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The Modern Regulatory Framework for Generic Drugs Encourages Active Price Competition

A Booming Market for Generic Drugs

The importance of generic drugs[1] in the United States pharmaceutical landscape has grown steadily since their initial boom a few decades ago. Today, nine out of ten prescriptions in the U.S. are filled with generic drugs.[2] In the past decade, generic drugs saved the American healthcare system $2.2 trillion in healthcare costs.[3] The regulatory framework for pharmaceuticals has evolved alongside this boom to facilitate the safe and affordable access to medicine as consumers increase their use of generics. This article reviews the historical development of the regulatory framework for generic pharmaceuticals in the U.S. and its economic impact, particularly in facilitating price competition.

The modern regulatory framework for generic drugs in the U.S. was established under the Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act. Under this act, the FDA approves generic drugs through the Abbreviated New Drug Application ("ANDA"), which requires a demonstrated bioequivalence between generic drugs and the referenced brand name drugs. This requirement allows the FDA to approve generic

[1] Chemically-derived prescription pharmaceuticals sold in the U.S. generally fall into two categories: branded and generic. Brand name drugs are marketed under a trademarked name and are protected by patents or exclusivities granted by the Food & Drug Administration ("FDA") that proscribe the sale of direct copies of the drug for a limited time. Following the expiration of such patents or exclusivities on branded drugs, generic drug manufacturers can seek FDA approval to produce generic versions of those drugs. To gain FDA approval, these manufacturers must demonstrate bioequivalence with the branded drug. While generic drugs are thus therapeutically equivalent to brand name drugs, they almost always sell at a substantial discount to brand name drugs.

[2] https://www.fda.gov/drugs/generic-drugs/office-generic-drugs-2020-annual-report.

[3] https://www.fda.gov/drugs/generic-drugs/office-generic-drugs-2020-annual-report.

drugs without requiring manufacturers to repeat the costly clinical trials that are required for new branded drugs to enter the market.[4]

Once their bioequivalence has been established, generic drugs are permitted to be sold in lieu of the referenced brand name drug after the patent and/or exclusivity of the referenced brand name drug has expired (or upon a successful challenge to the patent of the referenced brand name drug).[5] Because the FDA deems generic drugs to be therapeutically equivalent to the referenced brand name drug, they may be directly substituted for prescribed brand name drugs at pharmacies without physician intervention.

While laws regarding generic drug substitution vary considerably by state, state pharmacy substitution laws in all states of the U.S. allow and, in some cases, mandate that the generic substitute be dispensed when available.[6] In particular, nineteen out of the fifty states require pharmacists to substitute generics when available, while the remaining thirty one allow for generic substitution.[7] Moreover, most states also protect pharmacists from greater liability that may arise due to drug substitution.[8]

To facilitate the substitution of generic drugs under the drug laws of various states, the FDA publishes the *Approved Drug Products with Therapeutic Equivalence Evaluations*, more commonly known as the Orange Book. The Orange Book lists drug products approved on the basis of established bioequivalence with branded drugs and was proposed in 1979 to aid states in determining which drugs can be substituted for branded equivalents.[9]

The regulatory features that facilitate the substitution of branded drugs for generic drugs also allow generic drugs to be substituted for one another fairly easily. This is due to the established bioequivalence of acceptable generic drugs, which means that generic drugs are not merely substitutable with their branded equivalents but, rather, among themselves as well.

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[4] "Abbreviated New Drug Application (ANDA)." *Food and Drug Administration* (May 22, 2019). <https://www.fda.gov/drugs/types-applications/abbreviated-new-drug-application-anda> (accessed Apr. 29, 2021).

[5] The "Orange Book" published by the FDA lists generic drugs that are bioequivalent to brand name drugs. "Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations." *Food and Drug Administration.* <https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm> (accessed May 18, 2021).

[6] Sacks, Chana A., Victor L. Van de Wiele, Lisa A. Fulchino, Lajja Patel, Aaron S. Kesselheim, and Ameet Sarpatwari. "Assessment of Variation in State Regulation of Generic Drug and Interchangeable Biologic Substitutions." *JAMA Internal Medicine* 181.1 (Jan. 2021): 16-22 at 16.

[7] *Id.*

[8] *Id.*

[9] https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface. ("Because of the number of requests in the late 1970s for FDA assistance in preparing both positive and negative formularies, it became apparent that FDA could not serve the needs of each state on an individual basis. The Agency also recognized that providing a single list based on common criteria would be preferable to evaluating drug products on the basis of differing definitions and criteria in various state laws. As a result, on May 31, 1978, the Commissioner of the Food and Drug Administration sent a letter to officials of each state announcing FDA's intent to provide a list of all prescription drug products that are approved by FDA for safety and effectiveness, along with therapeutic equivalence determinations for multisource prescription products.")

The Economics of Generic Drug Markets Facilitates Price Competition Among Pharmaceutical Companies

Given the high substitutability of generic drugs and pharmacists' discretion in dispensing available substitutes, drug producers who are competing on quality or branding are unlikely to receive greater sales.[10] Instead, producers of generic drugs and their branded equivalents compete primarily on price, as is recognized by a large volume of academic research.[11]

Price competition among producers is encouraged by the structure of the market for generic drugs. Generic drug manufacturers typically sell their products via auctions to retail pharmacies and institutionalized consumers, rather than advertise directly to consumers or physicians.[12]

A report published by the FDA in 2019 confirms the extent of price competition for generic drugs based on a study of drugs that entered the market between January 2015 and December 2017.[13] The FDA found that a greater number of entrants in the analyzed markets was associated with a significant reduction in prices.[14] The FDA also concluded that prices declined even in situations where the number of competitors was stable, as manufacturers competed for market share.[15]

The extent of price competition among generic drugs is evidenced by the U.S. experience in the past two decades. Starting in the early 2000s, the U.S. generic drug market has seen sustained price declines as low-cost generic manufacturers from India and other countries entered the

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[10] In fact, generic drug manufacturers often market the drug under the name of the active ingredient, such that several producers market a product that has the same name. Furthermore, promotional spending in prescription drugs is typically undertaken for brand-name drugs rather than generics. See http://www.cbo.gov/sites/default/files/cbofiles/ftpdocs/105xx/doc10522/12-02-drugpromo_brief.pdf.

[11] *See, e.g.*, Berndt, Ernst R., and Murray L. Aitken. "Brand Loyalty, Generic Entry and Price Competition in Pharmaceuticals in the Quarter Century after the 1984 Waxman-Hatch Legislation." *International Journal of the Economics of Business* 18.2 (July 2011): 177-201; Boehm, Garth, Lixin Yao, Liang Han, and Qiang Zheng. "Development of the Generic Drug Industry in the US after the Hatch-Waxman Act of 1984." *Acta Pharmaceutica Sinica B* 3.5 (Sept. 2013): 297-311; Dave, Chintan V., Abraham Hartzema, and Aaron S. Kesselheim. "Prices of Generic Drugs Associated with Numbers of Manufacturers." *New England Journal of Medicine* 377.26 (Dec. 28, 2017): 2597-98; Olson, Luke M., and Brett W. Wendling. "Estimating the Causal Effect of Entry on Generic Drug Prices Using Hatch-Waxman Exclusivity." *Review of Industrial Organization* 53.1 (Aug. 2018): 139-72; Reiffen, David, and Michael R. Ward. "Generic Drug Industry Dynamics." *The Review of Economics and Statistics* 87.1 (Feb. 1, 2005): 37-49; Saha, Atanu, Henry Grabowski, Howard Birnbaum, Paul Greenberg, and Oded Bizan. "Generic Competition in the US Pharmaceutical Industry." *International Journal of the Economics of Business* 13.1 (Feb. 2006): 15-38; Saha, Atanu, and Heather Roberts. "Pharmaceutical Industry's Changing Market Dynamics." *International Journal of the Economics of Business* 27.2 (May 3, 2020): 159-75.

[12] Olson, Luke M., and Brett W. Wendling. "Estimating the Causal Effect of Entry on Generic Drug Prices Using Hatch-Waxman Exclusivity." *Review of Industrial Organization* 53.1 (Aug. 2018): 139-72 at 142.

[13] Conrad, Ryan, and Randall Lutter. "Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices." *Food and Drug Administration* (Dec. 2019). <https://www.fda.gov/media/133509/download> (accessed Apr. 29, 2021).

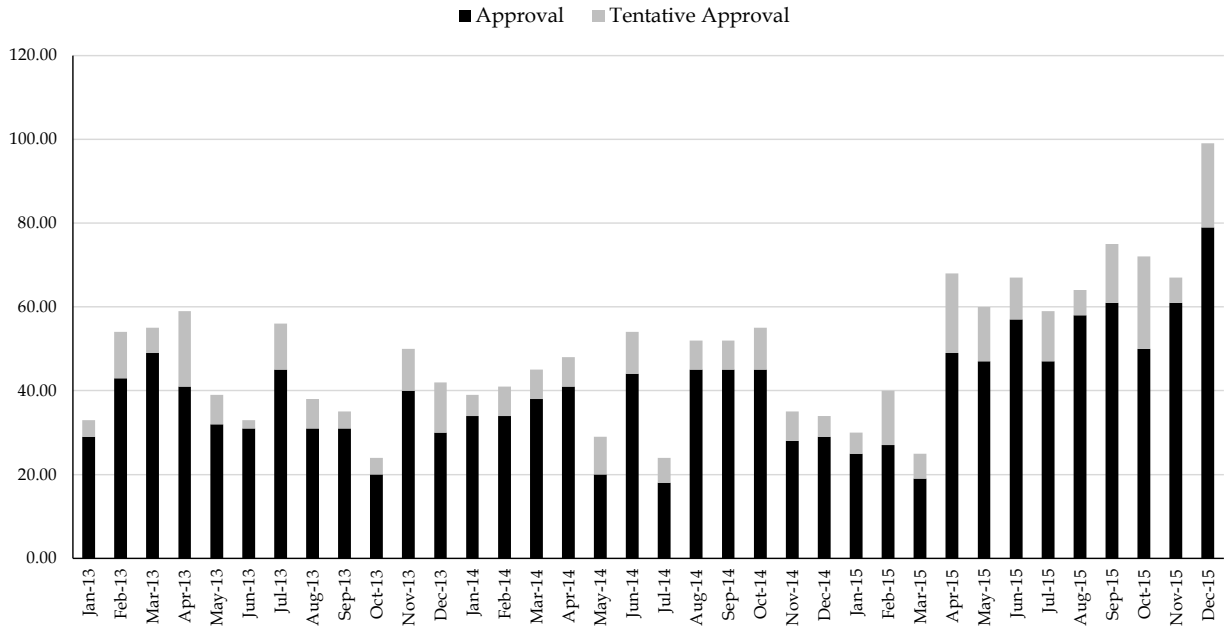
[14] *Id.*

[15] *Id.*

market.[16] For instance, in 2005, despite an increase in U.S. generic sales, most leading U.S. generic manufacturers experienced a drop in their revenues due to price erosion caused by the entry of additional suppliers from low-cost countries, among other factors.[17]

Due to the inverse relationship between the number of competitors and drug prices, policies that lower entry barriers and encourage new participants in drug markets tend to encourage lower prices. To see this relationship clearly, consider the change in FDA policy that led to a dramatically increased number of approved ANDAs.[18] *See* **Figure 1:** *FDA Approval of ANDAs, 2013-2015*. As a result, prices for generic drugs fell markedly in the following years.[19]

Figure 1: *FDA Approval of ANDAs, 2013-2015*[20]



[16] Greene, William. "The Emergence of India's Pharmaceutical Industry and Implications for the U.S. Generic Drug Market." *United States International Trade Commission* (May 2007). <https://www.usitc.gov/publications/332/EC200705A.pdf> (accessed May 17, 2021) at 21-24.
[17] *Id.* at 23.
[18] The total number of new drug approvals was 580 in 2015, relative to 421 in 2014, representing an increase of approximately 38 percent. *See* "Activities Report of the Generic Drug Program (FY 2014)." *Food and Drug Administration.* <https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/generic-drugs-program-activities-report-monthly-performance> (accessed June 22, 2021) and "Activities Report of the Generic Drug Program (FY 2015)." *Food and Drug Administration.* <https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/generic-drugs-program-activities-report-monthly-performance> (accessed June 22, 2021).
[19] DeBenedette, Valerie. "Prices for Generic Drugs Fall by About 9%; Third Decrease in Three Years." *DrugTopics* (April 11, 2019) <https://www.drugtopics.com/view/prices-generic-drugs-fall-about-9-third-decrease-three-years > (accessed June 29, 2021).
[20] "Activities Report of the Generic Drug Program (FY 2013-2015)." Food and Drug Administration. <https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/generic-drugs-program-activities-report-monthly-performance> (accessed June 22, 2021).

The regulatory environment in the U.S. is generally conducive to competitive pricing pressures. In fact, studies on pricing indicate that policies encouraging the substitution of generic drugs while allowing drug manufacturers to set drug prices are more effective at lowering drug prices than the type of price controls used in some European countries.[21]

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[21] Wouters, Olivier J., Panos G. Kanavos, and Martin McKee. "Comparing Generic Drug Markets in Europe and the United States: Prices, Volumes, and Spending." *The Milbank Quarterly* 95, no. 3 (2017): 554-601 at 571-572.