PhRMA
RESEARCH • PROGRESS • HOPE

NASEM Committee on Processes to Evaluate the Safety and Efficacy of Drugs for Rare Diseases or Conditions in the United States and the European Union

December 4, 2023

Lucy Vereshchagina, PhD
Senior Vice President, Science & Regulatory Advocacy, PhRMA

About PhRMA

- PhRMA is a voluntary, nonprofit association that represents the country's leading biopharmaceutical research and biotechnology companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Over the last decade, PhRMA member companies have more than doubled their annual investment in the search for new treatments and cures, including nearly $101 billion in 2022 alone.

Challenges in Rare Disease Drug Development

- Lack of regulatory precedent, small trial populations, heterogeneous patient populations, and/or limited understanding of disease natural history
  - Determining the appropriate efficacy endpoints for clinical trials
  - Feasibility of randomization and use of a concurrent control arm
  - Assessing dose response and exposure
  - Developing Clinical Outcome Assessments (COAs)
- Lack of relevant animal models
- Varying regulatory requirements across regions

Opportunities for Regulatory Flexibilities

- FDA's expedited development and review programs (i.e., Fast Track, Breakthrough Therapy Designation, Priority Review, and Accelerated Approval)
- Novel trial designs, including adoptive and decentralized clinical trials
- Innovative use of biomarkers and novel endpoints
- Novel approaches to statistical analysis
- Adoption of a flexible framework for the development and modification of COAs
  - Integrating perspectives of patients, family, and caregivers
- Advancing international harmonization

PDUFA VII Will Enhance Rare Disease Drug Development

- Establishes a Rare Disease Endpoint Advancement (RDEA) pilot program for supporting efficacy endpoint development
  - Additional engagement opportunities with FDA to sponsors of development programs that meet specific criteria
  - Develops staff capacity to enable and facilitate appropriate development and use of these types of novel endpoints.
  - Up to 3 public workshops by the end of FY 2027 to discuss relevant topics
- For cell and gene therapies, continue stakeholder discussions on the use of existing approaches (e.g., surrogate endpoints, real world evidence, complex innovative designs, natural histories) and explore new approaches for obtaining efficacy and safety information with specific consideration and attention to rare and ultra-rare diseases.
- Establishes a digital health technologies framework to guide the use of DHT-derived data in regulatory decision-makings for drugs and biological products.
- Advances the use of complex adaptive and other novel clinical trial designs and facilitates the use of decentralized clinical trials which can also increase diversity of clinical trial participants
  - FDA issued a draft guidance on the implementation of decentralized clinical trials in May 2023

Increase Acceptance of Data Generated Outside RCT

- Non-randomized observational data (e.g., from natural history studies, patient registries, expanded access programs) may generate evidence acceptable for regulatory decision-making regarding treatment safety and effectiveness
- PDUFA VII Advancing RWE Program
  - Improve the quality and acceptability of RWE-based approaches in support of new intended labeling claims, including approval of new indications of approved medical products or to satisfy post-approval study requirements
- FDA should consider providing recommendations to improve data collection and analysis under expanded access so that it may be considered fit-for-purpose as confirmatory evidence

PhRMA
RESEARCH • PROGRESS • HOPE

Thank You