FDA Encourages Use of Real-World Evidence to Support New Drugs

The agency hopes to make better use of information from patients and providers.

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Statement from FDA Commissioner Scott Gottlieb, MD, on FDA's new strategic framework to advance use of real-world evidence to support development of drugs and biologics

The health care system is integrating more effective ways to leverage electronic tools to gather and use vast amounts of health-related data. These tools offer new opportunities to use data collected during the routine care of patients to advance medical care. Leveraging such data — typically called real-world data (RWD) — to improve regulatory decisions is a key strategic priority for the FDA. Today, the FDA is announcing our new 2019 strategic Framework for how we'll continue to advance these opportunities.

RWD collected from a variety of sources offer new opportunities to generate evidence and better understand clinical outcomes. These data may be derived from a diverse array of sources, such as electronic health records (EHR), medical claims, product and disease registries, laboratory test results and even cutting-edge technology paired with consumer mobile devices. These data are being used to develop information and real-world evidence (RWE) that can better inform regulatory decisions. Because they include data covering the experience of physicians and patients with the actual use of new treatments in practice, and not just in research studies, the collective evaluation of these data sources has the potential to inform clinical decision making by patients and providers, develop new hypotheses for further testing of new products to drive continued innovation and inform us about the performance of medical products.

RWE provides us with a potential source of information that can complement, augment and expand our understanding of how best to use medical products — improving what we know about our medical care.

RWD and RWE can be especially useful for postmarket monitoring of the safety of products during their use in real world settings. To give some examples, our use of RWD and RWE, derived from our Sentinel system, eliminated the need for postmarketing studies on nine potential safety issues involving five products, making our postmarket evaluation of safety timelier and more effective. The aim is to get reliable, high-quality, actionable safety information to patients and providers much faster. Traditional post-market studies typically require years to design and complete and

cost millions of dollars. By using RWD and RWE, we may be able to provide patients and providers with important answers sooner — identifying a broader range of safety signals and following up on them more efficiently. We've also used Sentinel to understand patterns of opioid use.

These tools will gradually allow us to shift some studies and data collection to the point of care, making the collection of data and the development of actionable evidence more efficient. These opportunities are already being recognized. In the oncology setting, for example, we currently have new drug applications under review where RWD and RWE are helping to inform our ongoing evaluation as one component of the total complement of information that we're evaluating. This is especially relevant when it comes to the evaluation of treatments for uncommon conditions, such as very rare tumor types. To take advantage of these opportunities, the identification, evaluation, and addressing of post marketing safety issues has now become a much more multidisciplinary venture within the agency. In addition, these endeavors increasingly involve closer interactions between the FDA, global regulatory authorities, and industry.

Advances in technology are also promoting these opportunities. New innovations such as natural language processing (NLP) are rapidly maturing and expediting the review of inputs such as single case reports, literature, EHRs, and social media. This coincides with an increasing use of RWD and RWE to help inform health care decisions. The FDA's Sentinel safety capability continues to expand, making active surveillance a greater reality. In more cases, active post-market risk identification and analysis (ARIA) is replacing the need for post-marketing studies as a more effective, comprehensive, and achievable tool for post-market evaluation of products. As a result of these opportunities, these tools are becoming an increasingly important part of pre-market planning for post-market safety evaluation.

The FDA recognizes how important RWD and RWE are. This is a top strategic priority for the FDA. We're committed to realizing the full potential of these tools in advancing the development of novel therapeutic products and strengthening our regulatory oversight of medical products across the life-cycle continuum.

To that end, today we're releasing a new, strategic, approach — the Framework for the Real-World Evidence Program, to apply across our drug and biologic review programs. This Framework is aimed at leveraging information gathered from patients and the medical community to inform and shape the FDA's decisions across our drug and biologic development efforts. This strategic Framework will form a cornerstone of our efforts to advance the use of these tools. In the coming months, we'll advance other new initiatives to better leverage RWD and RWE in our programs.

The FDA has already begun to incorporate RWE in regulatory decisions. The 21st Century Cures Act required the FDA to release a comprehensive plan for how we'll continue to advance these efforts.

As I noted, in the postmarketing space we've been using RWD and RWE to monitor and evaluate the safety of drug and biologic products through our Sentinel System. This system accesses data from large amounts of electronic health care sources — including electronic health records,

insurance claims data and registries — from a diverse group of data streams. In appropriate cases, we've also accepted RWE to support the evaluation of efficacy in product approvals using data from registries, natural history studies and chart reviews to establish a comparison arm in single arm trials in oncology and rare diseases. RWE captured throughout the totality of a product's post-approval lifecycle has been a significant aid in informing both the development of new products and changes to existing products. We're also exploring ways to better harness patient-reported information, such as our recently announced MyStudies mobile application.

The strategic Framework we're announcing today will serve as a roadmap for more fully incorporating RWD and RWE into the regulatory paradigm. The Framework outlines a number of important RWE-related efforts to explore the potential for using RWE to help support approval of new indications for approved drugs or to support or satisfy post-approval study requirements. This new Framework will help the FDA and industry evaluate the potential use of RWE to support regulatory decisions that have visible outcomes for consumers.

Potential advances to be explored under the Framework include the use of RWE and RWE to help support revisions to labeling about drug and biologic product effectiveness or safety, including adding or modifying an indication, such as a change in dose, dose regimen, or route of administration; adding a new population; or adding comparative effectiveness or safety information. The Framework involves the establishment of demonstration projects and stakeholder engagement, as well as the use of internal processes to bring senior leadership input into the evaluation of RWE and promote shared learning and consistency in applying the Framework. We'll also work to develop new guidance documents to assist sponsors interested in developing and using RWE.

For example, earlier this year, we issued guidance on the use of electronic health records in prospective clinical investigations, to support sponsors who want to leverage this data during clinical development. We're developing other guidance documents to advance these opportunities. This includes a new guidance that will address types of evidence that can be used to support drug review decisions.

In implementing this new strategic Framework, we'll work on identifying relevant standards and methodologies for collection and analysis of RWD. This is a key strategic priority that's already actively underway. Our Framework calls on us to develop new guidance on considerations for designing clinical trials that include pragmatic design elements as one tool for generating evidence of effectiveness for regulatory decisions. We'll also evaluate the potential role of observational studies in contributing to the body of evidence for demonstrating drug and biologic product efficacy. The goal is to develop a path for ensuring that RWE solutions are an integral part of the drug development and regulatory life cycle at the FDA.

There's more data available to inform medical decisions than ever before. But we need to provide clear guidance on the appropriate collection and evaluation of this information. This Framework is intended to advance the collection of data that are appropriate, consistent and provide information and knowledge that can better inform regulatory decision-making. For example,

currently used EHRs and medical claims data may not capture all of the data elements needed to answer significant questions of interest. That's why part of our new Framework is to explore strategies for filling the gaps other sources of RWD, which may include the use of mobile technologies, electronic patient reported outcome tools, wearables, and biosensors. Recording individual patient data accurately and consistently while ensuring the utmost privacy will be an important challenge as we aim to shape the future of evidence generation.

This Framework is the culmination of a longstanding effort that's been underway inside the FDA; and it's another milestone in our effort to advance the use of RWD and RWE to better inform patients and providers. Last September, the agency helped sponsor a meeting to discuss a structure for evaluating the use of RWE in regulatory decisions. During this meeting – along with our participation in other public workshops — we heard industry, academia, and patient advocacy groups share new opportunities on the horizon as well as some of the challenges they face with using RWD and RWE.

To advance all of these goals, the FDA has other efforts underway. For example, the agency is funding a project to evaluate the potential of observational RWE to replicate the results of 30 clinical trials from several therapeutic areas. Being able to replicate the findings of trials is a cornerstone of the scientific method. This project should give us greater insight into which RWE methods and trial designs can provide insight into the opportunities and limitations of using these designs in regulatory decisions.

The FDA will continue to engage in projects and programs with academia, patient advocacy groups, as well as organizations like the National Academy of Sciences, Engineering, and Medicine. We've partnered with U.S. agencies such as the Centers for Medicare and Medicaid Services, the Veterans Health Administration and the Centers for Disease Control and Prevention on ways to increase our availability of data. We'll continue to work with international groups such as those in Europe to better understand how similarities and differences between health care systems can advance these efforts.

Through all of this new work, we hope to make better use of the information from patients and providers during the lifecycle of a marketed medical product. Soon, the FDA will have more to say in guidance about how to interpret our evidentiary standard in the context of today's modern informatics and advanced analytics, which provide new openings for the collection of data and the generation of evidence. Today's data comes from a broader variety of sources than ever before. And we have more tools to leverage this information to inform patient care. As we look toward the future, finding ways to collect and apply that evidence will bring us closer to providing better overall health care.

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