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FDA User Fee Reauthorization and the Value of Real-World Evidence

ISSUE BRIEF

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Increasing use of real-world evidence (RWE) in regulatory decision-making has the potential to provide advantages, including more efficient drug development and the ability to collect more robust information about the benefits and risks of new therapies. The result is potentially increased uses of RWE among key stakeholders, including regulators, providers, product developers, health systems, and patients/patient advocates, who are key to facilitating and broadening access to innovative, safe, and effective medical products for patients.

The United States Food and Drug Administration (FDA) utilized RWE in several cases to inform regulatory reviews of medical products, and the Prescription Drug User Fee Act (PDUFA) has provided critical support to advance the use of RWE. The foundation of the user fee programs is the understanding that collaboration and partnerships are essential to improve regulatory science and unlock innovation. User fees have provided resources for the FDA to engage in several multi-stakeholder discussions, including those convened by the Duke-Margolis Center for Health Policy, to identify key RWE policy considerations and gain experience working with this evidence as part of pilot studies and demonstration projects that inform regulatory reviews of medical products.

Congress is currently considering a reauthorization of FDA's user fee authorities that will continue to drive exploration into the use of RWE for regulatory decision-making. The Duke-Margolis Real-World Evidence Collaborative has synthesized input from a range of stakeholders to recommend important opportunities for the use of RWE amid Congress' consideration of reauthorizing FDA user fees. This issue brief considers this stakeholder input and the Center's ongoing work to highlight current opportunities for advancing RWE implementation in support of regulatory decision-making and more.

Prescription Drug User Fee Act Reauthorization and RWE

Since its initial enactment in 1992, PDUFA and related user fee authorizations have provided critical funding to the Agency, which allow the FDA to hire additional staff and develop important programs that have reduced review and development times and advanced the availability of innovative drugs, while maintaining FDA standards for safe and effective medical products. In its current iteration, PDUFA VI, is set to expire on September 30, 2022. The PDUFA VII commitment letter which outlines agreements made between the FDA and the stakeholder community on how user fees will fund a range of actions, has been sent to Congress for approval. Although the House passed its Energy & Commerce Committee's PDUFA VII legislation (H.R. 7667), the Senate Committee on Health, Education, Labor and Pensions has yet to approve its version and is currently considering competing bills–one that includes additional provisions and another that would only authorize the user fees. Given that user fee funding comprises approximately 46 percent of the FDA's operating budget, the expectation is that Congress will find a path to bridge differences and enact this "must pass" legislation.

Important provisions will remain to advance the use of RWE. PDUFA VI and the 21st Century Cures Act (passed in 2016) included a range of initiatives intended to

improve stakeholder engagement and understanding of how and when to use real-world data (RWD) and RWE in medical product development and regulatory decision-making processes. PDUFA VI also supported stakeholder discussions that informed the development of the 2018 "Framework for FDA's Real-World Evidence Program" and a series of guidance documents issued in 2021 and 2022 on key regulatory considerations in the review and evaluation of RWD and RWE.

How User Fee Support Has Addressed the Role and Potential of RWE

In addition to supporting the development of FDA's RWE framework and guidance documents, PDUFA VI provided critical resources for FDA to conduct pilot studies and other analyses that are helping the agency gain experience with RWE. Currently, the FDA is supporting approximately twenty demonstration projects across three buckets: (1) increasing the use of RWE (2) improving RWE study design, and (3) creating and refining RWD and RWE tools. Through these efforts, FDA is gaining key insight into appropriate uses of RWE from exploring important considerations around data quality, to improving study methodologies, and developing statistical tools and evaluation frameworks.

One demonstration project recently highlighted by the FDA was the RCT-DUPLICATE Demonstration. A methods demonstration project, it aims to understand and improve the validity of RWE studies to support regulatory decision-making. Results of the project revealed that RWE studies utilizing fit-for-purpose data, combined with rigorous design and analysis, can result in conclusions like those derived from randomized controlled trials. Continued and enhanced support for such demonstration projects and pilot studies are necessary to continue building on these critical lessons learned.

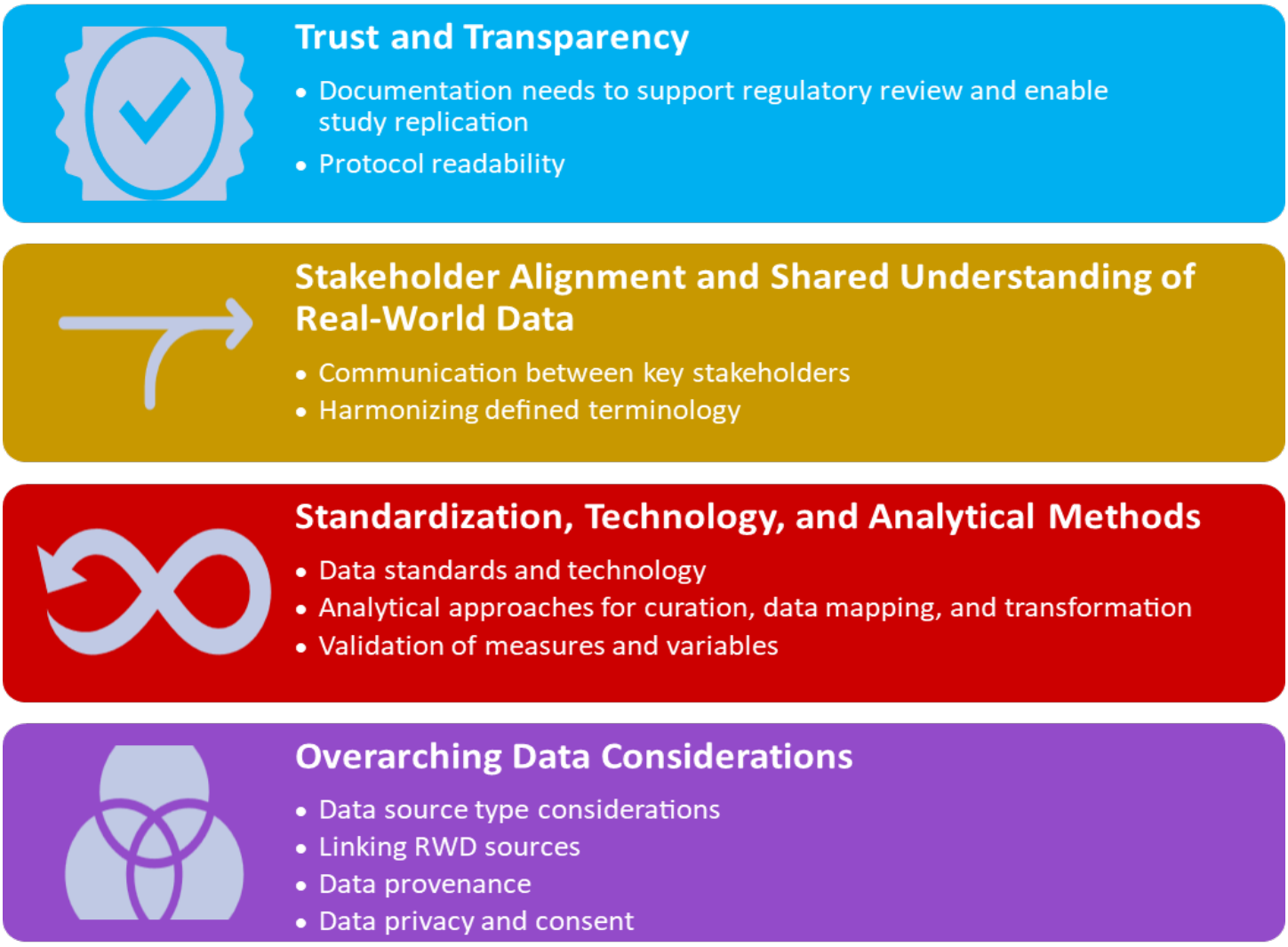
Building on these findings, the Advancing RWE Program, a pilot program described in the PDUFA VII commitment letter, aims to further clarify use cases for RWE in regulatory approvals. Specifically, the pilot program will aid in identifying approaches that meet regulatory requirements, developing agency processes to foster consistent decision-making and shared learning regarding RWE, and promoting awareness around the use of RWE to support regulatory decisions. In 2025, the agency has committed to convening a public forum to discuss case studies, with the intention of revising existing guidance on RWE by 2026. Public sharing of information learned from pilot studies will be an essential element of the Advancing RWE Program to help the broader community gain a better understanding of why and how to effectively consider and use RWE to support decision making. It is important that the user fee reauthorizations pass in a timely fashion not only for the overall health of the FDA, but also to enable this program to obtain generalizable knowledge about the use of RWE in regulatory decision and make it available to the broader stakeholder community.

FDA's Draft RWE Guidance Document Releases Under PDUFA VI

PDUFA VI required FDA to issue draft guidance on how to incorporate RWE into regulatory submissions, building on multi-stakeholder workshop discussions and pilot studies. In late 2021, the FDA released a series of draft guidance documents intended to guide the medical product industry in their endeavors to leverage electronic health records (EHRs), claims, and registry data—three sources of RWD in regulatory submissions. In response, stakeholders submitted comments to these draft guidance documents and the Duke-Margolis Center for Health Policy synthesized and categorized responses into the following thematic areas: 1) trust and transparency; 2) stakeholder alignment and shared understanding of RWD; 3) standardization, technology, and analytic methods; and 4) overarching data considerations themes are illustrated on page 3 in **Exhibit 1**.

EXHIBIT 1

Key Themes Among Stakeholders in Response to FDA's Draft RWE Guidance



This analysis was presented at a public workshop convened by the Duke-Margolis Center for Health Policy's Real World Evidence Collaborative entitled the State of Real-World Evidence Policy on May 12, 2022. At the workshop, RWE Collaborative members discussed key policy recommendations submitted by the Duke-Margolis Center for Health Policy in response to FDA's draft RWE guidance on: EHRs and claims data, registries, data standards, and study considerations encourage furthering RWD and RWE commitments in PDUFA VII, including the importance of standardizing definitions (e.g., defining patient visits consistently across clinical study data platforms and EHRs) and supporting more consistency in the use and consideration of RWE across centers and divisions within the FDA.

Key Next Steps for Enhancing the Value of RWE: Strengthening Partnerships, Engagements, and Collaborations

FDA has been clear that regulatory standards for assessing medical product effectiveness through the deliberation of substantial evidence will not change. Despite substantial progress in considering RWD/RWE to assess medical products for both safety and effectiveness, challenges remain. Challenges include addressing the inherent variability of data sources, quality, and governance of this burgeoning data ecosystem. Addressing these challenges are critical for integrating RWD/RWE into the health care ecosystem yet are only possible through meaningful and intentional stakeholder collaboration and engagement. Notably, over recent years FDA and other public and private stakeholders have witnessed how collaborations and partnerships can help inform the development of FDA's RWE policy. There is also growing interest internationally for collaborations across regulatory authorities to harmonize understanding of concepts and address common challenges for integrating RWE into regulatory processes.

The FDA has made considerable progress in understanding the challenges and opportunities associated with leveraging RWE to drive and support their decision-making. This commitment has brought an unprecedented array of industry, patient, and other health system stakeholders together to engage in meaningful and collaborative discussions to strengthen the use of RWE for regulatory decision-making. Policymakers and other key stakeholder should not miss opportunities to support these meaningful collaborations as the FDA implements PDUFA VII commitments.

Learn More about the Duke-Margolis Center for Health Policy's RWE Collaborative here.

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Disclosures

Dr. Rachele Hendricks-Sturrup reports employment with the National Alliance Against Disparities in Patient Health.