



Policy Proposal: Expedited Review of Generic Drug Applications

A series that examines policies to manage drug spending

What problem is this policy meant to address?

Competition from generic drugs can significantly reduce spending on pharmaceuticals. The number of competitors in a market can also affect drug prices. A Food and Drug Administration analysis of national sales data found that the first generic version of a drug is typically priced only slightly lower than the brand product but that the availability of a second generic version is associated with an average price of about half that of the brand drug.¹ Competition from additional generic competitors can drive prices down even further, reaching, on average, prices that are 80 to 85 percent lower than their brand equivalents.² Under its new agreement with manufacturers (the reauthorization of the Generic Drug User Fee Amendments), FDA will typically act on a generic drug application within 10 months of submission.³ Despite a recent increase in the approvals of generic drug applications, as well as an FDA policy that prioritizes the review of an application when a single manufacturer produces the drug or when fewer than three generic versions of a drug are approved,⁴ some eligible drugs still face limited or no generic competition. According to FDA, as of March 2017 more than 180 off-patent brand drugs were on the market without any generic competitors.⁵ In many cases, there may be only one or two manufacturers approved to market a particular drug,⁶ which allows these companies to charge higher prices than if there were more competitors. Incentivizing generic developers to submit applications for drugs that face limited competition and expediting FDA review of those applications may drive down costs.

How could this policy work?

Members of Congress have proposed policies to encourage the development of generic drugs when limited competition exists by (1) reducing the statutory FDA review time frame for any such product and (2) providing an additional incentive by awarding the sponsor of such an application a voucher that could be used to obtain priority review for a second generic drug application (or sold to another company at fair-market value for that purpose).

The Lower Drug Costs Through Competition Act (H.R. 749), introduced in 2017, would require FDA to prioritize the review of generic applications for drugs in shortage (i.e., where currently approved manufacturers are unable to meet market demand) and for drugs (1) that have been recently introduced to market by a single manufacturer in the last three months and (2) for which two or fewer generic applications have been tentatively approved.⁷ FDA would be required to review these generic drug applications within 180 days of submission. In addition, a transferable generic drug priority review voucher⁸ would be awarded to the sponsor of an approved generic drug application if the drug establishes “a sustained market presence.” Senate legislation introduced in 2017, the Increasing Competition in Pharmaceuticals Act (S. 297), is similar but would require FDA review of priority and voucher applications within 150 days and would waive user fees for priority applications, except those that include a patent challenge to the innovator product.⁹

Another approach is included in the Generic Drug User Fee Amendments' reauthorization agreement (GDUFA-II), as part of the FDA Reauthorization Act (FDARA), which Congress passed in August 2017.¹⁰ This requires FDA to review within eight months applications for drugs that have three or fewer competitors, if certain requirements are met.¹¹ And it codifies recent FDA policy updates to expand priority review to more applications for generic drugs with limited competition¹² as well as FDA's agreement with industry¹³ to review 90 percent of priority applications within eight months. The reauthorization act also requires FDA to publicly report information related to generic application review, including the volume and status of priority applications, approval times, and the number of review cycles prior to approval. Additionally, FDA is required to publish both a semiannual list of drugs with limited competition and monthly information on drugs withdrawn from the market.

The act also creates a program that extends priority review and pre-application support to generic applications for drugs with a single manufacturer. In some cases, a qualifying generic may also be eligible for six months of exclusivity, barring additional competitors from entering the market.¹⁴

What should policymakers consider?

A range of factors can influence a generic drug developer's decision to bring a product to market. These may include a drug's market size; manufacturer production costs; costs associated with the development of the drug, including conducting tests that are required for FDA approval; anticipated revenue; and time and resources needed to obtain FDA approval, including user fees paid to FDA to review marketing applications. How manufacturers weigh these considerations may vary significantly from product to product and company to company. Policies to expedite review of generic drug applications target only the last of these factors, and it is not clear whether they would increase the amount of competition from generic drugs.

While FDA currently prioritizes the review of applications for the first generic version of a drug and applications for drugs with only a single manufacturer, and an eight-month review timeline was included in FDARA, some of the proposals would create a statutory time frame for FDA action that is shorter than eight months. Whether this requirement would improve current approval times is unknown. According to FDA officials, it may be difficult to review a generic drug application in less than eight months, due in part to the time necessary to inspect manufacturing facilities, many of which are overseas.¹⁵ FDA has also stated that eight months allows the agency to effectively communicate with generic developers on any deficiencies in their applications, which enables developers to quickly make necessary changes to a submission so that it may be approved in the first review cycle, rather than waiting to receive a formal response from FDA in the form of a Complete Response Letter before making any necessary revisions to the application.¹⁶ Any additional requirements for a faster review that have not been agreed to by FDA and industry as part of GDUFA-II may not accelerate generic approvals. If the agency is required to act on some applications in less than eight months, FDA may not have adequate time to conduct any necessary facility inspections and communicate with sponsors to request clarifications or changes to the application. This could increase the share of applications requiring multiple review cycles, which would lengthen the overall time to approval and delay access to generics.

Not enough information exists to determine whether a priority review voucher program would provide sufficient incentive to overcome the underlying reasons that generic developers have declined to enter markets with limited competition. However, the FDA experience with other voucher programs should be considered. FDA has had a Tropical Disease Priority Review Voucher program since 2007, but as of January 2017 the program had awarded only three vouchers.¹⁷ The Pediatric Voucher Program, an FDA initiative that rewards development of innovator drugs for rare pediatric diseases, has resulted in six vouchers. Four of them have been sold to other manufacturers for prices ranging from \$67.5 million to \$350 million.¹⁸ A 2016 Government Accountability Office

report found that FDA officials did not see any evidence that the Pediatric Voucher Program had been effective in incentivizing drug development for rare pediatric diseases.¹⁹ Officials also expressed concern that the program had strained agency resources and affected the agency's ability to set its public health priorities.

The market for innovator drugs differs significantly from the generic market, as innovators are granted patent protections and exclusivity periods that shield them from generic competition. These protections allow innovator products to command higher prices than generics. Therefore, the market value of generic priority review vouchers is likely to be lower than that of innovator products. In addition, it is not clear in what situations a generic developer would find a priority review voucher to be of high utility. Under FDARA, first, second, and third generics could all be granted priority review status without a voucher. Therefore, an application for which a sponsor could use a priority review voucher would be limited to cases where (1) multiple manufacturers sell the drug on the market, or (2) FDA is already considering multiple applications for the same drug on a priority review timeline. A voucher would not allow an application to move ahead of other applications with priority review status. Additional study may be needed to determine whether a voucher program, as structured in current proposals, would be sufficient incentive for generic developers to bring products to market in cases of limited competition.

Policies to expand priority review and create a voucher program are likely to increase FDA's workload, but it is not clear what additional resources, beyond those negotiated in the user fee agreements, the agency would need. Absent additional resources, it is not known what effect these policies would have on FDA's ability to review other generic applications on the timelines outlined in GDUFA-II. Proposals that waive user fees for priority applications may be especially challenging, because they pair faster FDA review with a reduction in resources.

Endnotes

- 1 Food and Drug Administration, "Generic Competition and Drug Prices," accessed May 17, 2017, <http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm>.
- 2 Food and Drug Administration, "Facts About Generic Drugs," accessed May 17, 2017, <https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingGenericDrugs/ucm167991.htm>.
- 3 Food and Drug Administration, "GDUFA Reauthorization Performance Goals and Procedures, Fiscal Years 2018-2022" (2016), <https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM282505.pdf>.
- 4 Food and Drug Administration, Center for Drug Evaluation and Research, "Manual of Policies and Procedures: Prioritization of the Review of Original ANDAs, Amendments, and Supplements" (2017), <http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM407849.pdf>.
- 5 Examining FDA's Generic Drug and Biosimilar User Fee Programs, Before United States House of Representatives Committee on Energy and Commerce Subcommittee on Health, 115th Cong. (2017) (video of Dr. Janet Woodcock, director of the Center for Drug Evaluation and Research, U.S. Food and Drug Administration), <https://energycommerce.house.gov/hearings-and-votes/hearings/examining-fda-s-generic-drug-and-biosimilar-user-fee-programs>.
- 6 Ravi Gupta et al., "Generic Drug Approvals Since the 1984 Hatch-Waxman Act," *JAMA Internal Medicine* 176, no. 9 (2016): 1391-93, <http://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2534150>.
- 7 Lower Drug Costs Through Competition Act, H.R. 749, 115th Cong. (2017).
- 8 A voucher may be sold to any sponsor of a generic drug application. The voucher could be used by the sponsor to have the Food and Drug Administration review its application within 180 days of submission.
- 9 Increasing Competition in Pharmaceuticals Act, S. 297, 115th Cong. (2017).
- 10 FDA Reauthorization Act of 2017, S. 934, 115th Cong. (2017); FDA Reauthorization Act of 2017, H.R. 2430, 115th Cong. (2017).
- 11 FDA Reauthorization Act of 2017, H.R. 2430.
- 12 Food and Drug Administration, Center for Drug Evaluation and Research, "Manual of Policies and Procedures."

- 13 Food and Drug Administration, “GDUFA Reauthorization Performance Goals and Procedures, Fiscal Years 2018-2022.” This letter is a joint FDA-industry developed agreement on GDUFA performance goals.
- 14 FDA Reauthorization Act of 2017, H.R. 2430.
- 15 Examining FDA’s Generic Drug and Biosimilar User Fee Programs, Before United States House of Representatives Committee on Energy and Commerce Subcommittee on Health.
- 16 Ibid.
- 17 Jonathan Berman and Tanya Radhakrishna, “The Tropical Disease Priority Review Voucher: A Game-Changer for Tropical Disease Products,” *American Journal of Tropical Medicine and Hygiene* 96, no. 1 (2017): 11-13, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5239674/>.
- 18 Government Accountability Office, “Rare Diseases—Too Early to Gauge Effectiveness of FDA’s Pediatric Voucher Program” (March 2016), <http://www.gao.gov/assets/680/675544.pdf>.
- 19 Ibid.

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