



# Global Collaborations to Advance Innovation in Regulatory Science

October 27, 2015 “Better Science, Better Health”

**Dr. Lynn Hudson**  
**Chief Science Officer**  
**Critical Path Institute**



# C-Path Consortia in the Pre-Competitive Space



Twelve global consortia collaborating with 1,300+ scientists and 61 companies



**Coalition Against Major Diseases**  
*Focusing on diseases of the brain*



**Multiple Sclerosis Outcome Assessments Consortium**  
*Measuring drug effectiveness in MS*



**Coalition For Accelerating Standards and Therapies**  
*Data standards*



**Polycystic Kidney Disease Outcomes Consortium**  
*New imaging biomarkers*



**Critical Path for Parkinson's Consortium**  
*Enabling clinical trials in Parkinson's Disease*



**Patient-Reported Outcome Consortium**  
*Assessing treatment benefit*



**Critical Path to TB Drug Regimens**  
*Accelerating the development of TB drug regimens and diagnostics*



**Electronic Patient-Reported Outcome Consortium**  
*Electronic capture of treatment benefit*



**The Duchenne Regulatory Science Consortium**  
*Duchenne Muscular Dystrophy*



**Predictive Safety Testing Consortium**  
*Drug safety*



**International Neonatal Consortium**  
*Neonatal clinical trials*



**Pediatric Trials Consortium**  
*Developing effective therapies for children*

- ✓ Biomarkers
- ✓ Clinical outcome assessment instruments

- ✓ Clinical trial simulation tools
- ✓ Data standards
- ✓ In vitro tools

# Collaborating When Challenges Are Too Big For Any One Organization

## International Neonatal Consortium



- Develop practical tools to incorporate in clinical trials in neonates.
- McCune, S.K., Mulugeta, Y.A. “Regulatory science needs for neonates: a call for neonatal community collaboration and innovation.” *Front Pediatr.* 2: 135-137 (2014)

## Pediatric Trials Consortium



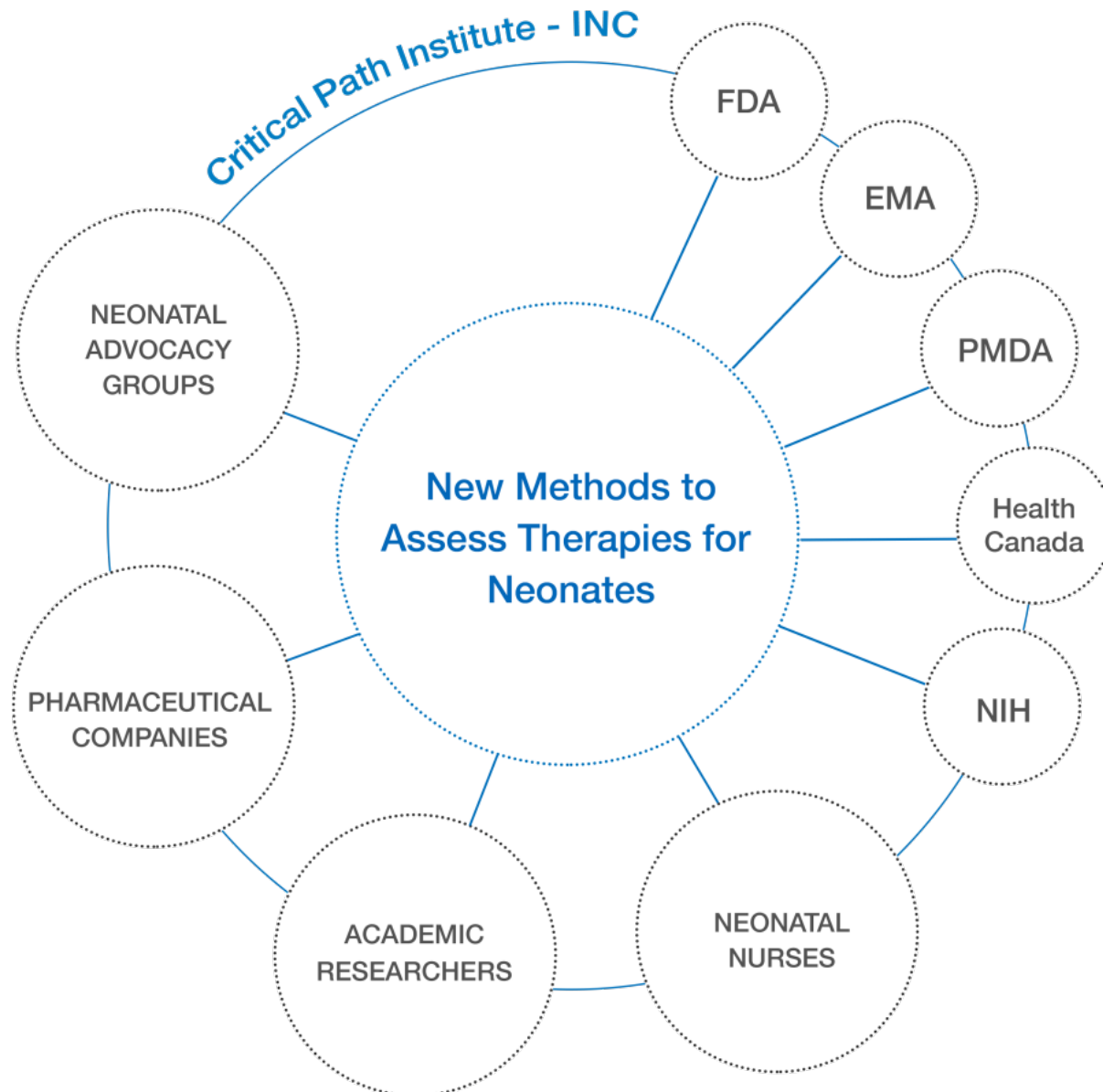
- Consortium will provide C-Path with recommendations to form a new non-profit organization.
- The new non-profit organization will provide the **sustainable infrastructure** needed to plan, start up,

conduct, and close out pediatric clinical studies that deliver the **high-quality data** necessary for **regulatory standards and review**.

### Primary outcomes:

Clinical trial efficiency & speed, High quality data, Increase in pediatric labels, Better clinical guidance for physicians and parents, Improved child health.

# INC Members Spanning the Globe



## Neonatal Nurses

- NANN
- COINN

## Founding Companies

- AstraZeneca
- Janssen
- Lilly
- Novartis
- Pfizer
- Sanofi
- Shire

## Families/Advocacy

- Graham's Foundation
- March of Dimes



# Prioritizing Initiatives to Address Unmet Needs

## INC AND THE NICU

The International Neonatal Consortium will concentrate its efforts on those conditions most commonly encountered in Neonatal Intensive Care Units (NICUs), and on the prevention of pre-term birth.



International Neonatal Consortium



**NEONATAL LUNG INJURY  
AND CIRCULATORY FAILURE**

**PERINATAL/NEONATAL  
INFECTIONS**

**NEONATAL ABSTINENCE  
SYNDROME (NAS)**

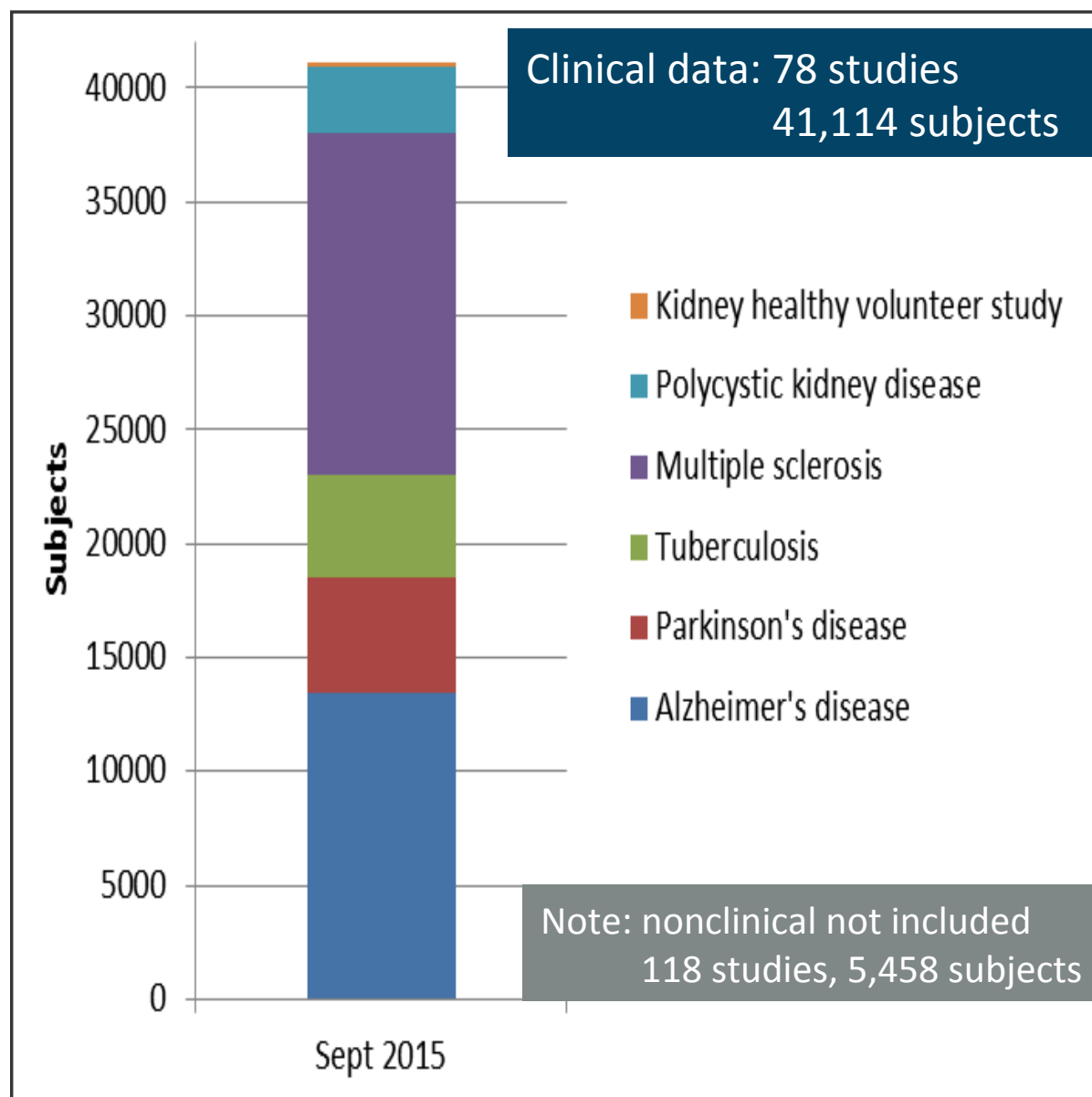
**RETINOPATHY OF  
PREMATURITY (ROP)**

**NEONATAL  
GASTROINTESTINAL INJURY**

**NEONATAL BRAIN INJURY**

**DRUGS TO PREVENT  
PRETERM LABOR**

# Sharing Data is Central to Developing New Methods to Evaluate Safety and Efficacy of Therapies

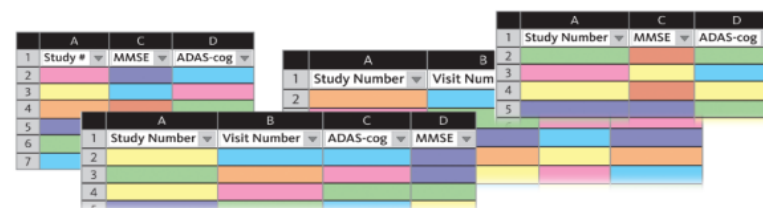


- Data contribution agreements implemented per dataset
- Level of allowable sharing defined in advance
- Data privacy assessment and anonymization must conform to all applicable regulations

# Value of Data Sharing, Standards, and Pooling

## Start Point

- Nine member companies agreed to share data from 24 Alzheimer's disease (AD) trials
- The data were not in a common format
- All data were remapped to the CDISC AD standard and pooled

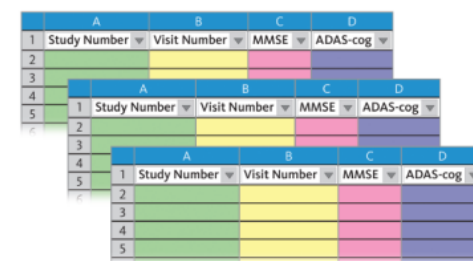


The diagram illustrates 'Disparate Legacy Data' by showing several overlapping and differently structured tables. Each table represents a different study with its own unique column headers and data organization, making them incompatible for direct pooling.

Disparate Legacy Data



CDISC Data Standards



The diagram illustrates 'Integrated Data' by showing multiple tables that have been standardized into a common format. All tables now share the same column headers: 'Study Number', 'Visit Number', 'MMSE', and 'ADAS-cog'. This standardization allows the data from all 24 studies to be pooled together for analysis.

Integrated Data

## Result

- A new clinical trial simulation tool was created and has been the first model endorsed by the FDA and EMA
- Researchers utilizing database to advance research

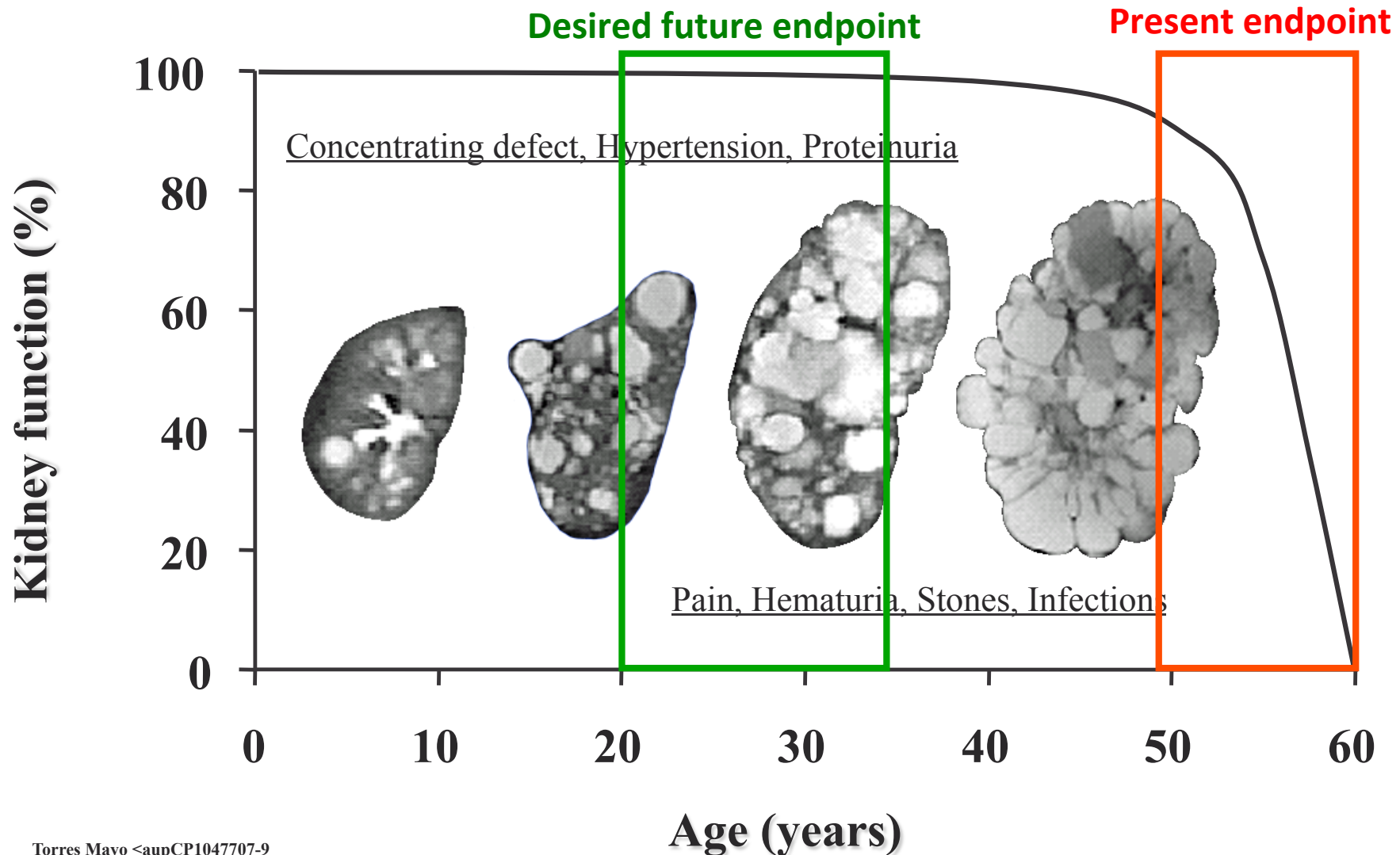


The screenshot shows the 'C-PATH ONLINE DATA REPOSITORY' interface. A blue banner at the top right reads 'Data integration'. Below the banner, there are search and filter options. A list of studies is displayed, including 'Study #', 'Study Name', 'Study Status', and 'Study Date'.

- Integrated database
- 24 studies, > 6500 patients
- Database accessed by > 200 qualified researchers in 35 countries

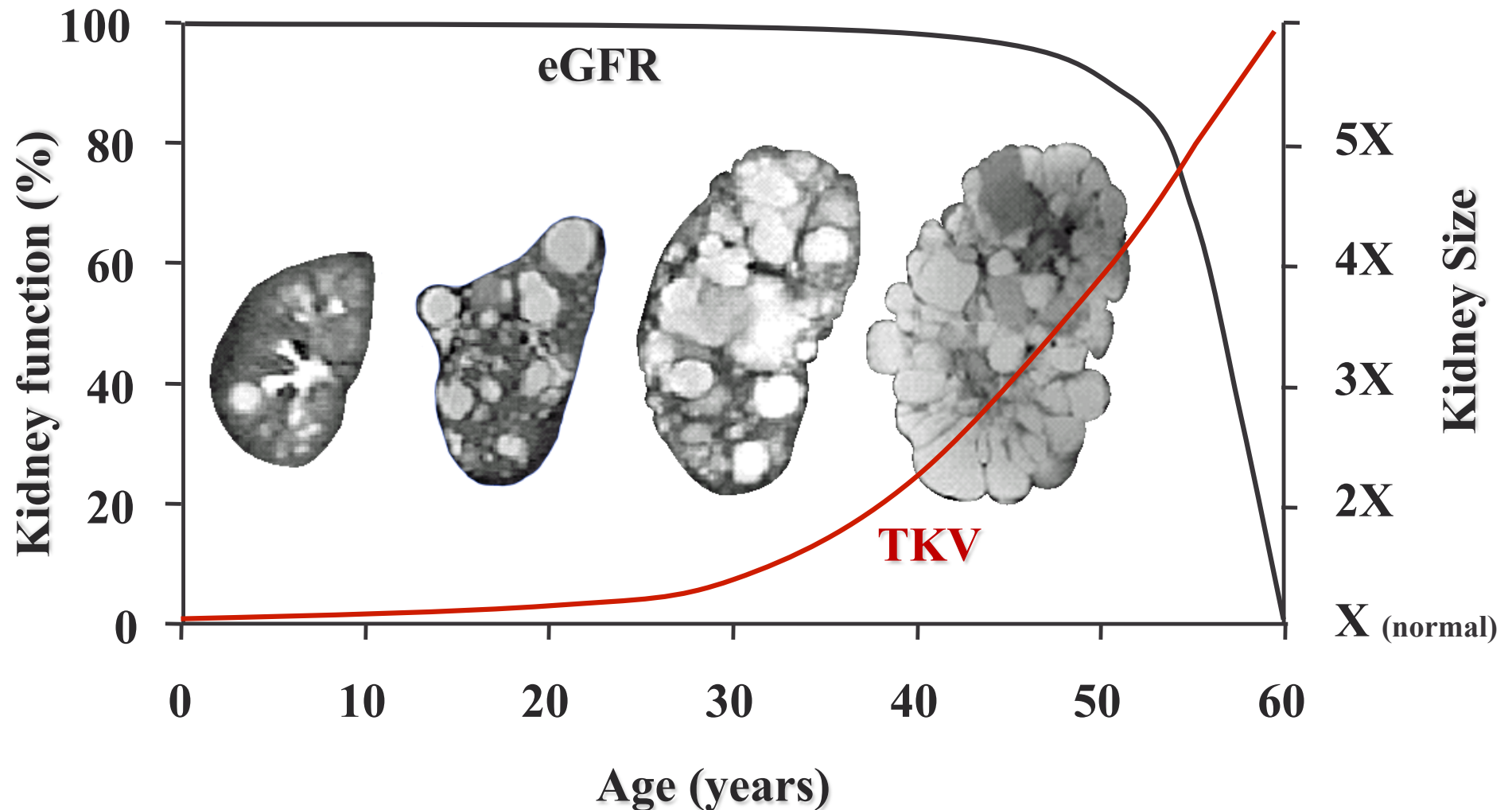
# Changing the Paradigm in Drug Development

## *Progressive kidney enlargement in Autosomal Dominant Polycystic Kidney Disease (PKD)*





# Biomarkers for Polycystic Kidney Disease: Baseline TKV and Baseline eGFR



# Qualification of Biomarker - Total Kidney Volume in Studies for Treatment of Autosomal Dominant Polycystic Kidney Disease



**August 17, 2015**

The Critical Path Institute's Polycystic Kidney Disease Outcomes Consortium Secures FDA Qualification for Enrichment Biomarker (**Total Kidney Volume**) in Autosomal Dominant Polycystic Kidney Disease (ADPKD)

## EMA Qualification Status:

CHMP has issued positive qualification opinion for TKV that is currently undergoing public review.

*Contains Nonbinding Recommendations*

*Draft — Not for Implementation*

## Qualification of Biomarker— Total Kidney Volume in Studies for Treatment of Autosomal Dominant Polycystic Kidney Disease

### Draft Guidance for Industry

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not create any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the Center for Drug Evaluation and Research (CDER) Biomarker Qualification Program (email: [CDER-BiomarkerQualificationProgram@fda.hhs.gov](mailto:CDER-BiomarkerQualificationProgram@fda.hhs.gov)).

Drug Development Tool (DDT) Type: Biomarker  
Referenced Biomarker(s): Total kidney volume (TKV)

TKV is defined as the sum of the volume of the left and right kidneys.

### I. SUMMARY OF GUIDANCE

#### A. Purpose of Guidance

This draft guidance provides a qualified context of use (COU) for the biomarker TKV in studies for the treatment of autosomal dominant polycystic kidney disease (ADPKD). This draft guidance also describes the experimental conditions and constraints for which this biomarker is qualified through the CDER Biomarker Qualification Program. This biomarker can be used by drug developers for the qualified COU in submissions of investigational new drug applications (INDs), new drug applications (NDAs), and biologics license applications (BLAs) without the relevant CDER review group reconsidering and reconfirming the suitability of the biomarker.

#### B. Application of Guidance

This guidance applies to the use of TKV in studies for the treatment of ADPKD. It does not change any regulatory status, decisions, or labeling of any medical imaging device used in the medical care of patients.

TKV use in drug development outside of the qualified COU will be considered by FDA on a case-by-case basis in regulatory submissions. In such cases, additional information relevant to the expanded use may be requested by the CDER product review team.

# Collaborating with other Partnerships to Biomarkers to Detect Kidney Injury



Press Contact  
Jenna R.M. Palfrey  
301.435.2613  
jmills@fnih.org

## The FNIH Biomarkers Consortium Launches Project to Improve Diagnosis of Kidney Injury

Researchers aim to advance acceptance of new biomarkers for monitoring kidney safety in the clinic

Bethesda, MD (October 25, 2011) – The Foundation for the National Biomarkers Consortium announced today the launch of a two-year study to advance the acceptance of new biomarkers designed to detect kidney injury in clinical trials. The study is being conducted in collaboration with the Biomarkers Consortium (PSTC), a public-private partnership founded by the Critical Path Institute (C-Path).



**IMI Contact**  
Catherine Brett  
+32 2 541 82 14  
[catherine.brett@imi.europa.eu](mailto:catherine.brett@imi.europa.eu)

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May 23, 2013



**C-Path Contact:**  
Allison Schott  
520 647 8380  
[aschott@c-path.org](mailto:aschott@c-path.org)

## LEADING US AND EUROPEAN MEDICAL PUBLIC-PRIVATE PARTNERSHIPS ANNOUNCE AGREEMENT Critical Path Institute and Innovative Medicines Initiative Collaborate on Development of Important New Drug Safety Tests

Tucson, AZ - The Predictive Safety Testing Consortium (PSTC) led by the Critical Path Institute (C-Path) and the Safer and Faster Evidence-based Translation (SAFE-T) consortium sponsored by the Innovative Medicines Initiative (IMI), announced today the



**Thank You**

[www.c-path.org](http://www.c-path.org)