MILKEN INSTITUTE

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Access Point:

Trends in Clinical Trials Transformation #3

Introduction

The FasterCures *Access Point* brief examines how emerging trends, organizations, and initiatives are innovating to improve clinical trial access and efficiency. Released quarterly, *Access Point* highlights breakthrough technologies, regulatory and industry advancements, and innovative partnership models shaping the future of clinical research. *Access Point* provides new market entrants and their established health ecosystem partners with the strategic intelligence needed to navigate an evolving clinical trial landscape and translate real-world insights from their data into meaningful research impact.

Clinical Trials in a Time of Policy Revolution

The clinical research landscape is experiencing a significant transformation driven by changes to policy regarding how evidence is generated, evaluated, and translated into patient access and value. Regulators are signaling greater openness to real-world data (RWD) and streamlined clinical trials to support decision-making, while federal support for clinical research is becoming inconsistent and unpredictable. These shifts are creating new impetus for data partnerships, digital health integration, and faster approval. At the same time, broader health and social policies—including funding disruptions, insurance instability, and changes to vaccine review—are directly affecting who can access trials and therapies and whether research can proceed uninterrupted. Together, these shifts reflect a clinical trial policy revolution, requiring research stakeholders to adapt quickly while safeguarding system integrity.

Evolving Approaches to Evidence and Review

FDA Eliminates Blanket Patient-Level Data Requirement for RWE in Medical Device Applications

In final guidance related to the use of real-world evidence (RWE) for regulatory decision-making, the Food and Drug Administration (FDA) revised its requirement that all medical device applications provide patient-level data. Previously, FDA mandated the inclusion of such data, which complicated the use of registry, claims, and electronic health record data in marketing applications, despite significant growth in the volume of real-world data (RWD) and the value of population-level insights that can be generated from them.

The agency will now assess the quality and reliability of RWE in medical device applications on a case-by-case basis. Despite increases in trust, data quality, and dedicated FDA programming on RWE, its use in regulatory applications has been tepid over the past decade; RWE has been used in only 35 drugs and biologics applications and 250 medical device authorizations since 2016. FDA and its partners expect this new approach to unlock insights from a wealth of available RWD, ultimately accelerating therapeutic access. However, it may place additional strain on review teams within the Center for Devices and Radiological Health (CDRH), which must apply this new guidance on a case-by-case basis in the wake of staffing cuts that have, in part, led to extended review timelines, fewer market authorizations for devices, and increased uncertainty from sponsors about FDA response.

Is FDA's Plan to Eliminate Requirement of Two Controlled Clinical Trials an Opening for RWE?

FDA is expected to lower the number of well-controlled clinical trials required to support medical product applications from two to one. In an interview, FDA Commissioner Marty Makary signaled that the agency will roll out policies regarding this change over the next three to six months. With this change, RWE could play a larger role in the medical product review process as RWD is used to supplement single pivotal trials to demonstrate effectiveness and safety. In the wake of this news, experts have commented that the change occurred outside of established policymaking pathways and may impact evidentiary standards and drug safety. Although FDA already approves drugs based on single trials with confirmatory evidence of effectiveness in many cases—over half of drugs approved in 2022 used just one pivotal trial—the formal policy change could standardize the use of RWE as supplemental evidence and reduce the overall cost of conducting research, potentially accelerating RWE's acceptance and integration into regulatory decision-making.

FDA Details Common Reasons for Rejection of RWE in Regulatory Applications

During a public meeting about FDA's efforts to support industry in generating regulatory-grade RWE, FDA officials described common reasons for denied admission into FDA's Advancing Real-World Evidence Program. The program offers a pathway for sponsors, if selected, to interact with experts from across the agency to better understand how to incorporate RWE that meets regulatory decision-making standards into their applications. Commonly cited reasons for rejecting applications include (1) the heterogeneity in patient populations and evolving treatment plans made it difficult to interpret study data; (2) the study provided supportive, not primary, evidence for product review; and (3) the study was deemed to better fit another FDA review pathway. Overall, FDA officials emphasized that early alignment on study design, data quality, and regulatory intent is critical for sponsors seeking to use RWE as decision-grade support for medical product review.

Reduced FDA Reliance on Expert Advisory Committees Increases Concern About Agency's Decision-Making Criteria

In 2025, FDA held significantly fewer advisory committee meetings than in recent years and diverged from advisory committee recommendations on nearly half of the cases it reviewed, a notable departure from historical patterns. This shift has raised concerns about reduced transparency and predictability in FDA decision-making, as industry stakeholders and the general public have fewer opportunities to understand how the agency is evaluating complex clinical benefits and risks. It also heightens uncertainty among sponsors about the application of regulatory standards amid broader policy changes under new leadership at the Department of Health and Human Services and FDA, including limits on industry participation and discussions about phasing out advisory committees for individual drug applications altogether.

Proposed Shifts in Vaccine Review Approach Could Limit Access, Former FDA Heads Say

Former FDA commissioners warned that proposed changes to the agency's vaccine approval policies, such as higher evidence thresholds, pregnancy-specific requirements, and data from longer outcome-based trials, could undermine the long-standing regulatory framework that has supported timely vaccine availability and innovation. They argued that more burdensome trial requirements would impede development, raise costs, and erode public trust, ultimately reducing vaccine availability and affordability. The debate over FDA's approach to vaccine review occurs amid a controversial overhaul of the US childhood immunization schedule that has dramatically reduced the number of vaccinations recommended for children and limited access to vaccines for some conditions to high-risk children.

The former FDA heads expressed particular concern that the new review approach could delay updates to vaccines for rapidly evolving viruses responsible for global pandemics and make regulatory processes less predictable for sponsors. Sponsors such as Pfizer, however, state that despite these changes, they intend to continue their long-term investments in their vaccine pipelines.

Advancing the Use of RWD, Digital Health, and AI

CMS and FDA Announce Plans to Test New Model for Technology-Supported Care and Accompanying RWE Generation

In December 2025, the Centers for Medicare & Medicaid Services (CMS) and FDA announced the initiation of two complementary pilots that, by offering stable clinical and reimbursement pathways, will encourage and test the use of health technology in real-world settings to manage chronic diseases. FDA's CDRH will select 40 digital health tools that have not yet been cleared for participation in its Technology-Enabled Meaningful Patient Outcomes (TEMPO) pilot, which connects to the newly available CMS Advancing Chronic Care with Effective, Scalable Solutions (ACCESS) reimbursement model. The selected tools will span therapeutic areas and will be used by patients in outpatient settings under the supervision of a clinician who can receive up to $100 per patient referred to the ACCESS program.

FDA also expects that participating manufacturers will leverage this pilot opportunity to collect RWD on the use of their products to inform FDA's eventual review, acknowledging that "under certain circumstances, RWD may be used to generate RWE that can help inform or augment FDA's understanding of the benefit-risk profile of devices at various points in their life cycle." CMS did not take a position on RWD's potential within the context of the pilots but released guidance earlier in 2025 on the critical elements of study protocols that rely on RWD for items or services seeking a National Coverage Determination.

FDA Priority Voucher Pilot Signals Focus on Faster Approvals and Growing Importance of Data Partnerships to Demonstrate Product Value

FDA's first approval and proactive priority voucher issuance under the new National Priority Voucher Pilot Program signal a focus on faster approvals for high-impact therapies that target national priorities and unmet medical needs. However, the program has faced criticism that faster approval may lead to politicized review and perceived lower standards of evidence, and members of Congress have expressed concern that FDA may be acting outside its authority.

For new indications in the context of the voucher program, RWD on therapeutic access and concordance may help identify unmet needs and strengthen confidence that trial benefits will translate at scale in real-world settings. As speed and proof of value become central to market access and regulatory success, data partnerships may play an increasingly important role in shaping regulatory and market strategies for pharmaceutical companies.

The Regulatory Science Effort to Make RWD Decision-Grade

FDA has issued a request for proposals to advance RWD methods that support evidence generation and regulatory decision-making. In its 2026 Broad Agency Announcement, the agency emphasizes the needs to improve observational study design, data quality, and methods to assess whether RWD are fit-for-purpose in RWE generation. This initiative reflects a broader policy push to strengthen the scientific foundations of RWD use, recognizing that data sources such as electronic health records, registries, and claims can provide valuable insights in both clinical and regulatory decision-making if collected and analyzed with validated methodologies.

This new announcement connects to contemporary and historical efforts to increase quality and trust in RWE for decision-making, including FDA's Advancing RWE Program and related grant awards, which show a trend toward proactive engagement with sponsors on the topic, as well as an interest in lowering barriers to the use of RWE in regulatory submissions.

FDA Announces Changes to Oversight of AI in Trials and Care

These policy developments are contextualized by the FDA's release of guidance on the use of AI in clinical trials for drugs and biologics and the development and marketing of AI-enabled medical devices. This regulatory momentum coincides with Anthropic's Claude integration with ClinicalTrials.gov to support research operations, as well as Anthropic's release of Claude for Healthcare and OpenAI's release of ChatGPT Health, which are chatbots that allow users to upload their medical records to obtain more personalized answers to medical questions.

White House Blocks Enforcement of State AI Regulations, Favors National Framework

A recent executive order aims to preempt state-level AI regulations and establish a single national framework for AI governance, which could centralize authority over health AI tools and limit the ability of individual states to impose stricter safety or transparency standards for the use of AI tools in care delivery and trials. By blocking enforcement of state AI laws and creating a federal task force to challenge those inconsistent with the federal framework, the executive order impedes states' capacity to protect patient data and privacy. Policymakers frame this movement toward federal preemption as necessary to avoid a patchwork of conflicting rules that could slow innovation and complicate the deployment of AI. Critics argue that diminishing state authority may weaken oversight mechanisms for health AI, potentially leaving gaps in protections around bias, accountability, and patient safety.

Policy Impacts on Trial and Therapeutic Access

NIH Funding Cuts, Now Blocked, Have Impacted More Than 74,000 Clinical Trial Participants

A new *JAMA* report indicates that changes in funding policies at the National Institutes of Health (NIH) led to the cessation of financial support for 383 clinical studies between late February and mid-August 2025, directly affecting more than 74,000 people enrolled in these trials. Many of the affected studies were testing treatments for serious conditions such as cancer, heart disease, brain disease, and infectious diseases. Because funding stopped abruptly, some participants lost access to medications or ongoing monitoring, while other trials were paused or ended with no guarantee of data publication, undermining both access to the trial and the collection of data to support future therapeutic access.

Subsequent federal court decisions found that this mass termination of grant funding violated federal law because NIH failed to follow required administrative procedures and acted beyond its statutory authority. Although some studies were eventually allowed to resume after court orders, judges acknowledged that the interruptions had already caused irreversible harm, including loss of participants' access to experimental therapies, disrupted data collection, and damage to research infrastructure.

The ACA Subsidy Debate Threatens Patient Access to Trials and Therapeutics

Congress is deadlocked over whether to extend enhanced Affordable Care Act (ACA) premium tax credits that expired at the end of 2025, with the House passing a temporary three-year extension and the Senate still undecided. Without these subsidies, millions of Americans are facing dramatic premium increases, with 4.8 million ultimately expected to drop insurance coverage altogether. Loss of coverage would directly interrupt access to essential therapies, including ongoing treatments for cancer, autoimmune disorders, and rare diseases, because patients may be unable to afford the medications or specialist visits needed to safely continue therapy. Patients without insurance are also less likely to enroll or remain in clinical trials because consistent coverage is often required to access trial-related care, monitor treatment safety, and manage side effects. Gaps in insurance coverage can also force participants to drop out, which can impede study progress.

In Drug Policy Overhaul, EU Proposes Shorter Market Exclusivity Period, Opening Door for RWD Collaborations

The EU has reached a provisional agreement on a sweeping pharmaceutical policy overhaul that could reshape how drugmakers think about trial speed, access, and RWE. By shortening baseline market exclusivity and tying extensions to factors such as unmet medical needs and broad patient access, the new framework aims to boost the availability of innovative therapeutics that provide substantial clinical benefits over existing products. Further, it may create new opportunities for health-care data partnerships with drugmakers that may be increasingly interested in RWD platforms that deliver population-level insights to identify and address unmet medical needs. If approved, the overhaul could accelerate data partnerships to better define product value, improve access, and extend market exclusivity.

About Us

The Milken Institute is a nonprofit, nonpartisan think tank focused on accelerating measurable progress on the path to a meaningful life. With a focus on financial, physical, mental, and environmental health, we bring together the best ideas and innovative resourcing to develop blueprints for tackling some of our most critical global issues through the lens of what's pressing now and what's coming next.

Milken Institute Health bridges innovation gaps across the health-care continuum to advance whole-person health throughout the lifespan by improving healthy aging, public health, biomedical science, and food systems.

The Milken Institute's FasterCures is working to build a system that is effective, efficient, and driven by a clear vision: patient needs above all else. We believe that transformative and life-saving science should be fully realized and deliver better treatments to the people who need them.