August 14, 2025

The Honorable Martin Makary
Commissioner
US Food and Drug Administration
Silver Spring, MD 20993

Re: Reauthorization of the Prescription Drug User Fee Act; Public Meeting; Request for Comments

Dear Commissioner Makary,

FasterCures at the Milken Institute is honored to provide our response to the Reauthorization of the Prescription Drug User Fee Act; Public Meeting; Request for Comments [FDA–2025–N–0816].

As a nonprofit, nonpartisan think tank, the Milken Institute believes in the power of capital markets to address urgent social and economic challenges, thereby improving lives. Its guiding belief is that societies thrive when they cultivate an educated, healthy workforce, foster transparent and efficient capital markets, and sustain effective social institutions. FasterCures, part of Milken Institute Health, appreciates the opportunity to comment as the FDA, industry, Congress, and stakeholders work toward a Prescription Drug User Fee Act (PDUFA) VIII reauthorization.

FasterCures' mission is to accelerate biomedical innovation and access and strengthen the systems that connect research to patients. Since 2024, we have submitted comments urging practical, near-term steps the FDA and manufacturers can take to reduce inefficiency, improve the evidentiary rigor, and embed patients' lived experience across development and review. Those prior filings focused heavily on two related priorities that we again elevate for PDUFA VIII: **(1) Advancing Community-Based Clinical Research for Better, Faster, More Representative Evidence; and (2) Strengthening Patient Engagement Across the Total Product Lifecycle.**

FasterCures' ENRICH-CT (Enabling Networks of Research Infrastructure for Community Health Through Clinical Trials) networks[1] —now comprising more than 60 organizations across biopharma, community health systems, data/technology firms, and advocacy groups—stand ready to work with FDA to pilot many of these elements: community site readiness tools, workforce training curricula, data interoperability templates, and pragmatic monitoring models. We invite the FDA's continued participation and believe PDUFA VIII resources could accelerate field testing and scale.

With science advancing rapidly and health care delivered across increasingly diverse settings, PDUFA VIII is the right moment to align user fee commitments with targeted resourcing and clear performance goals; the resulting operational improvements ripple outward across the biomedical innovation ecosystem.

Summary of Recommendations:

I. **Make Regulatory Priority for Increasing Community Proximity of Clinical Trials and Research:** We urge that PDUFA VIII require FDA to produce an integrated, practical companion to its existing decentralized-trial and real-world-evidence guidance documents—mapping key design questions to specific regulatory provisions—to make it easier for sponsors to run pivotal drug and biologic studies in the community settings where most patients actually receive care.

II. **Enforce Community-Based Research Infrastructure with Practical and Streamlined Regulations and Support:** We ask FDA to build on its recent trial-modernization efforts by issuing harmonized, risk-proportionate guidance—coupled with master-contract templates and new efficiency incentives—that aligns human-subject protections across agencies, streamlines low-risk study requirements, clarifies community-clinician roles, and actively rewards sponsors who conduct high-quality, patient-accessible trials in everyday care settings.

III. **Build Data Connectivity and Accountability: From Community Sites to Regulatory and Coverage Decisions:** We urge FDA to embed in PDUFA VIII a joint FDA–CMS workplan that pilots secure linkage of community-generated real-world data to regulatory and payment systems—supplemented by concrete case studies showing how such data inform labeling, safety monitoring, and coverage—to accelerate the translation of evidence from point of care to patient access.

IV. **Elevate Patient Expertise as Core Evidence Input for Advisory Committee Meetings:** We ask that PDUFA VIII require every therapeutically focused FDA advisory committee to include voting patient and patient-organization representatives and employ standardized PFDD-based question sets, while encouraging sponsors to embed early community input in trial design, so that patient expertise consistently informs both development and regulatory benefit-risk decisions.

V. **Ensure Continuity of Patient Voice Beyond Approval:** We request that PDUFA VIII commits FDA to piloting continuous, structured patient-reported outcome collection in post-approval studies—linked where possible to CMS claims data—and to issuing clear, multilingual summaries of advisory-committee outcomes, major safety updates, and annual performance reports, thereby sustaining patient engagement across the entire product life cycle.

Advancing Community-Based Clinical Research for Better, Faster, More Representative Evidence

I. Make Regulatory Priority for Increasing Community Proximity of Clinical Trials and Research

Today, most US patients, especially those in rural counties and socioeconomically disadvantaged neighborhoods, receive care in community hospitals, federally qualified health centers, and local practices rather than large academic medical centers.[2] Yet, regulated drug and biologic clinical trials remain concentrated in those academic hubs, producing data that may not fully generalize to populations with different comorbidities, access constraints, or demographic profiles. Analyses in oncology show that the most socially vulnerable counties are markedly less likely to host cancer clinical trials,[3] and enrollment shortfalls are common: as many as 85 percent of trials fail to meet accrual targets on schedule, with ~80 percent experiencing recruitment delays—operational problems that are exacerbated when participation is geographically narrow.[4]

PDUFA VIII should stipulate that expanding the geographic and care-setting footprint of clinical development is a goal for research sponsors. Evidence used to support approval should increasingly be generated in (or linked to) the settings where products will be used. The FDA can reinforce this priority in guidance document development.

Over the last several years, the FDA has issued a suite of guidance documents that, taken together, provide the regulatory building blocks for shifting meaningful portions of trial activity out of single tertiary centers and closer to where patients live. These include the guidance on conducting clinical trials with decentralized elements (telehealth visits; home testing; remote sensor monitoring; mobile units; local laboratory and provider office involvement; electronic informed consent; direct investigational product distribution), the guidance on assessing electronic health records and medical claims data as sources of real-world data (RWD) to support regulatory decisions, and the broader considerations for RWD/real-world evidence (RWE). Stakeholders consistently report that these documents do not conflict; however, they can be challenging to apply in combination, especially when designing randomized clinical trials (RCTs) embedded in routine practice.[5] In addition, examples of new product approvals that leverage the RWD/RWE, beyond external control, labeling expansion, and post-marketing studies, and decentralized clinical trials are still too few for product sponsors to risk more trials in community-based settings.

In comments on FDA's draft guidance on RCTs integrated into clinical practice, **FasterCures urged the agency to present these documents as a coherent "how-to" package and to cross-reference the operational flexibilities they contain.** A concise implementation companion (even a dynamic web landing page) that maps common design questions (such as Where may consent occur? How can telehealth supervision be documented? What constitutes acceptable data provenance for community EHR extracts?) to specific sections in guidance would reduce perceived regulatory risk and accelerate adoption of community-proximal models. We recommend including the development of such a compendium as a PDUFA VIII commitment deliverable.

II. Enforce Community-Based Research Infrastructure with Practical and Streamlined Regulations and Support

The FDA has taken several important steps in recent years to bring regulated clinical research closer to the communities in which patients live and receive care. Guidance documents referenced above and the creation of the CDER Center for Clinical Trial Innovation all signal the agency's willingness to pilot solutions that reduce geographic, logistical, and administrative barriers to participation. These moves are widely welcomed, yet the day-to-day experience of investigators and sponsors shows that **additional, well-targeted efforts would further streamline study start-up and oversight without compromising participant protection or data integrity.**

A first area for continued progress is the alignment of human subject-protection requirements across oversight bodies. Divergent interpretations of waiver provisions, exempt categories, and single-IRB mandates by the FDA and the Office for Human Research Protections can lead institutions to duplicate reviews even when a central IRB has already approved a protocol, expending effort that adds little substantive value. Clear, harmonized guidance that reconciles these interpretations would reduce confusion and shorten activation timelines. Second, greater use of risk-based oversight is needed. Because "minimal-risk" research remains poorly defined in practice, many sponsors default to the most conservative documentation, monitoring, and safety-reporting standards for all studies, including those that evaluate marketed therapies with well-established profiles. Adopting explicit, proportionate expectations would relieve low-risk trials of unnecessary burdens while preserving rigorous scrutiny of higher-risk investigations.

Moreover, data collection policies could be modernized to focus on critical elements. Streamlined case report forms, limited core datasets, and electronic documentation of essential regulatory records would lighten the load on study teams and reduce analytical noise. In parallel, FDA can continue clarifying how local clinicians, pharmacists, and community-health workers may contribute to FDA-regulated trials without assuming extensive regulatory or legal liabilities; fit-for-purpose Good Clinical Practice training modules tailored to these providers would encourage broader participation. Remote and decentralized monitoring tools complement these changes. Still, sponsors remain uncertain about the record-keeping obligations that accompany their use, especially for investigational products with long marketing histories and well-characterized safety. Further guidance on simplified

drug-accountability procedures would address that hesitation. Similarly, protracted contract negotiations are routinely cited as the single biggest obstacle to launching multisite studies. FDA's endorsement of master contracts and template agreements that suit adaptive, platform, or other innovative designs would significantly shorten start-up and enable direct comparisons of new therapies without excessive reliance on placebo arms.

While the FDA has issued a series of guidance documents that encourage pragmatic designs, real-world evidence integration, and decentralized approaches, sponsors often remain risk-averse and revert to familiar practices. **The agency could consider formal incentive mechanisms**—analogous to those it already employs for technological innovation—explicitly aimed at efficient, community-accessible, high-quality trials. Existing models, such as CDRH's Total Product Lifecycle Advisory Program, the START Pilot for rare disease studies, and the CMC Development and Readiness Program, demonstrate that targeted regulatory engagement can meaningfully shift sponsor behavior. **A comparable initiative devoted to operational efficiency and inclusivity, built on internationally recognized good-trial-practice principles, would help embed a culture of streamlined research across the biomedical enterprise.**

III. Build Data Connectivity and Accountability: From Community Sites to Regulatory and Coverage Decisions

Evidence generated in community settings has the greatest value when it is efficiently integrated into regulatory review, labeling, post-marketing studies, and coverage determination. FDA's RWD/EHR guidance provides a framework for assessing data fitness. What stakeholders need now are practical examples demonstrating how community data can inform regulatory decision-making. In addition, FasterCures has recommended that FDA and the Centers for Medicare & Medicaid Services (CMS) pursue a staged interoperability agenda—a shared "digital nervous system"[6]—linking trial, post-market studies, and longitudinal claims/clinical data (Medicare, Medicaid, CHIP, Marketplace) to shorten the path from approval to access, reinforce signal detection, and inform payment models. Including an FDA–CMS data connectivity workplan in the PDUFA VIII commitments would set expectations, resource the technical work, and create a transparent forum for multi-stakeholder learning.

Strengthening Patient Engagement Across the Total Product Lifecycle

IV. Elevate Patient Expertise as Core Evidence Input for Advisory Committee Meetings

The FDA has spent decades building a patient engagement architecture, including the Patient-Focused Drug Development (PFDD) meetings, the Patient Preference Initiative, the Patient Engagement Advisory Committee, the FDA Patient Council, and the Patient Representative Program. Through these programs, individuals with lived experience contribute to advisory activities. Yet in many formal drug and biologic advisory committee meetings, patient input remains intermittent, non-voting, or narrowly framed. Patients are experts in living with their conditions, and their insights are critical to contextualizing benefit-risk. **PDUFA VIII should solidify patient participation as a standing component of advisory committee meetings rather than an ad hoc addition.**

We recommend that each therapeutically focused advisory committee include, by default, at least one trained individual patient representative and one representative of a qualified patient organization as standing members, with voting privileges, except where conflicts arise or the committee's scope is purely technical (e.g., manufacturing). Establishing clear expectations in committee charters will improve consistency, reduce post-decision controversy, and ensure lived experience informs evidence interpretation.

The first PFDD guidance, *"Collecting Comprehensive and Representative Input,"* outlines the major domains of patient experience that matter for benefit-risk assessment: symptoms and their day-to-day impact, disease trajectory, treatment burdens, outcome preferences, and how patients weigh potential benefits against risks. In advisory committee meetings, however, these domains are not consistently or systematically elicited. FasterCures has

recommended that the FDA develop standardized, scientifically grounded question sets aligned to PFDD domains for use across advisory committees and in sponsor briefing packages. Structured elicitation tools would help committees compare patient perspectives across products and indications, reduce reliance on anecdote, and surface tradeoffs that matter in labeling discussions.

Because no single person can represent an entire patient community, we also recommend that the FDA routinely pair an individual patient representative with a vetted patient-organization representative who can speak to aggregated community experience and preference data. This dual-input model broadens perspective and helps ensure that the full diversity of patient priorities—age groups, severities, comorbidities—is reflected in deliberations.

The same engagement principles that argue for patient representation in advisory committees apply upstream in development. **FasterCures urges the Agency to tie operational flexibilities, such as local healthcare provider involvement, telehealth, home testing, and EHR-enabled data capture, to the overarching objective of increasing patient access to clinical trials and research**. When sponsors solicit community input early on, schedules that work, outcomes that matter, language and literacy needs, and supports such as transportation or childcare trials become more feasible and more relevant.

V. Ensure Continuity of Patient Voice Beyond Approval

Patient engagement should not end with an approval. Community-based research infrastructure, such as local EHRs, registries, and patient-reported outcome tools, can feed post-marketing studies that matter to patients in the settings where they receive care. FDA's RWD/EHR and RWE guidance already contemplate regulatory use of such data. **PDUFA VIII's commitment to pilot for capturing structured patient-reported data in post-approval studies (coordinated, where possible, with CMS longitudinal claims and utilization data) would demonstrate how lifecycle learning can incorporate patient voice continuously**.

Plain-language and multilingual communication are critical to sustaining engagement. We encourage the FDA to include in PDUFA VIII a commitment to produce patient-friendly summaries—translated where needed—of advisory committee outcomes, major safety communications, and annual PDUFA performance updates relevant to patient participation and diversity. Sponsors can assist by supplying lay summaries as part of submission packages; FDA's amplification lends credibility and reach.

Integrating the Two Domains Under PDUFA VIII

Community-proximal evidence generation and lifecycle patient engagement are mutually reinforcing. Studies conducted in the settings where patients live improve representation, (1) when those patients and their advocacy organizations help shape protocols, burdens fall and accrual improves; (2) when the resulting data are considered in advisory meetings that include standing patient members using structured PFDD question sets, benefit-risk discussions become more grounded in lived experience; and (3) when post-market data flows back from community care, potentially through an FDA–CMS interoperability "digital nervous system," labeling, safety monitoring, and coverage decisions can adapt more quickly to real-world use. These linkages are achievable under current law; what is needed is alignment, resourcing, and accountability—exactly what PDUFA user fee commitments are designed to provide.

If we want evidence that applies to all who will rely on a therapy, we must generate it in the communities where those patients receive care, and we must welcome their voices when that evidence is interpreted. Community-based clinical research and robust patient engagement across the total product lifecycle are not parallel aspirations. They are interdependent components of a modern, learning, equitable biomedical ecosystem. PDUFA VIII can knit

them together through targeted commitments that clarify expectations, reduce operational friction, and make progress visible. FasterCures and the broader Milken Institute Health community look forward to partnering with the FDA, manufacturers, community health providers, and patient organizations to implement these recommendations for the benefit of all patients.

Sincerely,

Esther Krofah
Executive Vice President, Health
Milken Institute

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