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Operation Trailblazer Launches to Restore U.S. Leadership to Clinical Trials

On June 22, the U.S. Department of Health and Human Services (HHS) launched an "unprecedented" department-wide effort, Operation Trailblazer, to bring the world's clinical trials back to the HHS is partnering with the U.S. Food and Drug Administration (FDA), the National Institutes of Health (NIH), the Advanced Research Projects Agency for Health (ARPA-H), the Office of the Inspector General (OIG), and other relevant HHS components. In particular, HHS noted that the impetus for this is in part from a warning from the National Security Commission on Emerging Technology that the U.S. has a "critical window, measured in years, not decades, to act decisively or risk ceding military, geopolitical, and economic advantages to China." For clinical trials, China's global share of early phase clinical studies (Phase I) surpassed the U.S. in 2021, and its total registered clinical trials surpassed the U.S. in 2024, representing 39% of global clinical trials.

FDA is soliciting comments on a proposal to develop a pilot program to shorten the time from drug identification to first-in-human Phase I (typically healthy subjects given an investigational product) and clarifying regulatory expectations for sponsors that could reduce early trial timelines by six to 12 months. FDA already issued draft guidance identifying when one high-quality clinical trial with confirmatory evidence could support a new drug approval.

In addition, FDA plans to offer additional resources to accelerate and modernize its investigational new drug (IND)-phase to late-phase pivotal clinical trials including:

- Phase I IND Navigator Webpage (consolidated resources and practical examples)

- Phase I IND Chemistry, Manufacturing, and Controls (CMC) Webpage (clarify key CMC requirements for first-in-human INDS to reduce excessive data submissions, which may save six to 12 months of development time)
- Phase I Contact Center (real-time responses and agency engagement)
- Quantitative Systems Pharmacology-Based Dose Section for Minimum Anticipated Biological Effect Level (new approach methodologies (NAMs) like organ-on-a-chip instead of animal studies, AI-powered models, and real-world data to facilitate dose selection)
- Master Protocols to evaluate multiple diseases, conditions, or disease subtypes in one framework or to evaluate multiple drugs and eliminate duplicative infrastructure, data collection, and evidence generation.

NIH plans to strengthen its support for informative, well-powered clinical trials incorporating advanced modalities like artificial intelligence (AI), human cell-based models, real-world data, and practical clinical trial tools. NIH's components will help accelerate therapies for rare diseases, cancer, connect patients with ongoing clinical studies to become subjects as part of routine care.

ARPA-H has launched initiatives to modernize clinical research including developing new approaches to test multiple treatments and diseases simultaneously and leveraging AI and machine learning to predict safety, optimize dosing, and improve trial efficiency before patient enrollment begins. Some of ARPA-H's newer programs include Treating Hereditary Rare Diseases with In Vivo Precision Genetic Medicine (intends to develop platform technologies to accelerate precision genetic medicines to slow, reverse, or prevent chronic diseases at genetic level) and Computational ADME-Tox and Physiology Analysis for Safer Therapeutics program (intends to develop computer models that mimic real human biology to predict safety and effectiveness for new therapies).

In addition, the OIG has published a Request for Information to obtain input on whether additional safe harbors are needed under the federal antikick statute or exceptions to the civil monetary penalty provision prohibiting inducements for remuneration for individuals to participate in clinical studies.

Takeaways

Now is the time to ride the wave to help accelerate early-stage clinical studies in the US. Tools like AI will be critical to design early-stage clinical studies relying on NAMs as well as analyze clinical data real-time versus only after a clinical study has been completed and the database closed. But even with AI, it will be important to utilize institutional knowledge and experience to pressure test clinical trial models to make sure that they are viable and appropriate for the investigational products and indications or conditions tested for in relevant patient populations.

This blog was drafted by Brian Malkin, a Spencer Fane attorney on the FDA Pharmaceutical and Biologics Market Team. For more information, visit spencerfane.com.

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