

Key Themes and Suggestions

Advancing Rare Disease Therapies Through an FDA Rare Disease Innovation Hub

Engagement - External

1. Hub Processes:

- a. Create procedures for engaging with the new Hub Director of Strategic Coalitions.
- b. Provide information on the scope of the Hub, including what will and will not be under its purview.
- c. Develop a detailed strategic plan with short- and long-term goals.

2. Centralized Communication Platforms:

- a. Establish a centralized Hub portal to provide interested parties, including patients and advocacy groups, sponsors, and academia, with regular updates on regulatory guidance, and policy changes.
- b. Utilize accessible tools such as newsletters, webinars, and publicly available Q&A documents to educate and engage stakeholders.

3. Educational Outreach:

- a. Create plain-language resources to guide patients and caregivers through regulatory pathways.
- b. Develop training sessions for sponsors and advocacy groups to clarify FDA requirements for rare disease drug development.
- c. Publish case studies and learnings to inform future rare disease applications.
- d. Provide guidance on “ultra-rare” vs. rare diseases, accelerated approval, and surrogate endpoints.
- e. Launch public awareness campaigns to improve understanding of rare diseases and their impact.

4. Transparency in Decision-Making:

- a. Publish standardized explanations of advisory committee decisions and establish real-time feedback mechanisms to ensure stakeholders understand and trust regulatory processes.

5. Building Trust with Stakeholders:

- a. Foster partnerships with advocacy groups and others in the rare disease community to establish platforms for engagement to ensure patient and

- other stakeholder perspectives are integrated into policy decisions, including regulatory processes.
- b. Utilize community initiatives such as Rare Disease Day events to highlight shared goals and challenges.

6. Equal Participation:

- a. Implement targeted outreach to underserved and underrepresented populations, including ultra-rare disease groups and pediatric patients, to ensure inclusivity.
- b. Address systemic barriers, such as geographic and economic disparities, to broaden clinical trial participation.
 - i. Reduce patient burden through decentralized trial models and incorporation of flexible participation requirements.

7. Continuous Engagement:

- a. Sustain dialogue through advisory boards, focus groups, etc., to ensure advocacy groups and others in the rare disease community are involved throughout the drug development lifecycle.
- b. Create a mechanism for early engagement with non-sponsors in the pre-competitive space to allow for practical advice on
 - i. the development of biomarkers, clinical endpoints, registries, and natural history studies that contain quality fit-for-purpose data
 - ii. clinical trial design and risk-benefit assessment considerations
 - iii. regulatory decision-making and frameworks.
- c. Expand FDA's START Program to expedite early phase IND-enabling rare disease drug development.
- d. Provide additional support for academic rare disease developers.

8. Cross-Sector Partnerships:

- a. Strengthen partnerships among FDA, industry, academia, and advocacy groups through joint workshops, Patient-Focused Drug Development (PFDD) meetings, and advisory boards. Consider Science-Focused Drug Development meetings or similar workshops to address issues common to rare disease, or to classes of rare diseases or conditions.
- b. Foster public-private partnerships to advance research and develop innovative therapies.

9. Global Collaboration:

- a. Work with international organizations to facilitate global access to therapies.
- b. Assist with international rare disease drug development collaborations.
- c. Coordinate with global regulators to harmonize standards, reducing duplicative efforts and expediting approvals.
- d. Collaborate on shared goals, such as improving diagnostic tools and establishing cross-border clinical trial frameworks.

10. Funding and Incentives:

- a. Advocate for increased public and private funding to address the unmet needs of rare diseases.
- b. Introduce incentives such as extended orphan drug benefits and tax credits to encourage industry participation in rare disease drug development.

Engagement - Within and Cross Agency**1. Internal FDA Alignment:**

- a. Create a Rare Disease Advisory Committee to standardize decision-making and ensure consistent application of regulatory processes across CDER, CBER, and review divisions.
 - i. Provide consistent advice to sponsors across FDA review divisions.
 - ii. Standardize application processes and approval timelines to provide sponsors with greater confidence in regulatory outcomes.
- b. Develop cross-division communication mechanisms to harmonize reviews for rare disease therapies, including use of flexibility in review and approvals.
- c. Train FDA reviewers in rare disease complexities to enhance consistency and expertise in rare disease regulatory decisions.

2. Interagency Collaboration:

- a. Strengthen partnerships with agencies such as the National Institutes of Health (NIH), Centers for Medicare & Medicaid Services (CMS), and Social Security Administration (SSA) to streamline policies on reimbursement, disability evaluations, and clinical research.

Innovation**1. Revolutionizing Clinical Trials:**

- a. Embrace master protocols (e.g., basket or platform trials) and adaptive trial designs to accommodate the small, diverse populations characteristic of rare diseases.
- b. Incorporate digital health technologies, wearable devices, and patient-reported outcomes (PROs) to enhance trial efficiency and relevance.
- c. Expand the use of surrogate endpoints, including biomarkers, for accelerated approvals, especially in progressive or severe diseases.
- d. Leverage real-world evidence (RWE) and natural history studies to inform regulatory decisions and reduce trial burdens.
- e. Utilize novel endpoints, biomarkers, and statistical methods.
- f. Focus on drug repurposing for rare disease drug development.
- g. Advance “ultra-rare” drug development policies.

2. Technological Integration:

- a. Support of artificial intelligence (AI) and machine learning (ML) to optimize dose selection, patient stratification, and trial design.

- b. Apply advanced modeling techniques to predict outcomes and accelerate the development of therapies.

3. Centralized Data Sharing:

- a. Create and support shared registries and data repositories to enable efficient data collection and sharing to avoid redundancies in regulatory processes and clinical trials and improve transparency within the rare disease drug development community.