STATEMENT
OF
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FOOD AND DRUG ADMINISTRATION

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SUBCOMMITTEE ON REGULATORY REFORM, COMMERCIAL AND ANTITRUST LAW
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"Antitrust Concerns and the FDA Approval Process"

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INTRODUCTION

Good Morning Chairman Marino, Ranking Member Cicilline, and Members of the Committee. I am Dr. Scott Gottlieb, Commissioner of the Food and Drug Administration (FDA). Thank you for the opportunity to be here today to discuss some of the barriers to generic drug competition. Today, too many patients continue to be priced out of the medicines they need. There are complex reasons for this, and FDA doesn't have a direct role in how drugs are priced. That is why the Administration has begun the process of soliciting ideas and solutions to develop a more comprehensive strategy to address the complexities that have resulted in high prices, while continuing to foster innovation and competition. The goal of the Administration's strategy is to 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.

FDA does play a key, if indirect, role in the eventual cost of medicines. To the extent that FDA can make sure its regulatory requirements are efficient, predictable, and science-based, FDA can help reduce the time and uncertainty of drug development for both generic and branded drugs. Ultimately the steps FDA is taking to improve its regulatory requirements can help reduce the cost of drug development. To achieve these goals, FDA is undertaking a careful review of its requirements and processes to ensure that they meet these objectives in support of the broader public health mission.

There is another important way FDA can have an impact on reducing drug costs -- by encouraging competition. In short, consumers derive greater value when they have access to more choice and competition. We have a system that supports market-based pricing for innovation, as a way to provide proper incentives to entrepreneurs for taking on the uncertainty

of these costly and high-risk endeavors. That system also allows for vigorous competition once the patent and exclusivity rights no longer preclude generic approval. This is the careful balance that Congress struck when it created the modern generic drug framework in 1984 with the passage of the Hatch-Waxman Amendments. This compromise has enabled Americans to maintain a careful balance between access and innovation for more than thirty years. We need to ensure the continued success of this model.

But I am concerned that, in some cases, this model is not working as Congress intended. For example, we know that sometimes statutory and regulatory requirements, established to ensure the safety and quality of drugs approved by FDA, may also be leveraged – or "gamed" – in an effort to delay generic drug approvals beyond the timeframe the law has intended. This can serve to thwart expected competition. We are actively considering the ways our rules and laws are being used and, in some cases, misused, to diminish competition, and in turn, reduce access to medicines. As part of our efforts, and consistent with our public health goals, we have taken steps to curb this misuse. Our goal is to help maintain the balance between access and innovation that Congress established in the Hatch-Waxman Amendments. In connection with this effort, on June 21, 2017, I announced that FDA has begun work on a Drug Competition Action Plan. The announcement is available at *https://blogs.fda.gov/fdavoice/index.php/2017/06/fda-working-to-lift-barriers-to-generic-drug-competition/*.

As part of this plan, we have already announced a number of efforts currently underway. First, we announced in the Federal Register a public meeting that we held last week to solicit input on places where FDA's rules are being used in ways that may create obstacles to generic access. We specifically requested comment on several of the issues that we are discussing at today's hearing.

The FDA public meeting, "Administering the Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access," was held on July 18, 2017. It provided FDA, along with our partners at the Federal Trade Commission (FTC) whom we invited to participate, with an opportunity to hear from the public about the administration of the Hatch-Waxman Amendments. The docket for this meeting will remain open for public comment until September 18, 2017. We are evaluating the input we received from the public meeting and will consider the comments we receive from the docket to inform our actions moving forward. This feedback will inform where we need to take action to better serve patients in fostering an environment that fulfils Congress' vision for balancing the need to reward innovation with the imperative to enable timely competition once the patent and exclusivity rights no longer preclude generic approval. In other words, we are going to engage and act where we need to in areas where the balance sought by the Hatch-Waxman Amendments is not being achieved.

In addition, shortly after the announcement of the public meeting, on June 27, 2017, FDA announced two new steps we are taking to increase competition in the market for prescription drugs and facilitate entry of lower-cost alternatives. First, FDA published a list of off-patent, off-exclusivity branded drugs without approved generics in order to encourage development and submission of applications for generic versions of such products. Second, we are implementing a policy to expedite the review of generic drug applications for products with limited competition.

These steps are the first in a series of actions FDA intends to take to help promote competition. Our hope is that through increased competition, we will be able to improve access, and promote the public health, by reducing the overall burden on patients who have a difficult time paying for

the medicines they need. The Drug Competition Action Plan is a broad initiative intended to result in a comprehensive review of our drug review and approval process to ensure that it remains calibrated to serving as the gold-standard for safety and efficacy while simultaneously ensuring that our marketplace for drugs is delivering on the competition that Congress intended. Some of our efforts will target broad issues that impact drug applications generally, such as an assessment of our own internal generic drug application review processes that will result in increased review efficiency, among other benefits. Other efforts in the Drug Competition Action Plan will be focused on more targeted issues, such as the policies and regulatory approaches for establishing "sameness" for generic versions of complex drug products as a way to facilitate more generic competition for "hard to copy" complex drug products.

I have provided you this broad update on our Drug Competition Action Plan today because, among other things, the plan is intended to make strides in each of the areas that we are discussing today: (1) Restricted distribution systems and access to necessary reference listed drugs for bioequivalence testing; (2) Requirements for single-shared systems in the context of drugs with risk evaluation and mitigation strategies (REMS); (3) The citizen petition process; (4) the unapproved drug initiative; and (5) "Pay-for-delay" agreements.

I will provide some background on how we consider each of these areas below.

Reference Listed Drug ("RLD") Access and Limited Distribution Systems

In order to get approval for a generic drug, the generic company needs to show, among other things, that its version of the product is bioequivalent to the brand drug, also known as the "reference listed drug" or "RLD." This usually requires the generic company to conduct

bioequivalence studies comparing its product to the RLD. In general terms, bioequivalence testing is designed to show that the proposed generic drug reaches the site of action at a rate and to an extent not significantly different from the RLD. To conduct these kinds of bioequivalence studies, the generic company needs to obtain certain physical amounts of the RLD. A generic applicant typically needs between 1,500 and 5,000 units of the RLD for drug development purposes. Often, generic companies are able to get these RLD samples through normal drug distribution channels – i.e., via wholesalers. Sometimes, however, samples of the RLD are not available through normal distribution channels.

A drug may not be available through standard distribution channels because the brand company limits the distribution of the drug on its own initiative for a variety of business reasons, for example, by selling it through a central or small group of pharmacies. In other cases, a REMS program with elements to assure safe use (ETASU) might impact the way the product is distributed. For example, a pharmacy certification requirement might limit the pharmacies to which the product is distributed to ensure that the pharmacist is aware of the specific safe-use measures required for the particular drug and help to ensure that these measures are followed.

As background, the Food and Drug Administration Amendments Act of 2007 authorized REMS to ensure that a drug's benefits outweigh its risks. These risk management programs may be used and established for the approval of particularly risky drugs. These measures can include ETASU that, for example, limit where or how the drug can be dispensed, impose patient monitoring requirements, or impose prescriber or pharmacist training or certification. These kinds of REMS programs allow products that could not otherwise be approved because of safety issues to be approved and available to patients.

We understand that some brand companies selling products under limited distribution -- sometimes as part of a REMS ETASU or, otherwise-- have refused to sell the RLD to generic companies for testing. In other cases, some brand companies have included provisions in their distribution agreements prohibiting the sale of the branded drug product to generic companies for testing purposes. FDA has received more than 150 inquiries from generic companies that want to develop generic drugs but tell us they are unable to do so because they cannot get access to supplies of the RLD to do the testing needed for a generic application. We have referred such matters that have been brought to our attention to the FTC and encouraged generic companies to also raise these matters with the FTC.

To address cases where some brand companies have argued that their products' REMS prohibit them from selling RLD supplies to generic companies for testing, we developed a process, where appropriate, for informing the brand company in writing that FDA will not consider provision of the RLD for these purposes to be a violation of the REMS. This process is described in our 2014 draft guidance *How to Obtain a Letter from FDA Stating that Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable REMS for RLD*. As described in that draft guidance, when requested to do so, we review the bioequivalence study protocols of companies that want to develop generic versions of these REMS drugs to assess whether they contain safety protections comparable to those in the applicable REMS. If we determine that they do, we send a letter to the brand company stating that selling the RLD to the generic company for testing and development will not be considered a violation of the REMS. Despite these actions, we understand that some brand companies have continued to refuse to sell their product to the generic developer for testing purposes. We are currently taking a close look at that guidance and actively considering whether it achieves its goals or whether we can and should do more.

Single, Shared System REMS

We also continue to have concerns about situations where brand companies may block or delay the approval of generic drugs by leveraging the single, shared system REMS requirement. This is a separate problem from the RLD access issue described above. For branded drug products approved with REMS ETASU, the Federal Food, Drug, and Cosmetic Act (FD&C Act) requires that the generic drug applicant and the branded drug manufacturer use a single, shared system to implement the ETASU, before the generic drug application can be approved. FDA can waive the requirement for one of the reasons set forth in the FD&C Act.

This requirement necessitates discussion and negotiation between two potential competitors – the brand and generic company – and their agreement on the terms of the single, shared system REMS and how it will operate. In part because this is a prerequisite to generic drug approval, brand companies often have an incentive to refuse to agree to a single, shared system REMS. By prolonging the negotiations over a single, shared system REMS, they further delay generic drug approval and competition. We see prolonged negotiations and inability to agree on the terms of a single, shared system REMS regularly. In addition to working to delay and frustrate generic drug approval, these negotiations are time- and resource- intensive on the part of both industry and FDA. To the extent that these negotiations are prolonged in an effort to delay competition, the negative impacts to the healthcare system are multiple. Not only is the approval of a generic competitor delayed, but the drug approval process is less efficient and more expensive for everyone involved.

As noted above, FDA does have the ability, when appropriate, to waive this single, shared system requirement. We are actively considering our authority and practices in this space and evaluating whether we can do more here to alleviate any unnecessary delay to generic drug approval and related regulatory cost. Our policy goal remains to pursue a single, shared system in most circumstances. This helps reduce the burden that REMS place on the healthcare system. But we need to balance the benefits of a shared system against the public health impact of delays to generic entry.

Citizen Petitions

A citizen petition is a vehicle that stakeholders outside of FDA can use to ask FDA "to issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action" (21 Code of Federal Regulations 10.25(a)). Petitioners can request, for example, that FDA require warnings to be added to the labeling of a drug or not approve drug product applications without such warnings included in the labeling.

Section 505(q) was added to the FD&C Act in 2007 to limit the potential for certain citizen petitions to be employed as a means to delay approval of generic and certain other applications. The requirements in Section 505(q) apply to certain petitions that request that FDA take any form of action related to a pending generic application, as well as certain applications for other abbreviated approval pathways. Most commonly, these 505(q) petitions ask FDA not to approve the generic application unless certain conditions are met. In 2012, FDASIA added some procedural requirements and changed some timelines in an effort to discourage submission of baseless petitions and petitions with a primary purpose to delay approval of follow-on

applications. Among other things, section 505(q) now requires FDA to take final agency action on a petition not later than one hundred and fifty days after the date on which the petition is submitted. Further, section 505(q) prohibits FDA from delaying the approval of a generic drug application during consideration of a pending citizen petition, unless certain limited circumstances exist.

Citizen petitions often raise relevant issues and provide useful information for FDA. They provide interested parties with a vehicle to bring their concerns before FDA, and are therefore an important element of good governance and public accountability. But significant FDA resources are often required to answer a citizen petition, which include careful consideration of the issues by appropriate FDA staff, and preparation, review, and vetting of the response through multiple groups across FDA whose work may be impacted by it. As part of its public health mandate, FDA takes care to create an appropriate record to support FDA's actions. Where citizen petitions raise genuine issues for scientific consideration, this process can be well worth the resources it consumes. In such cases, the petition process may improve FDA's scientific understanding or otherwise improve our review or approval processes.

In other cases, however, section 505(q) petitions may not raise valid scientific issues that ultimately, when reviewed and considered, persuade FDA to change its evaluation of pending generic applications. A very high percentage of these petitions are denied as without merit. Although some of these petitions raise difficult and important questions of public health that FDA should consider (even if the petitions are ultimately rejected), others do not. It can be difficult in many cases to know prior to review which petitions are which. But all such petitions

require the dedication of FDA resources and time. Further, because of the statutory obligations limiting FDA's timeframes for answering these petitions, such resource issues are exacerbated.

FDA continues to be concerned that the 2012 changes to section 505(q) may not be discouraging the submission of petitions that are intended primarily to delay the approval of competing drug products and do not raise valid scientific or public health issues. For example, the number of 505(q) petitions submitted to FDA each year has remained relatively steady since the enactment of section 505(q). This could suggest that the provision has had limited impact in discouraging the submission of petitions intended primarily to block or delay generic competition.

FDA is actively considering the impact that 505(q) petitions have on generic drug approvals. For example, even if a particular 505(q) petition does not delay the approval of the generic drug application(s) that it specifically relates to, because of their resource-intensive and time-sensitive nature, responses to these petitions necessarily draw resources away from review and approval of generic drug applications more generally. To the extent that these petitions do not raise issues, the consideration of which would benefit the public health, then these diverted resources introduce an unneeded and unhelpful inefficiency and cost into the generic drug approval process generally. We are considering what actions we can take, within our existing authorities, to reduce the unnecessary burden these petitions continue to place on the generic drug program.

Unapproved Drug Initiative

Building on pre-existing requirements that new drugs be evaluated for safety, in 1962 Congress amended the FD&C Act to require that all new drugs, including prescription drugs, must also be

shown to be effective for their intended use(s) before they can be legally marketed in the United States. As a result of this requirement to evaluate new drugs for effectiveness, thousands of drugs previously approved only for safety had to be reevaluated in light of the new legal requirements, as did many marketed unapproved drugs that were identical, related, or similar to the previously approved products. However, FDA estimates that more than 1,000 prescription drug products have never gone through the approval process and remain on the market. Few, if any, of these unapproved prescription drug products are likely to be exempt from statutory approval requirements.

The lack of evidence demonstrating that unapproved prescription drugs are safe and effective, as well as the lack of a review to ensure that the drugs' labeling include accurate and complete information, is a significant public health concern. These unapproved new drugs have not undergone the rigorous FDA drug review process, which helps ensure that new drug products are safe and effective, manufactured according to Federal quality standards, and bear labeling that conveys accurate, clear and complete information to health care professionals and patients regarding the drugs' risks, benefits and safe use. Many healthcare providers are unaware that some of the drugs they prescribe are unapproved.

In June 2006, FDA launched a new drug safety initiative, the "Unapproved Drugs Initiative," to bring marketed unapproved drugs into the approval process, ensuring that they meet modern standards for safety, effectiveness and quality, and that they bear labeling for safe and effective use. In implementing this policy, FDA uses a risk-based enforcement approach. FDA concentrates its resources on unapproved products that pose the highest threat to public health to avoid imposing undue burdens on consumers or unnecessarily disrupting the market.

FDA encourages all makers of unapproved new drugs to submit new drug applications (NDAs). Patients and practitioners can have confidence that FDA-approved drugs have been shown to be safe and effective for their intended use(s) and that they are manufactured according to Federal quality standards. In addition, once an NDA is approved, there is a clear pathway for generic entry since the approval results in a product that can be designated as an RLD. Generic approval, in turn, greatly facilitates substitution because many state and other formularies permit automatic substitution of an FDA-approved generic product when the RLD is prescribed.

Sometimes, however, only one company will seek FDA approval of a product that has been on the market for a long time. When there is only one of an FDA-approved version of a drug, market dynamics may enable the company that sought and received approval to set a higher price than when the drug was unapproved, unless and until competitive products, generic or otherwise, are approved. As we contemplate additional actions to facilitate patient access to safe, effective, and high quality drug products, FDA will continue to consider possible improvements in all areas, including the Unapproved Drugs Initiative. In addition, we note that the benefits of the Drug Competition Action Plan that are intended to improve the predictability, efficiency, and overall competitiveness of the drug approval process generally also apply to drug product applications resulting from this initiative.

Pay-for-Delay Agreements

"Pay-for-delay" agreements are another way that brand companies extend the period of time during which the brand drug is the only drug on the market. These agreements occur when brand drug companies resolve patent litigation over potentially infringing generic products by reaching

a settlement under which a generic company agrees to delay marketing of its generic product for a period of time in exchange for a benefit.

The Hatch-Waxman Amendments to the FD&C Act provide that certain generic companies that are first to submit generic drug applications that include challenges to a listed patent on the brand drug ("first applicants") may be eligible for 180 days of marketing exclusivity. During the 180-day exclusivity period, which is triggered by commercial marketing by a "first applicant," other generic applicants who are not "first applicants" cannot obtain approval of their drugs. Under these provisions, and subject to certain forfeiture provisions, a generic company that is eligible for such exclusivity can delay triggering such exclusivity for as long as the generic company postpones commercially marketing the drug. As a result, all other generic manufacturers who have submitted a generic drug application for the same drug are precluded from obtaining approval for their generic versions of the brand product for as long as the "first applicant" postpones marketing the drug, as well as during the 180-day exclusivity period which follows first commercial marketing. This exclusivity was established by the Hatch-Waxman Amendments, at least in part, to provide an incentive for such "first applicants" to challenge the brand company's patents and, potentially, begin generic competition before the patents would have otherwise expired. As a result of this exclusivity, however, "pay-for-delay" agreements between branded companies and 180-day exclusivity "first applicants" (in which a first applicant agrees to delay commercial marketing and, thus, to delay triggering its 180 day exclusivity) are particularly powerful because one such agreement has the potential to affect when the subsequent generic drug applicants for a given drug product can enter the market.

While many "pay-for-delay" agreements have resulted in generic products entering the market before the expiration of a patent (the period beyond which patent law would prohibit such agreements), we do not know when generic products would have entered the market if the patent litigation had continued and the companies had not settled with an agreement to delay marketing. If the patent litigation had been allowed to run its course, and the court had determined that the patent was invalid or not infringed, the generic product might have entered the market years before the date set forth in the relevant "pay-for-delay" agreement. However, a number of other outcomes would also have been possible. This problem is complex, and solutions will involve several stakeholders in addition to FDA, including the FTC, which is responsible for enforcement actions related to such agreements. However, we will continue to work with the FTC and our other partners to consider these critical issues and will determine whether there are any additional actions that can be taken to address them.

CONCLUSION

FDA will continue taking steps to address the concerns before us today, to make sure that we are facilitating appropriate competition in circumstances where Congress intended. The public meeting we held last week helped FDA to solicit public comment in order to inform us of circumstances where these and other techniques may upset the intended balance between innovation and access. FDA will continue to consider ways in which it can work to ensure that the balance between drug access and innovation is maintained.

As we solicit additional information, we will also be looking at policy and programmatic changes to address these issues. Some of these steps may be actions we can take by using our

own authorities more effectively. Other steps might involve collaborating with sister agencies. We intend to use every appropriate tool available to us to address these challenges.

We also plan to unveil additional aspects of our Drug Competition Action Plan in the near future. I will continue to communicate with the public as additional elements of this plan are implemented. I look forward to continuing to work with Congress and to providing updates on our efforts to accomplish the goal of broadening access to safe and effective generic drugs that can help consumers lower their healthcare costs. As in all of the things we do, we will steadfastly maintain FDA's gold standard for rigorous, science-based regulation.