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Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
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Majority (202) 225–2927
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January 17, 2020

The Honorable Stephen Hahn, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Hahn:

We write to request information and certain reports from the Food and Drug Administration (FDA) concerning the approval process for complex generic drug products.

We are interested in identifying ways to help reduce the costs of health care for patients, including the costs of prescription drugs. Generic versions of brand-name drugs provide substantial cost savings for patients and third-party payers and account for nine out of ten prescriptions filled in the U.S.[1] With their large market share and a cost that is typically 75 to 90 percent less than their brand name versions, generic drugs have resulted in savings of more than $1 trillion over a decade and $265 billion in 2017.[2] However, competition from complex generic drugs, a subset of these products is lagging.

Complex drug products are critical to the care of many serious medical conditions, such as multiple sclerosis, schizophrenia, metastatic breast cancer, osteoporosis, chronic obstructive pulmonary disease (COPD), and diabetes mellitus. Some of these drugs are high-cost medicines, like metered dose inhalers used to treat asthma, as well as costly injectable drugs not easily accessible to patients.

When the Hatch-Waxman Amendment created the generic drug pathway in 1984, generic drugs were generally easy to characterize and evaluate through traditional methods, including

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[1] Association for Accessible Medicines, Generic Drug Access & Savings in the U.S. (2018) (accessiblemeds.org/sites/default/files/2018_aam_generic_drug_access_and_savings_report.pdf).

[2] *Id.*

traditional bioequivalence studies.[3] In contrast, complex drugs are harder to formulate and manufacture for many reasons. Some complex drugs have a larger, more complex molecular composition or contain complex active ingredients. In other cases, complex drugs target conditions differently than other products by acting in a localized manner, like an inhaled medicine that acts directly on the lung or an eye drop that acts on the surface of the eye. It is more difficult to measure the therapeutic effect of these products and, thus, harder to measure bioequivalence than in conventional generic drugs.[4]

In some cases, intellectual property and exclusivity protections have lapsed on complex and costly branded drugs and there is still no generic competition, therefore, limited patient access to more affordable options.[5] As former FDA Director of the Office of Generic Drugs Dr. Kathleen "Cook" Uhl noted, many complex drugs have relatively small market capitalization and are less enticing for generic drug developers.[6] Moreover, similar to barriers faced by some small-molecule generic drugs, brand-name companies have put up barriers to approving complex generics.[7] These factors contribute to a lack of complex generic drug product development and Abbreviated New Drug Application (ANDA) submissions.[8] Because brand-name versions of complex drugs are often higher-priced than many other brand-name drugs, the development of generic competitors for complex drugs may have an outsized impact on access and drug spending.[9]

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[3] FDA, Remarks by FDA Deputy Commissioner Anna Abram to the FDA/DIA 2018 Complex Generic Drug-Device Combination Products Workshop (Oct. 9-10, 2018).

[4] FDA, Statement from FDA Commissioner Scott Gottlieb, M.D. responding to report from GAO and updating on FDA's ongoing efforts to increase access to complex generic drugs (Jan. 16, 2018) (press release).

[5] *Id.*

[6] Sharif Ahmed, *No Easy Solutions for Complex Generics Yet*, Lachman Consultants (Sept. 13, 2018), (www.lachmanconsultants.com/2018/09/no-easy-solutions-for-complex-generics-yet/) (accessed November 11,2019).

[7] Thomas J. Bollyky and Aaron J. Kesselheim, *Can Drug Importation Address High Generic Drug Prices?* Hutchins Center Working Paper #29, Brookings Institution (May 2017) (www.brookings.edu/wp-content/uploads/2017/05/wp29_bollykykesselheim_drugimportation.pdf).

[8] *Id.*

[9] FDA, FDA Acting Commissioner's Remarks to the 2019 FDLI Annual Conference (May 2, 2019).

The length of time leading to the approval of some recently approved complex generics raises questions of whether additional actions may be necessary to encourage the development of these products.[10]

For example, in August 2018, FDA approved the first generic versions of EpiPen and EpiPen Jr. (epinephrine) auto-injectors for the emergency treatment of allergic reactions, including those that are life-threatening (anaphylaxis).[11] This approval came nearly 10 years after FDA accepted the ANDA for filing in November 2008.[12]

In making this request, we acknowledge FDA's recent work to approve a record-setting number of generic drugs[13] and publish product-specific guidance documents that address complex generic drug development.[14] We also acknowledge FDA's recent announcement that it would maintain an updated list of planned new and revised product-specific guidance documents.[15]

Congress has acted to help advance complex generic drug development through the 2017 reauthorization of the Generic Drug User Fee Act (GDUFA).[16] Reauthorization of GDUFA supported the establishment of a pre-ANDA program and mid-cycle review meetings for complex generic drugs, improving communication between FDA and industry regarding

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[10] *See, e.g.*, FDA Statement, Statement from FDA Commissioner Scott Gottlieb, M.D., on new agency actions to further deter 'gaming' of the generic drug approval process by the use of citizen petitions (Oct. 2, 2018) (www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-new-agency-actions-further-deter-gaming-generic-drug).

[11] FDA, FDA approves first generic version of EpiPen (Aug. 16, 2018) (press release).

[12] FDA ANDA Approval Letter to Teva Pharmaceuticals USA, Inc. (Aug. 16, 2018) (www.accessdata.fda.gov/drugsatfda_docs/appletter/2018/090589Orig1s000ltr.pdf). First, there was a delay by the filing of a citizen petition in early 2015 by the company with exclusivity, in an attempt to persuade FDA not to approve this generic version to its EpiPen device. Ed Silverman, *How Mylan tried to keep Teva from selling a generic EpiPen*, STAT (Aug. 31, 2016). FDA denied the petition in June 2015. Second, FDA rejected the generic product application in a February 2016 Complete Response Letter (CRL) due to unspecified deficiencies. *Id.*

[13] Jill Wechsler, FDA Promotes Complex Generics and Combination Products, Pharmaceutical Technology (Oct. 19, 2018) ("One sign of success is the agency's approval of a record 971 new generic drugs this past fiscal year, largely due to devising a more streamlined and efficient review process and providing added advice and assistance on product development to manufacturers.").

[14] FDA, Upcoming Product-Specific Guidances for Complex Generic Drug Product Development (Sept. 16, 2019) (www.fda.gov/drugs/guidances-drugs/upcoming-product-specific-guidances-complex-generic-drug-product-development) (accessed Nov. 21, 2019).

[15] *Id.*

[16] FDA Reauthorization Act, Pub. L. No. 115-52 (2017).

regulatory expectations and potential deficiencies earlier in the approval process.[17] This is in addition to FDA issuing product-specific guidance documents under the GDUFA reauthorization.

In October 2017, former FDA Commissioner Gottlieb announced the Drug Competition Action Plan to promote new policies aimed at bringing more drug market competition.[18] Former Commissioner Gottlieb noted that if consumers are priced out of the drugs that they need, then that is a public health concern that FDA should address within the scope of FDA's mandate and authorities.

Our interest in this area is further reflected in the bipartisan request to the Government Accountability Office (GAO) that resulted in the December 2017 report, *FDA Should Make Public Its Plans to Issue and Revise Guidance on Nonbiological Complex Drugs*.[19] GAO identified several steps that have been taken that may help address the challenges associated with reviews. GAO also noted that FDA did not include product-specific guidance documents in its list of possible topics for guidance development or revision for 2018. In addition, GAO found that the lack of advance communication on guidance issuance and subsequent revisions can create setbacks for generic drug sponsors. GAO recommended that FDA should announce its plan to issue and revise product-specific guidance for drugs that are nonbiological and complex drugs. The Department of Health and Human Services, on behalf of FDA, concurred with the recommendations.

We would like to further understand whether FDA's initiatives and commitments are sufficient to address the particular challenge of approving complex generic drugs within existing authorities. A primary purpose of this request is to determine whether additional authority is needed to improve the approval process for complex generic drugs to increase access and reduce costs. FDA also may have internal and updated information that were not available or accessible to GAO at the time of their review for the 2017 report.

To assist our oversight, please provide the following by January 31, 2020:

1. A list of all complex generic drugs approved by FDA since October 1, 2016, including the date of the first submission, the dates of other milestones (e.g., issuance of complete response letters [CRLs], subsequent submissions), and the date of approval;

2. Copies of any after-action reports or internal reviews related to the review process of complex generic drugs approved since October 1, 2016;

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[17] FDA, *GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022* (May 12, 2016) (www.fda.gov/media/101052/download).

[18] FDA, FDA Drug Competition Action Plan (Oct. 23, 2019) (www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan) (accessed Nov.21, 2019).

[19] GAO-18-80.

3. The number of pre-ANDA meeting requests that FDA has received each year since the program was launched, the number of pre-ANDA meetings that FDA has held each year, and the number of ANDAs that have been submitted for products discussed during these meetings;

4. The number of product development meeting requests for complex products, as defined in the GDUFA II commitment letter, that FDA has received each year since August 1, 2017; the number of product development meeting requests for complex products that FDA has held each year; and the number of ANDAs that have been submitted for products discussed during these meetings; and

5. A list of product-specific guidances FDA has published for complex drug products, including the number of such guidances that are draft and the number of such guidances that are final.

We appreciate your attention to this matter, and if you have any questions, please contact Kevin McAloon of the Majority Committee staff at (202) 225-2927 or Alan Slobodin of the Minority Committee staff at (202) 225-3641. Thank you for your prompt attention to our request.

Sincerely,

Frank Pallone, Jr.
Chairman

Greg Walden
Ranking Member

Anna G. Eshoo
Chairwoman
Subcommittee on Health

Michael C. Burgess, M.D.
Ranking Member
Subcommittee on Health

Diana DeGette
Chair
Subcommittee on Oversight
and Investigations

Brett Guthrie
Ranking Member
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