TESTIMONY

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Introduction

Good morning Chairman Collins, Ranking Member Casey, and Members of the Committee. Thank you for the opportunity to testify today and for this Committee's distinguished record of focusing attention on policies to expand access to life-saving medications.

Access to affordable medicine is a matter of life and death for many Americans. Yet, too many Americans are unable to afford life-saving therapies because of their high costs. As the Director of FDA's Center for Drug Evaluation and Research, I can tell you that my colleagues and I take this issue very seriously.

FDA doesn't have a direct role in how drugs are priced; however, we can play an indirect role in holding down prices by bringing efficiencies to the drug development and review process and by promoting robust competition for established drugs, both of which are of great importance to the Center. We are committed to expanding access to high-quality, safe and effective, affordable therapies.

<u>Promoting Competition in Development of Drugs and Biologics</u>

Congress took care to promote innovation and access when it created the framework for generic drug development more than three decades ago and established a biosimilars pathway twenty-five years later. At FDA, we're proud of our record under these laws of fostering generic and biosimilar competition to expand access, lower drug prices, and promote public health.

FDA has worked hard to encourage applicants to enter the market with safe and effective generic drugs after legal barriers to approval, such as patents and exclusivities, have lapsed or otherwise been addressed. As a result the United States has one of the most competitive generic markets in the world.

Under FDA's Drug Competition Action Plan (DCAP), launched in 2017, we're enhancing our efforts to promote greater patient access to more lower-cost options via robust competition. More recently, we announced a Biosimilars Action Plan (BAP) to advance biosimilar development and approval — and facilitate access to lower-cost biological products to treat a growing number of chronic and life-threatening conditions.

Under the DCAP, we are taking steps across three main areas: 1) streamlining the abbreviated new drug application review process, 2) facilitating development of "complex" generic products, and 3) working to close loopholes that allow brand-name drug companies to "game" FDA rules in ways that delay generic competition. We kicked off our efforts in July 2017 with a public meeting to solicit input on ways to promote innovation in drug development and accelerate the availability of lower cost drugs to the American public. The Agency carefully reviewed all the input received and is actively considering new initiatives to help advance competition.

Of course, the foundation of our efforts is our generics review program. We committed under the Generic Drug User Fee Act (GDUFA II) (as part of FDARA) to timelier generic drug application assessments and to enhancements to help reduce the average number of generic review cycles –

and we are delivering. In FY 2018, the first full year of GDUFA II, FDA granted 971 approvals, of those 781 were full approvals and 190 were "tentative" approvals, that is, applications that are ready for approval from a scientific perspective but cannot be fully approved due to existing patents or exclusivities. Nearly 10 percent of the FY 18 approvals were first generics with no generic competition – and 12 percent were for complex, often difficult-to-copy, generic versions of branded products. The latter includes the first generic version of EpiPen and EpiPen Jr (epinephrine injection USP) auto-injector. FDA anticipates this approval means patients living with severe allergies who require constant access to lifesaving epinephrine should have a lower-cost option.

For the full year, FDA approved a record number of generic drugs, including first generics, high-priority medications, and drugs meeting vital public health needs. FDA's record-setting year for new generic approvals in 2018 continues a trend. In 2017, FDA surpassed it generic approval rate for 2016, which was itself another record-setting year.

FDARA recognized that consumers see significant price reductions when multiple FDA-approved generics are available. Based on that principle, we updated our internal procedures to prioritize the review of certain generic applications with not more than three approved generic drugs for a reference listed drug for which there are no blocking patents or exclusivities.

Generic competition is thriving for many products, but some products, including complex generics, have limited competition. Developing a generic version of a complex drug can offer a high-value opportunity at a time when the generics industry is facing economic pressures from rising costs, supply chain consolidation, increased competition and declining reimbursement on many generic products. Since brand-name versions of complex drug products are often higher-priced than many other brand name drugs, efforts to encourage generic competition for complex products also offers outsized potential to increase patient access and lower drug spending.

In February, FDA issued 74 product-specific draft guidances to assist industry in developing generic drugs, including 22 new guidances and 52 revised guidances. Four of the new draft guidances and 45 of the revised draft guidances are for complex drug products, including 16 complex products that, to date, do not have approved generics. Once finalized, these draft guidances will explain our current thinking and expectations on how to develop specific generic drug products that are therapeutically equivalent to the brand name drug products, providing an efficient path for these products to receive regulatory approval.

Recognizing that ready access to comprehensive, accurate, and reliable information on drugs is essential, we posted the inaugural List of Off-Patent, Off-Exclusivity Drugs without an Approved Generic in June 2017, and have subsequently posted more detailed, updated versions every 6 months. The list enables generic sponsors to more easily identify drugs without an approved generic. We intend to expedite the review of any generic drug application for a product on this list to ensure that they come to market as expeditiously as possible. We are also considering how we can enhance the *Approved Drug Products with Therapeutic Equivalence Evaluations* – known as the Orange Book – and clarify Orange Book processes. We are encouraged by congressional interest in improving the utility of the Orange Book for users who rely on its information for drug development. We hope to work with the Senate should it

consider H.R. 1503, the "Orange Book Transparency Act of 2019." Separately, we are undertaking efforts of our own to solicit public comment on Orange Book use and potential enhancements, including a re-examination of which pharmaceutical patents should be listed in the Orange Book.

We know there are still many branded products on the market without generic competition – and we are helping to encourage development of safe and effective generic competition to these sole source drugs. Since being granted new authorities in FDARA, the agency has moved quickly to designate drugs as Competitive Generic Therapies (CGT). The designation provides incentives for industry to develop generics for drugs lacking competition.

In February, FDA issued draft guidance on Competitive Generic Therapies to help provide even greater clarity to industry about the CGT pathway. This new guidance provides robust information on how drug developers can apply for CGT designation and when they may be eligible for CGT exclusivity. FDA's implementation of this new pathway is an important part of our broader effort to foster generic competition and help address the high cost of drugs and improve patient access to important medicines.

In addition, we are identifying abuses of the system that can impede competition and are doing our part to fix them. For example, many generic developers have reported difficulty obtaining brand drug samples needed for generic drug development, including bioequivalence testing, delaying or entirely preventing their efforts to develop more affordable generic drugs. In May of last year, we published a list on FDA's website of branded products for which generic drug developers have reported difficulties in obtaining access to samples. We also published a draft guidance to provide FDA's proposed response to some of the Risk Evaluation and Mitigation Strategies (REMS) competitor negotiation practices that can delay the entry of generic drugs.

We applaud congressional efforts to remove barriers to drug development and appreciate Congress' work on the "Creating and Restoring Equal Access to Equivalent Samples Act" (the CREATES Act). A path to securing samples of brand drugs for the purpose of generic drug development should always be available. We look forward to continuing to work with Congress on this legislation with the shared goal of reducing any opportunity for gaming.

Several proposals in the FY 2020 budget also target possible gaming. We would like to see statutory improvements to our citizen petitions process. Specifically, FDA would like greater authority to summarily deny petitions submitted with the primary purpose of delaying approval of an application and to incentivize timely filing of petitions. We would also like to eliminate the mandatory 150-day response timeframe from the statute. Operationally, the mandatory response timeframe is no longer needed to avoid delay of approval of follow-on applications as FDA already works under the goal dates set for these applications separate from this mandatory 150-day period.

Two other legislative proposals encourage competition, but with a focus on the 180-day exclusivity available to first-filers. First, we propose that Congress amend one of the existing 180-day forfeiture provisions to limit the ability of first filers with deficient ANDAs to game the system to avoid forfeiture. Forfeiture occurs under this provision when an applicant fails to

receive tentative approval within 30 months, unless the failure to obtain tentative approval is caused by a change in or a review of the requirements for approval imposed after the application filing date. Currently, first applicants with deficient applications may benefit from this provision by avoiding forfeiture even though they have deficiencies in their application unrelated to any change in or review of the requirements for approval. The proposal would clarify that the exception to forfeiture will only apply if the change in or review of the requirements for approval was the sole cause of the applicant's failure to obtain tentative approval.

The second proposal would address situations we see on a recurring basis where, after patent and exclusivity issues with the innovator drug have been resolved, first filers "park" their 180-day exclusivity and do not seek final approval, thereby delaying marketing and blocking competition for periods beyond which Congress envisioned. We suggest statutory modifications to trigger the start of the 180-day clock when: (1) a subsequent filer is ready for approval and the only barrier to final approval of the subsequent filer's application is a first filer's eligibility for 180-day exclusivity; and (2) certain other conditions are met, including that the first filer is past the 30-month timeframe to receive tentative approval and that any statutory stay of approval for the first filer has expired or terminated. This proposal will help ensure that generic competition occurs in a timely manner and that first filers who are unable or unwilling to obtain approval in a timely fashion cannot delay approval of subsequent applications indefinitely.

We are continuing to coordinate with the Federal Trade Commission, a vital partner in our efforts to address anti-competitive behavior in the drugs and biologics marketplace. Although we remain concerned about pay-for-delay agreements due to their anticompetitive impact, we are also concerned about *any* agreement that delays competition in the drug or biologic markets.

At FDA we have a number of pathways available to companies to get products to market more quickly than under our standard review. We offer those pathways (such as fast track and breakthrough, and even expedited consideration of applications for drugs currently in or vulnerable to a drug shortage). Let me make clear that although FDA may approve a drug, a company is under no obligation to market it. This is no small point given the scrutiny of drug prices and competition, and I raise it to highlight a dynamic outside of FDA's framework.

Every day we work to ensure that medical products are safe and effective, and that consumers can have confidence in the products they use. As regulators, we are on the front lines of the tension between upholding our standards of safety and efficacy and concerns over patient accessibility. I can't tell you how many times I have heard heartbreaking stories of families struggling with severe diseases, some of which are terminal, and others which are chronic and require a lifetime of care and close monitoring. At FDA, we have access to the best science and research in the world, and we do our level best to facilitate getting life-changing therapies to patients. Efforts to bypass our rigorous standards have unforeseen consequences, and I am always mindful of those challenges. The lessons we have learned since the establishment of FDA have helped inform our current thinking, which has also kept pace with scientific innovation and development.

Building a Strong Framework for Biosimilars

Similarly, an efficient, predictable development and approval pathway for biosimilars is a key to facilitating greater competition and innovation in the biologics marketplace. Biologic medicines have become a crucial tool in the treatment of many serious and life-threatening diseases. Biologics, which are typically complex molecules produced by living cells, are increasingly the backbone of modern therapy. But biologics are costly: they account for almost 40 percent of total prescription drug spending and 70 percent of the growth in drug spending between 2010 to 2015.

Until recently, biologics lacked effective competition because there was no abbreviated pathway for bringing follow-on versions of biologics to market under the Public Health Service Act (PHS Act), similar to the generic pathway we have for small molecule drugs created under the 1984 Hatch Waxman amendments to the Federal Food, Drug, and Cosmetic Act (FD&C Act). In 2010, Congress enacted the Biologics Price Competition and Innovation Act (BPCI Act), creating a pathway for approval of biosimilar and interchangeable products. This opened biologics to effective competition, with the ultimate goal of providing more treatment options, increasing access to lifesaving medications, and potentially lowering health care costs.

Since that time, FDA has approved 19 biosimilars and interest in these products remains high, with over 75 development programs currently enrolled in FDA's Biosimilar Biological Product Development Program for 36 different reference products. However, although the development pipeline for biosimilars is robust, fewer than half of the biosimilars approved by FDA have gone to market. We are very concerned that a large portion of the biosimilars that have been demonstrated to meet FDA's robust scientific standards for approval are not yet available to patients. We've set out in recent months to clarify and expand upon policies that promote more competition when it comes to biosimilar products and to advance our overall framework that improves the efficiency of the biosimilar and interchangeable product development and approval process.

FDA announced its Biosimilars Action Plan (BAP) in July 2018, recognizing that this is a crucial time in the emergence of biosimilars and a more competitive market for biologics. Under the BAP, FDA is focusing its efforts on: advancing the science and policies to make the development of biosimilars more efficient; increasing the understanding of biosimilars; and acting against regulatory gaming that can deter or delay competition.

Not only are we making the biosimilar development and review process more efficient and predictable, under the BAP we are also taking new steps to communicate with patients, payors, and providers to improve the understanding of biosimilar and interchangeable products. Further, we will act where appropriate to deter gaming of FDA requirements that unfairly delays competition among biologics.

The President's budget recommends a legislative proposal to encourage biosimilar development and innovation – and reduce gaming. Statutory provisions that relate to monograph standards issued by the U.S. Pharmacopeia, which include standards for strength, quality, packaging and labeling, were originally drafted for non-biologic drug products, but currently also apply to

biological products, including biosimilars. These provisions do not provide the flexibility needed to support innovation in product and test development. The proposal is meant to ensure that FDA can continue to approve biologic products with innovative changes that meet FDA's rigorous, approval requirements but nevertheless fail to meet static, prescriptive monograph standards – that, in some cases, have been outdated for decades. USP standards cannot be updated quickly enough to facilitate timely approval of novel products and/or novel manufacturing practices. The proposal would amend the Public Health Service Act so it is clear that biological products do not have to meet monograph standards, which could delay or impede licensure of a biosimilar and create substantial uncertainty for biosimilar applicants.

We're taking new steps to implement Congress's direction that we transition approved applications for biological products approved as drugs under the FD&C Act to biologics licenses under the PHS Act, opening them up to biosimilar competition. This will enable – for the first time – products that are biosimilar to, or interchangeable with, these biological products to come to market. Once an interchangeable product is approved and available on the market, it can then be substituted for the reference product without the involvement of the prescriber, potentially leading to increased access and lower costs for patients.

This transition is particularly important for insulin. Diabetes takes a tremendous toll on Americans, both physically and economically. It remains the seventh leading cause of death in the U.S. and accounts for $330 billion in annual health care spending. Insulin list prices have been regularly increasing by double digits annually despite the presence of numerous approved insulin products on the market. These increases have raised serious concerns about the ability for many patients to access the insulin needed to survive.

We must ensure that everyone who needs insulin has access to it. Under the FD&C Act, it has been hard to bring a substitutable generic insulin to the market. We believe the biosimilar pathway should help usher in a new era of competition for these products that we hope will lead to lower prices and better access.

As we transition to this pathway, FDA has been working to implement the statutory transition provision in a manner that promotes clarity, minimizes burden, helps ensure stability for patients using currently marketed products, and facilitates the development of biosimilar and interchangeable products. FDA has issued final guidance on the transition that provides recommendations to biological product sponsors to facilitate alignment of product development plans with FDA's interpretation of this statutory provision. We believe that FDA's recommendations to sponsors and performance goal dates for applications have made it unlikely that there would be any pending applications originally submitted under the FD&C Act that would need to be submitted and reviewed under the PHS Act. The Agency is also taking steps to minimize disruption and to provide clarity and certainty to application holders who seek to make changes to their approved products close to the transition date.

We're also working now – in advance of the March 2020 transition – to provide advice to sponsors on development programs for proposed biosimilar and interchangeable insulin products and to build a solid regulatory foundation for the review and approval of these products. In December 2018, we took a suite of actions designed to advance the agency's biosimilar

framework and to provide clarity and predictability to manufacturers, and earlier this month we published a final guidance outlining considerations for demonstrating interchangeability.

We're already seeing robust activity among sponsors seeking to develop products that are biosimilar to or interchangeable with insulin. Recently, we held a public hearing to discuss access to affordable insulin products, as well as the scientific and regulatory issues related to the development and evaluation of biosimilar and interchangeable insulin products. Stakeholders provided valuable input on data and information needed to support a demonstration of biosimilarity or interchangeability for insulin, and what factors the Agency should consider when evaluating data and other information submitted by an applicant, including from analytical and clinical studies. Importantly, we're also seeking input directly from patients about their experience with insulin products to inform our approach to regulating biosimilar and interchangeable products.

We have also closely reviewed legislation that affects biologic products. In many ways, the research, development and manufacturing of these products differs from small molecules. At FDA, we are cognizant of the many differences between drugs and biologics. Any proposal that attempts to import requirements of drug products that do not squarely fit within the biologics space could disrupt approval and access to these products.

We appreciate the Chairman's efforts to promote robust competition for biologics by introducing S. 659, the "Biologic Patent Transparency Act" and we hope to continue our constructive dialogue with your office on this important subject. We share your goal of enhanced transparency and are committed to making improvements to the Purple Book (a reference providing information relating to licensed biologic products).

We continue to evaluate additional steps necessary to strike the appropriate balance between encouraging ongoing innovation and facilitating the robust competition that can reduce costs to patients. We are committed to ongoing enhancements to reduce the time, uncertainty and cost of generic and biosimilar product development.

Modernizing Regulatory Oversight of New Drugs

Developing new medical therapies requires a challenging scientific process and significant financial investment. FDA has an important role to play in providing efficient, predictable, and science-based oversight to help reduce the time and uncertainty of bringing new drugs and biologics to market and, therefore, reduce the corresponding cost of drug development – and we are doing so.

Important new authorities and resources provided by Congress in the FDA Reauthorization Act of 2017 (FDARA) and the 21st Century Cures Act are helping transform the way we support medical product development and innovation while maintaining FDA's gold standard for safety and effectiveness. FDA is modernizing our science-based framework for clinical trials and embracing flexible, transparent, and innovative approaches to regulate new categories of products.

A cornerstone of our efforts is interactive communications with sponsors, which enables them to develop clinical trial designs and approaches, navigate key milestones, and understand submission requirements. Meaningful dialogue reduces the need for additional review cycles which can add significant time and expense to drug development.

In 2018, we approved many new drugs never before marketed in the United States, known as "novel" drugs, along with a wide variety of approvals for new and innovative uses of drugs already on the market. Many of these new approvals will have a significant impact on improving—and indeed, saving—countless patients' lives. All were approved within Prescription Drug User Fee Act (PDUFA) review goal dates. Approximately two-thirds used one or more of FDA's expedited development and review programs. We continue our efforts to keep pace with the rapidly changing scientific landscape and are working to modernize our regulatory framework. One legislative clarification we have sought in our FY 2020 budget proposal would codify FDA's active moiety approach for new chemical entity exclusivity determinations. This statutory change would help resolve uncertainty regarding applicability of our regulations in light of recent caselaw developments.

FDA is committed to enhancing achievement of its core mission, which includes efforts to help ensure and improve the safety and effectiveness of over-the-counter (OTC) Monograph drugs. Self-care through the use of OTC drugs empowers consumers to choose therapies which work best for them. Americans use OTC drugs every day, and these products will become increasingly important as patients take greater control of their own health. Reforms of the existing system are needed to promote innovation and choice for patients and consumers while also improving FDA's ability to address urgent safety issues in a timely fashion and help ensure the safety and effectiveness of OTC products. A wide range of stakeholders has come together to support these reforms and we hope to continue to work with Congress on legislation to make them a reality.

Conclusion

I look forward to continuing to work with the Committee as we address the problem of high drug prices, provide greater access to lifesaving medical products, and ensure that the United States remains a leader in biomedical innovation.

I am happy to answer questions from the Committee.