Holding the Industry Accountable for Post-Marketing Studies of New Drugs

Patients and providers must have the evidence that they need and deserve to inform effective medical care.

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Statement by FDA Commissioner Scott Gottlieb, MD, on the FDA's efforts to hold industry accountable for fulfilling critical post-marketing studies of the benefits, safety of new drugs

The FDA remains committed to ensuring that FDA-approved drugs are safe and effective for Americans. As part of this commitment, we require evidence from premarket clinical trials that the medicine will be both effective and safe for use when prescribed according to its labeling. However, it's not unusual for the FDA to identify issues that need additional evaluation either at the time of initial approval or later, once the drug has been marketed. These issues are evaluated through the conduct of additional post-marketing studies.

These post-approval studies are vital to enhancing patient safety and public health. They may be needed to further characterize the use of the product in the therapeutic armamentarium. Additionally, post-approval studies can allow for further evaluation of a potential safety issue or better characterize risk factors for a known safety issue. Once a drug is approved, invariably a larger population and wider range of patients will use the drug than were studied before approval. With this larger patient experience, new potential safety issues may emerge that were not seen in the studies conducted prior to approval. And such issues may require additional evaluation after the drug is marketed and used by patients for a period of time.

The results from completed post-market studies provide additional information that can lead to safety labeling changes, support expanded use of a drug, or alleviate concerns about a potential drug risk. The FDA is always looking at opportunities to facilitate the conduct and completion of these studies to ensure that patients and providers have the most complete data about a drug to inform their treatment decisions.

Recently, new tools for capturing data in the post-market period, including more sophisticated use of real world data and real-world evidence (RWE), are providing new approaches to address important questions about the safety and benefits of new drugs in real world settings. These approaches have the potential to do to so more rapidly and with greater efficiency than traditional methods.

For example, the FDA recently announced the MyStudies app, a new mobile technology created to foster the collection of RWE via patients' mobile devices. By releasing the open source code and technical documents, we hope that researchers will be able to customize and use the MyStudies app to collect different types of information from patients directly and more conveniently.

In addition, to further advance these opportunities, the FDA will soon publish a framework for the FDA's RWE program. This framework is intended to help evaluate the potential use of RWE to help support the approval of a new indication or to help support or satisfy post-approval study requirements.

The Food and Drug Administration Amendments Act of 2007 (FDAAA) gave the FDA additional authority to require safety-related post marketing requirements (PMRs). Prior to the implementation of this Act, if the FDA wanted to further evaluate the safety of a drug post-approval, it would generally have to request the applicant agree to conduct a post marketing commitment (PMC). The 2007 Act was a major step forward for drug safety in the U.S. as it gave the FDA explicit authority to require safety-related PMRs and hold manufacturers accountable for completing the PMRs through enforcement authorities.

There are two types of post-approval studies. The first are post-marketing requirements (PMRs). The FDA has the authority to require post-marketing studies in certain circumstances, for example to assess a known serious risk related to the use of the drug, to assess signals of serious risk related to the use of the drug, and/or to identify an unexpected serious risk when available data indicate the potential for a serious risk. The second type of post-approval studies are post-marketing commitments (PMCs). These studies are commitments by the drug manufacturer to conduct post-approval studies to provide additional information on the drug. For example, a sponsor may conduct a PMC to examine the natural history of a disease, or to evaluate the efficacy of a drug in a subpopulation of patients.

Today we're announcing our FY 2017 Report on the Performance of Drug and Biologics Firms in Conducting Postmarketing Requirements and Commitments. This report provides an update on how we're doing at holding companies accountable for completing these important studies on time to ensure that our understanding of a drug's safety and efficacy keeps pace with its use in all relevant populations once a product is approved. We're committed to ensuring that PMRs and PMCs are conducted and reported as required, and to providing transparent access to the progress of these studies for the public.

I'm pleased to report that 81 percent of open PMRs (1,056/1,298) and 76 percent of open PMCs (248/326) are progressing on schedule.

When studies are delayed, the FDA continues to provide guidance, oversight and monitor the manufacturers to ensure the studies are completed. We take the need to fulfill these requirements and commitments seriously given the health implications. The timely conduct of these studies is a major area of policy focus inside the FDA. When we see deficiencies in a company's progress, we take appropriate action.

It’s important to note that a delay does not mean a study isn’t taking place. The study may be ongoing, but the status is delayed because the sponsor is behind the originally planned schedule. There are many reasons a study might become delayed. Sometimes there are practical considerations that arise during the conduct of the study. For example, it may emerge that it’s more difficult than anticipated to get participants to enroll in the clinical trial. Or there may be other reasons for a need to change the study protocol. Our FDA review teams closely track milestones and communicate with companies when requirements are missed.

In addition, a great deal more information about the drug and the disease it treats often becomes available in the years after an approval. The FDA carefully reviews this emerging scientific information and may conclude that there are new safety concerns that warrant requiring the company to complete additional post-approval studies or changing the nature of the studies that we initially required. As a result, PMRs and PMCs may undergo modifications after they get underway. These modifications may serve an important public health purpose. But they could also extend the time required to bring them to completion.

As an additional part our commitment to ensuring that the FDA post-approval studies are being monitored, we regularly track and inform Congress on the status of a subset of PMRs and PMCs that were open at the time FDAAA was signed into law but have not yet been completed or fulfilled. This is referred to as the “backlog.” I’m pleased to report that we continue to make progress in closing the “backlog” as we reported earlier this year to Congress, in the FY2017 Report to Congress on the Backlog of PMRs/PMCs.

The report highlighted that the FDA Center for Drug Evaluation and Research (CDER) completed review for 1,468 of the 1,553 PMRs and PMCs in the backlog and the FDA Center for Biologics Evaluation and Research (CBER) completed review of 71 of 83 PMRs and PMCs in the backlog. The FDA is working to diminish the backlog by reviewing final reports and issuing fulfillment letters. The Fiscal Year 2017 report to Congress showed that 92 percent (1,422/1,553) of the PMRs/PMCs in the CDER backlog have been closed and 86 percent (71/83) of the PMRs/PMCs in the CBER backlog are now also closed.

We anticipate that the number of PMRs and PMCs in the backlog that aren’t yet fully completed will continue to diminish each year as applicants finish studies/trials and submit final reports. This progress is a reflection of the deep commitment of our team to ensure the program is functioning well so that we can focus on our efforts on the studies that we believe need to proceed. The timely completion of post-marketing studies remains a critical part of our regulatory responsibility. The post-market process must be unfailing.

As we work to modernize our body of knowledge about a drug’s performance throughout the product life cycle, post-marketing studies have an important role to play. We must continue to strive to leverage new tools, such as real world data and RWE and trials imbedded at the site of patient care to facilitate their timely and efficient conduct. We remain committed to keeping all of our programs robust and informed by the latest techniques and tools for collecting the data. And most importantly, we’re dedicated to ensuring that we have the evidence we need as regulators to

confirm that products are safe and effective. And that patients and providers have the evidence that they need and deserve to inform effective medical care.

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