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Statement for the Record
Submitted to the
United States House of Representatives
Judiciary Committee
Subcommittee on Regulatory Reform, Commercial and Antitrust Law
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The Pew Charitable Trusts

The Pew Charitable Trusts is an independent, non-profit research and public policy organization. Pew's drug spending research initiative seeks to understand the underlying drivers of rising drug costs and identify policy options to better manage spending on these products in ways that help to ensure that patients have access to needed treatments.

Pharmaceuticals account for 16.7 percent of health care expenditures, and drug costs continue to increase faster than health care overall. With patients and taxpayers increasingly shouldering this financial burden, lawmakers have introduced a wide range of policies to address rising pharmaceutical costs.

One such proposal, the Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2017,[i] would expedite legal review when generic developers sue innovator companies for withholding access to product samples. Generic and biosimilar manufacturers report that they have been unable to purchase samples of innovator drugs for their product development.[ii] Without access to these drugs, generic developers cannot conduct the testing required for Food and Drug Administration (FDA) approval. They can sue brand companies for violating antitrust law, but this type of litigation can take years to conclude,[iii] and it can be difficult for generic developers to demonstrate that a brand developer's actions caused harm to either them or consumers. As a result, patient access to generic drugs is delayed.

Risk Evaluation and Mitigation Strategies

Risk evaluation and mitigation strategies (REMS) are FDA-required management plans to help ensure that the benefits of certain prescription drugs outweigh their risks.[iv] As of May 2017, there were 71 different REMS in place for currently marketed medications.[v] Many REMS simply require the distribution of information to the patient, but 42 had elements to assure safe use (ETASU).[vi] For example, an ETASU REMS may include a requirement that pharmacies, practitioners, or health care settings dispensing a high-risk drug be specially certified to handle the product, which limits the distribution of these drugs to qualified entities. According to FDA, "restrictions on distribution, either required by innovators or as part of a REMS ETASU, can prevent generic companies from obtaining drug products for bioequivalence and other testing to support ANDA submissions."[vii]

While ETASU REMS are intended to reduce specific serious risks listed in the labeling of the drug, generic developers may have difficulty acquiring samples of innovator drugs subject to these requirements, as the statute contains no provision to explicitly require makers of these drugs to sell product samples to generic developers.

In addition to the necessity for a generic manufacturer to obtain product samples for testing, a generic version of a drug with an ETASU REMS requirement is subject to the same safeguards as the original product. Innovator and generic developers of drugs with ETASU REMS are required to participate in a single, shared REMS protocol, unless FDA waives the requirement.[viii] However, some generic

developers have raised concerns that innovator manufacturers make it difficult for them to participate in a joint REMS protocol.[ix] Patient access to these products can be delayed if the brand and generic manufacturers are unable to reach agreement on a shared REMS.

Creating and Restoring Equal Access to Equivalent Samples (CREATES) Act of 2017

The CREATES Act (HR.2212) would allow for expedited legal review when generic developers sue innovator companies for withholding access to product samples. Instead of having to prove that an innovator company has violated antitrust law, a generic developer would only need to demonstrate that a manufacturer has not complied with the generic developer's request to provide "sufficient quantities" of a drug for testing on "commercially reasonable, market-based terms." In the case of a product with an ETASU REMS, the generic developer may not sue unless it has received authorization from FDA to purchase product samples for testing. Authorization would be obtained after submitting a request to the agency. For product testing that involves clinical trials, the generic developer would have to submit testing protocols that provide safety protections comparable to the REMS of the innovator drug as well as meet any other requirements established by FDA.

If a generic developer brings a suit against an innovator company and is successful, the court could order the innovator company to sell samples of the requested drug to the generic developer; pay the generic developer's attorney fees and litigation costs; and pay the generic developer an additional monetary amount to deter the innovator company from refusing to sell sample product to other generic developers.

The CREATES Act would also allow a generic developer to establish its own ETASU REMS that uses "a different, comparable aspect of the elements to assure safe use," rather than participate in a single, shared REMS with the innovator drug developer. However, FDA could require manufacturers to participate in a single, shared REMS if it determines that "no different, comparable aspect of elements to assure safe use could satisfy" the REMS safety requirements.

The Congressional Budget Office (CBO) estimates that the CREATES Act would generate $3.3 billion in federal savings over 10 years.[x] An analysis funded by the Association for Accessible Medicines (AAM) concluded, based on a 2014 survey of generic manufacturers to identify instances of restricted access, that there could potentially be $5.4 billion in annual savings, including $1.8 billion in savings for the federal government, if generic versions of REMS and non-REMS brand drugs available only through limited distribution were to immediately come to market.[xi] A comparison of these assumptions is not possible, because the CBO analyses are not public. A critical assumption for producing any savings estimate is the amount of spending on drugs currently unavailable to generic developers due to REMS restrictions and other kinds of limited distribution. However, a recent analysis supported by AAM and based in part on a survey of its members found that drugs subject to restricted access had total sales of $22.7 billion in 2016.[xii]

Additional Considerations

While current proposals would not seek to reduce safety precautions for REMS drugs, policymakers may want to consider whether new approaches place unwarranted administrative and financial burdens on FDA. For example, requiring the agency to play a central role in mediating negotiations between manufacturers of innovator drugs and generic developers regarding the purchase of samples or the development of shared REMS protocols would likely be time-consuming and resource-intensive.

Another consideration is the trade-off between current policy that requires a single, shared REMS compared with allowing separate REMS protocols for brand and generic versions of a drug. In some

cases, separate REMS programs may require pharmacies and prescribers to spend additional time enrolling in or training to participate in multiple REMS systems.[xiii] This approach may be less efficient than mandating a single, shared REMS system.

Conclusion

It is important that generic developers comply with REMS standards. Negotiations on a shared REMS are complex and require agreement on several topics, but the existence of a REMS program should not be allowed to impede generic development. Policies that impose specific conditions, such as the price at which a product sample must be sold, may constrain the ability of manufacturers to negotiate a mutually beneficial agreement, resulting in further delays in settlement and generic approvals. However, policies that improve generic developer access to brand products, streamline the development of shared REMS protocols, and speed up the resolution of disputes between innovator and generic developers have the potential to improve consumer access to generics.

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[i] Creating and Restoring Equal Access to Equivalent Samples Act of 2017, S.974, 115th Cong. (2017), https://www.congress.gov/bill/115th-congress/senate-bill/974.

[ii] Federal Trade Commission's Brief as *Amicus Curiae*, Mylan v. Celgene, Case No. 2:14-CV-2094 (D.N.J. June 17, 2014), https://www.ftc.gov/system/files/documents/amicus_briefs/mylan-pharmaceuticals-inc.v.celgene-corporation/140617celgeneamicusbrief.pdf.

[iii] Lannett Co. Inc. v. Celgene Corp., Case No. 8-3920 (E.D. Pa.). A lawsuit brought by Lannett Co. Inc. in 2008 for denying access to samples of Celgene's Thalomid product for bioequivalence testing purposes was not settled until late 2011.

[iv] Food Drug and Cosmetic Act § 355-1.

[v] U.S. Food and Drug Administration, "Approved Risk Evaluation and Mitigation Strategies (REMS)," accessed March 27, 2017, https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm.

[vi] Ibid.

[vii] Federal Register Notice https://www.gpo.gov/fdsys/pkg/FR-2017-06-22/pdf/2017-12641.pdf

[viii] Food Drug and Cosmetic Act § 505-1(i)(1)(b).

[ix] The CREATES Act: Ending Regulatory Abuse, Protecting Consumers, and Ensuring Drug Price Competition, Before United States Senate Committee on the Judiciary, 114th Cong. (2016) (statement of Beth Zelnick-Kaufman, assistant general counsel, Amneal Pharmaceuticals), https://www.judiciary.senate.gov/imo/media/doc/06-21-16%20Zelnick-Kaufman%20Testimony.pdf.

[x] Senator Patrick Leahy, "Leaders of Senate and House Judiciary Committees Reintroduce Bipartisan Legislation to Counter Rising Prescription Drug Prices," news release, April 27, 2017, https://www.leahy.senate.gov/press/leaders-of-senate-and-house-judiciary-committees-reintroduce-bipartisan-legislation-to-counter-rising-prescription-drug-prices.

[xi] Alex Brill, "Lost Prescription Drug Savings From Use of REMS Programs to Delay Generic Market Entry," Matrix Global Advisors (July 2014), http://www.gphaonline.org/media/cms/REMS_Studyfinal_July2014.pdf.

[xii] Alex Brill, "REMS and Restricted Distribution Programs - An Estimate of the Market," Matrix Global Advisors (June 2017), http://www.gphaonline.org/media/cms/Alex_Brill_REMS_Study_June_2017.pdf

[xiii] Food and Drug Administration, "Memorandum."