Restricted Distribution Systems in the Pharmaceutical Supply Chain

Testimony of Janet Woodcock, M.D.
Director, Center for Drug Evaluation and Research

Before the
United States House
Committee on Oversight and Government Reform
Subcommittee on Health Care, Benefits, and Administrative Rules

March 22, 2017

U.S. Department of Health and Human Services
U.S. Food and Drug Administration
www.fda.gov

RELEASE ONLY UPON DELIVERY

INTRODUCTION

Mr. Chairman and Members of the Committee, I am Dr. Janet Woodcock, director of the Center for Drug Evaluation and Research (CDER) at the U.S. Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss restricted (referred herein as "limited") distribution systems in the pharmaceutical supply chain. This is an important topic that has implications for increasing generic competition and patients' access to affordable medicines.

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")[1]. This usually requires the generic company to do bioequivalence studies comparing their 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. Bioequivalence testing typically involves a relatively small number of human subjects and a small number of doses (often only one dose) and, therefore, a lower level of risk than other types of clinical testing during the drug development process. The regulatory regime applicable to bioequivalence testing – including the exemption of most bioequivalence testing from the investigational new drug (IND) requirements – reflects the lower level of risk associated with bioequivalence testing when compared with other kinds of clinical testing that occur during the drug development process. In addition, FDA

[1] For purposes of this testimony, we are using the term RLD to refer to the listed drug identified by FDA as the drug product upon which the applicant relies in seeking approval of its generic product or the drug product selected by FDA that an applicant seeking approval of a generic product must use in conducting a bioequivalence study.

regulations (at 21 CFR Part 56) require that before bioequivalence testing can begin, it must be approved by an Institutional Review Board (IRB) to ensure that risks are minimized.

To do these kinds of bioequivalence studies, the generic company needs to get access to a small quantity of the RLD. Typically, 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. This might happen because the brand company limits the distribution of the drug on its own initiative for a variety of legitimate business reasons (for example, by selling it through a central or small group of pharmacies). In other cases, a risk evaluation and mitigation strategy (REMS) program with elements to assure safe use (ETASU) might impact the way the product is distributed. 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 for particularly risky drugs, and 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.

A subset of REMS programs have features that may impact product distribution. For example, a pharmacy certification requirement might limit the pharmacies to which the product is distributed. The purpose of a requirement of this kind is to ensure that the pharmacist is aware of the specific safe use measures required for the particular drug and helps ensure that they have been followed before the product is dispensed. 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 that sell products under limited distribution have refused to sell the RLD to generic companies for testing or have included provisions in their contracts with pharmacies/third parties that prohibit the sale of the RLD to generic companies for testing purposes. This is a problem that affects both REMS and non-REMS products. FDA has received more than one hundred and fifty inquiries from generic companies that want to develop generic drugs but tell us they are unable to because they cannot get access to supplies of the RLD to do testing. We have referred such matters that have been brought to our attention to the Federal Trade Commission (FTC) and encouraged generic companies to also raise these matters with the FTC. We have taken a number of additional steps as well.

Because some brand companies have argued that their product's REMS prohibits them from selling RLD supplies to generic companies for testing, we have 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 guidance *How to Obtain a Letter from FDA Stating that Bioequivalence Study Protocols Contain Safety Protections Comparable to Applicable REMS for RLD* ("Protocols Guidance"), available at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm425662.pdf. As described in that 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 that they do, we send a letter to the brand company stating so and informing them that selling the RLD to the generic company for testing and development will not be considered a violation of the REMS. While FDA developed this

process to help facilitate access to RLD samples for generic companies, it is important to note that the protections in the REMS program are designed to mitigate risks that occur during real world, every day use by patients, and that safety concerns are likely to be lower in the more tightly-controlled context and limited scope of bioequivalence testing. We note that while the letters provided pursuant to the Protocols Guidance make clear that such sales will not subject the brand company to REMS-related enforcement action, some brand companies have argued that they have independent business reasons for not selling the RLD to the generic firm that are unrelated to their REMS and/or that they have no obligation to do so.

We have also received a significant number of RLD access inquiries about products that are not subject to a REMS for which the brand company has voluntarily limited their distribution. Because there is no REMS in place in such cases, there is, of course, no call for us to review bioequivalence study protocols to ensure they have safety protections comparable to a REMS. When generic companies contact us because they are experiencing difficulty getting access to brand products that are not subject to a REMS, we often confirm that the distribution restrictions they are describing are not required by FDA, and encourage the generic companies to raise the matter with the FTC.

CONCLUSION

We hope you found this information about how some limited distribution systems in the pharmaceutical supply chain can affect generic competition to be helpful.