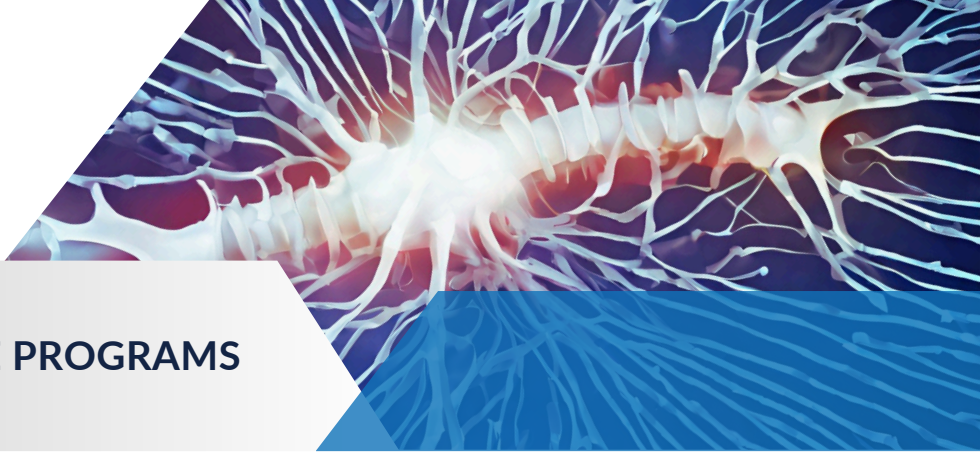
RARE AND ORPHAN DISEASE PROGRAMS

CRITICAL PATH INSTITUTE



RARE AND ORPHAN DISEASE PROGRAMS

RARE DISEASE DRUG DEVELOPMENT

Over 350 million people worldwide live with one of over 7,000 rare diseases, defined in the U.S. as affecting fewer than 200,000 individuals. While legislation like the Orphan Drug Act incentivizes drug development, only about 10% of rare diseases have FDA-approved treatments. Challenges include limited patient numbers and understanding of disease variability. Despite identification of new drug targets, slow development persists due to these challenges and lack of comprehensive disease characterization. Clear understanding of disease progression and use of defined outcome measures streamline clinical trial design, accelerating development and encouraging new companies to pursue rare disease drugs.

RARE AND ORPHAN DISEASE PROGRAM

C-Path's Rare and Orphan Disease Program is dedicated to addressing the unmet needs of more than 40 rare diseases, including Duchenne muscular dystrophy, rare neurodegenerative conditions such as ALS, Huntington's disease, the ataxias and more. Utilizing C-Path's core competencies, the program endeavors to devise drug development tools and other solutions endorsed by regulatory bodies like the FDA and EMA. These resources are accessible to developers, bolstering the progress of treatments and potential cures. Moreover, the program ensures the inclusion of individuals and families with lived experience at every stage.

RDCA-DAP®
Rare Disease Cures Accelerator
Data and Analytics Platform

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Critical Path Institute's Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP®) is central to the success of the Rare and Orphan Disease Program. RDCA-DAP is an FDA-sponsored initiative that provides a centralized and standardized infrastructure to support and expedite rare disease characterization, with the goal of advancing drug development solutions to accelerate the development of treatments for rare and orphan diseases.

RDCA-DAP integrates patient-level data across a multitude of rare diseases, contributed from academics, registries, clinical trials and hospital networks worldwide.

PROGRAM FOCUS

Eight dedicated pre-competitive collaborations that collectively accelerate rare disease drug development in areas of unmet need.

CPA-1 — CRITICAL PATH FOR ALPHA-1 ANTITRYPSIN DEFICIENCY

CPA-1 generates solutions for unmet drug development needs in AATD, with a specific focus on addressing its hepatic and pulmonary manifestations.

CPLD — CRITICAL PATH FOR LYSOSOMAL DISEASES

CPLD fosters collaboration among a broad spectrum of LD stakeholders – spanning industry, academia, patient advocacy, and regulatory entities.

CP-RND — CRITICAL PATH FOR RARE NEURODEGENERATIVE DISEASES

CP-RND brings together multiple experts in rare neurodegenerative diseases, including ALS, to dvance our understanding of disease pathology, treatment options, diagnostics and drug development.

CPTA — CRITICAL PATH TO THERAPEUTICS FOR THE ATAXIAS

CPTA brings together experts from across different fields of ataxia research, and drug development to create regulatory tools and strategies within a neutral forum that will catalyze clinical progress in the ataxias.

D-RSC — DUCHENNE REGULATORY SCIENCE CONSORTIUM

D-RSC has created an integrated database of patient-level clinical data from DMD studies, which is partially available for analysis by the Duchenne community as permitted by the owners of each dataset.

HD-RSC — HUNTINGTON'S DISEASE REGULATORY SCIENCE CONSORTIUM

HD-RSC leverages the deep knowledge of HD gained from working with patients, families, researchers, neurologists, and clinical scientists, as well as previous learnings from other C-Path neuroscience consortia to achieve success.

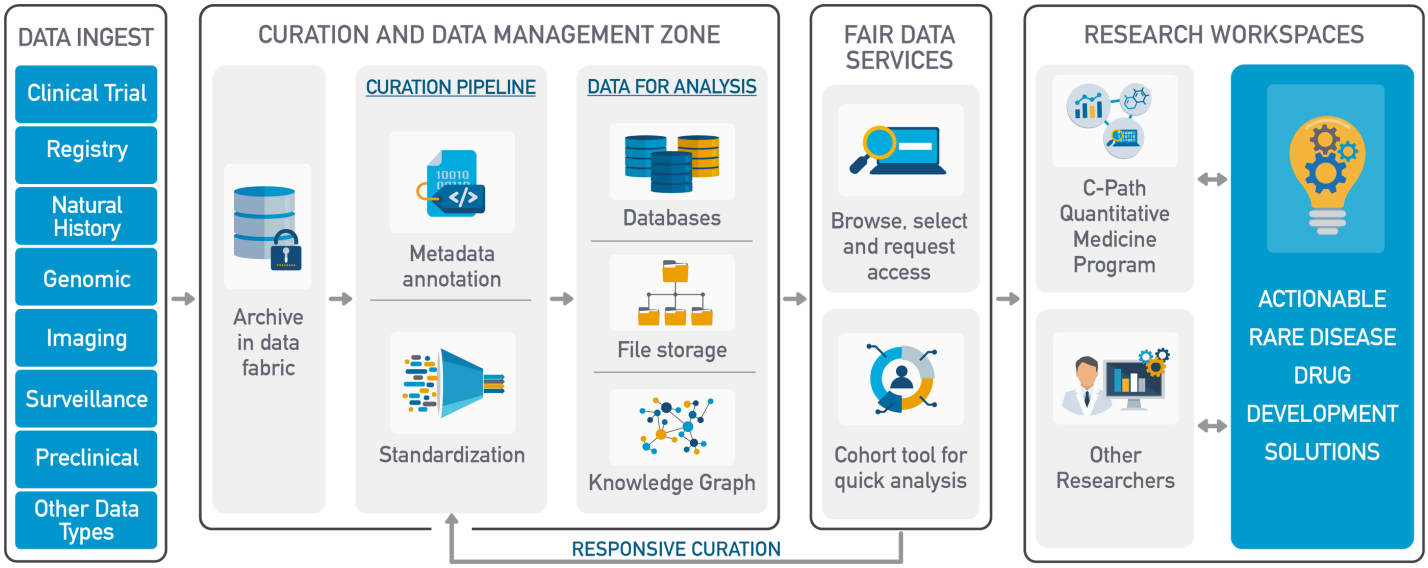
PKD — POLYCYSTIC KIDNEY DISEASE OUTCOMES CONSORTIUM

PKDOC is a collaborative partnership whose research leads to advancement of treatments for PKD.

RD-COAC — RARE DISEASE CLINICAL OUTCOME ASSESSMENT CONSORTIUM

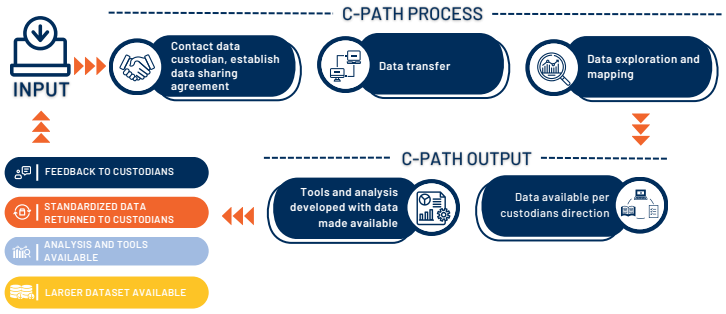
RD-COAC enables precompetitive, multi-stakeholder collaboration aimed at identifying scientifically sound tools and methodologies for collecting clinically meaningful outcomes data in treatment trials for rare diseases.

MAXIMIZING EVERY DATA POINT



C-PATH: A NEUTRAL CONVENER

C-Path provides expert pre-competitive peer guidance, validation, and regulatory grade tools to de-risk the path towards regulatory approval.



COLLECTIVE INFLUENCE

- Extensive, **multi-decade connections** with regulatory authorities
- Strict **neutrality** standards and values
- **Cutting edge guidance** in predictive analytics, pharmacometrics, data sequencing and methodologies
- **Leading collaborative innovation:**
  - AI for regulatory decision-making
  - Cell and gene-based therapies
  - Digital health technologies
  - Diverse and decentralized trials
  - Real-world evidence

Together, C-Path addresses unmet needs on a global scale, engaging the rare disease community to guide our focus.

TASK FORCES

C-Path Task Forces or collaborative efforts are designed to help, facilitate or accelerate drug development while improving the understanding of a disease.

Current task force and collaborative efforts include:

Friedreich's Ataxia Collaborative
- Launched February 2018
- Members: FARA, EFACTS
- Database: Natural history and multiple trials
- Deliverable: Clinical Trial Design, Drug Development Tools (Clinical Trial Simulation Tool obtained)

Progressive Supranuclear Palsy (PSP)
- Launched December 2023
- Members: Novartis, Cure PSP, The Association for Frontotemporal Degeneration, Rainwater Charitable Foundation (RCF), key opinion leaders
- Database: Natural history and multiple trials
- Deliverable: Drug Development Tool (early Disease Progression Model and Clinical Trial Simulation Tool obtained)

Rare Mitochondrial and Inherited Metabolic Diseases
- Launched January 2024
- Members: Astellas Pharma, 9+ patient advocacy groups, key opinion leaders
- Database: Registry, digital app PRO
- Deliverable: Data aggregation to inform data standardization and collection across diseases

Limb Girdle Muscular Dystrophy
- Launched June 2024
- Members: ML Bio Solutions, 4+ patient advocacy groups, key opinion leaders
- Database: Industry-led observational trial, 3 academic natural history studies (under negotiation)
- Deliverable: Drug Development Tool

c-path.org/fda-acknowledgement