government to purchase pharmaceutical drugs in the 1960s, but observing this practice "tailed off in the 1970s"). The only recent invocation of section 1498 in the health context occurred in 2001, when Tommy Thompson, then-Secretary of HHS, threatened to (but ultimately did not) rely on this authority to purchase generic versions of Cipro during the anthrax scare. *Id.* at 303.

[260] *See* Pub. L. No. 96-517, § 6, 94 Stat. 3015, 3019–27 (1980).

[261] 35 U.S.C. § 202(a); *see generally* Jennifer Penman & Fran Quigley, *Better Late than Never: How the U.S.*

the authority to "march in" and grant compulsory licenses to third parties for federally funded inventions under certain specified circumstances, such as the patent holder's failure to practice the patented invention or health or safety needs.[262] A license granted under Bayh-Dole's march-in provisions must be "upon terms that are reasonable under the circumstances," which may require the licensee to pay some compensation to the patentee.[263] The federal government has never exercised its march-in rights under Bayh-Dole.[264]

Patent Dispute Procedures for Generic Drugs and Biosimilars

As **Table 2** summarizes below, patent rights granted by the PTO and regulatory exclusivities granted by FDA are legally distinct.[265] They are motivated by similar purposes. Patents seek to encourage innovation by providing an economic incentive for inventors to invest their time and resources in developing novel inventions.[266] Analogously, regulatory exclusivities granted by FDA[267] provide an incentive for pharmaceutical manufacturers to undertake the investments necessary to complete the FDA approval process and bring new drugs and biologics to market.[268]

In some circumstances, patent rights can affect when a manufacturer can market a generic drug or biosimilar. For example, if a court hearing a patent dispute grants an injunction that prohibits a manufacturer from infringing by making a generic drug, the manufacturer cannot bring that product to market until after the patent expires and the injunction terminates.[269] In addition, as discussed below, the Hatch-Waxman Act's specialized patent dispute procedures can affect FDA's ability to approve an ANDA, even prior to a judicial decision.[270] Patent rights may also affect follow-on market entry indirectly, if a generic or biosimilar manufacturer declines to seek FDA approval because of the number of existing patents relating to a product or the costs of challenging them.[271]

Government Can and Should Use Bayh-Dole March-in Rights to Respond to the Medicines Access Crisis, 54 WILLAMETTE L. REV. 171, 177–78 (2017).

[262] 35 U.S.C. § 203(a)(1)–(4).

[263] *Id.* § 203(a); Penman & Quigley, *supra* note 261, at 178.

[264] Penman & Quigley, *supra* note 261, at 199.

[265] *See generally* Rebecca S. Eisenberg, *Patents and Regulatory Exclusivity*, *in* THE OXFORD HANDBOOK OF THE ECONOMICS OF THE BIOPHARMACEUTICAL INDUSTRY 167–200 (Patricia M. Danzon & Sean Nicholson eds., 2012).

[266] *See* Kewanee Oil Co. v. Bicron Corp., 416 U.S. 470, 480 (1974) ("The patent laws promote [the progress of the useful arts] by offering a right of exclusion for a limited period as an incentive to inventors to risk the often enormous costs in terms of time, research, and development.").

[267] *See supra* "Regulatory Exclusivities."

[268] *See* Ward, *supra* note 20, at 1; Morgan, *supra* note 15, at 98.

[269] *See supra* "Rights of Patent Holders."

[270] *See infra* "The Hatch-Waxman Act: Patents and Generic Drug Approval."

[271] If these patents are valid, such deterrence is the object of a functioning patent system. In some cases, patents may deter competition even if a court was likely to hold the patents invalid or not infringed. *See generally* Christopher R. Leslie, *The Anticompetitive Effects of Unenforced Invalid Patents*, 91 MINN. L. REV. 101, 113–39 (2006) (arguing that even invalid patents can deter market entry of competitors based on fear of litigation and high litigation costs); Rebecca S. Eisenberg & Daniel A. Crane, *Patent Punting: How FDA and Antitrust Courts Undermine the Hatch-Waxman Act to Avoid Dealing with Patents*, 21 MICH. TELECOMM. & TECH. L. REV. 197, 260–62 (2015) (arguing that pharmaceutical companies may deter or delay competition through assertion of "irrelevant" patents).

Table 2. Summary Comparison of Patents Versus Regulatory Exclusivities

	Patents	Regulatory Exclusivities
Purpose	Provide incentives to encourage creation of new technologies	Balance pharmaceutical innovation and generic competition
Specific to Pharmaceuticals?	No; available to any "process, machine, manufacture, or composition of matter"	Yes
Relevant Agency	U.S. Patent & Trademark Office (PTO)	Food & Drug Administration (FDA)
Requirements	New, useful, nonobvious, and sufficiently disclosed invention	Completion of FDA regulatory process for a particular drug or biological product
Term	Generally 20 years from the date the relevant patent application was filed	Variable (six months to 12 years) based on drug type, prior approvals, and other factors
Effect	Third parties cannot may, use, sell, or import the invention without the patentee's permission	Third parties cannot seek, obtain, and/or use data for FDA approval with respect to particular product
Enforcement	By the patentee, usually through a patent infringement lawsuit	By FDA

Source: CRS.

Rationale for Specialized Pharmaceutical Patent Procedures

One of the core aims of the Hatch-Waxman Act was to correct "two unintended distortions" in the patent term resulting from the temporally limited patent monopoly's interaction with FDA premarketing requirements for products such as prescription drugs.[272] The first distortion affected new drug manufacturers: because obtaining FDA marketing approval may take years, regulatory requirements shortened the effective patent term (i.e., the period during which the patentee can derive profit from the invention).[273] In response, the Hatch-Waxman Act granted a patent term extension for certain inventions relating to drug products or medical devices based on delays in obtaining regulatory marketing approval.[274]

The other distortion concerned the end of the patent term and affected generic-drug manufacturers. In general, once a patent expires, the patented invention should be available for anyone to use.[275] In the pharmaceutical context, generic manufacturers should, in theory, be able to enter the market once the applicable patents and regulatory exclusivities have expired. Prior to the Hatch-Waxman Act, however, some judicial decisions held that uses of a patented drug necessary to obtain FDA approval, such as conducting tests on a patented drug, constituted patent infringement.[276] Thus, as a practical matter, generic manufacturers could often not even *begin* seeking FDA approval until the applicable patents expired.[277] The result was an "effective extension of the patent term" based on the "combined effect of the patent law and the premarket

[272] Eli Lilly & Co. v. Medtronic, Inc., 496 U.S. 661, 669 (1990).

[273] *Id.* at 669–70.

[274] *Id.* at 670; 35 U.S.C. § 156. The patent term extension applies, among other things, to patents that claim a drug or medical device, a method of using a drug or medical device, or a method of manufacturing a drug or medical device. *See id.* § 156(a), (f)(1).

[275] Sears, Roebuck & Co. v. Stiffel Co., 376 U.S. 225, 230 (1964) ("[W]hen the patent expires the monopoly created by it expires, too, and the right to make the article . . . passes to the public.").

[276] *See, e.g.*, Roche Prods. v. Bolar Pharm. Co., 733 F.2d 858, 863 (Fed. Cir. 1984).

[277] *Eli Lilly*, 496 U.S. at 670.

regulatory approval requirement."[278] In response, the Hatch-Waxman Act created a "safe harbor," providing that making, using, or selling an invention "solely for uses reasonably related to the development and submission of information under a federal law which regulates the manufacture, use, or sale of drugs" is *not* patent infringement.[279]

A potential side effect of this safe harbor was to limit the ability of a pharmaceutical patent holder to file a lawsuit for patent infringement prior to the generic manufacturer's marketing of the follow-on product.[280] If actions relating to the FDA approval process are no longer infringing, patent litigation against an ANDA filer might not occur until the generic or biosimilar is marketed, after the completion of the FDA approval process.[281] Earlier resolution of patent disputes is usually regarded as beneficial, as it provides greater legal certainty to both the brand-name and generic-drug manufacturers.[282] In particular, generic manufacturers can obtain clarity on patent issues before they market a drug and expose themselves to monetary damages.[283]

To facilitate early patent dispute resolution, the Hatch-Waxman Act made the filing of an ANDA or paper NDA itself an "artificial" act of patent infringement.[284] For its part, the BPCIA contains an analogous provision making the filing of a biosimilar or interchangeable BLA an artificial act of patent infringement.[285] Functionally, these artificial acts of infringement enable the brand-name manufacturer to sue for patent infringement at the time of the follow-on application, allowing litigation of patent disputes before the generic drug or biosimilar is marketed.[286]

For all these reasons, both Hatch-Waxman and BPCIA enacted specialized patent dispute resolution procedures that complement the abbreviated pathways for the regulatory approval for follow-on products. This section reviews these procedures.

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[278] *Id.*

[279] 35 U.S.C. § 271(e)(1); Merck KGaA v. Integra Lifescis. I, Ltd., 545 U.S. 193, 200 (2005) (describing this provision as a "safe harbor").

[280] *Eli Lilly*, 496 U.S. at 678.

[281] Even in the absence of an actual act of infringement, either party could generally file a lawsuit seeking a declaratory judgment, asking a court to "declare the rights and other legal relations" between the parties, such as whether a patent is invalid or noninfringed. 28 U.S.C. § 2201(a). For a court to have jurisdiction, there must be an actual and "substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." MedImmune, Inc. v. Genentech, Inc., 549 U.S. 118, 127 (2007) (quoting Md. Cas. Co. v. Pac. Coal & Oil Co., 312 U.S. 270, 273 (1941)); *see also* Teva Pharm. USA, Inc. v. Novartis Pharm. Corp., 482 F.3d 1330, 1336–39 (Fed. Cir. 2007). In addition, both the Hatch-Waxman Act and the BPCIA limit declaratory judgement jurisdiction for pharmaceutical patents in some circumstances. 28 U.S.C. § 2201(b).

[282] *See* Natalie M. Derzko, *The Impact of Recent Reforms of the Hatch-Waxman Scheme on Orange Book Strategic Behavior and Pharmaceutical Innovation*, 45 IDEA: INTELL. PROP. L. REV. 165, 239 (2005) ("From society's perspective, early resolution of such patent disputes is generally considered beneficial since it helps clear the way for generic drug entry if a patent is in fact invalid. . . . Such resolution provides an early signal to the generic company of this fact before substantial resources are expended in launching, marketing and selling its generic copy of the brand-name drug.").

[283] *See id.* at 239–40; Laura J. Robinson, *Analysis of Recent Proposals to Reconfigure Hatch-Waxman*, 11 J. INTELL. PROP. L. 47, 78 (2003) ("[If patent issues are not resolved,] the generic [company] cannot go to market without risking a later infringement suit with substantial damages.").

[284] *Eli Lilly*, 496 U.S. at 678; *see* 35 U.S.C. § 271(e)(2)(A).

[285] 35 U.S.C. § 271(e)(2)(C).

[286] *Eli Lilly*, 496 U.S. at 678; *see generally* Elizabeth Stotland Weiswasser & Scott D. Danzis, *The Hatch-Waxman Act: History, Structure, and Legacy*, 71 ANTITRUST L.J. 585, 595 (2003) ("The Hatch-Waxman Act created a system that enabled the resolution of patent infringement disputes prior to the entry of generic competition.").

The Hatch-Waxman Act: Patents and Generic Drug Approval

Under the Hatch-Waxman Act, a drug manufacturer must list, as part of its NDA, any patent that claims the drug that is the subject of the application, or a method of using that drug.[287] FDA includes information on listed patents in the *Orange Book*.[288] When a generic drug manufacturer files an ANDA, it must provide a certification for each patent listed in the *Orange Book* for the RLD.[289] **Figure 1** diagrams the general patent dispute process under the Hatch-Waxman Act.

In particular, with some exceptions,[290] the generic applicant must make one of four certifications for each listed patent:

(I) there is no patent information listed;

(II) the patent has expired;

(III) the date the patent will expire; or

(IV) the patent is invalid or not infringed by the generic applicant's product.[291]

Paragraph (I) and (II) certifications do not affect FDA's ability to approve the ANDA.[292] If the generic applicant makes a paragraph (III) certification, FDA may not approve the ANDA until the patent at issue has expired.[293]

A paragraph (IV) certification triggers Hatch-Waxman's specialized patent dispute procedures, often leading to litigation.[294] First, the generic applicant must give notice of the ANDA and the paragraph (IV) certification to the patentee and the NDA holder, including "a detailed statement of the factual and legal basis" for patent invalidity or noninfringement.[295] The NDA or patent holder then has 45 days to sue the generic applicant for patent infringement.[296] If the NDA or patent holder declines to sue by the deadline, the generic applicant may file a "civil action for patent certainty" to obtain a declaratory judgment that the *Orange Book*-listed patents are invalid or not infringed.[297]

If the patent holder timely files suit after being notified of the paragraph (IV) certification, this lawsuit triggers the "30-month stay": FDA generally cannot approve the ANDA for 30 months while the parties litigate their patent dispute.[298] If, before the expiration of the 30-month stay, the

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[287] 21 U.S.C. § 355(b)(1); *see also* 21 C.F.R. § 314.53(b).

[288] U.S. FOOD & DRUG ADMIN., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (2020), https://www.fda.gov/media/71474/download [hereinafter *Orange Book*]; *see also* https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm (searchable version of the *Orange Book*).

[289] 21 U.S.C. § 355(j)(2)(A)(vii). While this summary discusses the patent dispute procedures with respect to an ANDA, NDAs that rely on reports and data to which they have no right of reference (e.g., published studies) are subject to a parallel certification and notification process. *See id.* § 355(b)(2)–(3), (c)(3).

[290] With respect to patents that claim a method of using a drug, the generic applicant may file a "section viii" statement when the applicant is seeking approval only for a use that is not claimed in a listed patent. *Id.* § 355(j)(2)(A)(viii).

[291] *Id.* § 355(j)(2)(A)(vii)(I)–(IV).

[292] *Id.* § 355(j)(5)(B)(i).

[293] *Id.* § 355(j)(5)(B)(ii).

[294] *Id.* § 355(j)(5)(B)(iii); Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S, 566 U.S. 399, 407 (2012).

[295] 21 U.S.C. § 355(j)(2)(B)(i)–(iv).

[296] *Id.* § 355(j)(5)(B)(iii).

[297] *Id.* § 335(j)(5)(C)(i); *see generally Caraco Pharm.*, 527 F.3d at 1285. In civil actions for patent certainty, federal courts have subject-matter jurisdiction so long as it is "consistent with the Constitution." 35 U.S.C. § 271(e)(5).

[298] *See* 21 U.S.C. § 355(j)(5)(B)(iii); *Caraco Pharm.*, 566 U.S. at 407–08. Following amendments to the Hatch-

district court concludes the patent is invalid or not infringed by the ANDA filer, FDA may approve the ANDA as of the date of the court's judgment or a settlement order to that effect.[299] If the court finds the patent is infringed (and the ANDA filer does not appeal that decision), then the effective date of ANDA approval must be "not earlier than the date of the expiration of the patent which has been infringed."[300] FDA approval of a generic drug application can thus be significantly delayed based on patent rights asserted by the NDA holder.

By statute, NDA filers must list patents that either (1) "claim[] the drug" that is the subject of the NDA or (2) claim "a method of using such drug."[301] FDA regulations make clear that "drug substance (active ingredient) patents, drug product (formulation and composition) patents, and method-of-use patents" *must* be listed, while "[p]rocess patents, patents claiming metabolites, and patents claiming intermediates" must *not* be listed.[302] As a result, patents on a process for manufacturing a drug, for example, should not be included in the NDA or listed in the *Orange Book*. (Because only certain patents relating to a drug are listed in the *Orange Book*, some patent litigation concerning generic drugs takes place outside the specialized notice-and-certification procedures of the Hatch-Waxman Act.)

FDA does not actively police the patent information listed in the *Orange Book*, viewing its role as merely "ministerial."[303] This approach has raised concerns among some commentators that NDA holders may list inapplicable patents in the *Orange Book* as a means to deter generic competition.[304] FDA does offer an administrative procedure through which "any person [who] disputes the accuracy or relevance of patent information" in the *Orange Book*, or believes that an NDA holder "has failed to submit required patent information," may notify the Agency and seek correction of the patent information.[305] With the availability of the 30-month stay and the requirement that ANDA filers make a certification for each patent listed in the *Orange Book*, it is generally in the interest of NDA holders to list all potentially relevant patents.[306] There is no

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Waxman Act in 2003, the NDA holder may receive one 30-month stay based on patents listed in the *Orange Book* with respect to an ANDA. *See* 21 U.S.C. § 355(c)(3)(C), (j)(5)(B)(iii); Colleen Kelly, *The Balance Between Innovation and Competition: The Hatch-Waxman Act, the 2003 Amendments, and Beyond*, 66 FOOD & DRUG L.J. 417, 439 (2011) ("[The 2003 amendments] effectively limited an innovator company to one 30-month stay per ANDA.").

[299] 21 U.S.C. § 355(j)(5)(B)(iii)(I).

[300] *Id.* § 355(j)(5)(B)(iii)(II); 35 U.S.C. § 271(e)(4)(A). If a judgment of infringement is appealed by the ANDA filer and reversed by the court of appeals (i.e., the Federal Circuit), FDA may approve the application as of the date of an appellate decision in favor of the ANDA filer. 21 U.S.C. § 355(j)(5)(B)(II)(aa)(AA).

[301] 21 U.S.C. § 355(b)(1). Additionally, the listed patents must be such that "a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." *Id.*

[302] 21 C.F.R. § 314.53(b)(1).

[303] *See* Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 68 Fed. Reg. 36,676, 36,683 (June 18, 2003) (codified at 21 C.F.R. pt. 314) ("[FDA's] patent listing role remains ministerial.") (citing aaiPharma Inc. v. Thompson, 296 F.3d 227, 242–43 (4th Cir. 2002)).

[304] *See, e.g.*, Eisenberg & Crane, *supra* note 271, at 260 (arguing that "the lack of administrative oversight" by FDA "has allowed innovators to defer competition through the listing of irrelevant patents").

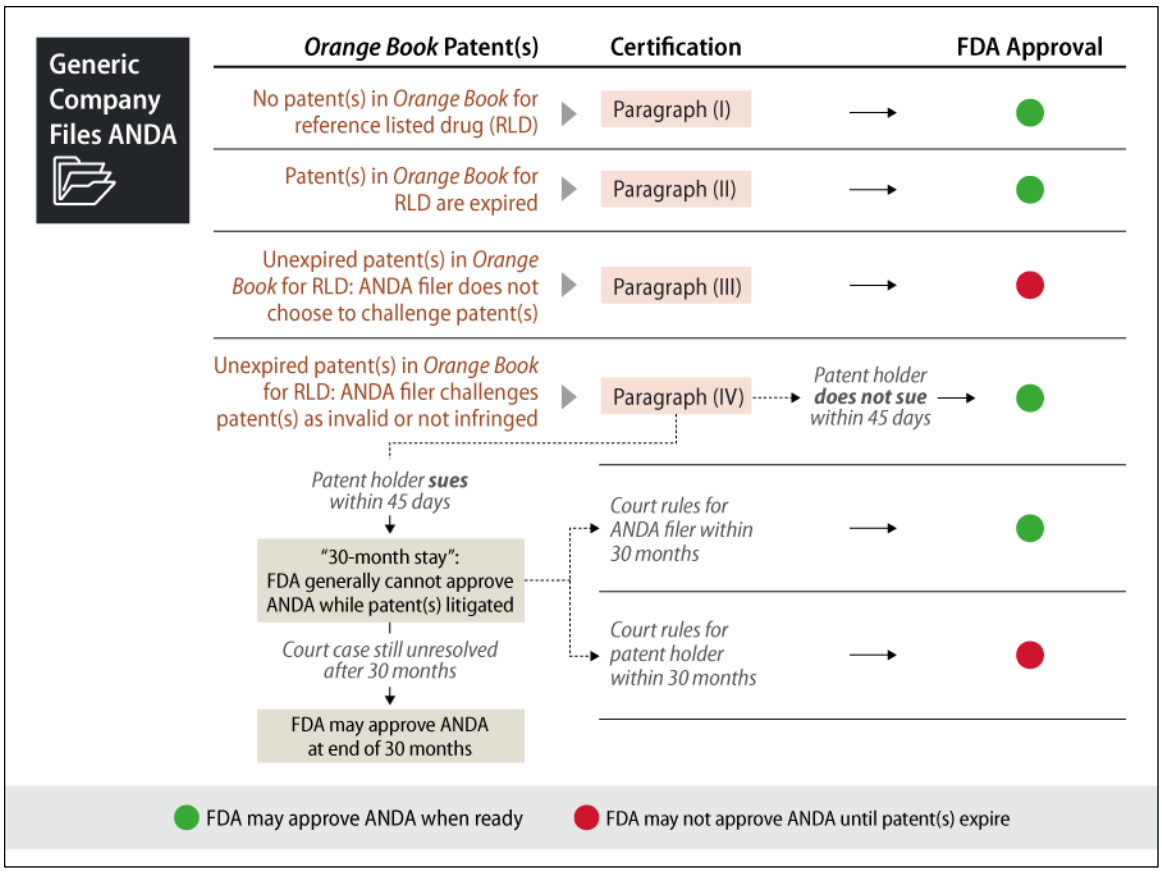
[305] 21 C.F.R. § 314.53(f)(1). Generally, FDA will not change the patent information in the *Orange Book* unless the NDA holder amends or corrects the information in response to a patent listing dispute. *Id.* § 314.53(f)(1)(i); *see generally* Ashley M. Winkler et al., *Requirements, Benefits, and Possible Consequences of Listing Patents in the FDA's Orange Book*, BNA PHARM. L. & INDUS. REP. 4–5 (July 3, 2018), https://www.finnegan.com/print/content/65249/Requirements-Benefits-and-Possible-Consequences-of-Listing-Patents-in-FDAs-Orange-Book.pdf. An ANDA filer may also make a counterclaim in patent infringement litigation to correct or delete patent information listed by the NDA holder. 21 U.S.C. § 355(j)(5)(C)(ii)(I).

[306] *See* Winkler et al., *supra* note footnote 305, at 3 ("Having a patent listed in the Orange Book provides significant

statutory provision providing that the patentee or NDA holder forfeits the right to sue if she fails to list the applicable patents, however.[307]

Figure 1. Patent Dispute Procedures for Generic Drugs

The Hatch-Waxman Notice-and-Certification Process



Source: CRS.

The BPCIA: The "Patent Dance" and Biosimilar Licensure

A different patent dispute resolution scheme applies to biological products and biosimilars, which are subject to regulatory licensure under the PHSA, as amended by the BPCIA.[308] Unlike the Hatch-Waxman approach, regulatory approval of biosimilars under the BPCIA is not directly contingent on resolution of patent disputes, and a BLA filer need not list patent information as

benefits to the NDA holder.").

[307] *See id.* at 4–5 (discussing the "possible consequences" of not listing or late listing, including the potential loss of the 30-month stay, but not a loss of patent rights); Brian D. Coggio & Ron Vogel, *Can Reference Sponsor Forfeit Right to Sue under BPCIA?*, LAW360 (July 25, 2016), https://www.law360.com/articles/820197, at n.32 ("It is worth noting that the Hatch Waxman Act does not have a 'list it or lose it' provision. A patentee can choose to assert any patents listed in the Orange Book, but it does not forfeit the right to later assert patents that were not part of the original litigation.").

[308] *See supra* "Biological Product and Biosimilar Licensure."

part of its BLA.[309] As a result, no patent information is currently listed in the *Purple Book*, FDA's list of approved biological products that is the biologics analogue of the *Orange Book.*[310]

Instead of the Hatch-Waxman certification process, patent disputes over biosimilars may be resolved through the BPCIA's "patent dance."[311] The patent dance is "a carefully calibrated scheme for preparing to adjudicate, and then adjudicating, claims of infringement" by reference product sponsors (i.e., the brand-name biologic manufacturers) against biosimilar applicants.[312] Depending on their participation in the patent dance, each party has an opportunity to litigate relevant patents in two phases. The first ("phase one") is at the conclusion of the patent dance—roughly six months after the biosimilar applicant files its BLA.[313] The second ("phase two") is when the biosimilar applicant provides a notice of commercial marketing, no later than 180 days before the date the biosimilar will be marketed.[314]

The first step in the patent dance process occurs when, not later than 20 days after FDA accepts a biosimilar BLA, the biosimilar applicant provides its application to the reference product sponsor, along with information on how the biosimilar is manufactured.[315] "These disclosures enable the [reference product] sponsor to evaluate the biosimilar for possible infringement of patents it holds on the reference product (i.e., the corresponding biologic)."[316] The biosimilar applicant and reference product sponsor next engage in a series of back-and-forth information exchanges regarding the patents that each party believes are relevant, as well as the parties' positions on the validity and infringement of those patents.[317] No later than 60 days after the initial disclosure by the biosimilars applicant, the reference product sponsor provides a list of patents that it reasonably believes it could assert, and whether it is willing to license them.[318] No later than 60 days thereafter, the biosimilar applicant provides a factual and legal basis for why the patents are invalid or not infringed, or whether it would accept a license.[319] After the reference product

[309] *See* 42 U.S.C. § 262(a); *Background Information: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations (Purple Book)*, U.S. FOOD & DRUG ADMIN. (Aug. 3, 2020), https://www.fda.gov/drugs/biosimilars/background-information-list-licensed-biological-products-reference-product-exclusivity-and [hereinafter *Purple Book Background Information*].

[310] *Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*, FOOD & DRUG ADMIN. (Aug. 3, 2020), https://purplebooksearch.fda.gov/ [hereinafter *Purple Book*]; Andrew Williams, *The Purple Book: The FDA Announces Welcome Enhancements*, WOLF GREENFIELD LIFE SCIS. IP BLOG (Feb. 27, 2020), https://blog.wolfgreenfield.com/wolf-tracks-life-sciences-blog/the-purple-book-the-fda-announces-welcome-enhancements. Unlike the *Orange Book*, FDA is not required by statute to publish the *Purple Book*. *See* Kurt R. Karst, *The "Purple Book Makes Its Debut*, FDA LAW BLOG (Sept 9. 2014), https://www.fdalawblog.net/2014/09/the-purple-book-makes-its-debut/. Legislation introduced in the 116th Congress would require FDA to publish the *Purple Book*, including certain patent information. *See* H.R. 1520, Purple Book Transparency Act, 116th Cong. (2019); S. 659, Biologic Patent Transparency Act, 116th Cong. (2019).

[311] *See* 42 U.S.C. § 262(*l*).

[312] Sandoz Inc. v. Amgen Inc., 137 S. Ct. 1664, 1670 (2017) (holding that injunctive relief to compel participation in the patent dance is not available under federal law); Amgen Inc. v. Sandoz Inc., 877 F.3d 1315, 1326–30 (Fed. Cir. 2017) (holding that the BPCIA preempts state law remedies for failure to commence the patent dance).

[313] *Sandoz*, 137 S. Ct. at 1672.

[314] *Id.*

[315] 42 U.S.C. § 262(*l*)(2).

[316] *Sandoz*, 137 S. Ct. at 1670–71.

[317] *Id.* at 1671–72.

[318] 42 U.S.C. § 262(*l*)(3)(A).

[319] *Id.* § 262(*l*)(3)(B)(ii)–(iii). The biosimilar applicant may also choose to supplement the reference product sponsor's list of relevant patents. *See id.* § 262(*l*)(3)(B)(i).

sponsor responds to the biosimilar applicant's invalidity and infringement contentions,[320] the parties engage in "good faith negotiations" over which patents (and how many) should be litigated immediately.[321] Once the parties determine the set of patents for "phase one" litigation, the reference product sponsor has 30 days to bring an action for infringement of those patents.[322]

"Phase two" litigation under the BPCIA begins once the biosimilar applicant gives notice to the reference product sponsor "not later than 180 days" before the first commercial marketing of the biosimilar product.[323] After receiving this notice, the reference product sponsor may seek a preliminary injunction for infringement of patents that were included on its initial patent list but not selected for phase-one litigation.[324] The biosimilar applicant may choose to give this "phase two" notice prior to FDA licensure of the biosimilar, so long as the notice is given 180 days before commercial marketing.[325] Thus, the biosimilar applicant can opt to "collapse" the two phases of litigation, if it so chooses.[326]

Reference product sponsors cannot obtain injunctive relief to compel the biosimilar applicant to engage in the patent dance.[327] In practice, this limitation means that biosimilar applicants can choose whether or not they wish to engage in the patent dance. If the biosimilar applicant chooses not to commence the patent dance, the BPCIA "authorizes the [reference product] sponsor, but not the applicant, to bring an immediate declaratory-judgment action for artificial [patent] infringement."[328] Thus, although the biosimilar applicant need not immediately reveal its manufacturing information if it chooses not to commence the patent dance, it exposes itself to an immediate declaratory-judgment lawsuit for patent infringement.[329] Biosimilar applicants thus may face complicated strategic tradeoffs in deciding whether to initiate the patent dance.[330]

Unlike patent listings in the *Orange Book* under Hatch-Waxman, the BPCIA contains an express statutory penalty for failing to list relevant patents. If the biosimilar applicant commences the patent dance, the reference product sponsor must provide a list of *all* "patents for which the reference product sponsor believes a claim of patent infringement could reasonably be asserted. . . if a person not licensed by the reference product sponsor engaged in the making, using, offering to sell, selling, or importing of [the biological product at issue]."[331] Under the "list it or lose it" requirement, the patent holder may forfeit his right to sue on patents that are not included on this

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[320] *Id.* § 262(*l*)(3)(C).

[321] *Id.* § 262(*l*)(4)(A), (*l*)(6). The BPCIA provides a procedure for a simultaneous exchange of patent lists if the parties cannot agree on the patents that should be litigated immediately. *Id.* § 262(*l*)(5).

[322] *Id.* § 262(*l*)(6).

[323] *Id.* § 262(*l*)(8)(A).

[324] *Id.* § 262(*l*)(8)(B).

[325] Sandoz Inc. v. Amgen Inc., 137 S. Ct. 1664, 1677 (2017).

[326] *See* Thomas J. Sullivan, *The Patent Dance*, EUR. BIOPHARM. REV. 70–74 (July 2018), *available at* https://www.finnegan.com/en/insights/articles/the-patent-dance-article.html ("A second mechanism to shorten a suit under the BPCIA would be to collapse the two phases of litigation . . . where the biosimilar applicant provides its 180-day notice of commercial marketing contemporaneously with its notification to the reference product sponsor of its [biosimilar application.]").

[327] *Sandoz*, 137 S. Ct. at 1675.

[328] *Id.*; *see* 42 U.S.C. § 262(*l*)(9)(C).

[329] *Sandoz*, 137 S. Ct. at 1675.

[330] *See generally* Limin Zheng, *Shall We (Patent) Dance?—Key Considerations for Biosimilar Applicants*, BIOSIMILAR DEV. (Feb. 27, 2018), https://www.biosimilardevelopment.com/doc/shall-we-patent-dance-key-considerations-for-biosimilar-applicants-0001.

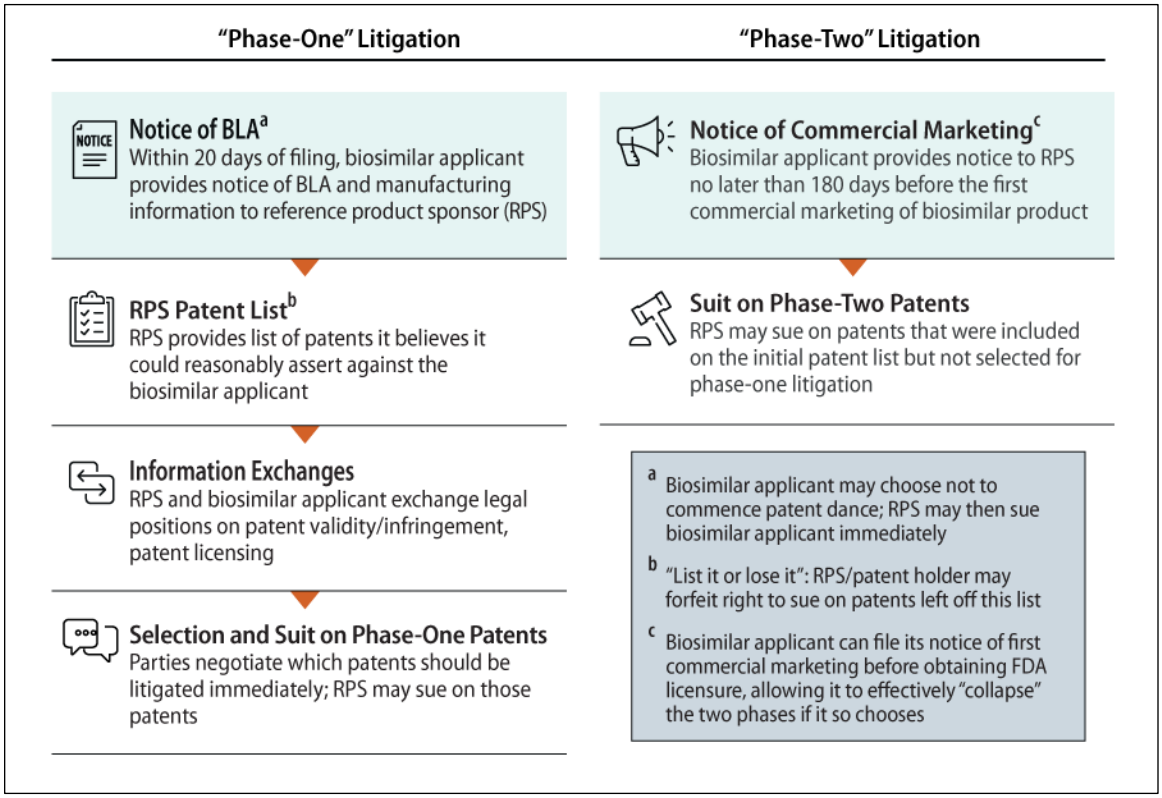
[331] 42 U.S.C. § 262(*l*)(3)(A)(i).

list.[332] Specifically, if a patent "should have been included in the list [as required during the patent dance], but was not timely included in such list," then the patent owner "may not bring an action under this section for infringement of the patent with respect to the biological product."[333]

Figure 2 diagrams the general patent dispute process under the BPCIA's patent dance. **Table 3** summarizes the key differences between the patent dispute resolution regimes for drugs under Hatch-Waxman and for biologics under the BPCIA.

Figure 2. Patent Dispute Procedures for Biosimilars

The BPCIA "Patent Dance"



Source: CRS.

[332] *See* Krista Hessler Carver et al., *An Unofficial Legislative History of the Biologics Price Competition and Innovation Act of 2009*, 65 FOOD & DRUG L.J. 671, 760 (2010) (describing this provision as the "list it or lose it" requirement); Coggio & Vogel, *supra* note 307 (same).

[333] 35 U.S.C. § 271(e)(6)(C). The statute is unclear as to whether the holder of a patent that was not timely listed loses his right to sue the biosimilar applicant only during the premarketing period (i.e., only with respect to the "artificial" act of infringement), or forfeits the right to sue on that patent for post-marketing infringement as well. *See* Coggio & Vogel, *supra* note 307 (analyzing the potential ambiguity as to whether the patentee is "precluded from asserting infringement of the nonlisted patent(s) under all subsections of section 271, or just subsection 271(e)(2)"); *but see* Hessler Carver et al., *supra* note 332, at 760 (describing the "list it or lose it" provision as reaching infringements both "before or after marketing of the biosimilar").

Table 3. Summary Comparison of Hatch-Waxman and BPCIA

Follow-on Regulatory Pathways and Patent Dispute Procedures

Feature	Hatch-Waxman and Generic Drug Approval	BPCIA and Biosimilar (or Interchangeable) Licensure
Regulatory Statute	FD&C Act	PHSA
Scope	A "drug" is, inter alia, a chemical compound "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease." 21 U.S.C. § 321(g)(1).	A "biologic" is a medical product derived from natural sources (human, animal, microorganism) and applicable to the prevention, treatment, or cure of disease. 42 U.S.C. § 262(i)(1).
Example	Aspirin: $C_9H_8O_4$	Adalimumab (a.k.a. Humira): $C_{6428}H_{9912}N_{1694}O_{1987}S_{46}$
Terminology	Drug is *approved* by FDA	Biological product is *licensed* by FDA
General Regulatory Standard	Safe and effective	Safe, pure, and potent
New Product Pathway	New drug application (NDA). 21 U.S.C. § 355(b).	Biologics license application (BLA). 42 U.S.C. § 262(a).
Abbreviated Pathway	Abbreviated new drug application (ANDA). 21 U.S.C. § 355(j).	Biosimilar (or interchangeable) BLA. 42 U.S.C. § 262(k).
Relationship Between New and Follow-on Product	*Chemical identity*: the active ingredient of the new drug is "the same as" that of the listed drug (if only one ingredient). 21 U.S.C. § 355(j)(2)(A)(ii).	*Biosimilarity*: "highly similar to the reference product" without "clinically meaningful differences." 42 U.S.C. § 262(i)(2); *see also* 42 U.S.C. § 262(k)(4) (interchangeability).
General Exclusivity Term for New Product	5-year new chemical entity exclusivity (3 years for other new products)	12-year new biologic exclusivity
Follow-On Exclusivity	180-day patent challenge exclusivity or 180-day competitive generic exclusivity	12- to 42-month exclusivity for first interchangeable product
Patent Listing Requirements	Required to list in NDA any patent that "claims the drug or a method of using the drug." 21 C.F.R. § 314.53(b); 21 U.S.C. § 355(b)(1).	Not required to list patents in BLA. If patent dance is initiated, BLA holder must list all patents "for which the [BLA holder] believes a claim of patent infringement could reasonably be asserted." 42 U.S.C. § 262(*l*)(3)(A)(i).
Patent Listing Consequences	ANDA filer need not certify; NDA loses opportunity for 30-month stay	"List it or lose it." 35 U.S.C. § 271(e)(6)(C).
FDA List of Approved Products	The *Orange Book* (includes patents)	The *Purple Book* (does not include patents)
Patent Dispute Procedures	Patent Certification/Notice. 21 U.S.C. § 355(b)(2)–(3), (c)(3), (j)(2)(A)–(B), (j)(5).	The "Patent Dance." 42 U.S.C. § 262(*l*).
Approval Contingent on Patent Disputes?	Yes, e.g., via the 30-month stay	No

Source: CRS.

Antitrust Law

How some drug and biologic manufacturers have obtained and enforced their patents may raise issues under federal antitrust laws. The Supreme Court has stated that the "primary purpose of the antitrust laws" is to protect and promote competition "from which lower prices can later

result."[334] To this end, antitrust law generally aims to "prohibit . . . anticompetitive conduct and mergers that enable firms to exercise market power."[335] The Sherman Antitrust Act of 1890 (the Sherman Act) "contains two main substantive provisions that prohibit agreements in restraint of trade and monopolization, respectively."[336] As discussed below, certain pharmaceutical patenting practices have been challenged by follow-on manufacturers under each of these two sections.[337]

Section 1 of the Sherman Act

Section 1 of the Sherman Act bars "[e]very contract, combination . . . , or conspiracy, in restraint of trade or commerce."[338] Although that language appears to sweep broadly, the Supreme Court has interpreted Section 1 to only bar *unreasonable* restraints on trade.[339] In evaluating the reasonableness of contractual restraints on trade under Section 1, courts have found that "some agreements and practices are invalid per se, while others are illegal only as applied to particular situations."[340] Unless the agreement falls within a per se illegal category, courts generally apply a "rule-of-reason" analysis to determine whether a restraint on trade is reasonable.

Per Se Illegal. Certain agreements are considered per se illegal "without regard to a consideration of their reasonableness"[341] because "the probability that these practices are anticompetitive is so high."[342] Only restraints that "have manifestly anticompetitive effects" and lack "any redeeming virtue" are held to be per se illegal.[343] Examples of per se illegal restraints include agreements for horizontal price fixing, market allocations, and output limitations.[344] To prevail on a claim of a per se illegal agreement, the plaintiff need only demonstrate that the agreement in question falls in one of the per se categories; in other words, "liability attaches without need for proof of power, intent or impact."[345]

The Rule-of-Reason Analysis. Challenged restraints that are not in the per se illegal category are generally analyzed under the rule-of-reason approach. While the Supreme Court has not developed a canonical framework to guide this totality-of-the-circumstances reasonableness inquiry, most courts take a similar approach in resolving rule-of-reason cases.[346] Under this burden-shifting approach, a Section 1 plaintiff has the initial burden of demonstrating that a

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[334] Leegin Creative Leather Prods. v. PSKS, Inc., 551 U.S. 877, 895 (2007) ("[T]he antitrust laws are designed primarily to protect interbrand competition, from which lower prices can later result."); State Oil Co. v. Khan, 522 U.S. 3, 15 (1997) ("Our analysis is also guided by our general view that the primary purpose of the antitrust laws is to protect interbrand competition.").

[335] CRS In Focus IF11234, *Antitrust Law: An Introduction*, by Jay B. Sykes.

[336] *Id.*

[337] 15 U.S.C. §§ 1–2; *see infra* "Pharmaceutical Patenting Practices."

[338] 15 U.S.C. § 1.

[339] *See, e.g.*, NCAA v. Bd. of Regents of Univ. of Okla., 468 U.S. 85, 98 (1984).

[340] United States v. E.I. du Pont de Nemours & Co., 351 U.S. 377, 387 (1956).

[341] United States v. Topco Assocs., Inc., 405 U.S. 596, 607 (1972).

[342] *NCAA*, 468 U.S. at 99, 103–04.

[343] Leegin Creative Leather Prods. v. PSKS, Inc., 551 U.S. 877, 886 (2007) (internal citations omitted).

[344] *See, e.g.*, United States v. Socony-Vacuum Oil Co., 310 U.S. 150, 218 (1940); *NCAA*, 468 U.S. at 99, 103–04; Stop & Shop Supermarket Co. v. Blue Cross & Blue Shield of R.I., 373 F.3d 57, 61 (1st Cir. 2004).

[345] *Stop & Shop Supermarket Co.*, 373 F.3d at 61; *see also Leegin Creative Leather Prods.*, 551 U.S. at 886; Nat'l Soc'y of Prof'l Eng'rs v. United States, 435 U.S. 679, 692–93 (1978).

[346] *See* DANIEL CRANE, ANTITRUST 53-6 (2014); *see also* Herbert Hovenkamp, *The Rule of Reason*, 70 FLA. L. REV. 81, 103 (2018) (collecting cases).

challenged restraint has anticompetitive effects in a "properly defined product" and geographic market—that is, that the restraint causes higher prices, reduced output, or diminished quality in the relevant market.[347] If the plaintiff succeeds in making this showing, the burden then shifts to the defendant to rebut the plaintiff's evidence with a procompetitive justification for the challenged practice.[348] For example, if a Section 1 plaintiff alleges that the challenged restraint produces higher prices, the defendant might attempt to contest that allegation or show that any price increases are offset by improvements in its products or services. If the defendant cannot produce such a justification, the plaintiff may prevail. If the defendant adequately demonstrates a procompetitive justification, the burden then shifts back to the plaintiff to show either (1) the restraint's anticompetitive effects outweigh its procompetitive effects or (2) the restraint's procompetitive effects could be achieved in a manner that is less restrictive of competition.[349]

Quick Look Analysis. In certain instances, courts may use "something of a sliding scale in appraising reasonableness," applying a more abbreviated rule-of-reason analysis to an agreement, referred to as a "quick look."[350] In identifying this intermediate standard of review, the Supreme Court explained that, because "[t]here is always something of a sliding scale in appraising reasonableness," the "quality of proof required" to establish a Section 1 violation "should vary with the circumstances."[351] As a result, the Court has concluded that in certain cases—specifically, those in which "no elaborate industry analysis is required to demonstrate the anticompetitive character" of a challenged agreement—plaintiffs can establish a prima facie case that an agreement is anticompetitive without presenting the sort of market power evidence traditionally required at the first step of the rule-of-reason analysis.[352]

While there is no universally accepted "quick look" framework, several courts of appeals have endorsed a modified burden-shifting approach in "quick look" cases.[353] Under this approach, if a Section 1 plaintiff can establish that a challenged restraint is obviously likely to harm consumers, the restraint is deemed "inherently suspect," and therefore presumptively anticompetitive.[354] A defendant can rebut this presumption by presenting "plausible reasons" why the challenged practice "may not be expected to have adverse consequences in the context of the particular market in question," or why the practice is "likely to have beneficial effects for consumers."[355] If the defendant fails to offer such reasons, the plaintiff prevails. However, if the defendant offers such an explanation, the plaintiff must address the justification by either explaining "why it can confidently conclude, without adducing evidence, that the restraint very likely harmed consumers" or providing "sufficient evidence to show that anticompetitive effects are in fact

[347] *See* CRANE, *supra* note 346, at 53-4; HERBERT HOVENKAMP, FEDERAL ANTITRUST POLICY: THE LAW OF COMPETITION AND ITS PRACTICE 103 (5th ed. 2015). The Supreme Court has explained that a properly defined market includes the product at issue and its substitutes—that is, other products that are "reasonably interchangebl[e]" with the relevant product. *See* Brown Shoe Co. v. United States, 370 U.S. 294, 325 (1962). Stated differently, whether two products compete in the same market depends on the extent to which an increase in the price of one product in a given geographic region would cause consumers to purchase the other product instead. HOVENKAMP, *supra*, at 111–17.

[348] *See* CRANE, *supra* note 346, at 54; Hovenkamp, *supra* note 347, at 103.

[349] *See* CRANE, *supra* note 346, at 54; Hovenkamp, *supra* note 347, at 104.

[350] Cal. Dental Ass'n v. FTC, 526 U.S. 756, 770 (1999).

[351] *Id*. at 780 (internal quotation marks and citation omitted).

[352] *Id*. at 770.

[353] *See* N.C. St. Bd. Dental Exs. v. FTC, 717 F.3d 359, 374, 374 n.11 (4th Cir. 2013); N. Tex. Specialty Physicians v. FTC, 528 F.3d 346, 361 (5th Cir. 2008); Polygram Holding, Inc. v. FTC, 416 F.3d 29, 35 (D.C. Cir. 2005).

[354] *Polygram Holding*, 416 F.3d at 35–36.

[355] *Id*. at 36 (internal quotation marks and citation omitted).

likely."[356] If the plaintiff succeeds in making either showing, "the evidentiary burden shifts to the defendant to show the restraint in fact does not harm consumers or has 'procompetitive virtues' that outweigh its burden upon consumers."[357] If the plaintiff fails to rebut the defendant's initial justification, its challenge is assessed under a full rule-of-reason framework.

Section 2 of the Sherman Act

Section 2 of the Sherman Act makes it unlawful to monopolize, attempt to monopolize, or conspire to monopolize "any part of the trade or commerce among the several States, or with foreign nations."[358] Despite the facially broad language of Section 2, the Supreme Court has clarified that monopolization is only illegal if "it is accompanied by an element of anticompetitive *conduct*."[359] It is not illegal to possess monopoly power that is the result of, for example, "a superior product, business acumen, or historic accident."[360] Thus, establishing a Section 2 violation requires proving the defendant "possessed monopoly power in the relevant market" and acquired or maintained that power using anticompetitive conduct.[361] Courts generally analyze whether conduct is anticompetitive (i.e., step two of the analysis) using a rule-of-reason approach.[362]

Enforcement

Federal antitrust laws are primarily enforced through three mechanisms: (1) enforcement actions brought by the U.S. Department of Justice's Antitrust Division, (2) enforcement actions brought by the Federal Trade Commission (FTC), or (3) lawsuits brought by a private party or by a state attorney general on behalf of a private party.[363] In particular, Section 5 of the FTC Act gives the FTC authority to combat "[u]nfair methods of competition" generally, which includes violations of the Sherman Act.[364]

FTC enforcement typically begins with a confidential investigation into the relevant conduct.[365] A company may resolve the investigation by entering into a consent order agreeing to stop or to address the potentially anticompetitive practices.[366] If the FTC and the company do not reach a

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[356] *Id*. (internal quotation marks and citation omitted).

[357] *Id*.

[358] 15 U.S.C. § 2.

[359] Verizon Commc'ns Inc. v. Law Offices of Curtis V. Trinko, LLP, 540 U.S. 398, 407 (2004).

[360] *Id.* (quoting United States v. Grinnell Corp., 384 U.S. 563, 570–71 (1966)).

[361] Schneiderman v. Actavis PLC, 787 F.3d 638, 651 (2d Cir. 2015).

[362] *Id.* at 652.

[363] *Antitrust Enforcement and the Consumer*, U.S. DEP'T OF JUSTICE, https://www.justice.gov/atr/file/800691/download (last visited Dec. 7, 2020); *The Enforcers*, U.S. FED. TRADE COMM'N, https://www.ftc.gov/tips-advice/competition-guidance/guide-antitrust-laws/enforcers (last visited Dec. 7, 2020) [hereinafter *The Enforcers*].

[364] 15 U.S.C. § 45; FTC v. Cement Inst., 333 U.S. 683, 690 (1948) (holding that the FTC may pursue violations of the Sherman Act as unfair methods of competition); FTC v. Motion Picture Advert. Serv. Co., 344 U.S. 392, 394 (1953) ("The 'Unfair methods of competition', which are condemned by § 5(a) of the [FTC] Act, are not confined to those that were illegal at common law or that were condemned by the Sherman Act.").

[365] *The Enforcers*, *supra* note 363.

[366] *Id.* ("If the FTC believes that a person or company has violated the law or that a proposed merger may violate the law, the agency may attempt to obtain voluntary compliance by entering into a consent order with the company. A company that signs a consent order need not admit that it violated the law, but it must agree to stop the disputed practices outlined in an accompanying complaint or take certain steps to resolve the anticompetitive aspects of its proposed merger.").

consent order, the FTC may begin an administrative proceeding or may seek relief in the federal courts.[367] The administrative proceeding is similar to a court proceeding, but is overseen by an administrative law judge (ALJ).[368] If the ALJ finds that there has been a violation, the FTC may issue a cease-and-desist order. The ALJ's decision is appealable to the full FTC, then to a U.S. Court of Appeals and, finally, to the Supreme Court.[369]

Pharmaceutical Patenting Practices

Patent holders generally seek to use their rights to the fullest extent permitted by law, regardless of their patent's technological field.[370] From the patent holders' perspective, the practices described below may be viewed as appropriate uses of the legal rights granted by their patents, which were obtained after a rigorous examination process that demonstrated compliance with patentability requirements.[371] Critics view these practices as harmful strategies that exploit the patent system in ways Congress did not intend.[372]

"Evergreening"

Definition

Evergreening, also known as patent "layering" or "life-cycle management," is a practice by which drug innovators allegedly seek "to prolong their effective periods of patent protection [through] strategies that add new patents to their quivers as old ones expire."[373] As discussed above, because different aspects of pharmaceutical products (and improvements thereon) are patentable,[374] dozens of different patents can protect a single pharmaceutical product. The average number of patents per drug has steadily increased since Hatch-Waxman was enacted in 1984.[375] On average, there are 2.7 patents listed for each pharmaceutical product listed in the *Orange*

[367] *Id.* ("If a consent agreement cannot be reached, the FTC may issue an administrative complaint and/or seek injunctive relief in the federal courts.").

[368] *Id.* ("The FTC's administrative complaints initiate a formal proceeding that is much like a federal court trial but before an administrative law judge: evidence is submitted, testimony is heard, and witnesses are examined and cross-examined.").

[369] *Id.* ("If a law violation is found, a cease and desist order may be issued. An initial decision by an administrative law judge may be appealed to the Commission. Final decisions issued by the Commission may be appealed to a U.S. Court of Appeals and, ultimately, to the U.S. Supreme Court.").

[370] Peter Thomas Luce, *Hiding Behind Borders in a Borderless World: Extraterritoriality Doctrine and the Inadequacy of U.S. Software Patent Protections in a Networked Economy*, 10 TUL. J. TECH. & INTELL. PROP. 259, 280 n.118 (2007) ("If the patent is legitimate, the patent holder would be a patent fool if he did not protect his rights to the fullest extent of the law.").

[371] GlaxoSmithKline, *GSK Public Policy Positions: Evergreening*, May 2019, https://www.gsk.com/media/2949/evergreening-policy.pdf [hereinafter *GlaxoSmithKline Positions*] ("GSK rejects the accusation that improvement patents are not justified within patent law. Patents for improvements to existing products, in the field of pharmaceutical and other technologies, are only available if they meet the requirements of patentability (i.e. that they are new, useful and involve an inventive step) as assessed by trained patent examiners.").

[372] *See, e.g.*, Michael A. Carrier & Carl J. Minniti III, *Biologics: The New Antitrust Frontier*, 2018 U. ILL. L. REV. 1, 3 (2018).

[373] Eisenberg, *supra* note 15, at 354; *see also* Marrs, *supra* note 37, at 83–89; Furrow, *supra* note 37, at 276.

[374] *See supra* "Types of Pharmaceutical Patents."

[375] C. Scott Hemphill & Bhaven V. Sampat, *When Do Generics Challenge Drug Patents*, 8 J. EMPIRICAL L. STUD. 613, 619–20 (2011).

Book.[376] Particularly profitable products are usually protected by many more patents. A 2018 study of the top 12 drugs by gross U.S. revenue found that pharmaceutical manufacturers obtained an average of 71 patents on each of these drugs.[377] For example, this study found that Celgene, the maker of the top-selling plasma cell myeloma drug Revlimid, filed 106 U.S. patent applications covering that product, resulting in 96 issued patents.[378] The study also found that the price of Revlimid increased by 79% since 2012.[379] The U.S. House of Representatives Committee on Oversight and Reform investigated the Revlimid's pricing and concluded that Celgene "stifled generic competition by filing for" numerous patents "and enforcing those patents against potential generic competitors."[380] Another House Committee on Oversight and Reform investigation into Amgen's biologic Enbrel, used to treat rheumatoid arthritis, concluded that "Amgen has leveraged its patent and lifecycle management strategies to prevent competitors from introducing lower-priced biosimilar versions of Enbrel."[381]

Debate

Because later-filed patents often claim aspects of a drug other than its active ingredient, these patents are sometimes called "secondary" patents.[382] Critics of evergreening maintain that, by obtaining secondary patents on improvements or ancillary aspects of a pharmaceutical product, manufacturers effectively extend patent protection beyond the term set by Congress. In doing so, according to these critics, secondary patents unfairly shield pharmaceutical products from generic or biosimilar competition, thereby resulting in higher drug prices.[383] In the view of evergreening critics, moreover, many of these secondary patents are of questionable validity.[384] While secondary patents tend to be challenged more frequently and more successfully than patents covering a pharmaceutical's active ingredient,[385] the combination of secondary patents and a

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[376] *Id.* Other commentators have found a similar average. *See, e.g.*, Ouellette, *supra* note 245, at 314 (finding, on average, 2.97 patents listed per drug in FDA's *Orange Book*).

[377] *See Overpatented*, *supra* note 245, at 6–8.

[378] *Id.* at 7.

[379] *Id.*

[380] STAFF OF H. COMM. ON OVERSIGHT & REFORM, DRUG PRICING INVESTIGATION: CELGENE AND BRISTOL MYERS SQUIBB—REVLIMID 20 (Sept. 30, 2020), https://oversight.house.gov/sites/democrats.oversight.house.gov/files/Celgene%20BMS%20Staff%20Report%2009-30-2020.pdf.

[381] STAFF OF H. COMM. ON OVERSIGHT & REFORM, DRUG PRICING INVESTIGATION: AMGEN—ENBREL AND SENSIPAR 25 (Sept. 30, 2020), https://oversight.house.gov/sites/democrats.oversight.house.gov/files/Amgen%20Staff%20Report%2010-1-20.pdf.

[382] *See supra* "Types of Pharmaceutical Patents."

[383] *See, e.g.*, Marrs, *supra* note 37, at 83–86; Feldman & Frondorf, *supra* note 8, at 555 ("Pharmaceutical company behavior [such as evergreening] that extends the period in which the company can hold off competition runs contrary to the patent bargain [leading to] losses to society in the form of higher prices."); Robin Feldman, *May Your Drug Price Be Evergreen*, 5 J.L. & BIOSCI. 590, 590 (2018) (criticizing drug companies for "recycling and repurposing old [medicines]" to stifle competition).

[384] *See, e.g.*, Aaron S. Kesselheim, *Think Globally, Prescribe Locally: How Rational Pharmaceutical Policy in the U.S. Can Improve Global Access to Essential Medicines*, 34 AM. J.L. & MED. 125, 136 (2008) ("Loose interpretation of patent laws has permitted patent evergreening, where overly broad or otherwise inappropriate patents have been granted on peripheral aspects of pharmaceutical products . . . ."); Eisenberg, *supra* note 15, at 354 (noting that although "innovating firms have succeeded in getting [secondary] patents issued by the PTO," "[t]he industry's track record in actually winning these infringement claims . . . has been considerably worse").

[385] C. Scott Hemphill & Bhaven V. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 21 J. HEALTH ECON. 327 (2012) (finding secondary patents relating to ancillary aspects of a drug are more frequently challenged by generics).

strong primary patent creates a barrier to generic entry because a generic manufacturer may delay or decline entry when faced with the prospect of defeating both patents.[386] According to *Bloomberg Law*, in 2017 the cost of litigating a Hatch-Waxman lawsuit was $1.8 million in cases involving over $25 million in risk.[387] Commentators have suggested that these costs can be compounded when there are several patents at issue, even if (some of) those patents are comparably weaker.[388] Thus, critics of evergreening argue that the costs of invalidating even comparatively weak patents strengthen the branded product's position in the market and can lengthen its effective period of exclusivity.[389]

Defenders contend that there is nothing inherently suspect about secondary patents, which must meet the same requirements for patentability and pass through the same examination procedures as any other patent.[390] Those requirements bar a secondary patent on an obvious variation of the primary patent or on another product or invention already available to the public.[391] "[I]t is often the case," defenders contend, "that the value of a follow-on patent is comparable to, or even might exceed, that of a primary patent."[392] One example arguably supporting this view is the drug Evista (raloxifine). Evista was "initially studied as a potential treatment for breast cancer" but, in 1997, FDA approved the drug for the prevention of osteoporosis.[393] At that time, there were a few years left on Evista's initial patent, which was filed in 1983.[394] If the brand could not patent the new use (i.e., for prevention of osteoporosis), one commentator has argued that insufficient incentives would have existed to make the investment in R&D necessary to bring the drug to market for the new use.[395] Thus, defenders of evergreening respond that the term is "inherently pejorative" because it creates the inaccurate impression that pharmaceutical companies are exploiting the patent system.[396]

Defenders also argue that the ability to receive a patent on a later-developed drug formulation provides a significant incentive to address problems with the original formulation. For example, the original formulation of Lumigan, which is used to treat glaucoma, resulted, at times, in sufficiently severe red eye that patients would discontinue its use.[397] Researchers subsequently

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[386] Hemphill & Sampat, *supra* note 375, at 621 ("These patents, though weak, nevertheless have the effect of making the patent portfolio stronger. If they overlap in duration with a strong composition of matter patent, they provide an additional barrier to generic entry prior to expiration of the strong patent, since the generic must defeat the weak patent in addition to the strong one.").

[387] Malathi Nayak, *Cost of Patent Infringement Litigation Falling Sharply*, BLOOMBERG LAW (Aug. 11, 2017), https://news.bloomberglaw.com/business-and-practice/cost-of-patent-infringement-litigation-falling-sharply.

[388] *See* Hemphill & Sampat, *supra* note 375, at 621.

[389] *Id.*; 35 U.S.C. § 103.

[390] *GlaxoSmithKline Positions*, *supra* note 371, at 1 ("Patents for improvements to existing products, in the field of pharmaceutical and other technologies, are only available if they meet the requirements of patentability (i.e. that they are new, useful and involve an inventive step) as assessed by trained patent examiners.").

[391] *Id.*

[392] Christopher M. Holman et al., *Patentability Standards for Follow-On Pharmaceutical Innovation*, 37 BIOTECH. L. REP. 131, 134 (2018).

[393] *Id.*

[394] *Id.*

[395] *Id.*

[396] *GlaxoSmithKline Positions*, *supra* note 371, at 1 ("'Evergreening' is an inherently pejorative term. It is used by some to convey the false impression that research-based pharmaceutical companies abuse the patent system by obtaining patents on what are characterised as 'minor' improvements to existing medicines in order to prevent competition by delaying the legitimate market entry of generic products.").

[397] Holman, *supra* note 392, at 135.

developed an improved formulation with significantly decreased risk of this side effect.[398] Defenders of secondary patents contend that without the possibility of patent protection, there would have been little incentive to perform this sort of research due to the significant costs involved.[399]

Secondary patents are also defended as necessary to recoup development costs. A recent study found that even though the patent term is generally 20 years, delays in PTO and FDA approval can decrease the nominal *Orange Book* patent term to 15.9 years, and generic competition can result in an effective market exclusivity of 12.2 years.[400] This effective market exclusivity is less than the 16 years that one commentator suggests is necessary to recoup the brand's fixed costs for research, development, and clinical testing.[401] Moreover, as secondary patents tend to be improvements to primary patents, brands argue they are necessarily narrower than those primary patents.[402] Thus, brands argue that when the primary patent expires, any other company—including a generic—may enter the market and produce the invention covered by that primary patent, assuming the generic can design around any unexpired secondary patents.[403] Doctors and patients can then decide whether the benefit conferred by a product covered by a secondary patent is worth the increased cost over the generic version of the product formerly covered by the primary patent.[404]

Defenders also note that congressional action has decreased the cost of challenging patents, reducing the impact of these later-filed "evergreening" patents. After Congress enacted the AIA in 2011, follow-on manufacturers can rely on administrative PTO procedures such as IPR, which was intended to "provide a more efficient system for challenging patents that should not have issued; and reducing unwarranted litigation costs."[405] Generally, any person who is not a patent's owner may file a petition for IPR beginning nine months after the patent issues.[406] The PTO then decides whether to initiate review of the patent.[407] If review is initiated, then the patent challenger must prove that the patent is invalid by a preponderance of the evidence[408]—a lower requirement than the clear-and-convincing-evidence standard used when challenging the patent in court.[409] The statute requires that the PTO's final decision be issued not more than one year after the decision to institute review.[410] The median cost for litigating an IPR to that final decision is

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[398] *Id.*

[399] *Id.*

[400] Hemphill & Sampat, *supra* note 385. "Nominal patent term" is "the time between brand approval and expiration of the last expiring patent." *Id.*

[401] Michiko Morris, *supra* note 5, at 267–68.

[402] *GlaxoSmithKline Positions*, *supra* note 371, at 2 ("Patents cannot give exclusive rights for things that are already known or obvious. Therefore, patents for modifications of existing products, sometimes referred to as 'secondary patents', are necessarily narrower in scope than what has gone before.").

[403] *Id.* ("It follows that, following expiry of an earlier patent, a secondary patent cannot preclude a generic competitor from selling products defined in that earlier patent and which are not covered by the secondary patent.").

[404] *Id.* ("It is the medical community and paying authorities that will decide whether a price premium for the [later-patented] product is worth paying.").

[405] H.R. Rep. No. 112-98, at 39–40 (2011).

[406] 35 U.S.C. § 311. A similar proceeding, PGR, allows for challenges in the initial nine months after the patent issues. *Id.* §§ 321–329.

[407] *Id.* § 314(a).

[408] *Id.* § 316(e).

[409] Microsoft Corp. v. i4i Ltd. P'ship, 564 U.S. 91, 95 (2011).

[410] 35 U.S.C. § 316(e)(11).

$324,000.[411] Thus, IPR provides a relatively fast and inexpensive method to challenge issued patents, particularly when compared to litigating in the courts.

Current Law

No statute specifically forbids evergreening. Instead, substantive patent law, particularly the law of obviousness, provides limits on whether the PTO may grant later-filed patents. Specifically, a patent may not be granted if "the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious" before the patent application was filed.[412] The Supreme Court has not articulated a specific test for whether an invention would have been obvious, instead preferring a flexible approach that takes the facts and circumstances of the state of the art into account.[413] The Court has identified, however, some situations in which an invention likely would have been obvious.[414] For example, if the invention involves "the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement," the invention likely would have been obvious.[415] At bottom, if the invention is "a predictable variation" of what came before, then the law of obviousness "likely bars its patentability."[416]

Other doctrines also affect the viability of later-filed patents. Because the patent statute limits a person to "*a* patent" for a new invention,[417] a single patentee may not obtain a later patent that covers the exact same invention as an earlier patent.[418] This doctrine is referred to as "statutory double patenting" because it derives from the patent statute and prevents patenting of the same invention twice by the same inventor.[419] The courts have extended double patenting to bar an inventor from patenting obvious variations of his earlier patents as well.[420] This second form of double patenting, referred to as "obviousness-type double patenting," prohibits a later patent that is not "patentability distinct" from an earlier commonly owned patent.[421] In other words, the doctrine bars a patent owner from receiving a patent on an obvious variation of one of its earlier-filed patents.[422] A patentee may overcome the obviousness-type double patenting issue, however, by using a "terminal disclaimer"—that is, by disclaiming any portion of the later patent's term after the expiration of the earlier patent.[423]

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[411] Stephen Yelderman, *Prior Art in Inter Partes Review*, 104 IOWA L. REV. 2705, 2706 (2019).

[412] 35 U.S.C. § 103.

[413] KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 416 (2007).

[414] *Id.* at 417–22.

[415] *Id.* at 417.

[416] *Id.*

[417] 35 U.S.C. § 101 ("Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain *a* patent therefor, subject to the conditions and requirements of this title." (emphasis added)).

[418] Sun Pharm. Indus., Ltd. v. Eli Lilly & Co., 611 F.3d 1381, 1384–85 (Fed. Cir. 2010).

[419] *Id.*

[420] *Id.*

[421] *Id.*

[422] *Id.*

[423] *See, e.g.*, Gilead Sci., Inc. v. Natco Pharma Ltd., 753 F.3d 1208, 1210 (Fed. Cir. 2014); STC.UNM v. Intel Corp., 754 F.3d 940, 942 (Fed. Cir. 2014).

"Product Hopping"

Definition

Critics of current pharmaceutical patenting practices have observed that patent evergreening can be used in conjunction with a practice they call "product hopping."[424] Product hopping is the process by which a brand, as the patents on an older branded drug are expiring, uses its current dominant market position to switch doctors, pharmacists, and consumers to a newer version of the same (or similar) drug with later-expiring patents. In other words, the brand forces a "hop" from one product to another.[425] The new version of the product may be, for example, an extended release form or new dosage (e.g., moving from twice-a-day to once-a-day), a different route of administration (e.g., moving from capsules to tablets, or tablets to film strips), or a chemical change (e.g., moving to a different enantiomer).[426] The switch to the new version may be accompanied by a marketing campaign or discounts and rebates to encourage doctors, insurers, and patients to switch to the new version; in some cases, production of the older version may be discontinued.[427]

Product hopping tends to take one of two forms: a "hard switch," where the brand removes the original product from the market, and a "soft switch," where the brand leaves the original product on the market.[428] The case of *Abbott Laboratories v. Teva Pharmaceuticals USA, Inc.*[429] provides one example of a hard switch. That case involved Abbott's changes to its drug TriCor, which was used to treat cholesterol and triglycerides.[430] Abbott allegedly lowered the drug's strength, switched it from a capsule to a tablet, stopped selling capsules, bought back supplies of capsules from pharmacies, and marked capsules as "obsolete" in the national drug database.[431] Once generics developed equivalents for the reformulation, Abbott allegedly again lowered the drug's strength, stopped selling the original tablets, and again changed the code for the old tablets to "obsolete."[432]

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[424] This term was coined by Professor Herbert Hovenkamp in the early 2000s. *See* Alan Devlin, *Exclusionary Strategies in the Hatch-Waxman Context*, 2007 MICH. ST. L. REV. 631, 658 (2007) (citing HERBERT HOVENKAMP ET AL., IP AND ANTITRUST: AN ANALYSIS OF ANTITRUST PRINCIPLES APPLIED TO INTELLECTUAL PROPERTY LAW § 12.5 (2002)).

[425] *See generally* Feldman & Frondorf, *supra* note 8, at 527–30; Carrier & Shadowen, *supra* note 37, at 171–73; Tobin Klusty, *A Legal Text for the Pharmaceutical Company Practice of "Product Hopping,"* 17 AM. MED. ASS'N J. ETHICS 760, 760 (2015).

[426] *See* Steve D. Shadowen et al., *Anticompetitive Product Changes in the Pharmaceutical Industry*, 41 RUTGERS L.J. 1, 25 (2009) (categorizing pharmaceutical reformulations); Feldman & Frondorf, *supra* note 8, at 529–32 (reviewing examples of product hopping); Carrier & Shadowen, *supra* note 37, at 172 (same).

[427] Shadowen et al., *supra* note 426, at 3 ("In addition to physically altering the product, manufacturers often also: (1) switch promotional efforts from the original product to the reformulated product; (2) introduce the redesigned product before generic entry; or (3) withdraw the original product from the market."); *accord* Feldman & Frondorf, *supra* note 8, at 527–29.

[428] Carrier & Shadowen, *supra* note 37, at 192.

[429] 432 F. Supp. 2d 408 (D. Del. 2006).

[430] *Id.* at 415.

[431] *Id.* at 415–17. As explained in more detail *infra*, making these types of changes may render any current generic version of a branded drug no longer therapeutically equivalent to the branded version, thus generally preventing a pharmacist from substituting the generic version for the branded version. *See infra* notes 443–448 and accompanying text.

[432] *Abbott Labs.*, 432 F. Supp. 2d at 415–17 A Delaware district court determined these allegations were sufficient to support an antitrust claim. *Id.* at 419–33.

A soft switch allegedly occurred in *Schneiderman v. Actavis PLC*.[433] There, Actavis produced Namenda IR (IR), a twice-daily drug designed to treat Alzheimer's disease.[434] As the patents on IR neared expiration and generics prepared to enter the market, Actavis introduced a once-daily version of the drug, Namenda XR (XR), and allegedly attempted to induce doctors and patients to switch from IR to XR.[435] Although the generic versions would have been substitutable for IR, the differences in dosing (10 mg in IR and 28 mg in XR) meant the generic versions would not be substitutable for the new XR product.[436] Initially, both IR and XR were on the market together.[437] During that time, Actavis allegedly stopped marketing IR and "spent substantial sums of money promoting XR to doctors, caregivers, patients, and pharmacists."[438] Actavis also sold XR at a discount, making it much less expensive than IR, and issued rebates to ensure patients did not have to pay higher copayments for XR than IR.[439] When it appeared the soft switch would only convert 30% of IR users to XR, Actavis allegedly implemented a hard switch by announcing it would discontinue IR and attempting to stop Medicare health plans from covering IR.[440]

Debate

Critics of product hopping deride it as an anticompetitive practice that inhibits the entry of generic and biosimilar competitors, allowing a brand to maintain its dominant market position (and higher prices) without substantial benefits for consumers.[441] In particular, critics contend that by shifting product demand from the previous product to a new product, the market for a generic form of the previous version dissipates by the time the generic can enter the market.[442]

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[433] 787 F.3d 638 (2d Cir. 2015). Since this case, Actavis has changed its name to Allergan. Andrew Berg, *Actavis Moves to Adopt New "Allergan" Corporate Name*, R&D, May 20, 2016, https://www.rdmag.com/news/2016/05/actavis-moves-adopt-new-allergan-corporate-name.

[434] *Schneiderman*, 787 F.3d at 642.

[435] *Id.*

[436] *Id.* at 647.

[437] *Id.* at 648.

[438] *Id.* (footnote omitted).

[439] *Id.*

[440] *Id.* The district court determined that Actavis's conduct was anticompetitive and issued a preliminary injunction ordering Actavis to make IR available on the same terms and conditions as before. *Id.* at 662. The Second Circuit affirmed the district court's determination and the preliminary injunction, although the court determined that it was only the *hard* switch that crossed the line into illegal behavior. *Id.* at 654. The court reasoned that as long as both IR and XR were on the market with generic drugs on the horizon, doctors and patients could evaluate whether the benefits of switching to once-daily XR outweighed the increased costs as compared to the generic form of IR. *Id.* at 655.

[441] *See, e.g.*, Carrier & Shadowen, *supra* note 37, at 168 ("The concern with [product hopping] is that some of these switches can significantly decrease consumer welfare, impairing competition from generic drugs to an extent that greatly exceeds any gains from the 'improved' branded product."); Justine Amy Park, *Product Hopping: Antitrust Liability and a Per Se Rule*, 35 CARDOZO ARTS & ENT. L.J. 745, 773 (2017) ("The use of product hopping to circumvent the entry of generic competitors is a gross violation of [antitrust law] and encourages brand name manufacturers to thinly disguise their products as innovative while maintaining patent monopolies on products."); Jessie Cheng, *An Antitrust Analysis of Product Hopping in the Pharmaceutical Industry*, 108 COLUM. L. REV. 1471, 1472 (2008) ("[P]roduct hopping amounts to little more than a thinly disguised scheme to manipulate the pharmaceutical industry's regulatory system and frustrate generic competition.").

[442] Vikram Iyengar, *Should Pharmaceutical Product Hopping Be Subject to Antitrust Scrutiny*?, 97 J. PAT. & TRADEMARK OFF. SOC'Y 663, 669–70 (2015) ("If the brand firm withdraws its existing product from pharmacy shelves and convinces doctors to write prescriptions for its new product, the market for the generic collapses."); Shadowen et al., *supra* note 426, at 7–18 (describing how the regulatory and economic context creates "price disconnect" that prevents generics from effectively competing on price following a product reformulation).

All 50 states have enacted drug product selection (DPS) laws, which aim to lower consumer prices by allowing, and sometimes even requiring, pharmacists to fill a prescription written for a brand-name drug with a generic version of that drug.[443] Typically, pharmacists may only substitute a generic drug for a branded drug if the generic version is "AB-rated" by FDA.[444] To receive an AB rating, the generic must be therapeutically equivalent to the branded drug, which means it must have the same active ingredient, form, dosage, strength, and safety and efficacy profile.[445] The generic must also be bioequivalent—in other words, the rate and extent of absorption of the generic cannot significantly differ from that of the brand drug.[446] Thus, if the brand's new version of a drug, for example, changes the form of the drug (e.g., capsule to tablet) or the dosage of the active ingredient (e.g., 10 mg to 12 mg) from the older version, the generic product may not receive the AB rating required to be substitutable by pharmacists.[447] Even if the generic is eventually able to obtain an AB rating to allow substitution, that process may take years to achieve.[448] Thus, the "hop" to a new product can prevent automatic substitution with a generic product, thereby giving the brand an additional period during which it is substantially unaffected by generic competition.

Defenders of product hopping counter that manufacturers have legitimate reasons to create new patented products and encourage doctors to prescribe the new product instead of an old product for which there is generic competition.[449] One commentator has argued that patent law encourages brands to create new drugs or switch to new versions of drugs because they receive an exclusive period during which they may charge higher prices.[450] That period is critical, it is argued, to recoup the estimated $2.6 billion average cost of bringing a new drug to market—compared to the $1-$2 million to bring a new generic product to market.[451] Once a branded drug's patents expire, however, the brand will lose 80% to 90% of its sales to generic drugs.[452] Thus, according to one commentator, brands have little incentive to keep marketing a product that is subject to generic competition; doing so would arguably transfer approximately 80% of the sales to their generic competitors. That is, even if the brand succeeds in convincing a doctor to prescribe the old product, DPS laws would allow a pharmacist to substitute a generic product instead.[453] Given these economic realities, defenders argue that the brand would be effectively paying to market its competitors' products.[454] Accordingly, it is argued that product hopping aims

[443] Carrier & Shadowen, *supra* note 37, at 175. Questions have been raised as to whether DPS laws are still important, considering the increased power of drug plans and pharmacy benefit managers. *See, e.g.*, Joanna Shepherd, *Deterring Innovation:* New York v. Actavis *and the Duty to Subsidize Competitors' Market Entry*, 17 MINN. J. OF L., SCI. & TECH. 663, 688–92 (2016) (arguing pharmacy benefit managers and insurers have adopted methods for providing patients with less-expensive alternatives to branded pharmaceuticals).

[444] Carrier & Shadowen, *supra* note 37, at 175.

[445] *Id.*

[446] *Id.*

[447] *Id.* at 176.

[448] *Id.*

[449] Shepherd, *supra* note 443, at 668; *see also* Tyler J. Klein, *Antitrust Enforcement Against Pharmaceutical Product Hopping: Protecting Consumers or Reaching Too Far?*, 10 ST. LOUIS U. J. HEALTH L. & POL'Y 213 (2016).

[450] Shepherd, *supra* note 443, at 668.

[451] *Id.*

[452] *Id.* at 668–69 (further noting that "eighty percent of marketed brand drugs never earn enough sales" to recoup development costs).

[453] *Id.* at 670.

[454] *See id.* at 670–71.

at maximizing profits for the brand (which can be used for additional R&D) and preventing free-riding by generics, not at preventing competition.[455]

Commentators also respond that generic manufacturers could reduce the impact of product hopping by marketing their own products.[456] In that view, generic manufacturers *choose* to rely on DPS laws for sales.[457] Instead, one commentator argues, the generic companies could promote their own products in the same way that brand manufacturers do.[458] In any event, patients and doctors can arguably choose to use the generic version of the old product if the brand's new product is not worth the cost.[459]

Current Law

There is no existing statute specifically prohibiting product hopping. Those practices have been challenged under the antitrust laws as anticompetitive attempts to maintain a monopoly in violation of Section 2 of the Sherman Act.[460] *Schneiderman* provides one example. In that case, the U.S. Court of Appeals for the Second Circuit (Second Circuit) held that the soft switch, described above, was not sufficiently anticompetitive to violate Section 2.[461] Specifically, the court determined that as long as Actavis continued to sell both XR and IR, with generic IR drugs on the market, "patients and doctors could evaluate the products and their generics on the merits in furtherance of competitive objectives."[462] The Second Circuit further held that once Actavis implemented a hard switch by withdrawing IR, it "crosse[d] the line from persuasion to coercion" and therefore violated Section 2.[463] The court next determined that Actavis's purported procompetitive justifications for the hard switch were pretextual because the hard switch was an attempt to impede generic competition[464] and, in any event, the procompetitive benefits were outweighed by anticompetitive harms.[465] Accordingly, the court affirmed the district court's grant of an injunction requiring Actavis to make IR "available on the same terms and conditions" as before the hard switch.[466]

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[455] *Id.* at 694.

[456] *See, e.g.*, Erika Lietzan, *A Solution in Search of a Problem at the Biologics Frontier*, 2018 U. ILL. L. REV. ONLINE 19, 27 (2018).

[457] *Id.*

[458] *Id.* ("[G]eneric companies choose to rely on automatic substitution but could in fact market their products.").

[459] *Id.* ("[R]ational payers and physicians will select the generic first-generation product if the innovative second-generation product is not meaningfully better.").

[460] *See, e.g.*, Schneiderman v. Actavis PLC, 787 F.3d 638 (2d Cir. 2015).

[461] *Id.* at 655 ("As long as Defendants sought to persuade patients and their doctors to switch from Namenda IR to Namenda XR while both were on the market (the soft switch) and with generic IR drugs on the horizon, patients and doctors could evaluate the products and their generics on the merits in furtherance of competitive objectives.").

[462] *Id.*

[463] *Id.* ("Defendants' hard switch crosses the line from persuasion to coercion and is anticompetitive.").

[464] *See id.* at 658.

[465] *Id.*

[466] *Id.* at 662.

"Patent Thickets"

Definition

Critics have argued that some pharmaceutical manufacturers develop "patent thickets" to protect their products. This term is used in two slightly different ways, both relating to products covered by a high number of patents. First, a patent thicket may describe a situation in which *multiple parties* have overlapping patent rights on one product, such that a "potential manufacturer must negotiate licenses with each patent owner in order to bring a product to market without infringing."[467] Patent thickets, in this sense, raise concerns about inefficient exploitation of a technology because the multiplicity of patent owners increases transaction costs and creates coordination challenges.[468] Second, the term may be used in a different sense to describe an incumbent manufacturer's practice of amassing a *large number of patents* relating to a single product, with the intent of intimidating competitors from entering the market, or to make it too costly and risky to do so.[469] It is this second usage that is usually intended when critics refer to the patent "thickets" protecting pharmaceutical products.

Debate

Commentators have observed that single products are frequently protected by multiple patents.[470] For example, it has been estimated that a single smartphone may be protected by as many as 250,000 patents.[471] Even the individual technologies in the phone may be covered by many patents. For example, Bluetooth 3.0 incorporates "contributions of more than 30,000 patent holders," and more than 800 patent holders contributed to the micro SD removable memory storage card.[472] Unlike pharmaceuticals, the patents on products like semiconductors or smartphones are typically not all owned by the same entity, and thus are examples of the first type of patent thicket (i.e., one in which multiple parties have overlapping patent rights on one product). Commentators contend that patent thickets on such technologies generally do not confer the same market power as a patent portfolio on a new pharmaceutical owned by a single drug manufacturer.[473]

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[467] Stu Woolman et al., *Evidence of Patent Thickets in Complex Biopharmaceutical Technologies*, 53 IDEA: INTELL. PROP. L. REV. 1, 2 (2013); Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard-Setting*, 1 INNOVATION POL'Y & ECON. 119, 119 (2001).

[468] *See* Gavin D. George, *What Is Hiding in the Bushes?* eBay*'s Effect on Holdout Behavior in Patent Thicket*s, 13 MICH. TELECOMM. & TECH. L. REV. 557, 558–60 (2007) (summarizing the economic literature); *see generally* Shapiro, *supra* footnote 467; Michael A. Heller & Rebecca Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698 (1998).

[469] Koons, *supra* note 39 (using "patent thicket" to refer to large patent portfolio amassed on one product by single biologics manufacturer); *see also America's Overspend*, *supra* note 6, at 4 (using term "thicket of patents" to refer to large patent portfolio claiming aspects of a single drug); Feldman, *supra* note 39 ("[D]rug companies build massive patent walls around their products, extending the protection over and over again.").

[470] Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1590–91 (2003) (stating that a one-to-one correspondence between patents and products "is the exception rather than the rule").

[471] Steve Lohr, *Apple-Samsung Patent Battle Shifts to Trial*, N.Y. TIMES, (July 29, 2012), https://www.nytimes.com/2012/07/30/technology/apple-samsung-trial-highlights-patent-wars.html. Notably, not all of the patents covering aspects of a smartphone are owned by the same entity. *Id.*

[472] Evan Engstrom, *So How Many Patents Are In A Smartphone?*, ENGINE (Jan. 19, 2017) https://www.engine.is/news/category/so-how-many-patents-are-in-a-smartphone.

[473] Burk & Lemley, *supra* note 470, at 159; *see also* Dmitry Karshtedt, *The More Things Change: Improvement*

In the pharmaceutical context, patent thicket concerns mainly relate to biologics. At least in part, this may occur because biologics are derived from living cells or other biological material.[474] Naturally occurring source material is generally not eligible for patenting under Section 101 of the Patent Act,[475] but methods for transforming source material into a biological product generally are patentable.[476] Manufacturing a pharmaceutical using living cells is often complicated, offering more opportunities for patenting relative to chemically synthesizing small-molecule drugs.[477] As changes are implemented to either the biologic product or its manufacturing process throughout the original patent term, those changes can be claimed as inventions and used to extend the effective patent protection.[478] For example, a company producing a biologic could attempt to patent the use of a different medium for cell growth or an adjustment to the dosing.[479]

The patent portfolio that covers Humira, pharmaceutical manufacturer AbbVie's flagship biologic, has been characterized as an example of the second type of patent thicket.[480] Critics contend this patent portfolio has helped keep Humira competitors off the market for an extended time period.[481] One study found that AbbVie filed 247 patent applications on various aspects of Humira, resulting in 132 issued patents.[482] The Biosimiliars Council alleges that AbbVie filed 75 patents relating to Humira in the three years before biosimilar competition was set to begin, extending nominal patent protection through 2034.[483] The Council alleges it will cost "roughly $3 million per patent" to challenge the Humira patents.[484]

In August 2017, just before biosimilar manufacturer Boehringer received FDA approval to launch its Humira biosimilar in the United States, AbbVie filed a lawsuit alleging that the biosimilar would infringe 1,600 claims across 74 of AbbVie's patents.[485] Boehringer settled the lawsuit two years later, in 2019, citing "the inherent unpredictability of litigation, [and] the substantial costs of what would have been a long and complicated legal process and ongoing distraction to our

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Patents, Drug Modifications, and the FDA, 104 IOWA L. REV. 1129, 1158 (2019).

[474] Koons, *supra* note 39 ("[B]iologic medicines such as Humira . . . are typically made in living cells rather than chemically manufactured. That process often involves more steps and a higher level of complexity, which opens the door to more potential steps to patent.").

[475] *See, e.g.*, Ass'n for Molecular Pathology v. Myriad Genetics, Inc., 569 U.S. 576, 590–94 (2013). Biologics that are genetically modified or otherwise altered by man into a non-naturally occurring form are generally patent-eligible. *See* Diamond v. Chakrabarty, 447 U.S. 303, 309–10 (1980) (upholding patent on genetically engineered bacterium).

[476] *See, e.g.*, Amgen, Inc. v. Coherus BioScis. Inc., 931 F.3d 1154, 1156 (Fed. Cir. 2019) (describing patent on purifying step of manufacturing a biologic).

[477] *See* Koons, *supra* note 39.

[478] *Id.* ("[C]ompanies can claim any changes to their drugs over the years—say, using a slightly different medium in which to grow cells or adjusting the dosing—warrant new legal protections that can keep generic competitors at bay.").

[479] *Id.*

[480] *See* AbbVie Inc. v. Boehringer Ingelheim Int'l GmbH, No. 17-CV-01065-MSG-RL, 2019 WL 917990, at *4 (D. Del. Feb. 25, 2019) (summarizing allegation that AbbVie created a "thicket of dubious and overlapping patents to delay biosimilar competition").

[481] *See Overpatented*, *supra* note 245, at 7.

[482] *Id.*

[483] *Failure to Launch*, *supra* note 40, at 8.

[484] *Id.*

[485] Complaint at 1, AbbVie v. Boehringer Ingelheim Int'l GMBH, No. 1:17-cv-01065-MSG-RL (D. Del. Aug. 2, 2017) (stating that Humira "has resulted in more than 100 issued United States patents . . . 74 of which AbbVie has identified as infringed"); Nicole D. Prysby, *Patent News: AbbVie Facing First-of-Its-Kind 'Patent Thicket' Antitrust Suit*, IP LAW DAILY (Mar. 19, 2019), https://lrus.wolterskluwer.com/news/antitrust-law-daily/abbvie-facing-first-of-its-kind-patent-thicket-antitrust-suit/75518/.

business."[486] AbbVie has similarly settled litigation with other potential manufacturers of Humira biosimilars.[487] Although the primary patent on Humira expired in 2016, no biosimilars will enter the U.S. market until January 31, 2023, at the earliest.[488]

The alleged patent thicket surrounding Humira has been the subject of litigation on other bases, including under the antitrust laws. In March 2019, a welfare fund filed an antitrust suit against AbbVie alleging that its patent thicket approach unreasonably restrained competition in violation of Sections 1 and 2 of the Sherman Act,[489] and sought billions of dollars in damages when AbbVie doubled the cost of Humira.[490] The trial judge dismissed the complaint without prejudice in June 2020, determining that "AbbVie has exploited advantages conferred on it through lawful practices and to the extent this has kept prices high for Humira, existing antitrust doctrine does not prohibit it."[491] That matter is currently on appeal before the U.S. Court of Appeals for the Seventh Circuit.[492]

Critics have voiced concerns that other drug manufacturers may attempt to amass similar large patent portfolios on their biologics, thereby postponing biosimilar competition from entering the market.[493] Johnson & Johnson, for example, protects its Remicade product with more than 100 patents.[494] Biogen/Genentech similarly protects its cancer treatment Rituxin with what some could characterize as a patent thicket.[495] Rituxin was the subject of 204 patent applications and 94 issued patents, potentially resulting in 47 years of blocking competition.[496]

Defenders of this patenting practice raise arguments that are similar to those supporting evergreening: that patents on these products represent innovations the patent laws were designed to encourage, and that each patent has passed through the rigorous examination process and been determined to be novel and nonobvious.[497] For example, AbbVie has stated that Humira

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[486] Andrew Dunn, *With Boehringer Settlement, AbbVie Completes Humira Sweep*, BIOPHARMADIVE (May 14, 2019), https://www.biopharmadive.com/news/abbvie-boehringer-ingelheim-settle-humira-patent-biosimilar/554729/.

[487] *Id.*

[488] *Id.* In Europe, by contrast, Humira biosimilars entered markets in October 2018, and within four months captured 15% of the European market. Ned Pagliarulo, *Humira Biosimilars Launch in Europe, Testing AbbVie*, BIOPHARMADIVE (Oct. 19, 2018), https://www.biopharmadive.com/news/abbvie-humira-biosimilars-launch-europe/539938/; Dunn, *supra* note 486 ("Humira biosimilars captured 15% of the European market in February, the fourth month since launching."). It is estimated that biosimilars could claim up to 50% of the Humira market in Europe within the first year. *Id.* ("[B]iosimilars growing to take 50% of the Humira market in Europe within a year remains a possibility.").

[489] Prysby, *supra* note 485. The complaint also presents "state law claims for conspiracy and combination in restraint of trade, monopolization, state consumer protection law violation, and unjust enrichment." *Id. See also* Complaint, *In re* Humira (Adalimumab) Antitrust Litig., No. 1:19-cv-01873, Dkt. No. 1 (N.D. Ill. Mar. 18, 2019).

[490] Prysby, *supra* note 485.

[491] *In re* Humira (Adalimumab) Antitrust Litig., 465 F. Supp. 3d 811, 819 (N.D. Ill. 2020), *appeal docketed*, UFCW Local 1500 Welfare Fund v. AbbVie Inc., No. 20-2402 (7th Cir. July 30, 2020).

[492] Khorri Atkinson, *Humira Buyers Take AbbVie Antitrust Challenge To 7th Circ.*, LAW360 (July 30, 2020), https://www.law360.com/articles/1296320.

[493] Koons, *supra* note 39 ("After seeing [AbbVie's strategy for protecting Humira] laid out in a company presentation, Ronny Gal, a research analyst for Sanford C. Bernstein & Co., said at a conference of makers of biosimilars (generic-like drugs, in biologic drug parlance) last fall: 'I'm pretty sure every CEO in biopharma sent that to their head of IP and said, Can we do that?'").

[494] *Id.*

[495] *See Overpatented*, *supra* note 245, at 7.

[496] *Id.*

[497] *See supra* "Evergreening"

"represents true innovation in the field of biologics,"[498] warranting protection through all the various patents. Other experts note that "[t]here's nothing unusual about the multilayered way AbbVie has sought to patent and protect Humira," and that patent thickets simply "tak[e] advantage of existing law."[499] Accordingly, companies with patents relating to numerous aspects of their products likely view each patent as protecting significant patentable innovations of the sort the patent system is designed to protect.[500]

Experts note that creating a biologic like Humira "isn't easy work."[501] Scientists must genetically engineer a cell line to secrete large amounts of the biologic, purify the results, and modify dosages for different diseases, among other "incremental tweaks."[502] Each of those steps in the process brings challenges that may require innovative solutions, and those solutions may be the subject of patents.[503] As AbbVie's CEO noted, the Humira "patent portfolio evolved as [AbbVie] discovered and learned new things about Humira."[504] Thus, defenders view alleged patent "thickets" as an ordinary and legitimate use of the patent system to protect the different aspects of their innovations.

Current Law

No statute specifically forbids patent thickets. Like evergreening, substantive patent law (including the nonobviousness requirement and prohibition on double patenting) provides some of the primary restrictions on patent thickets. In other words, the ability to receive secondary patents is limited by the rule that new patents cannot be an obvious variation on the prior art or on the patentee's own prior patents.[505] On the other hand, obviousness-type double patenting restrictions may have less impact on patent thickets than on evergreening due to the availability of terminal disclaimers. As explained above, a patentee may overcome obviousness-type double patenting issues by disclaiming any portion of the later patent's term after the earlier patent expires.[506] Because the alleged goal of evergreening is to extend the exclusivity period for as long as possible, there is little incentive to file a terminal disclaimer. By contrast, the purported goal of a patent thicket is to accumulate a large number of patents protecting a single product, a goal that would be unaffected by terminal disclaimers. Thus, restrictions on obviousness-type double patenting may not prevent patent thickets as effectively as evergreening.

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[498] *Id.*

[499] Sy Mukherjee, *Protect at All Costs: How the Maker of the World's Bestselling Drug Keeps Prices Sky-High*, FORTUNE (July 18, 2019), https://fortune.com/longform/abbvie-humira-drug-costs-innovation/.

[500] *See* Koons, *supra* note 39.

[501] Mukherjee, *supra* note 499.

[502] *Id.*

[503] *See id.*

[504] *Id.*

[505] *See supra* "Evergreening"

[506] *See, e.g.*, Gilead Sci., Inc. v. Natco Pharma Ltd., 753 F.3d 1208, 1210 (Fed. Cir. 2014); STC.UNM v. Intel Corp., 754 F.3d 940, 942 (Fed. Cir. 2014).

"Pay-for-Delay" Settlements

Definition

As described above, patent litigation can result when generic drug and biosimilar manufacturers challenge the validity of brand-name companies' patents and/or their applicability to follow-on products.[507] Some brand-name companies resolve such litigation through settlement agreements with generic manufacturers whereby the brand-name company pays the generic manufacturer a sum of money (or other compensation) in return for the generic manufacturer agreeing to delay market entry.[508] This practice, referred to as "reverse payment settlements" or "pay-for-delay settlements," allows the brand-name company to (1) avoid the risk that its patents will be invalidated, (2) delay the market entry of generic competition, and (3) effectively extend its exclusive right to market the listed drug.[509] Because these agreements terminate the litigation, the questions of patent validity and infringement remain open.[510]

Pay-for-delay settlements are not limited to cash payments from the brand to the generic. In 2017, the U.S. Court of Appeals for the Third Circuit (Third Circuit) addressed such a settlement involving Wyeth, Inc.'s branded antidepressant drug, Effexor XR.[511] In that case, the plaintiffs alleged that Wyeth and generic manufacturer Teva Pharmaceutical Industries Ltd. (Teva) reached an anticompetitive pay-for-delay settlement.[512] Teva filed an ANDA for a generic version of Effexor XR, and Wyeth sued for patent infringement.[513] According to the plaintiffs (a class of direct purchasers of Effexor XR), an unfavorable preliminary ruling caused Wyeth to fear that it would lose the litigation, allowing generic manufacturers to enter the Effexor XR market.[514]

Accordingly, Wyeth and Teva entered into a settlement in which

- the parties agreed to vacate the unfavorable preliminary ruling;
- Teva agreed not to enter the market with its Effexor XR generic until approximately five years after the agreement (nearly seven years before Wyeth's patents expired);
- Wyeth agreed not to market a competing "authorized generic" during Teva's 180-day exclusivity period;
- Wyeth agreed to permit Teva to sell a generic version of another product, Effexor IR, before the original patent on Effexor expired and without a Wyeth-authorized generic; and

[507] *See supra* "Patent Dispute Procedures for Generic Drugs and Biosimilars."

[508] *See, e.g.*, FTC v. Actavis, Inc., 570 U.S. 136, 144–45 (2013); *In re* Androgel Antitrust Litig., No. 1:09-MD-2084-TWT, 2018 WL 298483, at *3–4 (N.D. Ga. June 14, 2018).

[509] *See, e.g.*, *Actavis*, 570 U.S. at 154.

[510] *Id.*

[511] *In re* Lipitor Antitrust Litig., 868 F.3d 231 (3d Cir. 2017).

[512] *Id.* at 239.

[513] *Id.* at 247 ("On December 10, 2002, Teva obtained ANDA first-filer status for a generic version of Effexor XR. Teva's ANDA included paragraph IV certifications, asserting that Teva's sale, marketing, or use of generic Effexor would not infringe Wyeth's patents or that those patents were invalid or unenforceable. . . . Within the 45-day period prescribed by the Hatch-Waxman Act, Wyeth brought suit against Teva for patent infringement in the District of New Jersey.").

[514] *Id.*

- Teva agreed to pay royalties to Wyeth on its sales of both generic versions of Effexor.[515]

Pursuant to a consent decree, Wyeth and Teva submitted the agreement to the FTC.[516] The FTC did not object to the agreement.[517] Notably, Wyeth did not pay money directly to Teva. Instead, Wyeth's agreement not to market an authorized generic during Teva's 180-day exclusivity period would cause Teva to reap increased sales during that period. In other words, although Wyeth did not *directly* pay Teva to keeps its generic product out of the market, the agreement ensured that Teva would receive compensation in other ways.

Debate

The FTC and others have alleged that pay-for-delay settlements "have significant adverse effects on competition" in violation of antitrust laws, including Section 1 of the Sherman Act and Section 5 of the FTC Act.[518] When evaluating agreements for potential antitrust violations, the court focuses its inquiry on "form[ing] a judgment about the competitive significance of the [settlement] . . . 'based either (1) on the nature or character of the contracts, or (2) on surrounding circumstances giving rise to the inference or presumption that they were intended to restrain trade and enhance prices.'"[519] The Supreme Court has recognized that "reverse payment settlements . . . can sometimes violate the antitrust laws,"[520] and courts have allowed antitrust litigation challenging certain reverse payment settlements to proceed under existing law.[521]

Defenders of such agreements contend there are significant benefits from pay-for-delay settlements. For example, AbbVie has settled suits with each of the companies that sought to introduce biosimilars to Humira.[522] Even while accusing AbbVie of "patent abuses" relating to Humira, the Biosimilars Council has touted using settlements between brands and biosimilars to resolve patent thickets.[523] The Council contends that the Humira settlements are pro-consumer because, although biosimilar market entry will be delayed until seven years after the primary patent on Humira has expired, entry will still occur before several of the secondary patents covering Humira will expire.[524] As the Supreme Court has recognized, pay-for-delay settlements may provide significant procompetitive benefits, and whether a particular settlement is

[515] *See id.*

[516] *Id.* Pursuant to a 2002 consent decree, the FTC "possessed the right to weigh in on and raise objections to Wyeth's settlements." *Id.*

[517] *Id.* While "[t]he FTC offered no objection" to the settlement agreement, it "reserved its right to take later action." *Id.*

[518] *Id.* at 147–48; *see also* King Drug Co. of Florence, Inc. v. Smithkline Beecham Corp., 791 F.3d 388, 398 (3d Cir. 2015).

[519] NCAA v. Bd. of Regents of Univ. of Okla., 468 U.S. 85, 103 (1984) (quoting Nat'l Soc'y of Prof'l Eng'rs v. United States, 435 U.S. 679, 690 (1978)).

[520] FTC v. Actavis, Inc., 570 U.S. 136, 141 (2013).

[521] *See, e.g.*, *Smithkline Beecham Corp.*, 791 F.3d at 403; King Drug Co. of Florence, Inc. v. Cephalon, Inc., 88 F. Supp. 3d 402, 422 (E.D. Pa. 2015); *In re* Aggrenox Antitrust Litig., 94 F. Supp. 3d 224, 245–46 (D. Conn. 2015).

[522] Dunn, *supra* note 486.

[523] *Failure to Launch*, *supra* note 40, at 8 ("[A] critical element of biosimilar entry is the ability for two parties to reach a settlement agreement providing for competition earlier than the expiration of the last patent, rather than bear the time and expense of litigating through these thickets in court.").

[524] *Id.* (stating that fewer agreements of the kind at issue in *Actavis* "paved the way for pro-consumer patent settlement agreements and earlier entry while avoiding expensive and burdensome litigation costs").

procompetitive or anticompetitive will depend on a number of factors that vary from case to case.[525]

Pay-for-delay settlements may now be uncommon. A recent FTC report found that in Fiscal Year 2017, brand and generic pharmaceutical manufacturers settled 226 patent disputes.[526] According to that report, 3 of those 226 settlements restricted generic entry and provided compensation beyond the repayment of legal fees.[527]

Current Law

In *Actavis v. FTC*, the Supreme Court held that the rule of reason is the appropriate level of analysis in challenges to pay-for-delay agreements.[528] Although the Court recognized the potential for such agreements to have anticompetitive effects, it acknowledged that "offsetting or redeeming virtues are sometimes present."[529] Such justifications might include "traditional settlement considerations, such as avoided litigation costs or fair value for services."[530] Accordingly, the FTC (or other plaintiffs) has to prove the anticompetitive effects of a particular agreement before the burden shifts to the defendant.[531]

The Third Circuit case involving the Wyeth-Teva agreement provides an example of the current analysis. Although the FTC did not object to the agreement, purchasers of Effexor XR filed a class action lawsuit against Wyeth and Teva alleging, inter alia, that the settlement agreement was an unlawful restraint of trade under Section 1 of the Sherman Act.[532] The Third Circuit concluded that the plaintiffs plausibly alleged an anticompetitive pay-for-delay settlement.[533] The court determined that Wyeth's agreement not to manufacture a competing generic product during Teva's 180-day exclusivity period was an adequate allegation of a sufficiently large payment because it ensured Teva would be the only generic product on the market, and thus Teva would receive all generic Effexor XR sales during that period.[534] The court concluded that the payment could not be justified as a simple effort to avoid the costs of litigation.[535] Accordingly, the court determined that the plaintiffs adequately alleged that the agreement between Wyeth and Teva was anticompetitive under the *Actavis* standard.[536]

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[525] *Actavis*, 570 U.S. at 158–60.

[526] FED. TRADE COMM'N, BUREAU OF COMPETITION, AGREEMENTS FILED WITH THE FEDERAL TRADE COMMISSION UNDER THE MEDICARE PRESCRIPTION DRUG, IMPROVEMENT, AND MODERNIZATION ACT OF 2003: OVERVIEW OF AGREEMENTS FILED IN FISCAL YEAR 2017: A REPORT BY THE BUREAU OF COMPETITION (Dec. 4, 2020), https://www.ftc.gov/system/files/documents/reports/agreements-filed-federal-trade-commission-under-medicare-prescription-drug-improvement-modernization/mma_report_fy2017.pdf.

[527] *Id.*

[528] *Id.* at 159.

[529] *Id.* at 156.

[530] *Id.*; *see also id.* at 159.

[531] *Id.* at 159; *see also* United States v. Brown Univ., 5 F.3d 658, 668 (3d Cir. 1993) ("The plaintiff bears an initial burden under the rule of reason of showing that the alleged combination or agreement produced adverse, anti-competitive effects within the relevant product and geographic markets.").

[532] *In re* Lipitor Antitrust Litig., 868 F.3d 231, 248 (3d Cir. 2017).

[533] *Id.* at 258–62.

[534] *Id.* at 260 ("The no-[authorized-generic (AG)] agreement used by Wyeth to induce Teva to stay out of the Effexor XR market was alleged to have been worth more than $500 million.").

[535] *Id.* at 261.

[536] *Id.* at 262 (stating that the plaintiffs' complaints "contain sufficient factual detail about the settlement agreement between Teva and Wyeth to plausibly suggest that Wyeth paid Teva to stay out of the market by way of its no-AG

Combinations of Practices

Although this report describes various patenting practices in isolation, patent holders can also use them concurrently. For example, product hopping can be combined with pay-for-delay settlements to delay generic entry while a brand switches the market to a new product. A manufacturer considering product hopping will often be more successful in preventing competition from the generic if it can convert the market to the new product before the generic enters the market.[537] In one case, the brand estimated that it would sell ten times more tablets if it could switch doctors to the new product before the generic entered the market.[538]

One example of a drug manufacturer allegedly combining product hopping and pay-for-delay settlements to prevent competition for its product involves Cephalon, maker of the branded sleep-disorder medication Provigil.[539] Between its secondary patent and a period of regulatory exclusivity, protection of Provigil expired in April 2015.[540] Due to the secondary patent's narrowness, however, the generic companies planned to enter the market with noninfringing products in 2006.[541] Cephalon estimated that, once the generic versions entered the market, there would be a 75% to 90% price reduction in Provigil, reducing revenues by more than $400 million in the first year alone.[542] In 2006, Cephalon attempted to move the market to a new product, Nuvigil, which was patent-protected until 2023.[543] FDA had not yet approved Nuvigil in late 2005 when Cephalon settled its patent lawsuits with the generics, paying them more than $200 million to delay market entry until 2012.[544]

Although Cephalon argued its settlement would allow generic versions of Provigil to enter the market three years before the expiration of the Provigil secondary patent in 2015, following the settlement, Cephalon increased the price of Provigil and stopped marketing it.[545] At the same time, Cephalon promoted Nuvigil both through its sales force and by discounting its price.[546] Through the pay-for-delay settlement, Cephalon had until 2012 to switch the market to Nuvigil rather than begin competing against the generics with Provigil in 2006. Thus, Cephalon seemingly combined product hopping with pay-for-delay settlements to prolong its period of exclusivity.

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agreement [and] that is the very anticompetitive harm that the Supreme Court identified in *Actavis*").

[537] Carrier & Shadowen, *supra* note 37, at 176–77 ("Put simply, the brand firm will be much more successful in forestalling generic competition if it can switch the market to the reformulated drug *before* a generic of the original product enters the market.").

[538] *Id.* at 177 ("In the *TriCor* case, . . . the brand firm predicted that it would sell more than ten times as many tablets if it was able to switch doctors to the reformulated product before the generic version of the original product entered the market.").

[539] Carrier, *supra* note 41, at 1022–27.

[540] *Id.* at 1022.

[541] *Id.* at 1022–23 ("The four first-filing generic firms planned for a launch in June 2006, at the latest.").

[542] *Id.* at 1023 ("A Cephalon vice president projected a 75%–90% price reduction that would lower revenues by more than $400 million (nearly 75% of the drug's annual sales) within one year.").

[543] *Id.* at 1023–25.

[544] *Id.* at 1024 ("Cephalon paid more than $200 million to the four generic firms to agree to forgo entry until April 2012.").

[545] *Id.* at 1025 ("The easiest way to make Provigil less desirable was to increase its price. . . . Another means to reduce Provigil's attractiveness was to stop promoting it.").

[546] *Id.* at 1026.

Conclusion

IP rights play an important role in encouraging pharmaceutical innovation and development of new drugs and biologics; they may also contribute to the perceived high prices of pharmaceuticals in the United States. The effects that regulatory exclusivities, patents, and pharmaceutical patenting practices have on drug prices depend on a complex interplay between patent law, FDA law (particularly the specialized provisions of the Hatch-Waxman Act and BPCIA), and antitrust law. An important issue for Congress is whether current law effectively balances innovation and competition in the pharmaceutical market. An overview of selected legislative proposals relating to drug pricing and IP rights in pharmaceuticals may be found in CRS Report R46741, *Drug Pricing and Intellectual Property: The Legislative Landscape for the 117th Congress*.

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