PORTAL
Program On Regulation, Therapeutics, And Law

Division of Pharmacoepidemiology and Pharmacoeconomics
Harvard Medical School | Brigham and Women's Hospital
www.portalresearch.org

July 15, 2026

The Honorable Brett Guthrie
Chairman
Committee on Energy and Commerce
2123 Rayburn House Office Building
Washington, DC 20515

The Honorable Frank Pallone, Jr.
Ranking Member
Committee on Energy and Commerce
2123 Rayburn House Office Building
Washington, DC 20515

The Honorable Morgan Griffith
Chairman, Subcommittee on Health
Committee on Energy and Commerce
2123 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
Ranking Member, Subcommittee on Health
Committee on Energy and Commerce
2123 Rayburn House Office Building
Washington, DC 20515

Statement for the Record

Advancing Innovation in Early-Stage Clinical Trials

Policy Options for Reauthorization of the User Fee Agreements

Thomas Hwang, MD

Director, Cancer Innovation and Regulation Initiative
Program On Regulation, Therapeutics, And Law (PORTAL)
Brigham and Women's Hospital & Harvard Medical School

PORTAL
Program On Regulation, Therapeutics, And Law

Written statement submitted to the U.S. House of Representatives Committee on Energy and Commerce, Subcommittee on Health, on July 13, 2026 in advance of hearing on July 15, 2026.

Testimony

PORTAL Program On Regulation, Therapeutics, And Law

Date: July 15, 2026

Re: **U.S. House Energy and Commerce Health Subcommittee Hearing: "Maintaining America's Leadership in Biomedical Innovation: FDA's Role in Advancing U.S. Drug Development"**

Dear Chairman Griffith, Ranking Member DeGette, and Members of the House Energy and Commerce Subcommittee on Health,

Thank you for the opportunity to submit this written statement for today's hearing on the role of the Food and Drug Administration (FDA) in advancing biomedical innovation. I applaud the Subcommittee's interest in policies to support early-stage clinical trials ahead of the upcoming reauthorization of FDA's key user fee agreements next year, including the Prescription Drug User Fee Act VIII and the Medical Device User Fee Amendments VI.

I am a physician and health policy researcher at Harvard Medical School and the Brigham and Women's Hospital, where I lead the Cancer Innovation and Regulation Initiative as a core faculty member of the Program On Regulation, Therapeutics, And Law (PORTAL).[1] My research focuses on the clinical development, regulation, and payment of new medicines and other interventions in cancer care. I serve on the European Society for Medical Oncology's Working Group on the Magnitude of Clinical Benefit Scale, which is the most widely used framework for evaluating the clinical benefit of cancer drugs.[2]

My testimony first provides background on key connected points: the vital role of US public investment in biomedical innovation; an evolving geographic shift in early-stage clinical trial activity, particularly for cancer trials; the distinctive safety obligations of first-in-human testing; and the opportunity to harness global scientific discovery for US patients. I then provide six policy recommendations aimed at fostering early-stage clinical development.

Background

Clinical trials for new medicines and medical devices rely on a broader innovation ecosystem. That ecosystem includes the foundational research that led to their discovery; the preclinical models that support the start of human clinical testing; and the postmarketing monitoring of products in the same class or with similar biological mechanisms.

[1] Based in the Division of Pharmacoepidemiology and Pharmacoeconomics at Brigham and Women's Hospital and Harvard Medical School, the Program On Regula ion, Therapeutics, And Law (PORTAL) is one of the largest academic research centers in the U.S. dedicated to investigating the regulation, use, evidence, and cost of prescription drugs, medical devices, and other interventions.

[2] The opinions and conclusions expressed in this written statement are the author's alone and do not represent those of the author's affiliated institutions, funders, or research sponsors. Disclosures are enclosed with this written statement.

The US has historically been the engine for this biomedical innovation. Nearly every new drug approved by the FDA has been linked to National Institutes of Health (NIH)-supported research,[3,4] and nearly a third of US patents rely on federal research.[5] In 2025, 70% of novel drugs approved by the FDA were approved first in the US before any other country.[6] And among cancer drugs approved worldwide from 2007 to 2020, the FDA was the first regulator to approve 80% of new cancer therapies.[7]

The efficiency of the FDA among global regulators is attributable, in part, to Congressional authorization of multiple programs to expedite the drug development and regulatory review process: priority review, accelerated approval, fast track, breakthrough therapy designation, and regenerative medicine advanced therapy. Overall, 72% of new drugs approved in 2025 benefited from at least one expedited program.[6] The FDA's Oncology Center of Excellence has also developed the Real-Time Oncology Review, which provides for rolling review of new drug and biologics license applications to streamline the approval process for cancer treatments.

Geographic Shifts in Early-Stage Cancer Trials

First-in-human and other early-stage clinical trials hold ethical and regulatory significance for three main reasons. First, early-stage studies are typically located where the discovery occurs (or preclinical development is conducted). Second, first-in-human trials typically involve healthy volunteers; in oncology, recognizing the seriousness of disease and correspondingly different risk-benefit balance, early-stage cancer trials frequently enroll affected patients and may serve as the pivotal study supporting regulatory approval. And third, unanticipated safety events can and do occur when preclinical models fail to predict actual human response.

Recent studies have reported that the US and China are now tied as the most frequent sites of early-stage clinical trials and drug development.[8] Among early-stage trials in the US, European Union, and China that were registered on ClinicalTrials.gov, the US and EU collectively accounted for nearly 90% of early-stage cancer trials in 2015 but only about 50% of such studies by 2023.[8] The absolute number of cancer trials centered in the US and Europe stayed relatively stable during this period, indicating that this shift reflects rising Chinese trial activity rather than declining US research productivity. A separate analysis found that China-only trials accounted for over 30% of industry-sponsored cancer trials in 2024,

---

3 Cleary EG, Beierlein JM, Khanuja NS, et al. *Proc Natl Acad Sci USA* 2018;115(10):2329-2334; Galkina Cleary E, Jackson MJ, Zhou EW, Ledley FD. *JAMA Health Forum* 2023;4(4) e230511.

4 Vokinger KN, Avorn J, Kesselheim AS. *N Engl J Med* 2023;388(4):292-295; Nayak RK, Avorn J, Kesselheim AS. *BMJ* 2019:367:l5766; Nayak R, Lee CC, Avorn J, Kesselheim AS. *JAMA Intern Med* 2021;181(11):1522-1525; Kesselheim AS, Tan YT, Avorn J. *Health Affairs* 2015;34:286-294.

5 Fleming L, Greene H, Marx M, et al. *Science* 2019;364(6446):1139-1141.

6 Food and Drug Administration. Advancing Health Through Innovation: New Drug Therapy Approvals 2025. ("32 of the 46 novel drugs approved in 2025 (70%) were approved in the US before any other country" and "In 2025, 33 of the 46 of CDER's novel drug approvals (72%) used one or more of these expedited programs, which helped bring new therapies to the market sooner.")

7 Hwang TJ, Kesselheim AS, Tibau A, et al. *JCO Oncol Pract* 2022;18(9):e1522-e1532.

8 Izarn F, Henry J, Besle S, et al. *ESMO Open* 2025;10(1):104086; Kang SY, Ji Y. *JAMA* 2026;335(15):1355-1357.

up from about 5% in 2015, whereas the share of multi-country studies fell from nearly 40% of trial starts in 2015 to 20% in 2024.[9]

To see how these shifts are cascading into FDA approvals, my team reviewed the Phase 1 and other early-stage clinical trials supporting FDA-approved novel cancer drugs from 2018 to 2025.[10] Roughly a third of cancer drug approvals were approved by the FDA based on a pivotal Phase 1 study, a proportion that did not change during the study period. Between 2018-2021 and 2022-2025, the share of trials with at least one US trial site declined across every study type: from 82% to 74% for all early-stage cancer trials, 96% to 91% for pivotal Phase 1 trials, and 98% to 88% for first-in-human studies.

During the same period, early-stage trial activity in China rose substantially. Cancer drug approvals from 2018-2019 involved no first-in-human study sites in China. Since then, the share of early-stage trials with any Chinese trial site increased from 5% to 13% for all early-stage trials, 18% to 24% for pivotal Phase 1 trials, and 6% to 12% for first-in-human studies. Only one pivotal Phase I/II cancer trial from 2018 to 2025 was conducted exclusively in China.[11]

Our study indicates that rising Chinese contributions to early-stage clinical development, previously documented through trial registrations and industry-sponsored development programs, now extend to the first-in-human and pivotal early-stage studies supporting FDA approval of new cancer medicines.

Safety Risks in First-in-Human Clinical Testing

Early-stage clinical trials are at the leading edge of innovation and the point of maximum risk. Where early-stage trials are conducted matters not only for innovation leadership but also the safety of patients and trial participants.

In 2006, six healthy volunteers had a catastrophic systemic inflammatory reaction within 90 minutes of receiving a single dose of an experimental monoclonal antibody as part of a first-in-human study.[12]

In 2016, one participant became brain dead and two had irreversible neurological injuries in a phase 1 study of an oral fatty acid amide hydrolase inhibitor.[13]

In 2020, four children died of acute progressive liver failure, gastrointestinal hemorrhage, and septic shock in a phase 1 trial of an experimental gene therapy.[14]

---

9 IQVIA. Global Oncology Trends 2025. (“The average number of countries with sites in trials has been trending down both from the decline in the share of multi-country studies and from the increasing activity for single-country trials, especially in China. Multi-country studies represented 37% of trial starts in 2015 but have dropped to 20% in 2024.”)

10 Preliminary findings from our analysis are shared in this written statement for the Health Subcommittee ahead of submission for peer review and scientific publication; final estimates may differ from those presented here. This work is an ongoing collaboration with contributions from Ms. Kyoko Yamamoto, Ms. Linda Lin, and Dr. Aaron Kesselheim.

11 The POLARIS-02 study was a Phase I/II trial supporting regulatory approval of toripalimab for previously treated unresectable or metastatic nasopharyngeal carcinoma.

12 Suntharalingam G, Perry MR, Ward S. *N Engl J Med* 2006;355(10)1018-28.

13 Kerbrat A, Ferré JC, Fillatre P, et al. *N Engl J Med* 2016;375(18):1717-1725.

These cases underscore how narrow the margin for error is for early-stage clinical studies. In these and other cases, seemingly promising new therapies were advanced through substantial preclinical testing before the toxicity that seriously harmed or killed participants surfaced in the clinic. And the catastrophic outcomes in these cases underscored the urgent need for transparency: without knowledge of the safety issues unfolding, participants in trials of *other* treatments in the same class, as well as patients receiving already-approved products with similar biological mechanisms, were placed at risk.

The FDA holds arguably the world's largest repository of data on how new treatments work in humans. The entire biomedical enterprise suffers when clinical research moves to sites with inferior standards for diligence and disclosure of safety issues, data integrity, and ethical protection of trial participants. In addition to the potential harm to trial participants, simply rushing experimental agents through clinical testing deprives our patients of invaluable information they need on safety and efficacy once the product enters the US market. Adequate oversight of early-stage trials by the FDA cannot be weakened, or substantially delegated away, without incurring real costs.

Harnessing Global Scientific Discovery for US Patients

Our patients benefit from access to the world's best scientific discoveries that will ultimately generate safe, effective, and affordable treatments for their conditions. We should welcome competition in the global research enterprise, because competition fosters innovation. But such competition must be fair, transparent, and ethically sound.

Recently, the FDA has raised questions about data from single-country and non-US clinical trials that may not be generalizable to patients in the US. In 2022 and 2025, the FDA's Oncologic Drugs Advisory Committee voted against regulatory approval of two cancer drugs, in part due to concerns about the representativeness of their pivotal trials: one study was conducted exclusively in China and the other enrolled globally but still underrepresented American patients.[15] In one review of randomized controlled trials of cancer medicines authorized by Chinese institutional review boards from 2016 to 2021, roughly one in eight were judged to have a suboptimal control group, as compared to standard of care recommended in local practice guidelines.[16]

Faster but lower-quality clinical trials push costs and harms onto future patients. The US has more to gain from helping raise global practices for rigorous clinical research to our high standard than blanket exclusions of innovations based on origin alone.[17] In unpublished research, we evaluated the regulatory approval and clinical benefit of Chinese-originated novel cancer medicines from 2019 to 2025 across the FDA, EU, and Japan.[18] Since 2019, approximately one in ten new cancer medicines approved by one of

---

14 Shieh PB, Kuntz NL, Dowling JJ, et al. *Lancet Neurol* 2023;22(12):1125-1139.

15 Food and Drug Administration. Meetings of the Oncologic Drugs Advisory Committee on February 10, 2022 and July 17, 2025.

16 Zhang Y, Chen D, Cheng S, et al. *PLoS Med* 2023;20(12):e1004319.

17 The quality of clinical research in certain jurisdictions may be improving already due to scrutiny by international regulators. For example, the number of internationally accredited ethics committees in China was reported to have increased from 4 in 2009 to 82 in 2022. See Chen X, Chu H, Zhang X, et al. *J Evid Based Med* 2025;18(4):e70085.

18 Preliminary findings from our analysis are shared in this written statement for the Health Subcommittee ahead of submission for peer review and scientific publication; final estimates may differ from those presented here. We plan to present part of the results of this analysis at the European

these three major regulators were Chinese-originated. Chinese-originated cancer products were associated with longer FDA review (12 months vs. 7 months for non-Chinese-originated cancer drugs), particularly for those approved in the earlier years of our study period. Yet, Chinese-originated drugs were more than twice as frequently scored as providing substantial clinical benefit than non-Chinese-originated therapies (37% vs. 16%, respectively), according to the ESMO Magnitude of Clinical Benefit Scale. Several of these recently-approved cancer therapies were shown to extend patients' survival and are now recommended in US clinical practice guidelines.

Policy Considerations to Advance Early-Stage Clinical Innovation

As Congress considers policy proposals in view of the upcoming reauthorization of the user fee agreements for prescription drugs and medical devices, this Subcommittee can support our nation's leadership in biomedical innovation and ensure efficient development of safe and effective therapies. I provide six policy recommendations for consideration.

Importantly, although outside the scope of this effort, first-in-human clinical trials reflect where the underlying scientific discovery occurs, and policies seeking to advance US clinical development require concurrent investments in foundational research by NIH (and other public-sector research institutions) as well as adequate funding for FDA reviewers.

1. **Raising global standards for clinical research protects patients and US competitiveness.**

   The FDA remains the global model for regulatory approval of new medicines and medical devices (and the US is the most lucrative market for these products), so the agency's priorities can shape the trajectory of development programs around the world. The Subcommittee could explore options to raise global standards for clinical research. For non-US clinical trials to support approval, a defined minimum percentage of non-US trial sites could be required to undergo FDA inspection. The FDA could be directed to formally review and attest whether the control arms of clinical trials reflect US standards of care. Postmarketing trials that are representative of the US population could be required for products approved with limited US patient enrollment in preapproval studies.

2. **Fee incentives for sponsors conducting Phase 1 trials in the US should be targeted at small companies as well as academic and non-profit sponsors.**

   Fee waivers or other incentives based on company domicile are unlikely to be effective at increasing US patient representation in early-stage trials. Instead, we should encourage sponsors to enroll patients in the US, regardless of where their operations are based. If the location of early-stage clinical trials is incorporated as a condition into the FDA's application fee schedule, reduced or waived fees should be targeted to small companies as well as academic and non-profit sponsors that are the source of important translational discoveries and that may be most sensitive to these fees as a share

Society for Medical Oncology's Annual Congress later this year. This work is an ongoing collaboration with contributions from Ms. Kyoko Yamamoto, Mr. Adam Zhang, and Dr. Ariadna Tibau.

of their development costs. However, such incentives are unlikely to be sufficient to meaningfully increase early-stage clinical development.

3. **Targeted tax incentives tied to US clinical trial activity could complement fee-based measures.**

   Congress already prioritizes domestic research in its structuring of research and development tax credits. Building on this precedent, Congress could explore whether targeted, refundable tax incentives for qualified clinical trial expenses at US trial sites would effectively encourage US trial research, particularly by small companies and pre-revenue sponsors. Congress could also consider conditioning a portion of existing research-related credits on a minimum level of US trial site or patient enrollment. Coupled with fee-based measures, carefully designed tax credits could help lower the costs of conducting early-stage studies in the US.

4. **Improved transparency can accelerate early-stage clinical testing, protect patient safety, and ensure efficient regulatory review.**

   The FDA has recently proposed providing more information on reasons why new drugs are not approved, including publicly releasing “Complete Response Letters,” which can help other sponsors and future developers avoid similar application deficiencies and learn from past development failures. Congress should provide explicit statutory backing for the FDA’s transparency initiative and extend it to include reasons for halted early-stage trials (or “clinical holds”) and a summary of steps taken to resolve them. The FDA could also be directed to publish summary reports on common deficiencies leading to clinical holds for first-in-human and Phase 1 clinical trials. These transparency reforms could help prevent duplicative errors and unnecessary delays in the trial process.

5. **Coordinated early-stage trial review by comparable regulators could strengthen the global trial infrastructure and streamline clinical development.**

   Parallel to FDA’s Project Orbis, which provides for concurrent submission and review of oncology drug applications among international partners, Congress could authorize a pilot program for coordinated review of Investigational New Drug and Investigational Device Exemption applications, which allow new drugs and devices to begin human clinical testing, respectively. This pilot program for coordinated regulatory review could be coupled with policies to facilitate single institutional review board review for multi-site trials sponsored by industry.

6. **Congress should direct FDA to implement guardrails in its Expedited IND Pilot Program.**

   Effective oversight of first-in-human studies is a critical part of US leadership in clinical development, and proposals to speed up times to first-in-human studies should not introduce new risks or compromise patient safety. A proposal by the FDA envisages a network of “Qualified Research Institutions” that would partner with sponsors to develop and review protocols for first-in-human

clinical trials intended for Investigational New Drug applications and then submit recommendations to the FDA on a rolling basis.[19]

The FDA's proposed pilot program is worthy of further consideration, but, given several potential risks, such a program needs explicit deliberation and authorization by this Committee before it is launched. Some of these risks and possible remedies include a firewall to prevent conflicts-of-interest between Qualified Research Institution staff developing study protocols, ethics committees, and those reviewing relevant components; periodic lookback and independent FDA re-review of protocols to prevent shadow delegation of oversight from FDA to these third-parties; qualification requirements for Qualified Research Institutions to prevent over-concentration on review revenue from one or a small number of sponsors (which could advantage larger sponsors over small companies); and exclusion of pivotal Phase 1 and other high-risk trials that should remain primarily overseen by FDA.

* * *

The map of early-stage clinical research is being rapidly redrawn in real-time, with the US increasingly no longer at its center. Congress has the opportunity to accelerate clinical development of important new therapies as part of the reauthorization of user fee agreements for prescription drugs and medical devices. This could include minimum standards for global trial data; incentives for US clinical trials; improved transparency; coordinated regulatory review; and appropriate guardrails in proposals to streamline early-stage trials. And, ultimately, any durable effort to promote US clinical development requires investments in public support for foundational research and the FDA.

Thank you for highlighting the importance of early-stage clinical research in the development of new medicines and medical devices. Our team looks forward to working with the Subcommittee to help design and evaluate policies that will achieve these goals. †

[19] Food and Drug Administration. Request for informa ion: Expedited Investigational New Drug Pilot Program. 91 Fed. Reg. 37,996 (June 24, 2026).