Addendum to Winckler Testimony, July 15, 2026

Compilations of Recommendations to Reports by the Reagan-Udall Foundation for the FDA

1. Improving Oncology Multi-Regional Clinical Trials

Improving Oncology Site Activation, Enrollment & Study Start Up Timelines Is Imperative – Especially in the U.S.							
Solutions	**Collaborators**						**Time**
	Regulators	**Clinical Trial Sponsors**	**Clinical Trial Sites & Organiza-tions**	**Clinical Research Groups**	**Patient Groups**	**Medical Research Groups**	**Short,- Mid-, or Long-Term Endeavor**
Recommendation #1: Unlock the Potential of Network Approaches							
Collectively define specifics of operational and regulatory compliance processes for network approaches, ideally harmonized with international standards	✓ (FDA, ICH)	✓	✓	✓			
Recommendation #2: Improve Enrollment and Study Start Up Timelines by Advancing More Patient-Centric, Rather Than Trial-Centric, Approaches							
Improve Referral and Screening Processes							
Develop pre-competitive platform approaches to enable patients to be screened for a broad array of trials and referred to the trial(s) that best fit their needs		✓	✓	✓	✓	✓	
Build More Opportunities to Enroll in Oncology Clinical Trials							
Develop and promote policies and best practices that enable sites with little to no experience to build clinical trial capacity	✓ (FDA)	✓	✓	✓			
Clarify regulatory policies and remove barriers to the effective deployment of tools that support decentralized approaches such as remote monitoring and in-home data collection	✓ (FDA , ICH)	✓	✓	✓	✓		
Explore pre-competitive approaches to support sustainable long-term community engagement and educational models that enable patients and families to better locate and evaluate clinical trial opportunities		✓	✓	✓	✓	✓	

Time Endeavors: Short-Term Mid-Term Long-Term

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	Regulators	Clinical Trial Sponsors	Clinical Trial Sites & Organiza-tions	Clinical Research Groups	Patient Groups	Medical Research Groups	Short,- Mid-, or Long-Term Endeavor
Reduce Patient and Family Financial Burdens							
Promote policies that reduce financial burdens on patients and advocate for the removal of statutes that prohibit or limit trial sponsors' ability to reduce patient burdens	✓ *Federal and state policy leaders (some solutions may require statutory changes)	✓	✓	✓	✓	✓	
Recommendation #3: Explore Common Budget and Contract Processes for U.S. Trial Sites							
Develop base-line budget and contracting processes for U.S. clinical trials and establish an iterative process for publishing case studies and capturing data about how best to manage site budget and contract variabilities		✓	✓	✓			
Develop data-driven processes for clinical trial costs and how to structure budgets		✓	✓	✓			
Develop and implement streamlined payment processes		✓	✓	✓			
Develop a framework that promotes best practices and enables widespread adoption of AI and platform approaches to streamline clinical trial budget and contract processes		✓	✓	✓			
Develop common compensation for physician referrals and physician participation in clinical trials (*e.g.*, reimbursement for time spent and execution of specific tasks)		✓	✓	✓			
Develop multi-sponsor and site budget and contract templates		✓	✓	✓			
Develop actionable recommendations for building collective resources and funding for site budget and contract needs, including outsourcing certain functions		✓	✓	✓			

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Recommendation #4: Ensure Utilization and Deployment of Technology Yield Benefits							
Develop an industry-wide approach to site technology demands, such as a framework for determining when sites may select/use their own vendors/technology resources or when deploying a specifically requested technology is required		✓	✓	✓			
Recommendation #5: Align on Training Needs and Minimize Duplicative Activities							
Construct collective, or at least aligned, training requirements to minimize duplicative clinical trial site activities		✓	✓	✓			

Importance of Global Harmonization of Science-Based Approaches to Clinical Trial Representativeness Targets and Generalizability Analyses

Solutions	Collaborators						Time
	Regulators	Clinical Trial Sponsors	Clinical Trial Sites & Organiza-tions	Clinical Research Groups	Patient Groups	Medical Research Groups	Short,- Mid-, or Long-Term Endeavor
Recommendation A: Develop Scientific Principles for Representativeness Requirements and Adapt for Disease-Specific Application							
Define scientific principles for representative requirements and statistical and data quality principles to drive analyses of safety and effectiveness in trials with patients from different countries and different racial and ethnic groups that include activities to provide context for specific diseases	✓ (FDA , ICH)	✓			✓	✓	(Active Clinical Trials) Mid-term (Future Clinical Trials
Develop processes that enable timely inspections aligned with other clinical research requirements	✓ (FDA)	✓	✓				(Active Clinical Trials) Mid-term (Future Clinical Trials)
Recommendation B: Manage Heterogenous and Continuously Evolving Standard of Care by Articulating Contextualized Regulator/Researcher Understandings for Discrete Cancer Areas							
Develop and advance regulatory understandings about how to address evolving and varying standards of care for oncology patients in MRCTs that consider clinical context/discrete disease area, patients' needs, and operational feasibility	✓	✓			✓	✓	(Active Clinical Trials) Mid-term (Future Clinical Trials)

2. Recommendations from Expanding Regulatory Agility and Evidentiary Integrity in Developing Treatments for Rare Diseases

Table 1. Topics, Challenges, and Recommendations

Developing Regulatorily-Acceptable Patient-Relevant Endpoints				
Recommendations	**Challenges**	**Next Steps***	**Product**	**Stakeholders**
1. Enable Mutual Recognition of Endpoint Qualifications	• Misaligned Validation and Qualification Timelines with Patient Need • The Precedent Paradox That Limits Acceptance of Novel Approaches	FDA and key regulatory agencies collaborate with sponsors to develop processes for mutual recognition agreements	Mutual recognition agreements, data sharing platform that enables collaborative work between multi-regional regulatory authorities and sponsors	FDA, regulated industry, EMA, other key regulatory authorities
2. Establish Fit-for-Purpose Tiered Pathways for Patient-Relevant Endpoint and Biomarker Qualification	• The Precedent Paradox • Translation Gaps Between High-Level Principles and Real-World Operational Needs • Lack of Clarity on Pathways for Developing and Using Disease-Agnostic Endpoints and Measurement Tools	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Frameworks published by FDA	FDA, ICH, regulated industry, patient organizations, medical researchers
3. Advance Methodological Approaches for Patient Relevant Endpoints	• The Precedent Paradox • Translation Gaps Between High-Level Principles and Real-World Operational Needs • Difficulty Valuing Incremental (Inchstone) Progress • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework (and potential guidance) published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, patient organizations (specifically including patients and caregivers), medical researchers, clinical research organizations
4. Collaboratively Explore and Promote Best Practices for Video- and Sensor-based Functional Assessments	• Translation Gaps Between High-Level Principles and Real-World Operational Needs	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Guidance published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, patient organizations, clinical research organizations, medical researchers
5. Establish Stakeholder/FDA Consultations for Rare Disease Endpoint Development	• Misaligned Validation and Qualification Timelines with Patient Need • The Precedent Paradox • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development	FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	FDA publication of new meeting mechanism and/or FAQ on best practices for scheduling and preparing for a dedicated rare disease endpoint meeting	FDA, regulated industry, patient organizations
6. Align Evidentiary Thresholds for Slowly Progressive Diseases	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Difficulty Valuing Incremental (Inchstone) Progress • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers

7. Develop and Implement Training Programs on Data Collection for Patients and Caregivers	• Translation Gaps Between Principles and Operational Realities	Training program development for patient experience data reporting and collection	Training program deployed to clinical sites and to patient organization; patient organization to deploy training programs to patients and caregivers	Regulated industry, medical researchers, patient organizations, contract research organizations
8. Enable Use of Endpoint Triangulation and Composite Endpoints	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Endpoint Triangulation and Composite Endpoint Uncertainty	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers
9. Expand FDA Grants to Advance Composite Endpoint Methodological Approaches	• The Precedent Paradox • Endpoint Triangulation and Composite Endpoint Uncertainty	FDA to expand/prioritize funding	Grants provided; publication of funded studies	FDA
10. Support Development and Use of Disease-Agnostic Endpoints and Tools	• Difficulty Valuing Incremental (Inchstone) Progress • Unclear Pathways for Disease-Agnostic Endpoint and Measurement Tool Development	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Inclusion in frameworks, case studies and peer reviewed publication for recommendations to: enable use of endpoint triangulation and composite endpoints; develop alignment on evidentiary thresholds for slowly progressive diseases; collectively explore, develop and disseminate methodological approaches for patient relevant endpoints; advance regulatory understandings for use of patient experience data to support endpoint acceptance; develop and enable fit-for-purpose tiered patient-relevant endpoint qualification; and establish stakeholder–FDA rare disease endpoint consultations	FDA, ICH, regulated industry, patient organizations, medical researchers
11. Establish Incentives for Large-Scale, Pre-Competitive Disease-Agnostic Data Collaboration	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Fragmented and Burdensome Data Landscape	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Statutory and regulatory incentive proposals	FDA, regulated industry, medical researchers, patient organizations, data scientists
12. Create Function-Based, Domain-Driven Endpoint Libraries	• Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development	FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	A publicly available, government housed or government-adjacent, domain-based endpoint library	FDA, regulated industry, medical researchers, patient organizations

Optimizing Patient Perspective and Natural History Data Collection and Use

Recommendations	Challenges	Next Steps*	Product	Stakeholders
13. Advance Best Practices for Responsible Rare Disease Data Sharing	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Fragmented and Burdensome Data Landscape	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, EMA/global regulators, regulated industry, medical researchers, patient organizations, clinical research organizations, privacy lawyers, data/AI companies
14. Create Tiered Approaches for Natural History and Registry Data Acceptability	• The Precedent Paradox • Translation Gaps Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Fragmented and Burdensome Data Landscape	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, medical researchers, patient organizations, clinical research organizations, privacy lawyers, data/AI companies
15. Clarify Evidentiary Requirements for Utilizing Legacy Registry Data	• The Precedent Paradox • Translation Gap Between Principles and Operational Realities • Unclear Pathways for Disease-Agnostic Endpoints and Measurement Tools Development • Fragmented and Burdensome Data Landscape	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Guidance published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, medical researchers, patient organizations, clinical research organizations, privacy lawyers, data/AI companies

Advancing Shared Understandings of Evidentiary Expectations and Regulatory Requirements

Recommendations	Challenges	Next Steps*	Product	Stakeholders
16. Promote Shared Understandings of Scientific Principles Supporting Flexible Evidentiary Strategies	• Lack of Clarity on Scientific Principles Driving Different Evidentiary Expectations and Regulatory Requirements	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Frameworks updated and/or published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers
17. Enable Early Identification and Resolution of Issues for Novel Endpoints and Trial Designs	• Lack of Clarity on Scientific Principles Driving Different Evidentiary Expectations and Regulatory Requirements	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Rare disease meeting best practices or guidance published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, regulated industry, medical researchers (including statisticians), patient organizations

18. Enable Rare Disease Clinical Trials to Learn and Adapt More Effectively	• Successfully Incorporating Learnings Generated During a Clinical Trial	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	Best practices and/or framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers (including statisticians)
19. Define Evidentiary Thresholds for Rare Disease Second- and Third-Line 3rd Line Treatments	• Successfully Incorporating Learnings Generated During a Clinical Trial	**Stakeholder workshop(s)** (addressing targeted topics and enabling discussion to yield substantive solutions)	Framework published by FDA, case studies, peer-reviewed publications (illustrating reasons for success and failures)	FDA, ICH, regulated industry, patient organizations, medical researchers

Improving Cross-Stakeholder Knowledge Management

Recommendations	Challenges	Next Steps*	Product	Stakeholders
20. Build a Cross-Stakeholder, AI-Enabled, Rare Disease Knowledge Management System	• Difficulty Translating Siloed Knowledge Management Improvements into Broader Public Benefit	**Stakeholder workshop(s)** FDA public meeting with public speakers and public comment period (addressing targeted topics and enabling discussion to yield substantive solutions)	A publicly available, easily searchable, government housed (or government-adjacent), AI-enabled rare disease knowledge management system	FDA, regulated industry, medical researchers, patient organizations, clinical research organizations, privacy lawyers, data/AI companies

*** Bold and Purple Text = Potential Reagan-Udall Foundation for the FDA Led Activity**

3. Enhancing Early-Stage Drug Development in the United States

Consolidated Recommendations and Solutions

SOLUTIONS	STAKEHOLDER LEADS
Modernizing IND Requirements and Processes	
Recommendation #1: Adopt Risk-Proportionate IND Submission Requirements and Triage Review Processes	
a) Develop specific recommendations for risk-proportionate IND submission requirements and triaged review processes. Efforts could include: i. Developing and implementing risk-proportionate IND review timeline (e.g., 14-day IND review for well-characterized platforms, simple formulations, microdosing, exploratory INDs). ii. Developing and implementing a triaged IND classification based on drug risk vs. subject risk that determines the level of submission requirements and reviewer time. iii. Establishing principles and developing modality specific guidance that describes what data are required for low-, medium-, higher-risk INDs. iv. Developing FDA internal training and standard operating procedures (SOP) about how to triage FDA reviewer time based on need. b) Establish a dedicated first-in-human (FIH) specialist review unit at FDA for novel-modality or high-risk INDs, consolidating expertise currently distributed across multiple divisions. c) Invest in a specialized FIH-review workforce at FDA that delivers clear, consistent, and modality-aware early-phase regulatory expectations, reducing variable cross-division feedback.	**FDA:** Generate guidance documents; implementation of review, training, and organization reforms **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Recommendation #2: Advance Rolling IND Submissions	
a) Adopt a modular, rolling IND review pathway: a sequential nonclinical package and Phase-appropriate CMC data package enabling first-cohort dosing. Elements of the pilot could explore: i. Cases where FIH dosing could proceed based on non-GLP studies and GMP-like materials. ii. An Investigator Brochure (and draft study reports) to enable start of FIH plus SEND datasets submitted at a later date.	**FDA:** Develop and implement new pathway(s) implementation **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #3: Modernize Nonclinical Requirements and Practices	
a) Develop dose selection scientific principles that take into consideration disease severity and distinguishes first-in-healthy-humans needs from first-in-patient needs. b) Refine Project Optimus implementation through greater use of model-informed drug development (MIDD) and population PK modeling to optimize dose selection and escalation and address data gaps. c) Convene meetings among regulators, biopharmaceutical companies, CROs, and medical researchers to discuss how to advance the utilization of New Approach Methodologies (NAMs) and create a pathway for sponsors to secure endorsement to use a single species toxicology study including reliance on nonclinical platform data that can be carried forward to future IND submissions. This effort should include development and implementation of FDA internal training programs exploring a review posture in which applications are presumed adequate with in vitro/comparative biology data unless reviewers provide scientific rationale for an animal study and provide insight on which species is most predictive. The substance of these trainings may be strengthened with input from external experts. d) Formalize a structured pharm-tox reviewer rotation program across FDA divisions and centers to cross-pollinate risk-tolerance frameworks.	**FDA:** Develop and implement principles, rotation program **Collaborators:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA, medical researchers, patient organizations
Recommendation #4: Update and Streamline Chemistry, Manufacturing and Controls (CMC) Requirements	
a) Expand the January 2026 CBER CMC flexibility announcement into formal guidance covering cell and gene therapies, explicitly clarifying that cGMP under 21 CFR Part 211 is not required before Phase 2 or Phase 3, and extend analogous flexibility to other modalities when supported by risk-benefit determination. b) Streamline CMC content required for certain Phase 1 trials to allow short-term or accelerated CMC stability data with a scientifically justified shelf-life covering only the clinical dosing period, paired with a sponsor commitment to continue stability testing during the trial. This could be modeled after Belgium's Phase 1 CMC submission model. c) Issue a formal policy statement on cross-regional comparator characterization, enabling sponsors to rely on drug characterization accepted by EMA or other ICH regulators. d) Establish a risk-based pathway to waive or streamline routine Phase 1 CMC submission and review for defined categories, including: (i) products manufactured using well-established platforms or with extensive prior sponsor experience with analogous FDA submissions; (ii) products for serious, life-threatening, ultra-rare, or N-of-1 conditions; (iii) very low-risk study designs such as microdosing studies and exploratory INDs; and (iv) simple formulations using known excipients and standard manufacturing processes (e.g., immediate-release oral tablets, aqueous solutions). e) Routinely publish an anonymized list of common CMC deficiencies and remediation pathways.	**FDA:** Publish policy, guidance and top 10 list; implement new pathway **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #5: Clarify Required IND Data	
a) Publish updated, modality-specific guidance and case studies clarifying minimum IND data expectations for Phase 1 INDs by scenario (e.g., small molecule, oligonucleotide, oncology, viral vector, cell therapy). b) Develop Q&A-style or decision-tree guidance tools that supplement narrative guidance documents, allowing sponsors to arrive at a transparent articulation of minimum CMC and nonclinical package requirements for their specific Phase 1 study based on modality, therapeutic area, prior human data, and study design.	**FDA:** Develop and publish guidance, case study and decision-tree publications **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Recommendation #6: Improve "Safe-to-Proceed" and "Clinical Hold" Communications	
a) Establish "Safe-to-Proceed" coordinated processes within FDA including: i. Consistent, timely notifications across all review divisions within the 30-day statutory period. ii. Written rationale on all clinical holds that identify the deficiency, the regulatory basis, and the recommended resolution path. b) Reframe 30-day IND notification terminology for pre-dosing actions where no patient has been dosed and the action is informational from "clinical hold" to "notice of additional information required."	**FDA:** Develop and implement new processes and communications, organizational reform **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Recommendation #7: Enable Greater Use of a Phase 1 Clinical Trial Notification (CTN) Pathway	
a) Develop and implement FDA's proposed Clinical Trial Notification pathway for certain Phase 1 trials.	**FDA:** Develop and implement pathway **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Modernizing Phase 1 Clinical Trials and Tools	
Recommendation #8: Enable Use of Innovative Clinical Trial Designs	
a) Review and update innovative clinical trial design guidance and develop accompanying FAQs that: i. Provide early-phase-specific examples for Bayesian adaptive dose-escalation, seamless Phase 1/2 designs, and biomarker-stratified expansion cohorts. ii. Permit adaptive Phase 1 designs to allow modifications to dose range, escalation increment, indication focus, and therapy line based on emerging clinical data—without protocol amendment but operating under pre-specified guardrails. b) Modernize Form FDA 1572 to reflect decentralized-element trial models and facilitate state-level alignment on telehealth-delivered research activities.	**FDA:** Develop and issue new documents **Collaborators on Substance:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA; medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #9: Increase Inclusion of Patient Perspectives in Early-Stage Drug Development	
a) Develop a review matrix that documents when patient perspectives were used to inform toxicology requirements.	**FDA:** Develop and publish review matrix **Collaborators** Biopharmaceutical companies
Recommendation #10: Develop Artificial Intelligence (AI) Enabled Sponsor-Facing Decision Support Tools	
a) Develop a meeting series for FDA and stakeholders to collaborate on developing and implementing knowledge management initiatives that can serve as the basis for the development of AI-enabled sponsor-facing decision support tools.	**Reagan-Udall Foundation for the FDA:** Develop and implement meeting series **Collaborators:** Biopharmaceutical companies, FDA; medical researchers, patient organizations
Optimizing FDA–Sponsor Early-Stage Engagements and Processes	
Recommendation #11: Enhance Pre-IND Meeting and IND Review Best Practices	
a) Standardize pre-IND meeting outputs to produce three documented conclusions: (i) required; (ii) optional but potentially helpful; and (iii) unnecessary for the proposed initial study. Treat pre-IND alignment on specific elements (e.g., inclusion/exclusion criteria) as commitments the IND review will not revisit without written justification. b) Pilot an IND-stage sponsor "safe-to-proceed checkbox" enabling sponsors to elect minimum-comment Phase 1 safety review, deferring forward-looking protocol, endpoint, and development-strategy feedback to later meetings; FDA's clinical hold, safety reporting, and inspection authorities fully preserved. c) Pilot an iterative, weekly Australian-style engagement model for pre-IND and IND-stage interactions. This effort could be supported by updating and reviving the Target Product Profile (TPP) as a sponsor-facing tool rather than a binding guidance designed to support a more iterative engagement model that surfaces assumptions earlier and provokes structured dialogue before formal IND submission.	**FDA:** Develop and implement approach **Collaborators on Substance:** Biopharmaceutical companies, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #12: Capture IND Regulatory Decision-Making Trends	
a) Support stakeholder efforts to capture evidence and identify trends of consistent or differing feedback on distinct IND topics, such as BIO's BRIDGE platform, designed to capture regulatory trend data from sponsors describing their interactions with the FDA. b) Convene disease-area or modality-specific shared learning forums (e.g., rare disease, chronic disease, gene therapy) to share information about pre-IND meetings, IND submission packages, and IND reviews and discuss what has worked, what has not, and where expectations have shifted. c) Encourage FDA to develop internal mechanisms to capture trends of consistent or differing feedback on specific IND related topics and cross-pollinate learnings.	**Reagan-Udall Foundation for the FDA:** Institute meeting series **FDA:** Implement internal trend/ knowledge management **Collaborators:** Collect trend data and platform development
Recommendation #13: Incentivize Fit-for-Purpose IND Submissions and Engagements	
a) Develop incentives for high-quality, appropriately scoped IND submissions. For example, FDA should develop best-practice templates and Pre-IND checklists that, when followed, provide the sponsor reasonable assurance that regulatory expectations have been met, and IND-stage changes would be limited to instances of emerging safety or scientific knowledge. b) Establish an expedited pre-IND pathway for U.S. biotech sponsors developing truly novel modalities or molecule types, modeled on EMA's PRIME early-entry program.	**FDA:** Implement meeting reform and new pathway implementation **Collaborators:** Biopharmaceutical companies, medical researchers, patient organizations
Building a Streamlined and Dedicated U.S. Phase 1 Infrastructure as Part of a National Clinical Trial Infrastructure and Coordinating Strategy	
Recommendation #14: Build and Fund a Dedicated Network of Phase 1 Capable Clinical Trial Sites	
a) Direct NIH and FDA to develop and/or designate FIH/Phase 1 centers of excellence, including using a single IRB process and other streamlined site activation processes. b) Provide federal funds to support a national Phase 1 clinical trial infrastructure.	**FDA and NIH** **Collaborators:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #15: Create a National Phase 1 Coordinating Strategy (as part of an overall National Clinical Trial Strategy)	
a) Create a National Phase 1 Coordinating Strategy. The strategy should include: i. Establishing a National Biotechnology Coordination Office. ii. Jointly publishing a U.S. Life Sciences Competitiveness Roadmap with explicit benchmarks by NIH and the FDA. iii. Formally designating the U.S. life sciences industry as a national treasure that defines clinical trial infrastructure as a critical national infrastructure, enabling cross-agency resource allocation and sustained capital investment consistent with other strategically significant sectors. iv. Commissioning and annually maintaining a national Phase 1 clinical trial site inventory capturing site type, modality capability, activation and enrollment metrics, workforce composition, and continuity of trial activity. v. Creating a nation-wide communication campaign on the value of early-phase trial participation paired with expanding community-practitioner education about clinical trial opportunities. vi. Continuing investment in NIH basic research funding. vii. Developing of a competency/certification framework for research nurses, coordinators, and pharmacists (with loan-repayment incentives). viii. Developing a centralized investigator database consolidating investigator credentials, training records, and site qualifications to eliminate duplicative sponsor-specific training. *NOTE: These solutions should be part of an overall national clinical trial infrastructure and coordinating strategy.*	**FDA and NIH** **Collaborators:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA, medical researchers, patient organizations

SOLUTIONS	STAKEHOLDER LEADS
Recommendation #16: Streamline IRB and Site Activation Processes	
a) Finalize single-IRB rule. b) Develop a national strategy to support single and centralized IRB capacity needs including: i. Requiring an sIRB process. ii. Developing enhanced Phase 1 IRBs that could be used as an outside sIRB authority. iii. Creating a pool of FDA certified regulatory auditors who could augment centralized IRB processes at clinical trial sites by providing technical CMC/safety seals of approval. iv. Embedding FDA subject-matter experts within major academic medical centers to support centralized IRB processes at clinical trial sites. c) Pilot a hybrid FDA-IRB parallel-review model with FDA to focus on scientific sufficiency and safety and IRB focus on trial protocol, informed consent, and ethical considerations, both of which are completed on an agreed-upon parallel timeline rather than the current sequential approach. d) Develop standardized informed consent templates for Phase 1 studies to reduce site-by-site consent negotiation delays. e) Extend financial and career incentives to clinician-investigators (e.g., reimbursement for time spent and execution of specific tasks). (See Box 1.) f) Expand rural and underserved Phase 1 access via academic satellite locations and hub-and-spoke models with limited but defined FIH/FIP capabilities (e.g., lower-risk/less-complex studies).	**FDA:** Finalize sIRB rule, implement parallel-review model **FDA and NIH:** Implement national sIRB capacity and strategies **Collaborators:** Biopharmaceutical companies, Reagan-Udall Foundation for the FDA; medical researchers, patient organizations **Biopharmaceutical Companies and Clinical Trial Sites:** Develop standardized templates and hub-and-spoke models **Stakeholders:** Advocate for financial incentives and clinical trial reimbursement reforms **Trial Sites:** Develop standardized templates and hub-and-spoke models **Biopharmaceutical Companies and Clinical:** Advocate for financial incentives and clinical trial reimbursement reforms
Mitigating Litigation Risk for Phase 1 Clinical Trial Sites	
Recommendation #17: Explore Safe Harbors and Insurance Reforms for FIH and Phase 1 Trials	
a) Explore federal safe harbors for Phase 1 clinical research sites and examine insurance coverage practices for potential reforms that would help mitigate litigation risks.	**Congress:** Enact safe harbor and master insurance laws **Collaborators:** FDA, NIH, Biopharmaceutical companies, Reagan-Udall Foundation for the FDA; medical researchers, patient organizations