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Drug Pricing and Intellectual Property Law: A Legal Overview for the 116th Congress

April 4, 2019

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R45666

CRS REPORT
Prepared for Members and
Committees of Congress

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SUMMARY

R45666

April 4, 2019

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Drug Pricing and Intellectual Property Law: A Legal Overview for the 116th Congress

Intellectual property (IP) rights play an important role in the development and pricing of pharmaceutical products such as prescription drugs and biologics. In order to encourage innovation, IP law grants the rights holder a temporary monopoly on a particular invention or product, potentially enabling him to charge higher-than-competitive prices. IP rights, if sufficiently limited, 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 Food and Drug Administration (FDA). However, because they may operate to deter or delay competition from generic drug and biosimilar manufacturers, IP rights have been criticized as contributing to high prices for pharmaceutical products in the United States.

Two main types of IP may protect pharmaceutical products: patents and regulatory exclusivities. Patents, which are available to a wide range of technologies besides pharmaceuticals, are granted by the U.S. Patent and Trademark Office (PTO) to new and useful inventions. Pharmaceutical patents may claim chemical compounds in the pharmaceutical product, a method of using the product, a method of making 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. If a court concludes that a competitor's generic or biosimilar version infringes a valid patent, the court may issue an injunction precluding the competitor from making, using, selling, and importing that competing product until the patent expires.

In some circumstances, FDA grants regulatory exclusivities to a pharmaceutical manufacturer upon the completion of the process required to market pharmaceutical products. Before a new drug or biologic can be sold in the United States, companies must apply for regulatory approval or licensure from FDA, which determines if the pharmaceutical is safe and effective. For certain pharmaceuticals, such as innovative products or those that serve particular needs, FDA provides a term of marketing exclusivity upon the successful completion of the regulatory process. If a product is covered by an unexpired regulatory exclusivity, FDA generally may not accept and/or approve an application seeking FDA approval of a follow-on product (i.e., a generic drug or biosimilar). Regulatory exclusivities vary in length from as little as six months to as much as 12 years depending on the specific type of drug or biologic at issue and other factors.

Like regulatory exclusivities, patent rights can affect when generic and biosimilar manufacturers can market their follow-on products. Pharmaceutical patent disputes are subject to certain specialized procedures under the Hatch-Waxman Act and the Biologics Price Competition and Innovation Act (BPCIA). Under Hatch-Waxman, applicants seeking approval of a generic version of an existing FDA-approved drug must make a certification with respect to each patent that the brand-name drug manufacturer lists as covering the product. If the generic manufacturer challenges those patents, FDA generally cannot approve the generic drug application for 30 months while the patent dispute is litigated. For biologics, applicants seeking approval of a biosimilar version of an existing biological product may choose to engage in the BPCIA's "patent dance," a complex scheme of private information exchanges made in preparation for formal patent disputes between brand-name biologic and biosimilar manufacturers. The patent dance does not affect FDA's ability to approve a biosimilar application.

Some pharmaceutical companies have been criticized for charging high prices and engaging in practices that are perceived by some to exploit the existing legal system governing IP rights on pharmaceutical products. For example, some generic manufacturers have claimed that brand-name drug manufacturers have unreasonably refused to sell them samples of brand-name drugs in order to impede their ability to obtain FDA approval and delay market entry of generic competition. Other commentators have criticized the practice of "pay-for-delay" settlements, through which brand-name drug companies settle patent litigation with generic or biosimilar manufacturers by paying them to delay their entry into the market. Still others criticize so-called patent "evergreening," in which pharmaceutical companies are alleged to serially patent minor improvements or ancillary features of their products in order to extend the effective term of patent protection.

In recent years, a number of congressional proposals have been introduced that seek to address these and other issues in IP law that are perceived by some to contribute to high prices for pharmaceutical products. These proposed reforms range from relatively modest changes, such as increasing patent transparency, to more sweeping reforms such as pricing controls and government compulsory licensing provisions.

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The prices paid by consumers for prescription drugs have been a recent area of significant congressional interest. Several committees in the House and Senate have held hearings this year on drug pricing issues,[1] and a number of bills have been introduced in the 116th Congress that seek to address the perceived high costs of prescription drugs and other pharmaceutical products.[2] Because intellectual property (IP) rights, including patent rights and regulatory exclusivities, play an important role in the development and pricing of pharmaceutical products,[3] a key focus of this debate is whether existing IP law promptly balances the need for innovation with the costs that IP may impose on the public.[4] Understanding the interplay between several complex legal regimes is necessary in order to fully make sense of this debate.

IP law comprises a set of exclusive rights that prevent others from making, copying, or using certain intangible creations of the human mind.[5] Federal law contains several different varieties of IP, depending on the type of intellectual creation at issue.[6] For example, copyright law generally grants authors of original creative works (such as literary works or musical compositions) the exclusive right to reproduce their work, publicly perform and display it, distribute it, and adapt it, for a specified term of years.[7] Other species of federal IP include patent law,[8] which protects novel inventions, and trademark law,[9] which protects symbols used to identify goods and services. 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.[10]

Although each of these forms of IP is legally distinct, they broadly share a common motivation: providing incentives to create.[11] Patents and copyrights are typically justified by a utilitarian

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[1] *See, e.g.*, *Drug Pricing in America: A Prescription for Change, Part I, Hearing Before the S. Comm. on Finance*, 116th Cong. (2019); *The Cost of Rising Prescription Drug Prices, Hearing Before the H. Ways and Means Comm.*, 116th Cong. (2019); *Examining the Actions of Drug Companies in Raising Prescription Drug Prices, Hearing Before the H. Comm. on Oversight and Reform*, 116th Cong. (2019). The Trump Administration has also discussed how to address rising drug prices. *See* DEP'T OF HEALTH AND 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] *See infra* "Selected Drug Pricing Proposals in the 115th and 116th Congresses." This report uses the term "pharmaceutical product" or "pharmaceutical" as a catch-all term to encompass both chemical "drugs" (typically artificially synthesized small molecules) and naturally derived "biologics" (typically large molecules such as proteins), which are subjected to different regulatory regimes. *See infra* "Food and Drug Administration (FDA) Law." Similarly, the term "brand product" and "follow-on product" will be used as a catch-all term for "brand-name drugs or biologics" and "generic drugs or biosimilars," respectively.

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

[4] *See infra* notes 11-19 (discussing economic rationale for IP and the costs and benefits that it may impose on the public).

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

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

[7] *See* 17 U.S.C. §§ 102, 106, 302. Copyright is subject to a number of significant limitations such as fair use. *See id.* §§ 107-122.

[8] *See* 35 U.S.C. §§ 1-390.

[9] *See* 15 U.S.C. §§ 1051-1141n.

[10] *See* Hickey, *supra* note 6.

[11] 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*

rationale that exclusive rights are necessary to provide incentives to produce new creative works and technological inventions.[12] 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, and thereby reduce the incentive to create in the first place.[13] IP incentives are said to be particularly necessary for products, such as pharmaceuticals, that are costly to develop but easily copied once marketed.[14] 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."[15] 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.[16]

By design, IP rights may lead to increased prices for goods or services that are protected by IP. IP rights are often said to grant a temporary and limited "monopoly" to the rights holder.[17] 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

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Property, 77 GEO. L.J. 287, 296-314 (1988) (articulating justification for intellectual property as natural right deriving from the labor of the author) & 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).

[12] *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.").

[13] *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.").

[14] *See* Grabowski et al., *supra* note 3, 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."); WILLIAM M. LANDES & RICHARD A. POSNER, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 24, (2003) ("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.").

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

[16] *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.").

[17] *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"). It should be noted that 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 14, 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.").

for a set period of time.[18] 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.[19]

New pharmaceutical products generally benefit from two main[20] forms of IP protection: patent rights and regulatory exclusivities.[21] These two sets of exclusive rights are distinct, yet often confused. Patents, which are available to a wide variety of technologies beyond pharmaceuticals,[22] are granted by the U.S. Patent and Trademark Office (PTO) to inventions that are new, useful, nonobvious, and directed at patentable subject matter.[23] 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 patent is issued by the PTO and ending 20 years after the date of the patent application.[24]

The Food and Drug Administration (FDA) grants regulatory exclusivities upon the completion of the FDA regulatory process necessary to market pharmaceutical products (i.e., drugs and biological products).[25] Exclusivities are granted only to 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).[26] Regulatory exclusivities prevent FDA from accepting or approving an application by a competitor for FDA approval of a follow-on product (i.e., a generic or biosimilar version) of a previously approved pharmaceutical for a set time period, and/or preclude a competitor from relying on safety and efficacy data submitted by the original manufacturer for a period of time.[27] Depending on the type of pharmaceutical product

[18] 35 U.S.C. §§ 154(b), 271(a).

[19] *See* LANDES & POSNER, *supra* note 14, 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.").

[20] 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).

[21] Although not a traditional form of IP such as copyright or patent, regulatory exclusivities share many of the features of traditional IP rights and 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.").

[22] 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 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)).

[23] *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.

[24] *Id.* §§ 154(a)(2), 271(a).

[25] *See infra* "Food and Drug Administration (FDA) Law."

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

[27] *Id.*; *see also* Thomas, *supra* note 21, at 44-49.

at issue and other factors, regulatory exclusivities may last anywhere from six months to 12 years.[28] In overlapping ways, both patent rights and regulatory exclusivities can operate to deter or delay the market entry of a generic drug or biosimilar.

The 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 spending.[29] Many factors other than IP rights contribute to the price consumers pay for prescription drugs and biologics, including demand, manufacturing costs, R&D costs, the terms of private health insurance, and the involvement of a government insurance program such as Medicaid.[30] That said, pharmaceutical products are frequently protected by IP rights,[31] and some studies have shown that IP rights are among the most important factors driving high drug prices.[32] For example, FDA has found that increased competition from generic drug manufacturers is associated with lower prices for pharmaceuticals.[33] Given that IP rights may allow the rights holder to charge higher-than-competitive prices, and can deter or delay the market entry of generic drug or biosimilar competitors, changes to IP rights or otherwise facilitating competition is seen by some to offer a potential means of lowering prices for pharmaceutical products.[34] Accordingly, several current proposed congressional reforms to lower drug prices would reform the existing legal structure of IP rights in the pharmaceutical context.[35]

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[28] Thomas, *supra* note 21, at 48.

[29] DEP'T OF HEALTH AND HUMAN SERVS., OBSERVATIONS ON TRENDS IN PRESCRIPTION DRUG SPENDING 1 (March 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.

[30] *See generally* Kirchhoff et al., *supra* note 29, 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).

[31] *See, e.g.*, LANDES & POSNER, *supra* note 14, at 313 (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").

[32] *See, e.g.*, Kesselheim et al., *supra* note 30, 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/2017/11/Excess-Costs-Briefing-Paper-FINAL_-2017-10-24.pdf (finding that patenting strategies caused $55 billion in excess costs for the American health care system with respect to just three drugs).

[33] *See Generic Competition and Drug Prices*, *supra* note 32.

[34] *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 30, at 864 (proposing limits on secondary patents and increased policing of pay-for-delay patent settlements as possible means to curtail high drug prices).

[35] *See infra* "Selected Drug Pricing Proposals in the 115th and 116th Congresses."

This report explains how several of these congressional proposals to reduce drug prices would interact with and/or alter existing IP law for pharmaceutical products. First, the report reviews the basics of patent law, FDA law and regulatory exclusivities, and the interaction between patent rights and FDA approval of pharmaceutical products. With this legal background in hand, the report overviews the details of a number of current legislative proposals to change these laws in order to reduce the drug prices paid by consumers.

Legal Background

Several different legal and regulatory regimes create or affect IP rights in pharmaceutical products. As noted above, pharmaceuticals are subject to two principal forms of IP protection—patents and regulatory exclusivities—which are generally distinct, but at times overlap and interact. Complicating matters further is the fact that FDA regulates pharmaceutical products differently depending on whether they derive from natural sources. In particular, before they can be marketed or sold, nonbiological "drugs"[36] must be approved by FDA under the Federal Food, Drug, and Cosmetic Act (FD&C Act), whereas "biologics"[37] must be licensed by FDA under the Public Health Service Act (PHSA).[38] Finally, patents on pharmaceutical drugs or biologics are subject to specialized patent dispute resolution procedures that can affect a manufacturer's ability to bring a follow-on product (i.e., a generic drug or biosimilar) to market. Specifically, provisions of the Drug Price Competition and Patent Term Restoration Act of 1984[39] (the Hatch-Waxman Act) govern FDA approval and patent disputes for generic drugs, whereas the Biologics Price Competition and Innovation Act of 2009[40] (BPCIA) governs FDA licensure and patent disputes for biosimilars.

In light of these complexities, a fair amount of background is necessary to understand how IP rights are obtained in pharmaceuticals, how these rights may impact drug prices, and the various reforms that have been proposed in Congress to reduce drug prices for consumers. This section provides this background, proceeding in three parts. First, it reviews patent law, including the requirements for obtaining a patent, the rights granted to patent holders, and various limitations on those rights.[41] Second, 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 types of approved pharmaceutical products.[42] Finally, this section describes and compares the different specialized patent dispute procedures for generic drugs and biosimilars under Hatch-Waxman and the BPCIA, respectively.[43]

[36] 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).

[37] 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).

[38] *See infra* "Food and Drug Administration (FDA) Law."

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

[40] Pub. L. No. 111-148, Title VII, 124 Stat. 199, 804-21 (2010).

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

[42] *See infra* "Food and Drug Administration (FDA) Law."

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

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."[44] The IP Clause was included in the Constitution to create a national, uniform law governing IP rights.[45] In the view of the Framers, the states could not effectively protect copyrights or patents separately because obtaining IP rights in multiple states with differing standards would be difficult and expensive for authors and inventors, undermining the effectiveness of the legal regime.[46]

Patent rights do not arise automatically. Rather, to obtain patent protection under the Patent Act,[47] an inventor must file a patent application with the PTO, and a PTO patent examiner must review the application and conclude that the application meets the statutory requirements before the PTO will issue a patent.[48] This section briefly overviews the requirements for obtaining a patent, the scope of the legal rights granted to the holder of a valid patent, and an important limitation on patent rights: the authority of the federal government to grant compulsory licenses for a patent under certain circumstances.

Requirements for Obtaining a Patent

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."[49] To obtain a patent, the inventor must formally file an application for a patent with the PTO, beginning a process called patent prosecution.[50] During prosecution, a patent examiner at the PTO evaluates the patent application to ensure that it meets all the applicable legal requirements to merit the grant of a patent.[51] In addition to requirements regarding the technical disclosure of the invention,[52] the claimed invention must be (1) directed at patentable subject matter, (2) new, (3) nonobvious, and (4) useful.[53] If granted, patents typically expire twenty years after the date of the initial patent application.[54]

Patentable Subject Matter

The field of patentable inventions is broad, embracing nearly "anything under the sun that is made by man."[55] By statute, patents are available on any new and useful "process, machine,

[44] U.S. CONST. art. I, § 8, cl. 8.

[45] Bonito Boats, Inc. v. Thunder Craft Boats, Inc., 489 U.S. 141, 162 (1989) ("One of the fundamental purposes behind the [IP Clause] was to promote national uniformity in the realm of intellectual property.").

[46] *See* Goldstein v. California, 412 U.S. 546, 556 (1973); THE FEDERALIST NO. 43, at 238-39 (James Madison) (E.H. Scott, ed. 1894).

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

[48] 35 U.S.C. §§ 111, 131.

[49] *Id.* § 101.

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

[51] 35 U.S.C. § 131.

[52] *See id.* § 112.

[53] *See id.* §§ 101-103.

[54] *Id.* § 154(a)(2).

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

manufacture, or composition of matter, or . . . improvement thereof."[56] Examples of technological areas for patentable inventions include pharmaceuticals, biotechnology, chemistry, computer hardware and software, electrical engineering, mechanical engineering, and manufacturing processes.[57] 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."[58] 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."[59]

In a series of recent cases, the Supreme Court has established a two-step test for patentable subject matter, sometimes called the *Alice* test.[60] The first step addresses whether the patent claims are "directed to" ineligible subject matter, that is, a law of nature, natural phenomenon, or abstract idea.[61] If not, the invention is patentable. If it is 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* 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.[62]

Novelty and Nonobviousness

Perhaps the most fundamental requirement for patentability is that the claimed invention must be actually *new*. Specifically, 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 effective filing date of the claimed invention."[63] 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.[64]

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

Rep. No. 1923, 82d Cong., 2d Sess., 6 (1952)).

[56] 35 U.S.C. § 101.

[57] *See Patent Technology Centers Management*, U.S. PATENT & TRADEMARK OFFICE, https://www.uspto.gov/patent/contact-patents/patent-technology-centers-management (last visited April 3, 2019) (listing technological divisions for PTO examiners).

[58] Diamond v. Diehr, 450 U.S. 175, 185 (1981).

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

[60] *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).

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

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

[63] 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).

[64] 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.").

nonobvious to be patentable.[65] 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.[66] 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."[67] By its nature, obviousness is an "expansive and flexible" inquiry that cannot be reduced to narrow, rigid tests.[68] Nonetheless, if an invention does no more than combine "familiar elements according to known methods," yielding only "predictable results," it is likely to be obvious.[69]

Utility

In addition to being novel and nonobvious, an invention must be *useful* to be patentable, that is, it must have a specific and substantial utility.[70] The utility requirement derives from the IP Clause's command that patent laws exist to "promote the Progress of . . . *useful* Arts."[71] 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."[72] This standard for utility is relatively low, however, requiring only that the claimed invention have some "significant and presently available benefit to the public" that "is not so vague as to be meaningless."[73]

Disclosure Requirements

In addition to substantive requirements relating to the invention, the Patent Act imposes a number of requirements relating to the form of the patent application. These provisions are intended to ensure that the patent adequately discloses the invention to the public such that the public can use the invention after the expiration of the patent term.[74] 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.[75]

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[65] 35 U.S.C. § 103.

[66] *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).

[67] *Graham*, 383 U.S. at 17-18.

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

[69] *Id*. at 416.

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

[71] 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.

[72] *Brenner*, 383 U.S. at 534-35.

[73] *In re Fisher*, 421 F.3d at 1371-72.

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

[75] 35 U.S.C. § 112(a).

This statutory language yields three basic disclosure requirements for patentability.[76] 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.[77] 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."[78] Finally, to satisfy the *best mode requirement*, the specification must demonstrate 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.[79]

Patent Claims

If granted, the legal scope of the patent is defined by the *patent claims*, words which "particularly point[] out and distinctly claim[] the subject matter which the inventor . . . regards as the invention."[80] In essence, while the specification explains the invention in a *technical* sense, the claims set forth the *legal* effect of the patent.[81] Much as a deed may describe the boundaries of a tract of land, the claims define the "metes and bounds" of the patent right.[82] 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."[83]

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.[84] 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 sued by the patentee.[85] Patents have the attributes of personal property and may be sold or assigned to by the patentee to a third party.[86] A patentee may also *license* other parties to practice the invention, that is, grant them permission to make, use, sell, or import the invention, usually in exchange for consideration (such as monetary royalties).[87]

Patents thus provide a *negative* right to exclude another person from practicing the claimed invention. However, patents do not grant the patentee any affirmative right to practice the invention.[88] In the pharmaceutical context, this means that even if a manufacturer has a patent on

[76] *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).

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

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

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

[80] 35 U.S.C. § 112(b).

[81] *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).

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

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

[84] 35 U.S.C. § 271(a).

[85] *Id.* §§ 271, 281, 283-85.

[86] *Id.* § 261.

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

[88] Leatherman Tool Group v. Cooper Industries, Inc., 131 F.3d 1011, 1015 (Fed. Cir. 1997) ("[T]he federal patent laws

a particular drug (or inventions related to making or using that drug), it nonetheless cannot market that drug without FDA approval.[89]

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."[90] The Patent Act includes provisions that may modify the 20-year term, including to account for excessive delays in patent examination at the PTO,[91] or delays associated with obtaining marketing approval from other federal agencies (including FDA).[92] In the pharmaceutical context, patents claiming a drug product or medical device (or a method of using or manufacturing the same) may be extended for up to five years to account for delays in obtaining regulatory approval, if certain statutory conditions are met.[93]

Patents are not self-enforcing: to obtain relief from infringement, the patentee must sue in court.[94] Patent law is an area of exclusive federal jurisdiction,[95] and the traditional forum for most patent disputes is federal district court.[96] Although patent suits may be filed in any district court across the country with jurisdiction over the defendant and proper venue, all appeals in patent cases are heard by a single specialized court, the U.S. Court of Appeals for the Federal Circuit (the Federal Circuit).[97]

If the patentee succeeds in proving infringement, the patent holder may obtain two major forms of judicial relief: monetary damages and injunctive relief.[98] Damages must be "adequate to compensate for the infringement,"[99] and typically take the form of either (1) *lost profits*, that is,

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do not create any affirmative right to make, use, or sell anything.").

[89] *See infra* "New and Generic Drug Approval." The same is true of biological products. *See infra* "Biological Product and Biosimilar Licensure."

[90] *Id.* § 154(a).

[91] *Id.* § 154(b)(1).

[92] *Id.* § 156.

[93] *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); Stephanie Plamondon Bair, *Adjustments, Extensions, Disclaimers, and Continuations: When Do Patent Term Adjustments Make Sense?*, 41 CAP. U. L. REV. 445, 460 (2013).

[94] 35 U.S.C. § 281.

[95] 28 U.S.C. § 1338.

[96] In 2018, roughly 3,447 patent lawsuits were filed in federal district courts, as compared to 1,717 before the Patent Trial and Appeal Board (PTAB). *See 2018 Patent Dispute Report: Year in Review*, UNIFIED PATENTS (Jan. 2, 2019), https://www.unifiedpatents.com/news/2019/1/2/2018-patent-dispute-report-year-in-review [hereinafter *2018 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 April 2, 2019); *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 conducts 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. (Feb. 19, 2019), https://www.usitc.gov/intellectual_property/337_statistics_number_new_completed_and_active.htm (reporting 74 new complaints in fiscal year 2018).

[97] 28 U.S.C. § 1295(a)(1).

[98] 35 U.S.C. §§ 283-84. A declaratory judgment (i.e., a judicial declaration of the rights of the parties) is another important form of relief in patent suits that is sometimes available to patentees or accused infringers. *See* 28 U.S.C. § 2201; *infra* note 287.

[99] *Id.* § 284.

the net revenue "lost to the patentee because of the infringement,"[100] or (2) a *reasonable royalty*, which awards the amount that the patentee would have received in a "hypothetical negotiation" if the patentee and the infringer had negotiated a license in good faith prior to the infringement.[101] Courts have discretion to increase the damages "up to three times the amount found or assessed,"[102] but such enhanced damages are "generally reserved for egregious cases of culpable behavior" by the infringer.[103] Finally, courts have discretion to award attorneys' fees in "exceptional cases,"[104] that is, ones 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."[105]

In addition to monetary damages, a patent holder may also ask courts to order various forms of injunctive relief.[106] 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.[107] If a patent infringement lawsuit is successful, the patent holder may seek a *permanent injunction*, an order prohibiting the defendant from infringing the patent in the future.[108]

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*.[109] To prove invalidity, the accused infringer must show, by clear and convincing evidence, that the patent should never have been granted by the PTO because it failed to meet the requirements for patentability.[110] 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.[111] Second, the accused infringer may claim an "absence of liability" on the basis of *noninfringement*.[112] 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.[113] Finally, the accused infringer may argue that the patent is

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

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

[102] 35 U.S.C. § 284.

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

[104] 35 U.S.C. § 285.

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

[106] 35 U.S.C. § 283.

[107] 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)).

[108] 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).

[109] 35 U.S.C. § 282(a)-(b).

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

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

[112] 35 U.S.C. § 282(b)(1).

[113] 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.

unenforceable based on the inequitable or illegal activities of the patent holder, such as obtaining the patent through fraud on the PTO.[114]

Following the passage of the 2011 Leahy-Smith America Invents Act (AIA),[115] the Patent Trial and Appeal Board (PTAB) has become an increasingly important forum for patent disputes.[116] The AIA created several new administrative procedures for challenging patent validity,[117] 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;[118] (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;[119] and (3) a transitional program for *covered business method patents* (CBM), a PGR-like process limited to certain patents claiming "business methods" that will be available only through September 2020.[120] Of these procedures, IPR is by far the most widely used.[121]

Types of Pharmaceutical Patents

If a person is the first to synthesize a particular chemical believed to be useful for the treatment of human disease, she may file for a patent on that chemical itself, and—presuming that the application meets all requirements for patentability—the PTO will grant the patent.[122] Patents on a pharmaceutical product's active ingredient may be of particular value to the manufacturer because these patents are unusually difficult, if not impossible, to "invent around" (i.e., develop a competing product that does not infringe the patent).[123] However, active ingredient patents are hardly the only patents relating to pharmaceuticals and not necessarily the most important to manufacturers as a practical matter.[124] Indeed, in the case of biological products, if the active

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).

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

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

[116] 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); CRS Report R44962, *Patent Law: A Primer and Overview of Emerging Issues*, by Kevin J. Hickey and Kathryn B. Armstrong, at 6-9.

[117] 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 116, 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.

[118] 35 U.S.C. §§ 321-329.

[119] *Id.* §§ 311-319.

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

[121] *See 2018 Patent Dispute Year in Review*, *supra* note 96 (finding that IPRs constituted 93.9% of petitions submitted to the PTAB in 2018).

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

[123] *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.").

[124] *See* Kyle, *supra* note 123, 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

ingredient is naturally occurring, it may not be legally possible to patent the biologic itself because it constitutes patent-ineligible subject matter.[125]

Pharmaceutical patents may cover many different features of a drug or biologic beyond a claim on the active ingredient itself.[126] Such patents may claim, among other things:

1. a formulation of the drug (e.g., an administrable form and dosage);
2. a method of using the pharmaceutical (e.g., an indication or use for treating a particular disease);
3. technologies used to administer the pharmaceutical or a method of administration;
4. a method of manufacturing or manufacturing technology used to make the pharmaceutical;
5. other chemicals related to the active ingredient, such as crystalline forms, polymorphs, intermediaries, salts, and metabolites.[127]

To be patentable, all of these types of inventions must be new, useful, and nonobvious, and sufficiently described in the patent application, like any other invention.[128]

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, a different manufacturing process, etc.—then the inventor can file for a patent on that improvement, which receives its own patent term.[129] 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."[130] Any person wishing to practice the improved form of the invention will need permission from both the holder of the patent on the original technology and the holder of the improvement patent (who need not be the same entity), if neither patent has yet expired.[131] In the case where the original patent has expired

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delivery routes, etc.").

[125] *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. CIRCUIT 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").

[126] Indeed, 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 AFF. 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).

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

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

[129] 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).

[130] KSR Int'l Co. v. Teleflex, Inc., 550 U.S. 398, 417 (2007); *see also supra* notes 65-69 and accompanying text (discussing the nonobviousness requirement).

[131] *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

but the improvement patent has not, permission from the improvement patentee is required to practice the improved version, but as a matter of patent law any person is free to make and use the original, unimproved version.[132]

Because many different aspects of pharmaceutical products (and improvements thereon) are patentable, some pharmaceutical products are protected by dozens of different patents. For example, one recent study of the top 12 drugs by gross U.S. revenue found that pharmaceutical manufacturers had obtained an average of 71 patents on each of these drugs.[133] AbbVie, the maker of the top-selling arthritis biologic Humira, was found to have filed 247 patent applications relating to that product, resulting in 132 issued patents claiming methods of treatment, formulations, methods of manufacturing, and other related inventions.[134]

The number and timing of nonactive ingredient patents (sometimes called "secondary" patents) have contributed to long-standing concerns by some commentators about so-called patent "evergreening." Evergreening, also known as patent "layering" or "life-cycle management," is an alleged practice by which "drug innovators [seek] to prolong their effective periods of patent protection [through] strategies that add new patents to their quivers as old ones expire."[135] Critics of evergreening maintain that, by obtaining later patents on improvements or ancillary aspects of a pharmaceutical, pharmaceutical manufacturers effectively extend patent protection beyond the term set by Congress, deterring follow-on competitors and keeping prices high.[136] In the view of evergreening critics, many secondary pharmaceutical patents are of questionable value and validity.[137]

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of the original patent need each other's permission before either can practice the improved invention).

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

[133] *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. 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 307-308 (discussing the limitations on the types of patents that may be listed in the *Orange Book*).

[134] *Overpatented*, *supra* note 133, at 7; *see also* 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 (finding that AbbVie has secured "more than 100 patents" on Humira and that "[m]any of those patents were issued over the past few years as the expiration of Humira's [primary] patent grew closer").

[135] Eisenberg, *supra* note 21, at 354; *see* Julian W. Marrs, *Forever Green? An Examination of Pharmaceutical Patent Extensions*, 18 OR. REV. INT'L L. 81, 83-89 (2008); Michael Enzo Furrow, *Pharmaceutical Patent Life-Cycle Management After* KSR v. Teleflex, 63 FOOD & DRUG L.J. 275, 276 (2008).

[136] *See, e.g.*, Marrs, *supra* note 135, at 83-86; Feldman & Frondorf, *supra* note 34, 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*, J.L. & BIOSCI. 8 (forthcoming 2019), https://doi.org/10.1093/jlb/lsy022 (criticizing drug companies for 'recycling and repurposing old [medicines]" to stifle competition).

[137] *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 21, 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, however, has been considerably worse."); *see also* C. Scott Hemphill & Bhaven V. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 21 J. HEALTH ECON. 327 (2012) (finding that later-issued patents relating to ancillary aspects of a drug are more frequently challenged

A similar, but distinct, concern voiced by some commentators is the notion of a patent "thicket." This term is used in two slightly different ways, both relating to products with a high number of patents. First, a patent thicket may describe the situation where 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."[138] Patent thickets, in this sense, raise concerns about inefficient exploitation of a technology because the multiplicity of owners increases transaction costs and creates coordination challenges.[139] Second, the term may be used in a looser sense to describe an incumbent manufacturer's practice of amassing of a large volume of patents relating to a single product, with the intent to intimidate follow-on competitors from entering the market (or to make it too costly and risky to do so).[140] AbbVie's Humira patent portfolio has been alleged to be an example of this sort of patent thicket.[141]

Although some critics deride patent thickets and evergreening, others assert that these are unfairly pejorative terms for legitimate uses of the patent system.[142] On this view, much innovation is incremental in nature, and sound public policy permits patents on improvements: like any other form of technology, society ought to provide incentives to develop more effective formulations of a drug, methods of treatment, and the like.[143] Secondary pharmaceutical patents may represent inventions with true medical benefits to patients, in which case the effect they may have on competition is arguably justified.[144] Finally, even presuming that some improvement patents

by generic firms).

[138] Stu Woolman at 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).

[139] *See* Gavin D. George, *What Is Hiding in the Bushes?* eBay*'s Effect on Holdout Behavior in Patent Thickets*, 13 MICH. TELECOMM. & TECH. L. REV. 557, 558-60 (2007) (summarizing the economic literature); *see generally* Shapiro, *supra* note 138; Michael A. Heller & Rebecca Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCI. 698, 698 (1998).

[140] Koons, *supra* note 134 (using "patent thicket" to refer to large patent portfolio amassed on one product by single biologics manufacturer); *America's Overspend*, *supra* note 32, at 4 (using term "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.").

[141] *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").

[142] *See, e.g.*, GlaxoSmithKline, *Evergreening* (Jan. 2014), https://www.gsk.com/media/2949/evergreening-policy.pdf (rejecting "evergreening" as an "inherently pejorative term . . . used by some to convey the false impression that research-based pharmaceutical companies abuse the patent system by obtaining patents on what are characterized as 'minor' improvements to existing medicines").

[143] *See, e.g.*, Christopher M. Holman, *In Defense of Secondary Pharmaceutical Patents: A Response to the UN's Guidelines for Pharmaceutical Patent Examination*, 50 IND. L. REV. 759, 760-61 (2017) (arguing that secondary pharmaceutical patent claims are necessary for incentivizing pharmaceutical innovation and neither inherently less legitimate and nor less worthy of protection than primary patents).

[144] *See* GlaxoSmithKline, *supra* note 142, at 3 ("[B]y allowing patents for secondary developments, the patent system provides incentives for companies which may not have the commercial or scientific capability to invent and develop new chemical entities to engage in incremental innovation.").

granted by the PTO are obvious or not truly innovative,[145] defenders of evergreening may point out that existing law already has several mechanisms to challenge the validity of patents.[146]

Compulsory Licensing

As explained above, the patent holder generally has the exclusive right to practice the invention. Thus, any other person who wishes to make, use, sell, or import the invention will ordinarily need a license (i.e., permission) from the patent holder, or else be exposed to legal liability.[147] In certain cases, however, patents may be subject to a "compulsory license," which allows another person to use the invention *without* the prior consent from the patent holder.[148] Compulsory licenses are typically a creation of statute and usually require the sanction of a governmental entity and the payment of compensation to the patent holder.[149] 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 ordinarily determined by operation of law, not by private contractual negotiations between the licensee and the patent holder.

Current federal law contains a number of compulsory license provisions for patents.[150] For example, under 28 U.S.C. § 1498, which is sometimes described as an "eminent domain" provision for patents,[151] the U.S. government has the authority to use any patented invention "without license."[152] 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.[153] In no event, however, will a court issue an injunction against the United States to prevent its use of the invention.[154] In effect, then, section 1498 allows the United States to issue itself a compulsory license to use any patented invention without obtaining the permission of the patentee, in exchange for the payment of reasonable compensation.[155] The federal government

[145] Defenders of evergreening contest this notion. Holman, *supra* note 143, at 759 ("[The] assumption that many types of pharmaceutical inventions are inherently obvious and undeserving of patent protection is incorrect and based on an oversimplified view of how these inventions come about.").

[146] *See, e.g.*, 35 U.S.C. §§ 311-319 (inter partes review); *id.* §§ 321-329 (post-grant review).

[147] *Id.* § 271.

[148] *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.").

[149] *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).

[150] *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).

[151] *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).

[152] 28 U.S.C. § 1498(a).

[153] *Id.*

[154] 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.

[155] 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).

uses its section 1498 authority with some frequency,[156] although it has not been used recently in the pharmaceutical context.[157]

Compulsory licensing is also available for inventions made with federal funding under the provisions of the Bayh-Dole Act.[158] In general, the Bayh-Dole Act permits certain government contractors to obtain patents on inventions produced with federal funding.[159] However, the federal government retains the authority to "march in" and grant compulsory licenses to third parties for federally funded inventions under certain specified circumstances, such as a failure to practice the patented invention or health or safety needs.[160] A license granted pursuant to Bayh-Dole's march-in provisions must be "upon terms that are reasonable under the circumstances," which may require some compensation to be paid by the licensee to the patentee.[161] The federal government has never exercised its march-in rights under Bayh-Dole.[162]

Food and Drug Administration (FDA) Law

Unlike patent law, which is centrally motivated by promoting innovation, FDA law generally arose to promote public health by protecting consumers from pharmaceuticals that are adulterated, misbranded, unsafe, or ineffective.[163] To this end, new drugs and biologics cannot be marketed without FDA approval.[164] FDA regulates which drugs and biologics may be marketed in the United States through similar but distinct approval processes.[165]

Nonetheless, the principle of balancing advancement through innovation against the benefits of competition applies to FDA law as well as patent law.[166] To that end, federal law provides certain regulatory exclusivities for companies that obtain approval for pharmaceutical products that meet the requisite criteria.[167]

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[156] 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).

[157] *Id*. at 303-07 (describing various uses of section 1498 by the federal government to purchase pharmaceutical drugs in the 1960s but observing that 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.

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

[159] 35 U.S.C. § 202(a); *see generally* Jennifer Penman & Fran Quigley, *Better Late than Never: How the U.S. 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).

[160] 35 U.S.C. § 203(a)(1)-(4).

[161] *Id*. § 203(a); Penman & Quigley, *supra* note 159, at 178.

[162] Penman & Quigley, *supra* note 159, at 199.

[163] *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.

[164] 21 U.S.C. § 355(a); 42 U.S.C. § 262(a)(1).

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

[166] *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).

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

This section provides an overview of the approval processes for new and follow-on drugs and 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."[168] New drugs are those drugs that scientific experts do not generally recognize as safe and effective for their intended use.[169] A new drug may contain an active ingredient that FDA has not previously approved or 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.[170]

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"[171] demonstrating the drug's safety[172] and effectiveness[173] for humans.[174] 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.[175] When the company is ready to begin clinical trials, it submits an investigational new drug (IND) application to FDA.[176] 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.[177] It also includes a proposed clinical study design and written approval from an Institutional Review Board, which reviews the study design.[178] FDA has 30 days to review the IND application and object before clinical investigations proceed.[179]

[168] 21 U.S.C. § 321(g).

[169] *Id*. § 321(p).

[170] *Id*. § 355(a).

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

[172] 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.

[173] 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*.

[174] 21 C.F.R. § 314.50(d)(5).

[175] *Id*. § 312.21.

[176] *Id*. § 312.20.

[177] *Id*. § 312.22-23.

[178] *Id*. § 312.23.

[179] *Id*. §§ 312.40, 312.42.

Clinical testing occurs in three phases.[180] Phase I clinical trials test the drug in a small number of subjects and focus on evaluating the safety of the drug.[181] During Phase I clinical trials, the company 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 from the drug.[182] Phase II and Phase III clinical trials evaluate the drug's efficacy and effectiveness in addition to safety.[183] These trials use a larger group of test subjects who have the characteristic, condition, or disease the drug treats.[184]

Once clinical trials are complete, the company submits the results in an NDA to FDA's Center for Drug Evaluation and Research (CDER), along with a list of articles used as components of the drug; a statement of the drug's composition; a description of manufacturing methods, facilities, and controls; specimens of the proposed labeling; any required pediatric assessments; and patient information.[185] 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.[186] The NDA may also include a proposed Risk Evaluation and Mitigation Strategy as needed.[187]

The FD&C Act provides for two types of NDAs: 505(b)(1) and 505(b)(2).[188] Both types include "full reports of investigations of safety and effectiveness."[189] However, the nature of the company's relationship to the underlying studies differs. For 505(b)(1) NDAs, the company has a right to all of the studies that support the investigational reports, either because the studies were conducted by or for the company, or because the company obtained the right to reference or use the studies from the person who conducted them.[190]

For 505(b)(2) NDAs, by contrast, at least some of the information contained in the application relies on studies that were *not* conducted by or for the company and for which the company has not obtained a right of reference or use.[191] This information to which the company does not have reference takes two forms: (1) published literature where the applicant has not obtained a right to the underlying studies or (2) the FDA's finding of safety and effectiveness for an approved drug.[192] The 505(b)(2) pathway is used to obtain approval for modifications of approved drugs—drugs that are "neither 'entirely new' nor 'simply a generic version of a branded drug.'"[193]

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[180] *Id*. § 312.21.

[181] *Id*. § 312.21(a).

[182] *Id*.

[183] *Id*. § 312.21(b)-(c).

[184] *Id*.

[185] 21 U.S.C. § 355(b).

[186] 21 C.F.R. § 314.50.

[187] 21 U.S.C. § 355-1(a)(1).

[188] *Id*. § 355(b).

[189] 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 [hereinafter FDA 505(B)(2) GUIDANCE].

[190] *Id.*; *compare* 21 U.S.C. § 355(b)(1) *with id*. § 355(b)(2).

[191] *Id*. § 355(b)(2).

[192] *See* FDA 505(B)(2) GUIDANCE, *supra* note 189.

[193] Takeda Pharm., U.S.A., Inc. v. Burwell, 78 F. Supp. 3d 65, 72 (D.D.C. 2015) (quoting Ethypharm S.A. France v. Abbott Laboratories, 707 F.3d 223, 227 (3d Cir. 2013), *vacated in part, aff'd in part*, Takeda Pharm. U.S.A., Inc. v. Burwell, 691 F. App'x 634 (D.C. Cir. 2016).

FDA regulations also permit NDA holders to make changes to the drug or label after approval.[194] Minor changes require only notice, but changes to the drug's label, dosage, strength, or manufacturing methods require a supplemental NDA (sNDA).[195] Because the sNDA relates to a drug already on the market, sNDAs must include post-market information, such as commercial marketing experience and reports in scientific literature and unpublished scientific papers, in addition to descriptions and analyses of clinical studies.[196]

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.[197] The agency also reviews the proposed labeling and the manufacturing controls.[198]

When FDA completes its review, it sends a letter to the company with the agency's determination.[199] If the NDA meets the requirements for approval, FDA sends an approval letter or, if patent rights or exclusivities bar approval, a tentative approval letter.[200] 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.[201] 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 could be remedied.[202]

Generic Drug Approval

Before the Hatch-Waxman Act was enacted in 1984, every new drug submitted to the FDA for preapproval required a complete application under Section 505(b) supported by clinical trial data demonstrating safety and effectiveness.[203] To encourage generic drug entry, the Hatch-Waxman Act established a pathway for abbreviated new drug applications (ANDAs),[204] 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.[205] The ANDA pathway allows generic manufacturers to avoid the long, expensive process of conducting their own clinical trials.[206] Instead, the generic manufacturer need only conduct studies with its generic product and samples of the RLD[207] to demonstrate that the

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[194] 21 C.F.R. § 314.70.

[195] *Id.*; *see also Drugs@FDA Glossary of Terms*, FOOD & DRUG ADMIN. (Nov. 14, 2017), https://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm (entry for "Supplement Type").

[196] 21 C.F.R. § 314.50(d)(5)(iv).

[197] 21 U.S.C. § 355(d).

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

[199] 21 C.F.R. § 314.105.

[200] *Id*.

[201] *Id*.

[202] *Id*. § 314.110.

[203] 21 U.S.C. § 355(b) (1982). FDA did permit applicants to rely on published studies to meet the "full reports of investigations" requirement through its Paper NDA policy. *See* Publication of "Paper NDA" Memorandum, 46 Fed. Reg. 27,396, 27,396 (May 19, 1981).

[204] 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).

[205] 21 C.F.R. §§ 314.92, 314.94.

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

[207] The FD&C Act and FDA regulations presuppose that generic manufacturers have access to the brand-name drug to

generic drug is pharmaceutically equivalent[208] and bioequivalent[209] to the RLD.[210] The ANDA also includes the generic manufacturer's proposed labeling, which must be identical to the RLD labeling except for manufacturing information and any approved changes from the RLD specifications.[211] ANDA filers submit this information, its proposed labeling, and any patent certifications[212] to FDA to obtain approval.[213]

Biological Product and Biosimilar Licensure

A biological product is derived from biological material, such as a virus, toxin, vaccine, blood component, or protein, and used for "the prevention, treatment, or cure of a disease or condition of human beings."[214] 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."[215] "Inherent variations" between different batches of the same biological product are "normal and expected."[216] 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."[217] 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 applicable license number; and the product's expiration date.[218] 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.[219] The BLA must include, among other things:

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conduct these studies. They do not provide any mechanisms for the generic manufacturer to force an NDA holder to provide samples of its brand-name drug.

[208] 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*.

[209] Bioequivalence means the drugs work the same inside the body; 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. 21 C.F.R. § 320.1(e).

[210] 21 U.S.C. § 355(j)(2)(A); 21 C.F.R. §§ 314.94, 320.21.

[211] 21 U.S.C. § 355(j)(2)(A)(v).

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

[213] 21 U.S.C. § 355(j)(2)(A).

[214] 42 U.S.C. § 262(i); 21 C.F.R. § 600.3.

[215] U.S. FOOD & DRUG ADMIN., BIOLOGICAL PRODUCT DEFINITIONS, https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/UCM581282.pdf (last visited Apr. 1, 2019).

[216] *Id*.

[217] *Id*.

[218] 42 U.S.C. § 262(a)(1).

[219] 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,

- "data derived from nonclinical laboratory and clinical studies";
- "[a] full description of manufacturing methods; data establishing stability of the product through the dating period";[220]
- representative samples of the product; the proposed labels, enclosures, and containers to be used;
- "the address of each location involved in the manufacture of the biological product"; and
- if applicable, a proposed Medication Guide.[221]

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.[222]

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."[223] As with drug approvals, FDA either issues the license or issues a complete response letter detailing the reasons for denying the license.[224] After approval, BLA holders must notify FDA of any changes to "the product, production process, quality controls, equipment, facilities, responsible personnel, or labeling."[225]

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."[226] To obtain a 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."[227] "[T]he condition or conditions of use prescribed,

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.

[220] The "dating period" is the "period beyond which the product cannot be expected beyond reasonable doubt to yield its specific results." 21 C.F.R. § 600.3(l).

[221] *Id*. § 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*.

[222] *Id*. § 601.20.

[223] 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 nature of the product 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).

[224] 21 C.F.R. § 601.3, 601.4.

[225] *Id*. § 601.12.

[226] 42 U.S.C. § 262(k).

[227] *Id*. § 262(i)(2).

recommended, or suggested in the labeling" must have been approved for the reference product.[228] 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.[229] 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."[230]

To obtain 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."[231] 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.[232] Interchangeable products "may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product."[233]

Regulatory Exclusivities

In order to balance interests in competition—which the abbreviated approval pathways aim to encourage—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.[234] This right to exclusivity aims to encourage new drug or biologics applicants to undertake the expense of generating clinical data and other information needed to support an NDA or BLA.[235] It also encourages follow-on product manufacturers to submit abbreviated applications as soon as permissible.[236]

There are two general categories of regulatory exclusivity: (1) data exclusivity, which precludes 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 the safety and effectiveness of the follow-on product; 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.[237] During a period of data exclusivity, a company

[228] *Id*. § 262(k)(2)(A)(i)(III).

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

[230] *Id*. § 262(k)(2)(A)(i)(V).

[231] *Id*. § 262(k)(4).

[232] *Id*. § 262(k)(4).

[233] *Id*. § 262(i)(3).

[234] *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."); Heled, *supra* note 166. For a comparison of regulatory exclusivities and patent exclusivities, see *infra* **Table 1.**

[235] Heled, *supra* note 166, at 427-30, 440.

[236] 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 166, at 428-29.

[237] 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

could submit an NDA or BLA for the same pharmaceutical product and use.[238] Functionally, however, 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 was or the nature of the treatment population. For new drugs, an NDA filer that 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.[239] During that period, no ANDA or 505(b)(2) NDA (i.e., applications that, by definition, would reference the NDA data) containing that same active ingredient may be submitted to FDA.[240] The 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 not infringed by the generic drug.[241]

NDA or sNDA[242] sponsors that obtain approval for significant changes to approved chemical entities that require additional clinical studies are eligible for **three years** of data exclusivity running from the time of NDA approval.[243] Significant changes would include new indications for or formulations of chemical entities that FDA previously approved.[244] Unlike 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.[245] The three-year exclusivity relates to when FDA may approve such applications.[246] 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.[247] In other words, the sponsor must have conducted or sponsored additional clinical trials that were necessary to obtain approval of the new use or formulation of the active ingredient in order to benefit from the three-year exclusivity for that new condition.

For brand-name biological products, the BPCIA establishes two applicable periods of exclusivity. First, no biosimilar applications can be submitted for **four years** "after the date on which the

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approach that ascribes distinct meanings to the terms. *See generally* Heled, *supra* note 166, at 436 n.67.

[238] *Id*.

[239] 21 U.S.C. § 355(c)(3)(E)(ii), (j)(5)(F)(ii); 21 C.F.R. § 314.108(b)(2).

[240] 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.

[241] 21 U.S.C. § 355(c)(3)(E)(ii), (j)(5)(F)(ii); 21 C.F.R. § 314.108(b)(3).

[242] sNDA sponsors are only eligible for three-year exclusivity because sNDAs amend existing NDAs with approved chemical entities. 21 C.F.R. § 314.108(b).

[243] 21 U.S.C. § 355(c)(3)(E)(iii)-(iv), (j)(5)(F)(iii)-(iv).

[244] *Id*.

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

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

[247] *Id*.

reference product was first licensed."[248] Second, approval of biosimilar application cannot become effective until **12 years** "after the date on which the reference product was first licensed."[249] 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 would not 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.[250] 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 four and 12-year regulatory exclusivity periods.[251]

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 a patent listed for an RLD has not expired, potential ANDA applicants have two choices: (1) wait until the patent expires to be approved or (2) file a paragraph (IV) certification[252] that the patent is invalid or not infringed by the generic product.[253] The potential for ensuing patent litigation raises the expected costs for the first ANDA filer with a paragraph (IV) certification as compared to other ANDA filers.[254] To incentivize generic manufacturers to be the first filer and challenge listed patents, the Hatch-Waxman Act provides **180 days** of exclusivity to the first ANDA applicant that successfully challenges an active patent listed for the RLD using a paragraph (IV) certification that the patent is invalid.[255] This exclusivity period precludes FDA from approving another ANDA for the same RLD during the 180-day period.

The BPCIA similarly awards regulatory exclusivity to the first interchangeable biological product for a particular reference product.[256] 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

[248] 42 U.S.C. § 262(k)(7)(B).

[249] *Id*. § 262(k)(7)(A).

[250] This issue has been the subject of discussions between FDA and some lawmakers. *See* Letter from Representative Anna G. Eshoo et al., to FDA (Dec. 21, 2010), http://patentdocs.typepad.com/files/letter-to-fda.pdf (signed by Representatives Barton, Eshoo, and Inslee); Letter from Senator Sherrod Brown et al., to Dr. Margaret Hamburg, Commissioner, FDA (Jan. 24, 2011), http://patentdocs.typepad.com/files/senator-letters-exclusivity.pdf (signed by Senators 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 that FDA may consider the exclusivity periods to provide 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.

[251] 42 U.S.C. § 262(k)(7)(C).

[252] ANDA applicants must provide one of four certifications for each listed patent for the reference listed drug. 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."

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

[254] *Id*.

[255] 21 U.S.C. § 355(j)(5)(B)(iv), (j)(5)(D)(iii)(II).

[256] 42 U.S.C. § 262(k)(6).

of a relevant patent dispute.[257] Specifically, the exclusivity period ends at the earlier of one 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.[258]

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, the FD&C Act provides a **180-day** exclusivity to an ANDA filer if—at the applicant's request—FDA designates the drug as a "competitive generic therapy" (CGT) due to "inadequate generic competition."[259] To receive the exclusivity, the first ANDA approved for the CGT drug must have submitted the ANDA when there were "no unexpired patents or exclusivities listed in the Orange Book for the relevant RLD,"[260] and the applicant must commercially market the drug within 75 days of approval.[261]

In addition, Congress passed the Orphan Drug Act in 1983 to encourage the development of drugs and biologics to treat rare diseases and conditions.[262] Because these drugs—called "orphan drugs"[263]—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.[264] 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.[265] To receive this exclusivity, (1) the drug must treat "rare diseases or conditions,"[266] and (2) FDA must not have approved another drug "for the same use or indication."[267]

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

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[257] *Id*.

[258] *Id*.

[259] 21 U.S.C. § 356h(b).

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

[261] 21 U.S.C. § 355(j)(5)(B)(v), (j)(5)(D)(iv).

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

[263] 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." 21 U.S.C. § 360bb(a)(2).

[264] *Id*. § 360cc(a).

[265] *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).

[266] 21 U.S.C. §§ 360bb, 360cc.

[267] 21 C.F.R. § 316.3(b)(12); *see also* 21 U.S.C. § 360cc. 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).

population and the filer completes pediatric studies at FDA's request.[268] Pediatric exclusivity adds **six months** to any existing exclusivity the NDA or BLA filer has obtained.[269] 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.[270]

Patent Dispute Procedures for Generic Drugs and Biosimilars

As **Table 1** summarizes below, patent rights granted by the PTO and regulatory exclusivities granted by FDA are legally distinct as a general matter.[271] They are, however, motivated by similar purposes. Patents are designed to encourage innovation by providing an economic incentive for inventors to invest their time and resources in the development of novel inventions.[272] Analogously, regulatory exclusivities granted by FDA[273] can be viewed as providing an incentive for pharmaceutical manufacturers to undertake the investments necessary to complete the FDA approval process and bring new drugs and biologics to market.[274]

In some circumstances, patent rights can affect when a follow-on generic or a biosimilar can be marketed. For example, if a court hearing a patent dispute grants an injunction against a generic drug manufacturer that prohibits that manufacturer from infringing by making the generic drug, that product cannot be brought to market until after the patent expires.[275] 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.[276] 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.[277]

[268] 21 U.S.C. § 355a(b)-(c); 42 U.S.C. § 262(m).

[269] 21 U.S.C. § 355a(b)-(c); 42 U.S.C. § 262(m).

[270] 21 U.S.C. § 355a(b)-(c).

[271] *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).

[272] *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.").

[273] FDA administers more than a dozen different regulatory exclusivities. *See* Thomas, *supra* note 21, at 42 n.40.

[274] *See id.* at 46; Morgan, *supra* note 21, at 98.

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

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

[277] Of course, if these patents are valid, such deterrence is the intended result of a patent system. However, in some cases, patents may deter competition even if the patents are invalid, inapplicable, 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 or listing of "irrelevant patents").

Table 1. 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)
Basic Requirements	Invention that is new, useful, nonobvious, and sufficiently disclosed in patent application	Successful completion of FDA regulatory process for a particular drug or biological product
Term	Generally 20 years from the date of the relevant patent application	Variable based on drug type and whether FDA approval has been previously obtained with respect to that product
Effect	Third parties cannot may, use, sell, or import the invention without the permission of the patentee	Third parties cannot seek, obtain, and/or use data for FDA approval with respect to particular product
Enforcement	By the patentee, usually in a judicial 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 interaction between the temporally limited patent monopoly and FDA premarketing requirements for products such as prescription drugs.[278] The first distortion affected new drug manufacturers: because obtaining FDA marketing approval could take years, the effective patent life (i.e., the period during which the patentee can derive profit from the invention) was shortened by FDA regulatory requirements.[279] 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.[280]

The other distortion concerned the end of the patent term and affected generic manufacturers. In general, once a patent is expired, the patented invention should be available for anyone to use.[281] As a result, in the pharmaceutical context, generic manufacturers can (at least in theory) enter the market once the applicable patents and/or regulatory exclusivities have expired. However, prior to the Hatch-Waxman Act, some judicial decisions had held that uses of a patented drug necessary to obtain FDA approval, such as conducting tests on a patented drug, constituted patent infringement.[282] Thus, as a practical matter, generic manufacturers could not even *begin* the process of seeking FDA approval until the applicable patents expired.[283] The result was an "effective extension of the patent term" based on the "combined effect of the patent law and the

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

[279] *Id*. at 669-70.

[280] *Id*. at 670; 35 U.S.C. § 156.

[281] 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.").

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

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

premarket regulatory approval requirement."[284] 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.[285]

A potential side effect of this safe harbor, however, 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.[286] 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 actually marketed, following the completion of the FDA approval process.[287] However, earlier resolution of such patent disputes is often considered beneficial, as it provides greater legal certainty to the parties.[288] In particular, generic manufacturers can obtain clarity on patent issues before they market a drug and expose themselves to monetary damages.[289]

For this reason, the Hatch-Waxman Act made the filing of an ANDA or paper NDA itself an "artificial" act of patent infringement.[290] For its part, the BPCIA contains an analogous provision making the filing of a biosimilar or interchangeable BLA an artificial act of patent infringement.[291] Functionally, these artificial acts of infringement enable the original manufacturer, in some circumstances, to sue for patent infringement at the time of the follow-on application, enabling patent disputes to be litigated prior to the marketing of the follow-on product.[292]

In short, both of the laws that created an abbreviated pathway for the regulatory approval for follow-on products enacted specialized patent dispute resolution procedures intended to facilitate the early resolution of patent issues. This section reviews these procedures.

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[284] *Id*.

[285] 35 U.S.C. § 271(e)(1); Merck KGaA v. Integra Lifesciences I, Ltd., 545 US 193, 200 (2005) (describing this provision as a "safe harbor").

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

[287] In general, even the absence of an actual act of infringement, either party could 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). However, 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 Maryland Casualty Co. v. Pacific 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 drug patents in some circumstances. 28 U.S.C. § 2201(b).

[288] *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.").

[289] *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.").

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

[291] 35 U.S.C. § 271(e)(2)(C).

[292] *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.[293] FDA includes information on listed patents in a publication known as the *Orange Book*.[294] When a generic drug manufacturer files an ANDA, it must provide a certification for each patent listed in the *Orange Book* with respect to the referenced listed drug (RLD).[295] In particular, with some exceptions,[296] the generic applicant must provide one of four certifications:

(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 and/or not infringed by the generic applicant's product.[297]

Paragraph (I) and (II) certifications do not affect FDA's ability to approve the ANDA.[298] If the generic applicant makes a paragraph (III) certification, however, FDA may not approve the ANDA until the patent at issue has expired.[299] A paragraph (IV) certification triggers Hatch-Waxman's specialized patent dispute procedures, often resulting in litigation.[300] First, the generic applicant must give notice of the ANDA and the paragraph (IV) certification to the patentee and the NDA holder.[301] The patent holder then has 45 days in which to bring a lawsuit against the generic applicant.[302] If the patent holder declines to file suit by the deadline, the ANDA 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.[303]

If the patent holder timely files suit after being notified of the paragraph (IV) certification, this lawsuit triggers the so-called "thirty-month stay": FDA generally cannot approve the ANDA for 30 months while the parties litigate their patent dispute.[304] If, prior to the expiration of the 30-month stay, the district court concludes that the patent is invalid or not infringed by the ANDA

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[293] 21 U.S.C. § 355(b)(1); *see also* 21 C.F.R. § 314.53(b).

[294] U.S. FOOD & DRUG ADMIN., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS (2019), https://www.fda.gov/downloads/drugs/developmentapprovalprocess/ucm071436.pdf [hereinafter *Orange Book*]; *see also* https://www.accessdata.fda.gov/scripts/cder/ob/ (searchable form of the *Orange Book*).

[295] 21 U.S.C. § 355(j)(2)(A)(vii). While this summary discusses the patent dispute procedures with respect to an ANDA, paper NDAs are subject to a parallel certification and notification process. *See id.* § 355(b)(2)-(3), (c)(3).

[296] 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 listed patent. *Id.* § 355(j)(2)(A)(viii).

[297] *Id.* § 355(j)(2)(A)(vii)(I)-(IV).

[298] *Id.* § 355(j)(5)(B)(i).

[299] *Id.* § 355(j)(5)(B)(ii).

[300] Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S, 566 U.S. 399, 407 (2012).

[301] 21 U.S.C. § 355(j)(2)(B)(i)-(iv).

[302] *Id.* § 355(j)(5)(B)(iii).

[303] *Id.* § 335(j)(5)(C); *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).

[304] *See id.*; *Caraco Pharm.*, 566 U.S. at 407-08. Following 2003 amendments to the Hatch-Waxman Act, the NDA holder may receive only 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.").

applicant, FDA may approve the ANDA as of the date of the court's judgment or settlement order to that effect.[305] If the court concludes that the patent is infringed (and that decision is not appealed or affirmed), then the effective date of ANDA approval must be "not earlier than the date of the expiration of the patent which has been infringed."[306] FDA approval of a generic drug application can thus be significantly delayed based upon patent rights asserted by the NDA holder.

By statute, the only patents that must be listed with an NDA are those that either (1) "claim[] the drug" that is the subject of the NDA or (2) claim "a method of using such drug."[307] FDA regulations make clear that "drug substance (active ingredient) patents, drug product (formulation and composition) patents, and method-of-use patents" *must* be listed, whereas "[p]rocess patents, patents claiming metabolites, and patents claiming intermediates" must *not* be listed.[308] 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*. However, FDA does not actively police the patent information listed in the *Orange Book*, viewing its role as merely "ministerial."[309] This approach has raised concerns among some commentators that irrelevant or inapplicable patents may be listed by NDA holders and included in the *Orange Book* as a means to deter generic competition.[310]

Because of 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 relevant patents.[311] However, there is no statutory provision providing that the patentee or NDA holder forfeits the right to sue if she fails to list the applicable patents.[312] In addition, because only certain types of patents relating to a drug may be included in the *Orange*

[305] 21 U.S.C. § 355(j)(5)(B)(iii)(I).

[306] *Id.* § 355(j)(5)(B)(iii)(II); 35 U.S.C. § 271(e)(4)(A).

[307] 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.*

[308] 21 C.F.R. § 314.53(b)(1).

[309] *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 v. Thompson, 296 F.3d 227, 242-43 (4th Cir. 2002)). However, FDA does have 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 of this issue. 21 C.F.R. § 314.53(f)(1). Generally, however, FDA will not change the patent information in the *Orange Book* unless the NDA holder amends or corrects the information in response to the 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. & INDUSTRY 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 applicant may also file a counterclaim in infringement litigation to correct or delete patent information listed by the NDA holder. 21 U.S.C. § 355(j)(5)(C)(ii)(I).

[310] *See, e.g.*, Eisenberg & Crane, *supra* note 277, at 260 (arguing that "the lack of administrative oversight" by FDA "has allowed innovators to defer competition through the listing of irrelevant patents").

[311] *See* Winkler et al., *supra* note 309, at 3 ("Having a patent listed in the Orange Book provides significant benefits to the NDA holder.").

[312] *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.").

Book,[313] some patent litigation concerning generic drugs takes place outside the specialized procedures of the Hatch-Waxman Act.

The BPCIA: Patents 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.[314] Under the BPCIA, regulatory approval of biologics is not directly contingent on resolution of patent disputes. In contrast to the Hatch-Waxman approach, a BLA filed need not list any patent information as part of its BLA.[315] As a result, no patent information is currently listed in the *Purple Book*, FDA's list of approved biological products that is the biologics analog of the *Orange Book*.[316] **Table 2** summarizes the key differences between the patent dispute resolution regimes for drugs under Hatch-Waxman and for biologics under the BPCIA.

Instead of the Hatch-Waxman certification process, patent disputes regarding biosimilars may be resolved through the BPCIA's "patent dance."[317] The patent dance is "a carefully calibrated scheme for preparing to adjudicate, and then adjudicating, claims of infringement."[318] The first step in the patent dance process is triggered when, not later than 20 days after FDA accepts a biosimilar BLA, the biosimilar applicant provides its application to the reference product sponsor (i.e., the brand-name biologic manufacturer), along with information on how the biosimilar is manufactured.[319] "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)."[320] The biosimilar applicant and reference product sponsor then 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 as to the validity and infringement of those patents.[321] Depending on their participation in this information exchange, each party has the opportunity to litigate the patents in two phases: either at the conclusion of the patent dance, or

[313] *See supra* notes 307-308 and accompanying text.

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

[315] *See* 42 U.S.C. § 262(a); Daniel M. Scolnick, *FDA's 'Purple Book' for Biologics: Patents Not Included* PEPPERHAMILTON LLP 1 (Sept. 9, 2014), https://www.pepperlaw.com/resource/159/26J3.

[316] Scolnick, *supra* note 315; *Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*, U.S. FOOD & DRUG ADMIN. (March 20, 2019), https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm411418.htm [hereinafter the *Purple Book*]. FDA maintains two separate lists of approved biological products, depending on the center within FDA that regulates them: either CDER or CBER. *See Background Information: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations (Purple Book)*, U.S. FOOD & DRUG ADMIN. (March 5, 2015), https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm411424.htm. Unlike the *Orange Book*, FDA is not required by statute to publish the *Purple Book*, but it has chosen to do so voluntarily. *See id*.

[317] *See* 42 U.S.C. § 262(*l*).

[318] 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).

[319] 42 U.S.C. § 262(*l*)(2).

[320] *Sandoz*, 137 S. Ct. at 1670-71.

[321] *Id*. at 1671-72.

when the applicant provides a notice of commercial marketing no later than 180 days before the date that the biosimilar will be marketed.[322]

BLA holders cannot obtain injunctive relief to compel the biosimilar applicant to engage in the patent dance.[323] In practice, this limitation means that biosimilar applicants can choose whether or not they wish to commence the patent dance. However, 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."[324] Thus, although the biosimilar applicant need not immediately reveal his manufacturing information if he chooses not to commence the patent dance, he exposes himself to an immediate lawsuit for a declaratory judgment of patent infringement.[325]

Unlike patent listing under Hatch-Waxman, the BPCIA contains an express statutory penalty for failing to list relevant patents during the patent dance. 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 [the biological product at issue]" without permission of the patentee.[326] Under the "list it or lose it" requirement, the patent holder may forfeit his right to sue if this list is not submitted or is incomplete.[327] 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."[328]

[322] *Id*. at 1672.

[323] *Id*. at 1675.

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

[325] *Sandoz*, 137 S. Ct. at 1675. In general, there are complicated tradeoffs for biosimilars applicants in deciding whether to initiate the patent dance. *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.

[326] 42 U.S.C. § 262(l)(3)(A)(i).

[327] *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 312 (same).

[328] 35 U.S.C. § 271(e)(6)(C). The statute is not clear as to whether the holder of a patent that was not timely listed loses his right to sue the biosimilar applicant just 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 312 (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 327, at 760 (describing the "list it or lose it" provision as reaching infringements both "before or after marketing of the biosimilar").

Table 2. 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 resources (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	Five-year new chemical entity exclusivity (three years for other new products)	Twelve-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 that." 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 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 applicant 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.

Selected Drug Pricing Proposals in the 115th and 116th Congresses

This section reviews a number of legislative proposals in the 115th and 116th Congresses that seek to reduce pharmaceutical drug and biological product prices through reforming IP laws and/or facilitating increased competition from generic drug and biosimilar manufacturers. This review is not intended to be comprehensive, nor does it evaluate the merits of these proposals. Rather, proposals are reviewed merely as representative examples of the various types of legal changes under consideration. Related or similar proposals are referenced in the footnotes.[329]

As noted above, IP rights are only one factor that may contribute to consumer prices in a highly complex pharmaceutical market.[330] Thus, congressional proposals related to IP rights are merely one potential means to reduce drug prices that is currently under consideration in Congress. Other legislative proposals seeking to reduce drug prices would, for example, permit the Secretary of HHS (the Secretary) to negotiate drug prices for Medicare Part D,[331] allow consumers to import (often cheaper) pharmaceuticals from Canada under certain circumstances,[332] or reform health insurance requirements to institute a cap on consumers' out-of-pocket costs for prescription drugs.[333] Because these and other similar proposals relate only indirectly to IP rights in pharmaceuticals, they are outside the scope of this report.

In part due to the complexity of the legal regimes governing IP rights in pharmaceutical products, there are many different approaches that legislators seeking to reduce drug and biologic prices might take. These approaches include efforts to facilitate generic and biosimilar market entry, curtail practices perceived to be anticompetitive, limit IP rights based on pricing behavior, and increase patent transparency. This section surveys some of the specific means used in existing legislative proposals.

Facilitating Follow-On Product Entry: The CREATES Act of 2019

For many looking at how to reduce drug prices, encouraging the entry of follow-on products—which provide lower-cost alternatives to brand products—is often an area of focus.[334] Accordingly, proposals have been made to overcome perceived barriers to follow-on product entry. One such proposal is the CREATES Act of 2019,[335] which aims to facilitate the timely entry

[329] *See infra* notes 335, 394, 469 and 478.

[330] *See supra* note 30; *see generally* AMERICAN PATIENTS FIRST, *supra* note 1, at 12-18 (overviewing "complex U.S. pharmaceutical market"); Henry Waxman et al., *Getting to the Root of High Prescription Drug Prices*, THE COMMONWEALTH FUND 6-10 (2017) (same).

[331] *See, e.g.*, Medicare Negotiation and Competitive Licensing Act of 2019, H.R. 1046, 116th Cong.; Empowering Medicare Seniors to Negotiate Drug Prices Act of 2019, S. 62, 116th Cong.

[332] *See, e.g.*, Safe and Affordable Drugs from Canada Act of 2019, S. 61, 116th Cong.

[333] *See, e.g.*, Capping Prescription Costs Act of 2018, S. 3194, 115th Cong.

[334] *See, e.g.*, *Statement from FDA Commissioner Scott Gottlieb, M.D. on New Steps to Facilitate Efficient Generic Drug Review to Enhance Competition, Promote Access and Lower Drug Prices*, U.S. FOOD & DRUG ADMIN. (Jan. 3, 2018), https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm591184.htm.

[335] Identical bills have been introduced in the House of Representatives, *see* H.R. 965, 116th Cong., and the Senate, *see* S. 340, 116th Cong. For simplicity, all citations herein are to the Senate version as of April 2, 2019. In addition to the CREATES Act, the FAST Generics Act of 2019, H.R. 985, 116th Cong. § 505-2(f) (2019) would also authorize a generic product manufacturer to sue the brand manufacturer for refusal to timely provide brand samples. The CREATES Act is discussed here simply as an example of the proposals addressing the sample refusal concern.

of certain follow-on products by addressing the concern that some brand manufacturers have improperly restricted the distribution of their products to deny follow-on product manufacturers access to samples of brand products (i.e., the reference drug or biological product).[336] Because brand samples are necessary to conduct certain comparative testing required for an ANDA or biosimilar BLA,[337] some have attributed the inability to timely obtain samples as a cause of delay in the entry of generic products.[338]

Restricted Distribution and Sample Denial

While follow-on product manufacturers can usually obtain brand samples by purchasing them from licensed wholesalers, some brand products are subject to restricted distribution that limits how they can be sold.[339] This restriction can occur in one of two ways. First, a brand manufacturer can voluntarily place its products into restricted distribution in order to have more control over who can purchase them.[340] Second, some high-risk drugs are subject to restricted distributions under statute and FDA regulations.[341]

Under the FD&C Act, as amended by the Food and Drug Administration Amendments Act of 2007 (FDAA Act),[342] where a pharmaceutical product entails serious safety concerns (e.g., potentially acute side effects that may warrant special monitoring), FDA may require the sponsor of the NDA or BLA to submit a proposed Risk Evaluation and Mitigation Strategies (REMS),[343] a risk-management plan that uses strategies beyond labeling to ensure that the benefits of a drug or biological product outweigh its risks.[344] Examples of less restrictive REMS requirements include medication guides for patients and communication plans for health care providers.[345] More restrictive REMS programs have elements to assure safe use (ETASU), which can include prescriber and dispenser certification requirements, patient monitoring or registration, or controlled distribution that limits how the product can be sold.[346] If a brand product is subject to REMS with ETASU, the brand manufacturer and the generic or biosimilar manufacturers generally must agree on a single, shared REMS system before the generic product goes on the

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[336] *See, e.g.*, *Antitrust Concerns and the FDA Approval Process: Hearing Before the H. Comm. on the Judiciary*, 114th Cong. (2017) (statement of Scott Gottlieb, Comm'r of Food and Drug Admin.) [hereinafter Gottlieb Statement], *available at* https://www.fda.gov/NewsEvents/Testimony/ucm568869.htm; SPECIAL S. COMM. ON AGING, 113TH CONG., REP. ON SUDDEN PRICE SPIKES IN OFF-PATENT PRESCRIPTION DRUGS: THE MONOPOLY BUSINESS MODEL THAT HARMS PATIENTS, TAXPAYERS, AND THE U.S. HEALTH CARE SYSTEM 113-16 (2016) [hereinafter SPECIAL S. COMM. ON AGING REP.], https://www.aging.senate.gov/imo/media/doc/Drug%20Pricing%20Report.pdf.

[337] *See supra* "Food and Drug Administration (FDA) Law."

[338] Gottlieb Statement, *supra* note 336; SPECIAL S. COMM. ON AGING REP., *supra* note 336, at 113-16.

[339] *See* Gottlieb Statement, *supra* note 336; SPECIAL S. COMM. ON AGING REP., *supra* note 336, at 113-15.

[340] *See* Gottlieb Statement, *supra* note 336; SPECIAL S. COMM. ON AGING REP., *supra* note 336, at 114-15.

[341] *See* 21 U.S.C. § 355-1(a)(1); 21 C.F.R. § 312.300. *See also* Gottlieb Statement, *supra* note 336; SPECIAL S. COMM. ON AGING REP., *supra* note 336, at 115-16.

[342] Pub. L. No. 110-85, 121 Stat. 823 (2007).

[343] *See* U.S. FOOD & DRUG ADMIN., Risk Evaluation and Mitigation Strategies (REMS) (Feb. 2, 2018), https://www.fda.gov/drugs/drugsafety/rems/default.htm.

[344] 21 U.S.C. § 355-1(a)(1); 42 U.S.C. 262(k)(5)(C).

[345] 21 U.S.C. § 355-1(e).

[346] *Id.* § 355-1(f)(3).

market.[347] However, FDA can waive the shared REMS requirement and allow the use of a different, comparable system by the generic or biosimilar manufacturer.[348]

Since the enactment of the FDAA Act, some generic manufacturers[349] have complained that they have been improperly denied access to samples through restricted distribution.[350] Some brand manufacturers have implemented voluntary, contractual restrictions that target generic manufacturers.[351] Alternatively, if their products are subject to REMS with ETASU, some brand manufacturers have either (1) invoked the restricted distribution component of a REMS with ETASU to deny sales to generic manufacturers, or (2) used the existence of REMS with ETASU to substantially prolong negotiations over the sale of samples or the development of a single, shared REMS system.[352]

Existing Law Governing Sample Denials

The existing statutory and regulatory framework provides limited legal recourse to generic manufacturers who have been denied access to or experience long delays in obtaining samples. As an initial matter, there are no statutes or regulations that specifically prohibit a company from imposing voluntary distribution restrictions on its products. For products subject to REMS, the brand manufacturers are generally prohibited from using their REMS to "block or delay approval of an application . . . to a drug that is subject to the abbreviated new drug application."[353] The statute, however, does not expressly authorize FDA to enforce this provision.[354] Accordingly, consistent with FDA's long-standing view that "issues related to ensuring that marketplace actions are fair and do not block competition would be best addressed by [the Federal Trade Commission],"[355] FDA has not asserted that it has the authority to compel the sale of samples for comparative testing.[356]

Given the lack of recourse under federal drug law, generic manufacturers have attempted to seek relief by suing withholding brand manufacturers for violations of antitrust law. Specifically, they argue that the brand manufacturer's refusal to sell samples or its delay in selling samples constitutes an anticompetitive effort to maintain a monopoly in the brand product market in violation of section 2 of the Sherman Act.[357] Whether this conduct violates antitrust law, however,

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[347] *Id*. § 355-1(i)(1)(C).

[348] *Id*.

[349] To date, concerns about sample refusal have primarily been raised by generic drug manufacturers. *See* Gottlieb Statement, *supra* note 336. However, biosimilar manufacturers can potentially face similar issues because biological products may also be subject to REMS. *See* 42 U.S.C. 262(k)(5)(C).

[350] Gottlieb Statement, *supra* note 336.

[351] *See id*.

[352] *See id*.

[353] 21 U.S.C. § 355-1(f)(8).

[354] *See id*.

[355] *See, e.g.*, U.S. FOOD & DRUG ADMIN., Letter Response to Dr. Reddy's Lab.'s Citizen Petition 7 (Aug. 7, 2013), *available at* https://www.regulations.gov/document?D=FDA-2013-P-0572-0003.

[356] *See* U.S. FOOD & DRUG ADMIN., HOW TO OBTAIN A LETTER FROM FDA STATING THAT BIOEQUIVALENCE STUDY PROTOCOLS CONTAIN SAFETY PROTECTIONS COMPARABLE TO APPLICABLE REMS FOR RLD: DRAFT GUIDANCE FOR INDUSTRY (2014), https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm425662.pdf.

[357] *See, e.g.*, *In re* Thalomid and Revlimid Antitrust Litig., 2015 WL 9589217, at *14-16 (D.N.J. Oct. 29, 2015); Mylan Pharm. v. Celgene Corp., 2014 WL 12810322, at *3-4 (D.N.J. Dec. 23, 2014); CRS Legal Sidebar LSB10272, *The CREATES Act of 2019 and Lowering Drug Prices: Legal Background & Overview*, by Wen S. Shen, at 2-3.

is unclear because courts have not defined a clear standard for when a refusal to deal is anticompetitive.[358] A generic manufacturer's ability to obtain relief for sample denial under antitrust law is therefore uncertain under existing law.

The Proposed Bill

The CREATES Act seeks to address the uncertainties in the existing legal framework by creating a private cause of action that follow-on product developers can use to initiate expedited litigation to obtain needed brand samples. Instead of asserting an antitrust claim, the bill would allow a follow-on product developer to sue to compel the provision of brand samples if specific statutory elements are met.

For brand products not subject to a REMS with ETASU (including a product that is subject to voluntary restrictive distribution imposed by the brand manufacturer), the follow-on product developer would need to show that:

1. it had made a request for samples;
2. the brand manufacturer failed to deliver, on commercially reasonable, market-based terms, sufficient quantities of the samples within 31 days of receiving the request; and
3. as of the filing date of the action, the follow-on product developer is still unable to obtain sufficient quantities of the needed samples on commercially reasonable, market-based terms.[359]

For products subject to REMS with ETASU, the bill would create a process by which the follow-on product developer can request from FDA an authorization to obtain sufficient quantities of the relevant samples.[360] FDA would issue the authorization if it determines that the follow-on product developer has agreed to comply with or otherwise met the safety conditions or requirements deemed necessary by FDA.[361] In this situation, the follow-on product developer would need to show the first and third elements above, and that the brand manufacturer failed to deliver, on commercially reasonable, market-based terms, sufficient quantities of samples either within 31 days of receiving the request *or* within 31 days of receiving notice of FDA's authorization, whichever is later.[362]

If a follow-on product developer prevails under either cause of action, the bill would require the court to issue injunctive relief compelling the brand manufacturer to provide the samples without delay and award attorney's fees and costs.[363] If the court finds that the brand manufacturer delayed providing the samples without a "legitimate business justification," the court could also award monetary damages.[364] Monetary damages are not to exceed the revenue the brand manufacturer earned on the product during the period beginning on the day that is 31 days after

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[358] *Compare In re Thalomid*, 2015 WL 9589217, at *14-16 *and Mylan*, 2014 WL 12810322, at *3-4 (denying motions to dismiss section 2 claims alleging refusal to sell samples by brand manufacturer), *with In re* Suboxone (Buprenorphine Hydrochloride and Naloxone) Antitrust Litig., 64 F. Supp. 3d 665, 685-88 (E.D. Penn. 2014) (granting motion to dismiss Section 2 claim alleging intentional delay in negotiating single shared REMS).

[359] CREATES Act of 2019, S. 340, 116th Cong. § 3(b)(2)(A).

[360] *Id*. § 3(b)(2)(B)(i).

[361] *Id*. § 3(b)(2)(B)(ii).

[362] *Id*. § 3(b)(2)(A).

[363] *Id*. § 3(b)(4)(A).

[364] *Id*. § 3(b)(4)(A)(iii).

the receipt of the request for samples (or, if the product is subject to REMS with ETASU, on the day that is 31 days after the receipt of the FDA notice of authorization, if that date is later), and ending on the date on which the follow-on product developer receives sufficient quantities of the brand sample.[365]

The bill would also provide FDA more latitude to approve a separate REMS system that the follow-on product developer could use if it cannot reach an agreement on a shared strategy with the brand manufacturer.[366] Specifically, rather than requiring the use of a shared system as the default, the bill would amend the relevant statutory provisions to permit the use of a shared system or a different but comparable system as available alternative options.[367]

To address the concern that a more relaxed REMS requirement may expose the brand manufacturers to liability, the bill includes a provision that limits the brand manufacturer's liability against claims arising out of a follow-on product developer's failure to follow adequate safeguards during the development and testing of the generic product.[368]

Facilitating Public Production of Follow-On Products: The Affordable Drug Manufacturing Act of 2018

Rather than promoting follow-on product entry by providing production incentives to private parties (as the Hatch-Waxman Act did), or by removing certain barriers to entry for private parties (as the CREATES Act would), the Affordable Drug Manufacturing Act of 2018[369] (ADMA) would direct the government itself to manufacture certain pharmaceuticals. In particular, ADMA aims to facilitate competition in the market for pharmaceutical products by establishing an Office of Drug Manufacturing within HHS that would oversee the production of certain "applicable drugs."[370]

ADMA would define an "applicable drug" as a drug or biological product that FDA has approved or licensed under specified provisions of the FD&C Act or PHSA, and which would further satisfy one of two conditions.[371] The first condition would require that any patent listed in the *Orange Book* with respect to such drug has expired, and that any period of regulatory exclusivity granted by FDA under listed provisions of the FD&C Act or PHSA has expired.[372] Moreover, to meet the first condition for an "applicable drug," the drug would have to either (a) not be currently marketed in the United States or (b) be marketed by fewer than three manufacturers.[373] In the case where the drug is being marketed by fewer than three manufacturers, the drug would

[365] *Id*. § 3(b)(4)(B).

[366] *Id*. § 4.

[367] *Id*. § 4(2).

[368] *Id*. § 3(c).

[369] Identical bills have been introduced in the House of Representatives, *see* H.R. 7348, 115th Cong., and the Senate, *see* S. 3775, 115th Cong. For simplicity, all citations herein are to the Senate version as of April 2, 2019.

[370] S. 3775 § 2 (proposed new PHSA § 310B(a)). Under the bill, the Office of Drug Manufacturing would be headed by a Director appointed by the President and confirmed by the Senate. *Id*. (proposed PHSA § 310B(a)(3)(A)). The Director would have the authority, in consultation with the Secretary, to appoint and direct all employees of the office. *Id*. (proposed PHSA § 310B(a)(3)(B)). The bill would place certain restrictions on who could be appointed as Director and who could work at the Office. *Id*. (proposed PHSA § 310B(a)(3)(C)).

[371] *Id*. (proposed new PHSA § 310B(e)).

[372] *Id*. (proposed PHSA § 310B(e)(1)(A)-(B)).

[373] *Id*. (proposed PHSA § 310B(e)(1)(C)(i)-(ii)).

be required to further meet one of a number of additional criteria such as experiencing a recent price increase or being included on FDA's drug shortage list.[374]

The second, alternative condition for meeting the "applicable drug" definition would be the existence of a license or other authorization of "patent use" under a number of provisions of federal law.[375] These provisions include the United States' "eminent domain" authority for patents under 28 U.S.C. § 1498,[376] and the United States' "march-in rights" under the Bayh-Dole Act,[377] both of which are discussed above.[378] In short, the "applicable drug" definition would generally limit the Office of Drug Manufacturing to producing drugs for which either (1) the applicable patent and regulatory exclusivities have expired (in addition to not being widely marketed currently) or (2) the government already has a patent license under current law.

With respect to an applicable drug, the Office would be required to (1) prepare and submit the relevant applications for FDA approval or contract with other entities to do so; (2) acquire the relevant manufacturing rights and then either manufacture the drugs or contract with other entities to do so; (3) sell the drugs at a fair price, which takes into account certain specified factors, and (4) use the money received for the activities of the Office.[379] In addition, the Office would also manufacture or contract with other entities to manufacture active pharmaceutical ingredients (APIs) under specified conditions, including if an API is not readily available from existing suppliers, and set the API's prices based on specified factors.[380]

The bill would set forth certain selection criteria for the applicable drugs and require a gradual increase in the number of drugs produced over time. Specifically, the bill would require the Office to prioritize the manufacturing of applicable drugs that would have the greatest impact on (1) lowering drug costs to patients, (2) increasing competition and addressing drug shortages, (3) improving the public health, or (4) reducing costs to Federal and State health programs.[381] In the first year following enactment, the Office would be required to manufacture, or enter into contracts with entities to manufacture, at least 15 applicable drugs.[382] During that time, the Office would also be required to begin the manufacturing of insulin.[383] Within three years of enactment, the Office would be required to manufacture, or enter into contracts with entities to manufacture, at least 25 applicable drugs.[384]

Beginning three years after the date upon which the Office first begins manufacturing a drug and annually thereafter, the Secretary would also be required to make available for sale the approved FDA application.[385] If the purchaser of the application either fails to market the applicable drug

[374] *Id*. (proposed PHSA § 310B(e)(1)(C)(ii)(I)-(III)).

[375] *Id*. (proposed PHSA § 310B(e)(2)(A)-(E)).

[376] *Id*. (proposed PHSA § 310B(e)(2)(A)).

[377] *Id*. (proposed PHSA § 310B(e)(2)(C)).

[378] *See supra* "Compulsory Licensing."

[379] S. 3775 § 2 (proposed PHSA § 310B(a)(4)).

[380] *Id*. (proposed PHSA § 310B(a)(4)(A)(vi) and § 310B(a)(4)(D)).

[381] *Id*. (proposed PHSA § 310B(a)(6)).

[382] *Id*. (proposed PHSA § 310B(a)(7)).

[383] *Id*. (proposed PHSA § 310B(d)).

[384] *Id*. (proposed PHSA § 310B(a)(7)).

[385] *Id*. (proposed PHSA § 310B(c)(2)). A sponsor of an NDA or BLA may transfer ownership of its application if the following information is provided to FDA at the time of transfer: (1) the former owner submits a letter to FDA providing notice of the transfer; and (2) the new owner submits an application form confirming its commitment to agreements and conditions made by the former owner, the effective date of the transfer, and a statement that it has a

within six months of purchase or increase its price above the fair price (as adjusted by the consumer price index), the Secretary would be required to revoke the purchaser's approved application and resume production of that drug.

The Office would be required to report to the President and Congress annually on specified topics, including a description of the status of applicable drugs for which manufacturing has been authorized.[386] The bill would authorize the Office to be appropriated such sums as may be necessary.[387]

Reforming Pay-for-Delay Settlements: The Preserve Access to Affordable Generics and Biosimilars Act

As described above, patent litigation can result when generic drug and biosimilar manufacturers seek to market a drug or biological product before patent rights expire by challenging the validity of the brand-name companies' patents and/or their applicability to the follow-on product.[388] Some brand-name companies have resolved or settled such litigation through agreements with the generic manufacturer wherein the brand-name company pays the generic manufacturer a sum of money in return for the generic manufacturer agreeing to wait to enter the market.[389]

This practice, referred to as "reverse payment settlements" or "pay-for-delay settlements," allows the brand-name company to avoid the risk that its patent will be invalidated, delay the market entry of generic competition, and effectively extend its exclusive right to market the listed drug.[390] A valid patent affords the owner the right to exclude infringing products from the market, but "an invalidated patent carries with it no such right," "[a]nd even a valid patent confers no right to exclude products or processes that do not actually infringe."[391] Because these agreements terminate the litigation, the questions of validity and infringement remain open.[392]

The FTC and private parties have alleged that these pay-for-delay agreements entail the brand-name company paying the follow-on applicant "many millions of dollars to stay out of its market" and, accordingly, "have significant adverse effects on competition" in violation of antitrust laws.[393] The Preserve Access to Affordable Generics and Biosimilars Act (PAAGBA) seeks to limit the ability of drug and biological product manufacturers (i.e., brand-name companies) to pay generic or biosimilar manufacturers to delay their entry into the market.[394]

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complete copy of the approved application. 21 C.F.R. § 314.72.

[386] *Id*. (proposed PHSA § 310B(a)(5)).

[387] *Id*. (proposed PHSA § 310B(f).

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

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

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

[391] *Id*. at 147.

[392] *Id*.

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

[394] S. 64, 116th Cong. preamble (2019). The Competitive DRUGS Act of 2019, H.R. 1344, 116th Cong., and the Protecting Consumer Access to Generic Drugs Act of 2019, H.R. 1499, 116th Cong., include similar provisions to S. 64. In the 115th Congress, several comparable bills were introduced. *See, e.g.*, Expanding Access to Low Cost Generic Drugs Act, S. 2476, 115th Cong. (2018); Competitive DRUGS Act of 2017, H.R. 4117, 115th Cong. (2017).

Antitrust Law

Pay-for-delay agreements may contravene existing antitrust laws if they have anticompetitive effects. Section 1 of the Sherman Act prohibits "contracts . . . in restraint of trade or [interstate] commerce."[395] The Supreme Court has held that the Sherman Act prohibits only *unreasonable* restraints, recognizing that all contracts operate as a restraint on trade.[396] Section 5 of the Federal Trade Commission Act (FTCA) further prohibits "unfair methods of competition,"[397]—a category that includes (but is not limited to) conduct that violates the Sherman Act.[398] When evaluating agreements for potential antitrust violations, the court focuses its inquiry on "form[ing] a judgment about the competitive significance of the restraint . . . '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.'"[399] The Supreme Court has recognized that "reverse payment settlements . . . can sometimes violate the antitrust laws,"[400] and courts have allowed antitrust litigation challenging certain reverse payment settlements to proceed under existing law.[401]

In evaluating the reasonableness of contractual restraints on trade, courts have found that "some agreements and practices are invalid per se, while others are illegal only as applied to particular situations."[402] Courts generally apply a "rule of reason" analysis unless the agreement falls within a per se illegal category. However, courts use "something of a sliding scale in appraising reasonableness"[403] and, in certain instances, apply a more abbreviated rule of reason analysis to an agreement, referred to as a "quick look."[404]

Rule of Reason Analysis. While the Supreme Court has not developed a "canonical" analytical framework to guide this totality-of-the-circumstances inquiry, most courts take a similar approach in resolving rule-of-reason cases.[405] Under the standard approach, a Section 1 plaintiff has the initial burden of demonstrating that a 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.[406] If the plaintiff succeeds in making

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[395] 15 U.S.C. § 1.

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

[397] 15 U.S.C. § 45(a).

[398] *See* FTC v. Cement Inst., 333 U.S. 683, 692 (1948).

[399] *NCAA*, 468 U.S. at 103 (quoting Nat'l Soc'y of Prof'l Eng'rs v. United States, 435 U.S. 679, 690 (1978)).

[400] *Actavis*, 570 U.S. at 141.

[401] *See, e.g.*, King Drug Co. of Florence, Inc. v. Smithkline Beecham Corp., 791 F.3d 388, 403 (3d Cir. 2015); King Drug Co. of Florence, Inc. v. Cephalon, Inc., 88 F. Supp. 3d 402, 422 (E.D. Pa. 2015); *In re* Aggrenox Antitrust Litigation, 94 F. Supp. 3d 224, 245-46 (D. Conn. 2015).

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

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

[404] *See, e.g.*, Leegin Creative Leather Prods., Inc. v. PSKS, Inc., 551 U.S. 877, 885-87 (2007); *Cal. Dental Ass'n*, 526 U.S. at 769-71.

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

[406] *See* CRANE, *supra* note 405, 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. U.S., 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.

this showing, the burden then shifts to the defendant to rebut the plaintiff's evidence with a procompetitive justification for the challenged practice.[407] If the defendant is unable to produce such a justification, the plaintiff is entitled to prevail. However, if the defendant rebuts the plaintiff's evidence, the burden then shifts back to the plaintiff to show either (1) that the restraint's anticompetitive effects outweigh its procompetitive effects or (2) that the restraint's procompetitive effects could be achieved in a manner that is less restrictive of competition.[408]

Per Se Illegal. Certain agreements are considered per se illegal "without regard to a consideration of their reasonableness"[409] "because the probability that these practices are anticompetitive is so high."[410] Only restraints that "have manifestly anticompetitive effects" and lack "any redeeming virtue" are held to be per se illegal.[411] The most common categories are agreements for horizontal price fixing, market allocation, or output limitation.[412] The plaintiff need only demonstrate that the agreement in question falls in one of the per se categories; "liability attaches without need for proof of power, intent or impact."[413]

Quick Look Analysis. A "quick look" is an abbreviated rule of reason analysis.[414] In identifying this intermediate standard of review, the Court has 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."[415] 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 rule-of-reason analysis.[416]

While there is no universally accepted "quick look" framework, several courts of appeals have endorsed an approach to "quick look" cases initially adopted by the FTC.[417] Under this approach, if a Section 1 plaintiff can establish that the nature of a challenged restraint makes it likely to harm consumers, the restraint is deemed "inherently suspect" and therefore presumptively anticompetitive.[418] 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."[419] If the defendant fails to offer such reasons, the plaintiff is entitled to prevail.

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[407] *See* CRANE, *supra* note 405, at 54; Hovenkamp, *supra* note 405, at 103. 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.

[408] *See* CRANE, *supra* note 405, at 54; Hovenkamp, *supra* note 405, at 104.

[409] *Topco*, 405 U.S. at 607.

[410] *NCAA*, 468 U.S. at 99, 103-04.

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

[412] *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).

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

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

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

[416] *Id*. at 770.

[417] *See* N. Car. St. Bd. Dental Exs. v. FTC, 717 F.3d 359, 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).

[418] *Polygram Holding*, 416 F.3d at 35-36.

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

However, if the defendant does offer such an explanation, the plaintiff must address the justification by either (1) explaining "why it can confidently conclude, without adducing evidence, that the restraint very likely harmed consumers," or (2) providing "sufficient evidence to show that anticompetitive effects are in fact likely."[420] 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."[421] However, if the plaintiff fails to rebut the defendant's initial justification, its challenge becomes a full rule-of-reason case.

In *Actavis v. FTC*, the Supreme Court held that the rule of reason is the appropriate level of analysis for pay-for-delay agreements.[422] Though it recognized the potential for such agreements to have anticompetitive effects, it acknowledged that "offsetting or redeeming virtues are sometimes present."[423] Such justifications might include "traditional settlement considerations, such as avoided litigation costs or fair value for services."[424] Accordingly, the FTC (or other plaintiff) has to fully prove the anticompetitive effects of a particular agreement before the burden shifts to the defendant.[425]

Proposed Legislation

PAAGBA seeks to prohibit brand-name manufacturers from compensating follow-on product manufacturers to delay their entry into the market by creating a presumption of illegality, moving away from a rule of reason analysis.[426] The proposed legislation would amend the FTCA to specifically authorize the FTC[427] to initiate enforcement proceedings against parties to "any agreement resolving or settling, on a final or interim basis, a patent infringement claim, in connection with the sale of a drug product or biological product."[428] Such agreements would be presumed to have anticompetitive effects and violate antitrust laws if the brand-name company agrees to provide the generic with "anything of value," including monetary payments or distribution licenses, in exchange for the generic company agreeing "to limit or forego research, development, manufacturing, marketing, or sales" of the generic product "for any period of time."[429] The presumption would not attach, however, to agreements where the only consideration from the brand-name company is the right to market the product before relevant patents or exclusivities expire, reasonable litigation expenses, or a covenant not to sue for infringement.[430]

The presumption would not make the agreement per se illegal. The parties to the agreement would have the opportunity to overcome the presumption with "clear and convincing evidence"

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

[421] *Id*.

[422] FTC v. Actavis, Inc., 570 U.S. 136, 159 (2013).

[423] *Id*. at 156.

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

[425] *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.").

[426] S. 64 preamble, § 3 (proposed FTCA § 27(a)(2)(A)).

[427] PAAGBA only addresses actions initiated by the FTC and does not modify the standards that apply to private suits. *See id*.

[428] *Id*. (proposed FTCA § 27(a)(1)).

[429] *Id*. (proposed FTCA § 27(a)(2)(A)).

[430] *Id*. (proposed FTCA § 27(c)).

that (1) the agreement provides compensation "solely for other goods or services" from the generic company or (2) the agreement's "procompetitive benefits . . . outweigh the anticompetitive effects."[431] In evaluating this evidence, the fact-finder cannot presume that entry would not have occurred—even without the agreement—until the patent or statutory exclusivity expired.[432] It also cannot presume that allowing entry into the market before the patent or statutory exclusivity period expires is necessarily procompetitive.[433]

If the FTC proves that parties to an agreement violated these provisions, the proposed legislation provides for assessment of a civil penalty against each violating party.[434] The civil penalty must be "sufficient to deter violations," but no more than three times the value gained by the respective violating party from the agreement.[435] In the event the NDA holder did not gain demonstrable value from the agreement, the value received by the ANDA filer would be used to calculate the penalty.[436] In calculating the penalty for a particular party, an FTC administrative law judge would consider "the nature, circumstances, extent, and gravity of violation," the impact on commerce of the agreement, and the culpability, history of violations, ability to pay, ability to continue doing business, and profits or compensation gained by all parties (i.e., the NDA or BLA holder(s) and ANDA or biosimilar BLA filer(s)).[437] Any penalties assessed would be in addition to, rather than in lieu of, any penalties imposed by other federal law.[438] The FTC would also be able to seek injunctions and other equitable relief, including cease-and-desist orders.[439] In addition, an ANDA filer that was party to such an agreement would forfeit its 180-day exclusivity awarded for challenging a patent using a paragraph (IV) certification.[440]

Compulsory Licensing of IP Rights: The Prescription Drug Price Relief Act of 2019

Some commentators have proposed using the government's authority to grant compulsory licenses on patents as a means to lower prices for pharmaceutical products.[441] This could be accomplished through reliance on existing legal authorities,[442] or through legislation that either

[431] *Id*. (proposed FTCA § 27(a)(2)(B)).

[432] *Id*. (proposed FTCA § 27(b)).

[433] *Id*. (proposed FTCA § 27(b)).

[434] *Id*. (proposed FTCA § 27(f)(1)).

[435] *Id*. (proposed FTCA § 27(f)(1)).

[436] *Id*. (proposed FTCA § 27(f)(1)).

[437] *Id*. (proposed FTCA § 27(f)(3)).

[438] *Id*. (proposed FTCA § 27(f)(4)).

[439] *Id*. (proposed FTCA § 27(f)(1) & (2)).

[440] *Id*. § 5 (amending FD&C Act § 505(j)(5)(D)(i)(V)). Other provisions of PAAGBA would amend Section 1112 of the Medicare Prescription Drug Improvement and Modernization Act of 2003. S. 64 § 4 (proposed Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (21 U.S.C. § 355 note) § 1112(d)). This section currently requires parties to submit to the FTC and Department of Justice any agreements between follow-on product applicants and brand-name manufacturers, or among follow-on product applicants for the same drug or biologic, regarding the "manufacture, marketing, or sale" of either the brand-name pharmaceutical product or the follow-on product, or the 180-day exclusivity period. 21 U.S.C. § 355 note. PAAGBA would amend this section to require the CEO or "company official responsible for negotiating any agreement" to file a certification affirming that the materials filed were the complete agreements between the parties, including any ancillary agreements or written descriptions of oral agreements. S. 64 § 4 (proposed Medicare Prescription drug, Improvement, and Modernization Act of 2003 (21 U.S.C. § 355 note) § 1112(d)).

[441] *See, e.g.*, Brennan et. al., *supra* note 156; *see also supra* "Compulsory Licensing."

[442] *See, e.g.*, 28 U.S.C. § 1498(a).

expands existing authority or specifies conditions for its exercise. An example of the latter approach is the Prescription Drug Price Relief Act of 2019 (PDPRA).[443] PDPRA would create a process by which the Secretary would review the pricing of all brand-name drugs and biological products to determine whether the prices of any such products are "excessive."[444] The Secretary would determine whether a brand-name drug price is excessive in part based on whether the average price in the U.S. exceeds the median price charged for the drug in five foreign "reference countries."[445] If the Secretary determines that the price of a brand-name pharmaceutical product is excessive, he would have the authority to waive or void any government-granted exclusivities, including FDA regulatory exclusivities, and issue compulsory licenses allowing any person to make, use, sell, or import the excessively priced drug despite applicable patents.

To accomplish this, the bill would require that NDA and BLA holders submit an annual report to HHS including detailed information about the pricing of "brand name drugs," including information on costs, revenues, R&D expenditures, and the "average manufacturer price of the drug in the United States and in the reference countries."[446] "Brand name drugs" are prescription drugs and biologics approved or licensed by FDA under a nonabbreviated regulatory pathway (i.e., not generic drugs or biosimilars) and that are "claimed in a patent or the use of which is claimed in a patent."[447]

Using this information, the Secretary would, on at least an annual basis, determine whether the price of any brand-name drug is excessive.[448] The bill envisions two ways in which the Secretary would determine that a brand-name drug price is excessive. First, the Secretary would be required to determine that a drug has an excessive price if the "average [U.S.] manufacturing price" exceeds "the median price charged for such drug in the 5 reference countries."[449] Second, the Secretary would determine that a drug has an excessive price if "the price of the drug is higher than reasonable" taking into account a number of factors, including the value of the drug to patients, R&D costs, health outcomes, revenues, and recent price increases.[450] Members of the public would be able to petition the Secretary to make an excessive price determination with respect to a particular drug under some circumstances.[451]

If the Secretary determines that the price of a brand-name drug is excessive, the Secretary would be authorized to (1) "waive or void any government-granted exclusivities" with respect to such drug, and (2) issue "open, non-exclusive [compulsory] licenses" that allow competitors to "make, use, offer to sell or sell, and import [the brand-name drug] and to rely upon the regulatory test data" of the brand-name drug manufacturer.[452] "Government-granted exclusivity" is defined to explicitly include common FDA regulatory exclusivities as well as "[a]ny other provision of law

[443] Identical bills have been introduced in the House of Representatives, H.R. 465, 116th Cong., and the Senate, S. 102, 116th Cong. For simplicity, all citations herein are to the Senate version as of April 2, 2019.

[444] *Id*. § 2.

[445] *Id*. § 2(b)(1). The five "reference countries" are Canada, the United Kingdom, Germany, France, and Japan. *Id*. § 2(b)(1)(B).

[446] *Id*. § 6(a).

[447] *Id*. § 8(3).

[448] *Id*. § 2(a).

[449] *Id*. § 2(b)(1)(A). If information about the price of the drug is not available for all the reference countries, the Secretary still must make a determination so long as pricing information is available for at least three of the reference countries. *Id*. § 2(b)(1)(C).

[450] *Id*. § 2(b)(2).

[451] *Id*. § 2(c).

[452] *Id*. § 3(a).

that provides for exclusivity . . . with respect to a drug."[453] The compulsory patent license, which the bill calls a "excessive drug price license," would permit the Secretary to authorize third parties to make and use the excessively priced drug despite patents that "claim[] a brand name drug or the use of a brand name drug."[454] It would also allow third parties to "rely upon regulatory test data for such drug."[455] However, any entity that accepts this compulsory license would be required to pay a "reasonable royalty" to the applicable patent holder and any NDA holder whose regulatory exclusivity was voided under the bill's provisions.[456] The royalty rate would either be based on an average rate for pharmaceuticals estimated by the Internal Revenue Service or set by the Secretary based on a number of factors.[457]

Any party accepting a compulsory license for an excessively priced drug would still need to apply for FDA approval (or licensure) in order to market a generic (or biosimilar) version. Accordingly, the bill would require FDA to expedite review of such applications and "act within 8 months."[458] During the period between the Secretary's excessive price determination and follow-on product approval, the bill would prohibit the brand-name drug manufacturer from increasing the price of the drug or biologic.[459]

In addition to excessive price determinations, the Secretary would use the information received pursuant to the bill to establish a "comprehensive, up-to-date database" of brand-name drugs and excessive price determinations.[460] Further, the Secretary would be required to submit an annual report to Congress describing its excessive price reviews and determinations for the preceding year.[461] The Secretary would be required to make both the report and the database available to the public online.[462]

Compulsory licensing provisions, like those of the PDPRA, may implicate the Takings Clause of the U.S. Constitution, to the extent that they retroactively affect property rights. The Takings Clause provides that private property shall not "be taken for a public use, without just compensation."[463] Presuming that patents are treated as "private property" under the Fifth Amendment,[464] and that the Secretary invoked the compulsory licensing authority, courts may be

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[453] *Id*. § 8(5).

[454] *Id*. § 8(7).

[455] *Id*.

[456] *Id*. § 4(a)(1).

[457] *Id*. § 4(a)(2)(A)-(B).

[458] *Id*. § 3(b).

[459] *Id*. § 3(c). Specifically, if the price increases during this period, the Secretary may file a civil action for damages "not less than" the total revenue attributable to the price increase. *Id*.

[460] *Id*. § 5(a).

[461] *Id*. § 5(b).

[462] *Id*. 5(c).

[463] U.S. CONST. amend. V.

[464] The Supreme Court has presumed, but not squarely held, that granted patents are private property subject to the Fifth Amendment. *See, e.g.*, Horne v. Dep't of Agric., 135 S. Ct. 2419, 2427 (2015) ("'[A patent] confers upon the patentee an exclusive property in the patented invention which cannot be appropriated or used by the government itself, without just compensation, any more than it can appropriate or use without compensation land which has been patented to a private purchaser.'" (quoting James v. Campbell, 104 U.S. 356, 358 (1882)). Although the Supreme Court's recent decision in *Oil States Energy Services, LLC v. Greene's Energy Group, LLC*, held that the grant of a patent was a "public right" (not a private right) under Article III of the Constitution, 138 S. Ct. 1365, 1374 (2018), the Court explicitly noted that its decision "should not be misconstrued as suggesting that patents are not property for purposes of the Due Process Clause or the Takings Clause." *Id*. at 1379.

asked to address: (1) whether compulsory licensing provisions constitute a "taking" of private property;[465] (2) whether any such taking was for "public use";[466] and (3) if so, whether the compensation (if any) provided to the rights holder suffices to provide the "just compensation" required by the Constitution.[467] Legislative provisions that retroactively void regulatory exclusivities may raise analogous Takings Clause issues.[468]

Limiting Regulatory Exclusivities Based on Price Increases: The FLAT Prices Act[469]

Just as compulsory licensing proposals may limit patent rights based on pharmaceutical product pricing, other proposed reforms would limit FDA regulatory exclusivities based on pricing behavior. For example, the FLAT Prices Act[470] aims to discourage pharmaceutical product manufacturers from significantly increasing the prices of their products. The bill would shorten the relevant periods of regulatory exclusivity for a pharmaceutical product if the manufacturer increases the price by certain percentages within specified time periods.[471] Specifically, the regulatory exclusivity period would be shortened by 180 days if the price[472] increases by more than: (1) 10% over a one-year period; (2) 18% over a two-year period, or (3) 25% over a three-year period.[473] For every price increase that is 5% over the 10%, 18%, or 25% thresholds for

[465] *See generally* Penn Cent. Transp. Co. v. City of New York, 438 U.S. 104, 123-24 (1978) (articulating factors for determining when government regulations with economic impacts on property rights are "takings" requiring compensation, including the economic impact, interference with investment-backed expectations, and the character of the government action).

[466] *See, e.g.*, Haw. Hous. Auth. v. Midkiff, 467 U.S. 229, 241 (1984) (requiring that a taking must be "rationally related to a conceivable public purpose" to satisfy the public-use requirement).

[467] U.S. CONST. amend V.

[468] The case for a compensable taking may be weaker as to the regulatory exclusivities because it is unclear whether a government-administered regulatory exclusivity would be treated as "private property," akin to a patent right. *Cf. supra* note 464 (authority suggesting that patents are private property under the Fifth Amendment). The regulatory takings analysis under the *Penn Central* factors would arguably be different for regulatory exclusivities, which are a restriction on government action (FDA approval), as opposed to a private right to exclude. *See supra* note 465 (*Penn Central* factors for regulatory takings).

[469] In addition to the FLAT Prices Act, several other bills contain provisions that would eliminate or shorten regulatory exclusivities under certain conditions. *See, e.g.*, The BLOCKING Act of 2019, H.R. 938, 116th. Cong. (reforming the 180-day generic drug exclusivity); Medicare Negotiation and Competitive Licensing Act of 2019, H.R. 1046, 116th Cong. § 2 (granting the Secretary authority negotiate drug prices for Medicare Part D and authorizing the Secretary to issue a compulsory license on all applicable patent rights and regulatory exclusivities if the Secretary is unable to successfully negotiate an appropriate price for a covered drug); Improving Access to Affordable Prescription Drugs Act, S. 771, 115th Cong. §§ 303-304 (shortening new biological product exclusivity from 12 to seven years, and reforming the new chemical entity exclusivity to allow FDA to accept ANDAs three years after approval of the referenced drug).

[470] Identical bills have been introduced in the House of Representatives, *see* H.R. 1188, 116th Cong., and the Senate, *see* S. 366, 116th Cong. For simplicity, all citations herein are to the Senate version as of April 2, 2019.

[471] FLAT Prices Act, S. 366, 116th Cong. § 2 (2019). The relevant regulatory exclusivity periods that would be subject to reduction for a drug under the bill include (1) the five-year data exclusivity for a drug that contains a new chemical entity (2) the three-year clinical trial exclusivity, and (3) the 180-day first generic exclusivity. *Id.* § 2(e). The relevant regulatory exclusivity periods for a biological product include (1) the 12-year market exclusivity for a new biological product and (2) the first interchangeable biological product exclusivity period. *Id.*

[472] Under the bill, the relevant price increase is the increase in the drug or biological product's wholesale acquisition cost, *id.* § 2(b), which is "the manufacturer's list price for the drug or biological to wholesalers or direct purchasers in the United States, not including prompt pay or other discounts, rebates or reductions in price . . . as reported in wholesale price guides or other publications of drug or biological pricing data." 42 U.S.C. § 1395w-3a(c)(6)(B).

[473] S. 366, § 2(a)(1), (b).

these three respective time periods, the exclusivity period would be shortened by an additional 30 days (i.e., a total of 210 days).[474]

The bill would also require manufacturers to report any relevant price increases described above to the Secretary within 30 days of the increase.[475] If a manufacturer fails to timely submit the report, the exclusivity period for the relevant drug or biological product would be shortened by an additional 30 days for each day that the report is late.[476]

The bill would authorize the Secretary to waive or decrease the reduction in the exclusivity period if (1) the manufacturer submits a report on the price increase that contains all the relevant information, and, (2) based on the report, the Secretary determines that "the price increase is necessary to enable production of the drug, does not unduly restrict patient access to the drug, and does not negatively impact public health."[477]

Orange Book and *Purple Book* Reform: The Biologic Patent Transparency Act[478]

Another potential reform under consideration concerns patent listings and other information included in FDA's lists of approved chemical drugs (the *Orange Book*) and biologics (the *Purple Book*).[479] One such proposal is the Biologic Patent Transparency Act (BPTA), which would amend the PHSA and patent law to do three principal things: (1) require that BLA applicants (and current BLA holders) provide patent information to FDA; (2) mandate by statute that FDA publish and maintain the *Purple Book* as a single, searchable list; and (3) require that patent and regulatory exclusivity information be included in the *Purple Book*.[480] The overall effect would be to make the *Purple Book* more similar to the *Orange Book* in some respects.[481] The stated aim of

[474] *Id*. § 2(a)(2).

[475] *Id*. § 2(c)(1).

[476] *Id*. § 2(c)(2).

[477] *Id*. § 2(d). The reduction in exclusivity periods may also raise issues under the Takings Clause, given that the right to regulatory exclusivity—essentially a right to exclude granted by federal law—may be a protected property interest. *See* Ruckelshaus v. Monsanto Co., 467 U.S. 986, 1001 (1984) (noting that property interest protected by the Takings Clause are those "defined by existing rules or understanding" independent from the Constitution). Thus, questions over whether the reduction would effect a taking for public use that must be justly compensated may arise. *See supra* notes 465-468 and accompanying text.

[478] Other proposed legislative proposals to reform the *Orange Book* and/or *Purple Book* include the Orange Book Transparency Act of 2019, H.R. 1503, 116th Cong. (limiting the patents in the *Orange Book* to exclude "any patent to the extent such patent claims a device that is used for the delivery of the drug," and requiring the Secretary to include regulatory exclusivity information in the *Orange Book* and remove patents determined to be invalid by the PTAB of a final judicial decision), and the Purple Book Continuity Act of 2019, H.R. 1520, 116th Cong. (requiring the Secretary to publish the *Purple Book* and ordering him to review an "formulate recommendations" on the types of biological patents that should be included in the *Purple Book*). Another bill on related issue would require generic drug and biosimilar manufacturers to certify that they will not petition the PTO to institute an IPR or PGR for certain patents claiming the referenced drug or product. *See* Hatch-Waxman Integrity Act of 2019, S. 344, 116th Cong.; *see also* H.R. 990, 116th Cong. (identical bill).

[479] *See supra* "The Hatch-Waxman Act: Patents and Generic Drug Approval" and "The BPCIA: Patents and Biosimilar Licensure."

[480] S. 659, 116th Cong. The bill indicates that patent and other information is to be submitted to and published by the Secretary. *See id*. § 2(a). However, for simplicity and clarity, this summary presumes that the Secretary will delegate these responsibilities to FDA.

[481] *See supra* notes 315-316 and accompanying text (describing differences between the *Purple Book* and the *Orange Book*).

the bill is to curtail patent thickets through greater transparency and limits on the enforcement of late-listed biologic patents.[482]

More specifically, the BPTA requires that, within 30 days, the holder of an approved BLA must submit to FDA "a list of each patent required to be disclosed."[483] The patents that would be required to be disclosed include "any patent for which the holder of [an approved BLA] believes that a claim of patent infringement could reasonably be asserted by the [BLA] holder, or patent owner that has granted an exclusive license to the holder" if "a person not licensed by the holder engaged in the making, using, offering to sell, selling, or importing" the biological product at issue.[484] The bill would also change the "patent dance"[485] to require that (if the patent dance is initiated) the list of relevant patents that the reference product sponsor provides to the biosimilar applicant must be drawn from the list provided to FDA.[486] Finally, the bill would enforce its patent listing requirement through a new "list it or lose it" provision,[487] providing that the owner of a patent that "should have been included in the list" given to FDA, but "was not timely included in such list, may not bring an action under this section for infringement of the patent."[488]

The BPTA would codify FDA's practice of publishing the *Purple Book* and further require that the *Purple Book* include more information that it does presently, in a more accessible form.[489] In particular, under the bill, the *Purple Book* would have to include:

- the official and brand name of each licensed biological product;
- the date of licensure for each licensed biological product;
- information about the marketing status, dosage, and route of administration of the biological product;
- if the product is a biosimilar or interchangeable, the relevant reference product (i.e., the brand-name biologic); and
- any determination related to biosimilarity or interchangeability for the biological product.[490]

Notably, FDA would be required to include patent information, information about whether the product is subject to a period of regulatory exclusivity, and when such exclusivity expires, and to make all the information publicly available as a "single, easily searchable list."[491] Currently, the

[482] *See* Allison Inserro, *Collins, Kaine Seek to Untangle Patent Thickets with Bill Requiring Transparency*, CTR. FOR BIOSIMILARS, Mar. 9, 2019, https://www.centerforbiosimilars.com/news/collins-kaine-seek-to-untangle-patent-thickets-with-bill-r-transparency; *see also supra* "Types of Pharmaceutical Patents" (overviewing allegations of patent "thickets").

[483] S. 659, 116th Cong. § 2(a) (proposed PHSA § 351(o)(1)(A)-(B)).

[484] *Id*. (proposed PHSA § 351(o)(3)).

[485] *See supra* notes 317-328 and accompanying text (overviewing the BPCIA's patent dance).

[486] S. 659, 116th Cong. § 2(b).

[487] *See supra* notes 327-328 (discussing BPCIA's "list it or lose it" requirement for the patent dance).

[488] S. 659, 116th Cong. § 2(c). As with the BPCIA's "list it or lose it" provision, it is not completely clear whether this provision reaches both pre- and post-marketing infringement, *see supra* note 328 (noting this ambiguity), but a natural reading of "this section" would refer to the entirety of 35 U.S.C. § 271, including both pre-marketing "artificial" infringement under § 271(e) and post-marketing direct infringement under § 271(a).

[489] S. 659, 116th Cong. § 2(a) (proposed PHSA § 351(o)(2)).

[490] *Id*. (proposed PHSA § 351(o)(2)(A)(i)-(viii)).

[491] *Id*.

Purple Book lacks any patent information, contains only partial information on regulatory exclusivities, and is published as two separate files as opposed to a single searchable database.[492]

Conclusion

Concerns about perceived high prices for prescription drugs and other pharmaceutical products implicate a complex set of legal regimes, including patent law, FDA law, and specialized patent dispute procedures for drugs and biological products. Much of the debate over allegedly high pharmaceutical prices is fundamentally a matter of public policy: in particular, finding the appropriate balance between providing incentives to create innovative new medicines versus the costs those incentives may impose on the public in the form of higher prices. Nonetheless, knowledge of the workings of the existing legal regimes governing IP rights in pharmaceutical products is necessary to fully understand the implications of the variety of legislative approaches to reduce pharmaceutical prices.

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[492] *See supra* note 316 and accompanying text.