What you want and need to know about the Rare Disease Cures Accelerator – Data and Analytics Platform

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Alone we are rare. Together we are strong.®
Opening
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Vanessa Boulanger, NORD
Michelle Campbell, FDA/CDER
Jane Larkindale, C-Path

Q&A
All Panelists
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NORD, an independent nonprofit, is leading the fight to improve the lives of rare disease patients and families.

We do this by supporting patients and organizations, accelerating research, providing education, disseminating information and driving public policy.
What you want and need to know about the Rare Disease Cures Accelerator - Data and Analytics Platform

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Director of Research, National Organization for Rare Disorders

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Sr. Clinical Analyst, Stakeholder Engagement and Clinical Outcomes, Office of Neuroscience, FDA/CDER

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Executive Director, Rare Disease Cures Accelerator-Data and Analytics Platform and Duchenne Regulatory Science Consortium, C-Path

NORD®
National Organization for Rare Disorders

FDA
U.S. Food & Drug Administration

CRITICAL PATH INSTITUTE
Challenges to rare disease drug development: obstacles for research and data collection

Vanessa Boulanger, MSc
Director of Research, NORD
Challenges to rare disease drug development

- Limited funding for the study of rare diseases
  - Impacts scientific discovery, the development of expertise
- Limited understanding of progression of many rare diseases
  - Over time and for different people
  - Impacts drug development interest, duration of development, design of clinical trials
- Small patient populations spread over diverse geographic area
  - Challenges clinical trial design and recruitment
  - Harder to detect and understand effects
Challenges to rare disease drug development

● Standardization of data and measures
  ○ Challenges the ability to combine and compare
  ○ Can shape quality, utility, and interpretation of data

● Data ownership and sharing
  ○ Restricted ownership
  ○ Multiple studies, same condition
  ○ Split already small communities across multiple efforts
    ■ Smaller number per study
    ■ Burden on participants in multiple studies
RDCA-DAP Solutions

- Aim for 360° view of disease characterization and natural history
- Promote sharing of existing data
- Greater standardization of existing data and new data collected
- Larger pools of data/datasets
- Encourage greater representativeness in study samples - steps toward more equitable and inclusive study designs
- Accelerate understanding of conditions and commercial/research interest; inform the design of trials
- Opportunity for cross-disease discovery
- Efficient, effective use of resources
Collaboration: Founding Partners
Rare Disease Cures Accelerator-Data and Analytics Platform

Michelle Campbell, PhD
Sr. Clinical Analyst, Stakeholder Engagement and Clinical Outcomes Office of Neuroscience
FDA/CDER
Context and Motivation

• Regulators are working with rare disease patients, investigators, and companies, mostly one at a time, and most struggling with the same challenges:

  • Vast knowledge gaps about the natural course of the disease and small dispersed patient populations that make it hard to do the randomized clinical trials that save lives.

• There is a need for a better solution.
<table>
<thead>
<tr>
<th>Discovery / Translational / Preclinical</th>
<th>Clinical Development</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characterization of Disease</strong></td>
<td><strong>Clinical Study of New Treatments</strong></td>
</tr>
<tr>
<td>What is known about the disease?</td>
<td>Is the investigational drug available in a form that can be administered?</td>
</tr>
<tr>
<td>Are there well-defined lab tests—to diagnose the disease?</td>
<td>Pre-clinical safety testing done to inform assessment of safety in humans?</td>
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<tr>
<td>What is the natural history of the disease?</td>
<td>A study design specified?</td>
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<tr>
<td>What causes the disease (pathogenesis)?</td>
<td>A study protocol?</td>
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<tr>
<td></td>
<td>IRB review and approval?</td>
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<td>IND submitted for FDA review?</td>
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<tr>
<td></td>
<td>Plan for patient enrollment?</td>
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<tr>
<td></td>
<td>Patient access to the trial site?</td>
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<td>Plan for study data collection?</td>
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**Getting Patient Perspectives on their Disease and Treatment**
- What disease impacts matter most to patients?
- What is the landscape of currently available treatments?
Congress provided FDA an Opportunity in its Fiscal Year 2019 Appropriation

Within the increases provided for a New Platform for Drug Development in FY 2019, Congress appropriated funding for Investment and Innovation for Rare Diseases

CDER is investing funds in Innovation for Rare Diseases to launch work on “Rare Disease Cures Accelerator.”
Need for a “Rare Disease Cures Accelerator”

- Adopting a cooperative research approach to accelerate the move from bench to bedside for rare disease cures.

- A “Rare Disease Cures Accelerator” would provide the infrastructure for a cooperative scientific approach to clinical trials readiness in rare diseases.

- Some key components include:
  - Centralized standardized infrastructure to support and accelerate rare disease characterization
  - Standard core sets of COAs measuring impacts that matter most to patients, ideally applicable to more than one rare disease
  - Global rare disease clinical trials network
Centralized Standardized Infrastructure to Support and Accelerate Rare Disease Characterization

• There is a compelling need for:
  • Efficient comprehensive characterization of the natural history of a given rare disease targeted for clinical development
  • Characterization conducted rigorously with attention to established data quality standards, in order to be most useful to clinical trial design and regulatory review

• A standardized rare disease natural history study data platform is needed to provide a sustainable approach
  • This platform would provide a disease-neutral background data framework for the conduct of standardized natural history studies.
  • Disease-specific needs would be layered onto this framework to provide a rapid means for standardized, yet customized, development of natural history studies for any given disease.
The Rare Disease Cures Accelerator- Data and Analytics Platform (RDCA-DAP) is intended to serve as a neutral, independent data collaboration and analytics hub to promote the sharing of critically important data across rare diseases in order to accelerate the understanding of disease progression.
RDCA-DAP

Critical Path Institute and NORD partnering on initiative
RDCA-DAP: Long-term Goal for Impact on Drug Development

- Centralized and standardized infrastructure to support and accelerate rare disease characterization, allowing development of more efficient and effective clinical trial protocols
- Standardized data that can be extracted in CDISC format for regulatory submissions
- Aggregated data will allow for a better understanding of the variance in disease progression across broad range of patients aiding in development of optimized clinical trial protocols (endpoints, inclusion criteria, length and size of trial)
- Analytics and simulation tools to help optimize your trial protocol for your therapy
- Ability to look at dynamics of change in outcome measures and biomarkers in individual disease states and in related diseases and understand sources of variation in rate of change.
- Ability to potentially find and match historical or contemporary control patients to enrich your placebo arm and reduce numbers of patients.
How do we add data to the RDCA-DAP, and what do we get out of it?

Jane Larkindale, DPhil
Executive Director, RDCA-DAP
Interacting with RDCA-DAP

Where does data come from?
- Clinical Trial Data
- Registry Data
- Natural History Data
- Genomic Data
- Imaging Data
- Surveillance Data
- Preclinical Data
- Other Novel Data

What do you do with the data?
- Data Curation
- Incoming Data Storage
- Standardization
- Integrated Data for Analysis

C-Path Online Data Repository

How can I see and use the data?
- Interface level I: Dashboard
- Interface level II: Data interrogator and data extraction
- Interface level III: Advanced analytics
RDCA-DAP – Where does the data come from?

• RDCA-DAP does not collect new data from patients or in new studies
• RDCA-DAP seeks to get copies of data from existing sources:
  ○ Clinical trial data
  ○ Natural history data
  ○ Registries (patient-entered, clinical etc.)
  ○ Other sources
• You cannot identify any individual in RDCA-DAP’s data
• Data is very secure
• Data is only used/shared as allowed by the patient’s consent AND the agreement of the data custodian (person or company that collected the data)
• Data source is not identified – data is fully integrated.
Process for incoming data

INPUT
- Clinical Trial Data
- Natural History Data
- Patient Registry
- Clinical Data
- Other Data

OUTPUT
- Tools and analysis developed with data made available
- Data available per custodian’s direction

RDCA-DAP contact with custodian, negotiate data sharing agreement
Data transfer
Data exploration and mapping
Process for incoming data

**INPUT**
- Clinical Trial Data
- Natural History Data
- Patient Registry
- Clinical Data
- Other Data

**RDCA-DAP contact with custodian, negotiate data sharing agreement**

**Data transfer**

**Data exploration and mapping**

**OUTPUT**

**Tools and analysis developed with data made available**

**Data available per custodian’s direction**

*Feedback to custodians on data gaps, gaps in standardization, other enhancements to collection*

*Standardized data returned to custodians*

*Analysis and tools available*

*Larger dataset available*
What are these “tools” you are talking about, anyway?

**Biomarkers:** Total Kidney Volume (TKV) qualified as a prognostic biomarker for polycystic kidney disease (PKD), now accepted as a reasonably likely surrogate endpoint

**Endpoints:** Understanding variability in Duchenne progression as measured by different endpoints

**Models:** Clinical trial enrichment tool for Parkinson’s Disease

![Graphs and data visualizations related to biomarkers, endpoints, and models.](image-url)
DMD Clinical Trial Simulator - Version 1.0

Simulate clinical trials on patients with Duchenne Muscular Dystrophy

Contact us:
By Karthik Lingireddi, Juan Francisco Morales & Sarah Kim on behalf of the Critical Path for Duchenne Regulatory Science Consortium. E-mail sarahkim@cop.ufl.edu with questions or comments.
What is unique about RDCA-DAP as a data sharing platform – data integration and cross disease searches?

- Data can be extracted from the entire database and used in various ways.
  - This helps you understand what to measure in clinical trials, how to measure it, and helps develop efficient trial designs – accelerating drug development.
- Single database with data from multiple rare diseases provides visibility to industry – may lead to new drug development projects in diseases represented in the database.
- Database is being developed in collaboration with FDA, who will have access to the data and analytics.
What is unique about RDCA-DAP as a data sharing platform – analytic capabilities?

Database will have an associated analytics platform that will include:

• Simple dashboards and visualizations of the data in the platform
• Ability to explore the data and do basic statistical tests on data (data interrogator)
• Ability to extract subsets of the data for analysis (data subset generator)
• Platform for more sophisticated analysis tool development (e.g. pharmacometric modeling, disease progression models)
• Artificial intelligence/machine learning interfaces to extract new knowledge from data
Interacting with RDCA-DAP

RDCA-DAP DATA COLLABORATION CENTER

C-Path Online Data Repository

Data Vault → Curation → Incoming Data Storage → Standardization → Integrated Data for Analysis

Interface level I: Dashboard
Interface level II: Data interrogator and data
Interface level III: Advanced analytics

Clinical Trial Data
Registry Data
Natural History Data
Genomic Data
Imaging Data
Surveillance Data
Preclinical Data
Other Novel Data

ACTIONABLE DRUG DEVELOPMENT SOLUTIONS
Engaging with Us

Vanessa Boulanger, MSc
Director of Research, NORD
How to engage with RDCA-DAP?

Defined pathway of engagement for all stakeholders

Our focus today is on different opportunities for patient organizations to get involved with RDCA-DAP:

- Organizations engaging in or leading research and data collection, including IAMRARE Community Partners
- Organizations in need of guidance to optimize or evolve their research plans
- Organizations supporting research activities
We want to hear from you!

Organizations engaging in or leading research and data collection, including IAMRARE Community Partners
  • Consider contributing data

Organizations in need of guidance to evolve their research plans
  • Tools to optimize data

Organizations not directly involved, but supporting research activities
  • Outreach and engagement, partnerships
Questions?
Please enter your questions in chat.

Further information is at:  [c-path.org/programs/rdca-dap/](c-path.org/programs/rdca-dap/)

To contribute data contact: rdcadap@c-path.org
Funding for this webinar was made possible, in part, by the Food and Drug Administration through grant U18 FD 005320. Views expressed in written materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does any mention of trade names, commercial practices, or organization imply endorsement by the United States Government.

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