The Rare Disease Cures Accelerator–Data and Analytics Platform

Rare Disease Drug Development

Over 350 million people in the world have one of more than 7,000 rare diseases. In the United States a rare disease is defined as one affecting fewer than 200,000 people. The Orphan Drug Act in the U.S., and similar laws in other countries, have created incentives for companies to develop rare disease drugs, nonetheless only about 600 or 10% of rare diseases have an FDA-approved treatment available, and drug development is frequently slowed by the low numbers of patients and limited understanding of the variability and progression of each disease.

Many new drug targets have been identified and new products are now in development for such diseases. Drug development, however, is frequently slowed by the low numbers of patients with each disease, and the lack of a comprehensive quantitative characterization of diseases. This means that design of clinical trials that can reliably evaluate the efficacy and safety of a potential therapy is challenging.

Developing a clear understanding of how each disease progresses, as measured by defined outcome measures and/or biomarkers, allows for development of clinical trial protocols that efficiently determine if a new therapeutic is effective or not. This accelerates clinical development, makes it less expensive and encourages new companies to develop rare disease drugs.

What is the Rare Disease Cures Accelerator-Data and Analytics Platform?

The Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP®) is an integrated database and analytics hub that is designed to be used in building novel tools to accelerate drug development across rare diseases. It has been developed by the Critical Path Institute (C-Path) and the National Organization for Rare Disorders (NORD) through a collaborative grant from the U.S. Food and Drug Administration.

RDCA-DAP promotes the sharing of existing patient-level data and encourages standardization for collection of new data. It includes both an integrated data platform containing data across rare diseases and an analytics platform based on this data. The analytics platform includes basic data interrogation tools allowing the user to understand the data in the system, a tool for extracting subsets of patient-level data for analyses and an advanced analytics platform where users (and C-Path's internal quantitative medicine team) are able to develop more advanced tools, such as disease progression models and clinical trial simulation tools, models of biomarkers across diseases and apply artificial intelligence/machine learning algorithms to address future needs.

What is the Value of the Rare Disease Cures Accelerator-Data and Analytics Platform?

By integrating available data in a regulatory-grade format suitable for analytics, RDCA-DAP accelerates the understanding of disease progression (including sources of variability to optimize the characterization of subpopulations), clinical outcome measures and biomarkers, and facilitates the development of mathematical models of disease and innovative clinical trial designs. RDCA-DAP is positioned to generate solutions to drug development, which can be made publicly available to qualified researchers in industry, government, regulatory agencies and academia. As such, the utility of the patient-level data is maximized and used to develop tools that will be accessible to the community, to optimize and accelerate drug development across rare diseases.

How do we do it?

RDCA-DAP houses integrated patient-level data from diverse sources, including clinical trials, longitudinal observational studies, patient registries and real-world data (e.g., electronic health records) across a multitude of rare diseases. Data

are, and will continue to be, contributed from different organizations and companies around the world and may include genomic data, imaging data and information about other novel biomarkers and outcome measures as well as clinical data. C-Path has extensive experience in building such integrated databases in many diseases, including existing rare disease databases (in Duchenne muscular dystrophy, Huntington's disease, Friedreich's ataxia and polycystic kidney disease).

C-Path has partnered with NORD to leverage its extensive expertise to identify potential data contributors and establish contacts with contributing organizations. Data contribution and use agreements will be negotiated to allow patient-level data transfers to the platform. C-Path will then standardize and integrate the data with other contributed data to make the data available at the appropriate user level (from regulatory agencies to qualified researchers), to the degree agreed to by the data contributors.

Collaboration

RDCA-DAP does not compete with ongoing efforts that are actively collecting (or plan to prospectively collect) patient-level data in rare diseases. RDCA-DAP contributes to the added value of such efforts, by providing a standardized platform for the integration of those patient-level data, with accessibility levels determined by each data contributor, as per C-Path's legal contract for Data Contribution Agreements. Additionally, RDCA-DAP will not compete with, or hamper the ability of ongoing efforts to provide access to patient-level data in rare diseases. RDCA-DAP contributes to the added value of such efforts, by partnering with the custodians of such datasets and provide regulatory-grade remapped versions of datasets back to ongoing platforms that make such data available in a non-monetized fashion.

Data Sharing Process with RDCA-DAP

RDCA-DAP integrates existing data sets to build a larger cross-disease database to provide new insights into disease progression and aid in the development of tools to help design efficient and effective clinical trials. RDCA-DAP promotes the sharing of existing patient-level data, makes such data available and provides an analytics platform to help interpret the data.

RDCA-DAP shares data with the original data custodian* who collected the data via the process below:

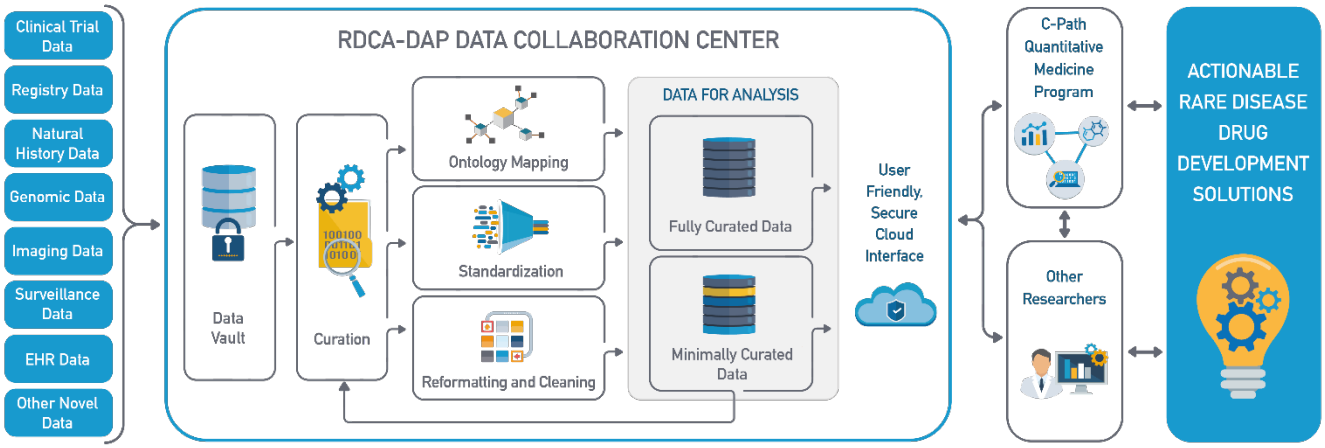
1. A dataset is identified (either through the data custodian approaching RDCA-DAP or external outreach by RDCA-DAP to the data custodian)
2. Discussion between the data custodian and RDCA-DAP to determine:
   a. What the data set contains (i.e., what data elements or type of data elements)
   b. Type of data included (registry/clinical trial, etc.) and whether the consent forms signed by the patients allows the data to be shared
   c. Whether the data was collected as a part of an ethical study (i.e., was the protocol reviewed by appropriate ethics panels)
   d. Whether the data can be appropriately de-identified**
   e. Where the data resides (different countries have different laws around data transfer)
   f. How widely the data custodian would like the data to be shared, and when it may be shared (all researchers, pre-selected groups of researchers or no sharing of patient level data, just tools developed from the data)
3. RDCA-DAP determines that the data will be of value to the research/drug development community and the custodian is willing to share.
4. RDCA-DAP sends a "Data Sharing Agreement" to the data custodian, an agreement signed by C-Path and the data custodian that:
   a. Affirms the custodian has the right to share the data
   b. Affirms the data can legally be shared (consent, ethics, de-identification)

***Data Custodian:** the entity that has collected the data and controls the use of the dataset. The patient owns their data and has given the custodian the right to use and share the data.

****De-identified:** patient's identity cannot be determined from the data. There are specific rules about what fields must be removed from a dataset for it to be considered de-identified.

c. Dictates the degree to which RDCA-DAP can share the data with others and use the data
d. Describes the data, the format of the data and any additional documentation that the custodian can share to help interpret the data (e.g., protocols, data dictionaries, case report forms)
e. Verifies RDCA-DAP will treat the data with appropriate data protection and ensure other users do the same

5. Custodian ensures that the data has had all identifiable fields removed (e.g., name, date of birth, address, etc.).
6. Custodian sends a copy of the data to RDCA-DAP through a secure link provided by C-Path, along with any available additional documentation.
7. C-Path will begin to curate the data and may go back to the custodian to clarify data elements.
8. After quality control steps, the data will be loaded onto the platform for use as described in the data sharing agreement.



For questions or additional information about RDCA-DAP or to share data, please email rdcadap@c-path.org.