



Modernization of the Clinical Trials Framework

Center Forward Basics

March 2026

Center Forward Basics

Center Forward brings together members of Congress, not-for profits, academic experts, trade associations, corporations and unions to find common ground. Our mission: to give centrist allies the information they need to craft common sense solutions.

Key Definitions:

- **Institutional Review Boards (IRBs):** An IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects for ethical considerations. IRB approval is required by the Common Rule as well as by other regulations.
- **Real-World Evidence:** Data relating to patient health status and/or the delivery of health care routinely collected outside of a clinical trial from a variety of sources (i.e. information from electronic health records, claims, or registries).
- **Investigational New Drug (IND) Application:** A request for authorization from the Food and Drug Administration (FDA) to administer an investigational drug or biological product to humans.
- **Prescription Drug FDA User Fee Amendment (PDUFA):** The Prescription Drug User Fee Act (PDUFA) was created by Congress in 1992 to address persistent funding shortfalls at FDA. It

Overview

Clinical trials are studies in which researchers assign participants one or more interventions to evaluate their effects on health-related biomedical or behavioral outcomes. Often, the intervention is investigational, which means it is not yet approved for doctors to prescribe to patients, while some Clinical trials study approved therapies.

Participants in clinical trials may choose to enroll for a variety of reasons. One common reason is to receive the newest, most cutting-edge treatment when other treatment options have failed or stalled. This can be a source of hope for individuals with rare diseases, aggressive forms of cancer, or other diagnoses with limited treatment options.

Clinical trials are characterized into four phases. Each phase seeks to answer different questions about the safety and efficacy of an intervention. Phase 1 trials are typically small, with anywhere from a few to a few dozen participants. These trials evaluate drug safety by monitoring for serious side effects. Phase 2 trials enroll more participants and refine which dosage will provide the most effective response while minimizing adverse reactions. Phase 3 trials are typically designed to definitively answer a question, such as whether a new drug is safe and sufficiently effective to be approved by regulatory agencies. Phase 4 trials occur after a treatment has been approved and can continue to monitor safety, effectiveness, risks, benefits, and optimal use in the general population.

Current Regulatory Framework

The [Federal Food, Drug, and Cosmetic \(FD&C\) Act](#) of 1938 is the foundational U.S. law authorizing the FDA to oversee the safety, efficacy, and labeling of food, drugs, medical devices, cosmetics, and tobacco. The Act has been amended numerous times, but the most consequential amendment for modern trials was the [Kefauver-Harris Amendments](#) of 1962, which required drug manufacturers to demonstrate not only safety but also effectiveness through “adequate and well-controlled investigations.” [The National Research Act](#) of 1972 mandated **Institutional Review Boards (IRBs)**, providing further oversight and protection for clinical trials and research subjects. Today, these laws continue to loom large in guiding the FDA’s mission.

More recently, the 2016 [21st Century Cures Act](#) was a bipartisan effort to accelerate medical product development, modernize clinical trials, and foster innovation. The Act sought to alleviate some of the administrative burdens prolonging the start of clinical trials by streamlining human subject research protection across the Department of Health and Human Services (HHS), and increasing the ability to use **Real-World Evidence** to support study conclusions. These efforts align regulations and consolidate IRBs to make multi-site and cooperative research projects easier, while avoiding regulatory delays and

duplicative efforts.

For further regulatory context, [Title 21 of the Code of Federal Regulations](#) governs food and drugs within the United States under the FDA. [Section 50](#) governs the protection of human subjects in clinical trials, mandating informed consent, upholding basic ethical principles, and providing safeguards for vulnerable populations, such as children, in FDA-regulated research. Other sections, such as [Section 312](#), detail **Investigational New Drug (IND) Application** requirements, including sponsor/investigator responsibilities and safety reporting.

Updated regulations can also come in the form of provisions attached to the **Prescription Drug FDA User Fee Amendment (PDUFA)** reauthorizations, which occur every 5 years. For example, provisions within 2022's PDUFA VII reauthorization require study sponsors to submit a **diversity action plan** for phase 3 or pivotal studies of new drugs, provides guidance on decentralized clinical trials, and more. These are just a few of the most important sections that govern clinical trials, creating a complex web of regulations, ethical guidelines, and protections for human subjects to which researchers must adhere.

Look Ahead

Innovations in digital technology, emerging methodological practices, and evolving incentive structures have prompted the FDA to reconsider traditional frameworks, creating pressure to modernize regulation and guidance in ways that preserve patient safety while fostering flexibility, inclusivity, and scientific advancement.

Although it may not be a one-size fits all approach, Community-based clinical trials (CBCTs) can enable faster, more efficient studies by conducting them primarily through primary-care physicians, community health centers, and other local outpatient facilities for certain trials that do not require a specialized center. Some advocates for updated CBCT regulations have called for clearer guidelines on how study investigators may provide oversight of local health care providers and other study staff by ensuring that those staff are appropriately qualified and trained for their trial-related activities through Title 21. This could include confirming proper education and qualifications, meeting state licensing requirements, and more.

Another potential area for modernization is the regulatory framework for offering financial support to patients participating in clinical trials. Currently, clinical trials may provide coverage of the direct trial costs, but offering additional financial support for personal expenses associated with participation in a clinical trial (e.g. travel costs) may currently be overly complex or blocked by financial rules. Some lawmakers sought to encourage participation in CBCTs and to make participant compensation easier through the 2025 [Clinical Trial Modernization Act](#). The Act would also allow cost-sharing by a drug or device manufacturer in clinical trials and ensure that payments people receive for participating in clinical trials are not counted as taxable income. Proposals for cost-sharing, and amendments to other financial rules must be carefully considered for any unintended consequences before passage.

Other ideas for reform include updating best practices for using AI to assist with data analysis and collection, integrating datasets, improving IRB and contracting processes, enhancing the use of electronic health records (EHRs) in research, developing guidelines for fully virtual participation models, widely sharing trial results in ways that promote accessibility while safeguarding patient privacy, and increasing collaboration among government agencies, industry, academia, and patients. These efforts are spearheaded by partnerships with independent organizations, such as the [Duke-Margolis Health Policy Institute](#) and the [Clinical Trials Transformation Institute](#) (CTTI), which produce research and provide recommendations to improve access, diversity of trial participants, and modern trial design. Cross-sector collaboration will be key to making U.S. clinical trials more efficient, accessible, technologically advanced, and globally competitive while maintaining rigorous standards for safety and scientific integrity.

authorizes FDA to collect user fees from entities that submit human drug applications for review or have approved products. Authorization to collect fees has to be renewed every 5 years and contains negotiated commitments from both industry and the FDA, such as standardized review timelines.

- **Diversity Action Plan:** Statutorily mandated plans from drug sponsors indicating planned demographic targets for pivotal clinical trials, along with justification for those targets and plans to meet stated enrollment targets.

Link to Additional Resources

- American Cancer Society: [Clinical Trial Modernization Act Fact Sheet](#)
- American Cancer Society and Allied Organizations: [CTMA Support Letter](#)
- AstraZeneca: [Clinical innovation](#)
- AstraZeneca: [Our commitment to clinical trial transparency](#)
- AstraZeneca: [Investing in the Future Through Clinical Trials](#)
- Biotechnology Innovation Organization (BIO): [Enhancing FDA Gold Standard](#)
- Clinical Leader: [Sponsors Collect Too Much "Non-Essential" Data, Say Tufts And TransCelerate](#)
- Clinical Trials Access Collaborative: [Clinical Trials Access Collaborative](#)
- Clinical Trials Transformation Initiative: [Modernizing Trials Together](#)
- Duke-Margolis Institute: [Clinical Trials Modernization](#)
- FDA: [CDER Center for Clinical Trial Innovation \(C3TI\)](#)
- Food and Drug Administration: [80 Years of the Federal Food Drug and Cosmetic Act](#)
- Friends of Cancer Research: [Advancing Cancer Research Through Collaboration](#)
- Friends of Cancer Research: [Seamless Clinical Trial Designs in Rare Cancers: Leveraging Operational and Adaptive Strategies to Accelerate Drug Development](#)
- Friends of Cancer Research: [Multi-Regional Clinical Trials: Addressing Standard of Care Variability](#)
- Milken Institute: [Enabling Networks of Research Infrastructure for Community Health Through Clinical Trials \(ENRICH-CT\)](#)
- Milken Institute: [The Future of US Biomedical Research and Innovation: Recommendations for Action](#)
- Multi-Regional Clinical Trials Center: [Defining and creating ethical, actionable, and practical solutions for global clinical trials.](#)
- NIH: [Learn About Studies](#)