The C-Path Vision: Sharing Data and Expertise to Accelerate the Development of Safe and Effective Therapies for Neonates

Martha Brumfield, President and CEO

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C-Path Mission

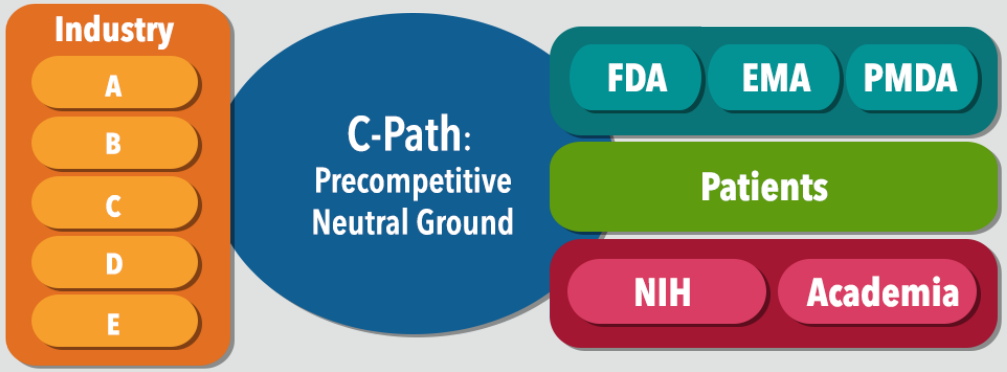
C-Path

The Critical Path Institute is a catalyst in the development of tools to advance medical innovation and regulatory science, accelerating the path to a healthier world. We achieve this by leading teams that share data, knowledge, and expertise, resulting in sound, consensus-based science.

C-Path: A Public-Private Partnership

- Act as a trusted, neutral third party
- Convene scientific consortia of industry, academia, and government for sharing of data/expertise

✓ The best science
✓ The broadest experience
✓ Active consensus building
✓ Shared risk and costs



- Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products

- Official regulatory endorsement of novel methodologies and drug development tools

Why Form A Global Collaboration

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Current State:

Underserved population

Underfunded area of research and investment

Knowledge, expertise, and experience is in silos

Future State:

More and better treatment options

Accepted standards of care

Accepted requirements for regulatory labeling for medical products

Mission Of INC

Accelerating the development of safe and effective therapies for neonates. The consortium will address the need for measurement and assessment of clinical outcomes in neonates through teams that share data, knowledge, and expertise to advance medical innovation and regulatory science.

<u>For neonates, we aim to add value by:</u>

- Adding more predictability in regulatory path for study in neonates
- Adding knowledge to enhance treatment for neonates
- Demonstrating principles of approach that are transferable

WHAT CAN INC DO?

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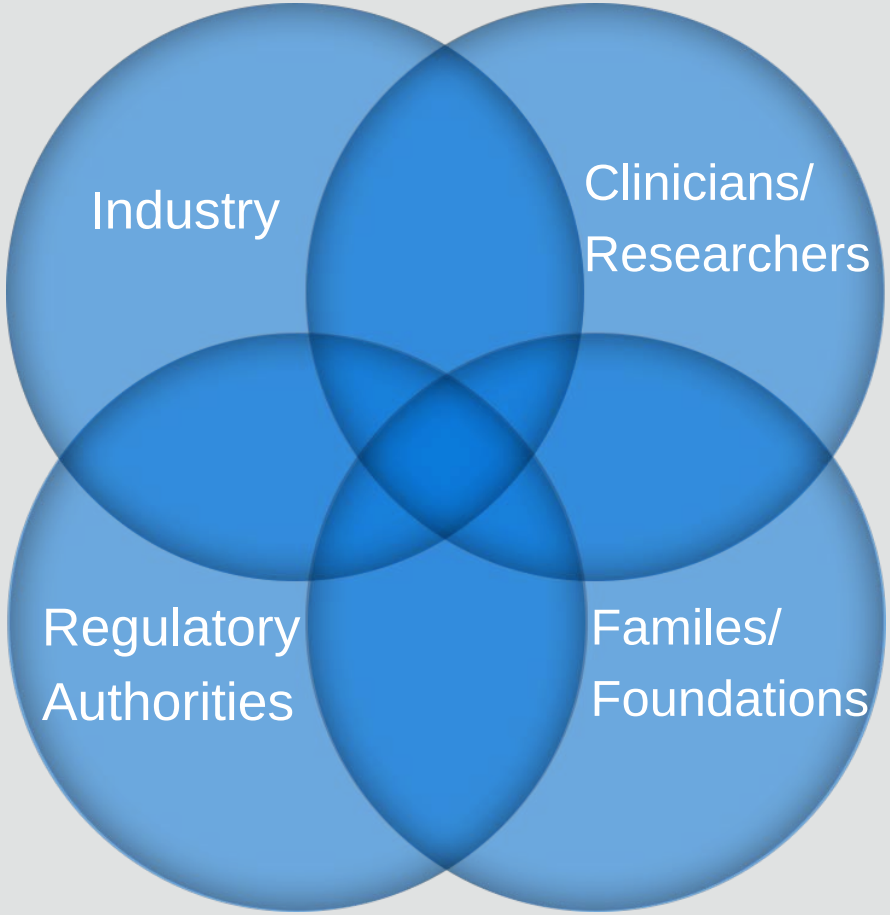
Roadmap to get there:

- ✓ Bring together industry, regulators and academic experts in a collaboration, to share knowledge, data, etc.
- ✓ Include patient groups and disease foundations as active participants
- ✓ Identify specific projects for which there is an unmet need
- Prioritize area(s) of initial focus and what specific objective(s) is(are)
- Develop a detailed research plan with specific timelines and deliverables early in the process

How it happens:

- Form consortium with structure, leadership support, processes to drive project forward and lead to meaningful deliverables for this population

Collaboration



- Define roles & responsibilities
- Communication
- Differing organizational priorities
- Keeping the end goal in mind

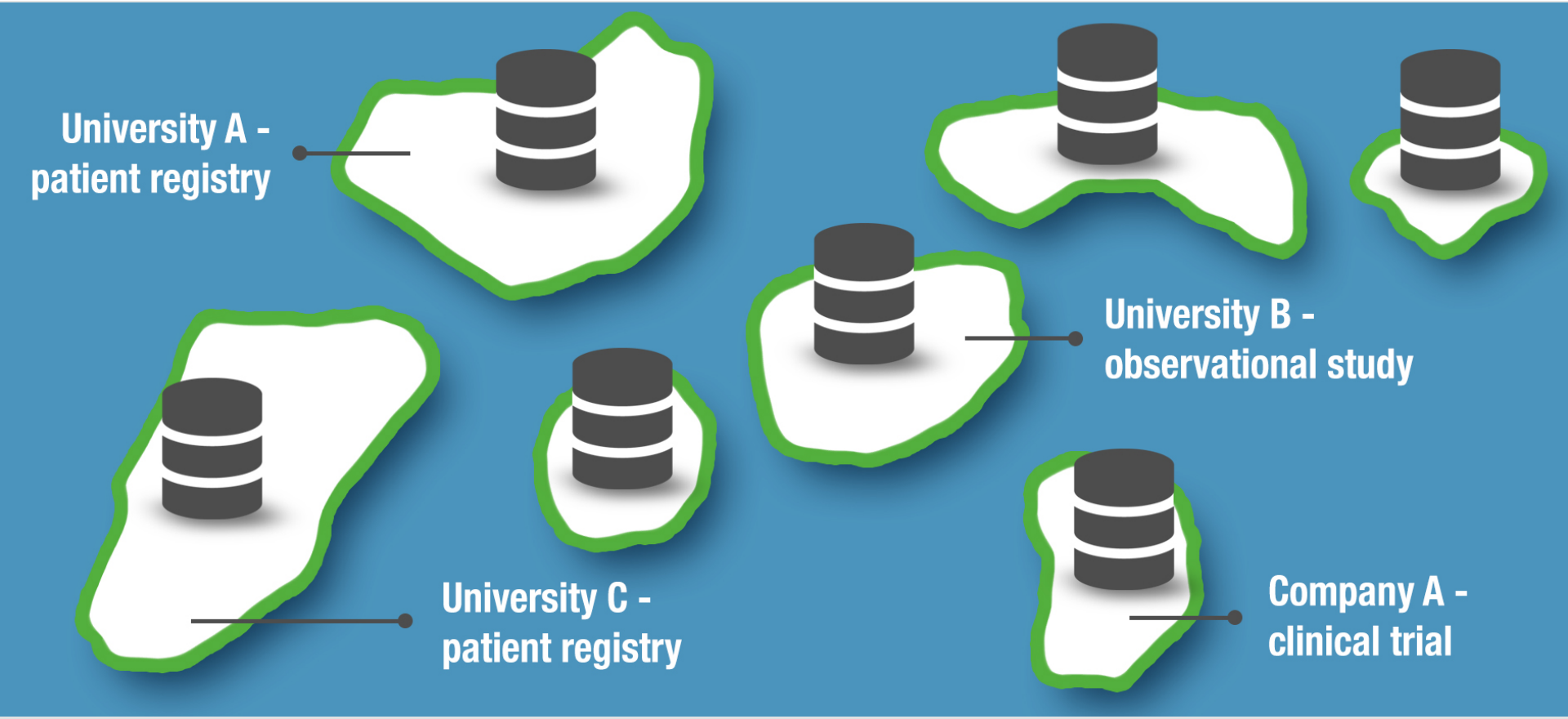
Factors Favoring Successful Collaborations

- We create a “trust accelerator” by doing our roles and doing them well
- We are data-led
- We are mindful of differences and work through them
- We embrace the concept of “constructive conflict”
  - learning from and being honest about failures
  - asking the important questions and not being afraid of the answer
  - using inquiry to seek truth, not to confirm we were right
- We engage in a collaborative process, all sharing knowledge, expertise, and data as appropriate
- Every part of the consortium contributes work (in-kind contribution)

Key Challenges To Overcome

- Potential for churn if each participant is not working in sync
- In-kind efforts from very busy people
- Scientific and regulatory uncertainty
  - maturity of science and regulatory “readiness”
  - uncertain evidentiary standards
- Sufficient funding to accomplish deliverables

Neonatal Data Archipelago



"We must be sober in our assessment of where we are…. We should know what we know now before we do more…."

Vasee Moorthy (WHO)

How: Data-Sharing

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Success Factors

- Utilization of same regulatory accepted data standard
- Establish the objective for data-sharing
- Determine what data are needed and define clear quality criteria
- Employ consistent and transparent data process
- Maximize data utility through standardization
- Engage in ongoing curation, validation, and reporting
- Manage range of data types: clinical trial, observational, registry, genotypic, phenotypic, treatment, and outcome data types

Processes and Safeguards

- Database access controls defined per consortium, with member agreement
  - access only by C-Path staff
  - access only by consortium members contributing data
  - access only by consortium members
  - access available to qualified external researchers
- De-identification procedures
  - fully de-identified data sets
  - documented by contributor with data-use agreement

How: Data-Sharing

Eventual Goals of Data-Sharing:

- Share organized curated data with range of researchers, optimizing utility
- User-friendly portal access and access criteria clearly established
- Address Competing Requirements
  - comply with applicable regulations
  - protect patient privacy
  - respect sponsor confidential information and IP
  - respect publication timeframes

Determine level of regulatory “endorsement” needed for deliverable

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Example mechanisms for regulatory “endorsement”:

- Regulatory qualification
- Co-publish with regulators
- Contribute to regulatory guidance
- Publication in the peer-reviewed literature with an editorial commentary from regulators
- Co-host scientific workshops with published proceedings

C-Path's Predictive Safety Testing Consortium

Mission: Improving tools for assessing drug safety

Project: Qualification of translational safety biomarkers for drug-induced kidney injury

Regulatory strategy: Qualification, publication, workshops

Phase 1 (2007-2009): Evaluation of biomarkers in rat; regulatory submission
Pharma (project leadership; funding; study conduct; data; toxicologists; vet pathologists; statisticians; regulatory experts; bioanalytical experts)
Academic labs (knowledge, data, assays)
Assay developers (specs. for assay validation)
FDA, EMA, PMDA (advice, review)

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Pharma (project leadership; funding; study conduct; data; toxicologists; vet pathologists; statisticians; regulatory experts; bioanalytical experts)	**Pharma** (as previous phase, plus: clinical safety expertise; samples from healthy volunteer studies)
Academic labs (knowledge, data, assays)	**Academic labs** (patient samples from DIKI setting)
Assay developers (specs. for assay validation)	**Phase 1 clinic** (healthy volunteer study)
FDA, EMA, PMDA (advice, review)	**Clinical assay developers and CLIA labs** (validation and run assays)
	FDA, EMA (advice, review)

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Pharma (project leadership; funding; study conduct; data; toxicologists; vet pathologists; statisticians; regulatory experts; bioanalytical experts)	**Pharma** (as previous phase, plus: clinical safety expertise; samples from healthy volunteer studies)	**Pharma** (predominantly funding and project leadership)
Academic labs (knowledge, data, assays)	**Academic labs** (patient samples from DIKI setting)	**Academic clinical trial sites** (patients, samples, data)
Assay developers (specs. for assay validation)	**Phase 1 clinic** (healthy volunteer study)	**CLIA lab** (performs sample tests and validates assay)
FDA, EMA, PMDA (advice, review)	**Clinical assay developers and CLIA labs** (validation and run assays)	**Foundation for the NIH** (partnership with C-Path)
	FDA, EMA, PMDA (advice, review)	**Innovative Medicines SAFE-T** (partnership with C-Path)
		FDA, EMA (advice, review)

C-Path's Polycystic Kidney Disease Consortium

Mission: Develop tools to create treatments for patients with PKD

Project: Qualification of total kidney volume as a prognostic biomarker for PKD

Regulatory strategy: Qualification

Phase 1 (2009 – 2011): Data standards development, data acquisition, curation and mapping
Tufts (Co-Director, scientific leadership)
Mayo; Emory Univ.; UC Denver (expertise, data & remapping)
PKD foundation (funding)
CDISC (data standards development)
pharma (funding; expertise)
NIH (data and expertise)
FDA (advice)

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Mayo; Emory Univ.; UC Denver (expertise, data & remapping)	**Mayo; Emory Univ.; UC Denver** (expertise)
PKD foundation (funding)	**PKD foundation** (funding)
CDISC (data standards development)	
pharma (funding; expertise)	**pharma** (funding; expertise)
NIH (data and expertise)	**Pharsight** (data analysis and modeling)
FDA (advice)	**FDA** (consultation/advice)

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Regulatory strategy: Qualification

Phase 1 (2009 – 2011): Data standards development, data acquisition, curation and mapping	**Phase 2 (2011 – 2012):** Data analysis and modeling including initial briefing package and BQRT meetings	**Phase 3 (2012 – 2015):** Regulatory submission and refinement of the model
Tufts (Co-Director, scientific leadership)	**Tufts** (Co-Director, scientific leadership)	**Tufts** (Write and review packages)
Mayo; Emory Univ.; UC Denver (expertise, data & remapping)	**Mayo; Emory Univ.; UC Denver** (expertise)	**Mayo; Emory Univ.; UC Denver** (Write and review packages)
PKD foundation (funding)	**PKD foundation** (funding)	**PKD foundation** (funding)
CDISC (data standards development)		
pharma (funding; expertise)	**pharma** (funding; expertise)	**pharma** (funding; review packages)
NIH (data and expertise)	**Pharsight** (data analysis and modeling)	**Pharsight** (writing and reviewing packages)
FDA (advice)	**FDA** (consultation/advice)	**FDA and EMA** (formal review) **Health Canada** (discussion)

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THANK YOU