Global Collaborations to Advance Innovation in Regulatory Science

October 27, 2015 "Better Science, Better Health"

Dr. Lynn Hudson
Chief Science Officer
Critical Path Institute

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a decade of excellence
10 YEARS

C-Path Consortia in the Pre-Competitive Space

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

Coalition Against Major Diseases
Focusing on diseases of the brain

Coalition For Accelerating Standards and Therapies
Data standards

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

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

The Duchenne Regulatory Science Consortium
Duchenne Muscular Dystrophy

International Neonatal Consortium
Neonatal clinical trials

Multiple Sclerosis Outcome Assessments Consortium
Measuring drug effectiveness in MS

Polycystic Kidney Disease Outcomes Consortium
New imaging biomarkers

Patient-Reported Outcome Consortium
Assessing treatment benefit

Electronic Patient-Reported Outcome Consortium
Electronic capture of treatment benefit

Predictive Safety Testing Consortium
Drug safety

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

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International Neonatal Consortium

INC
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- 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

PTC
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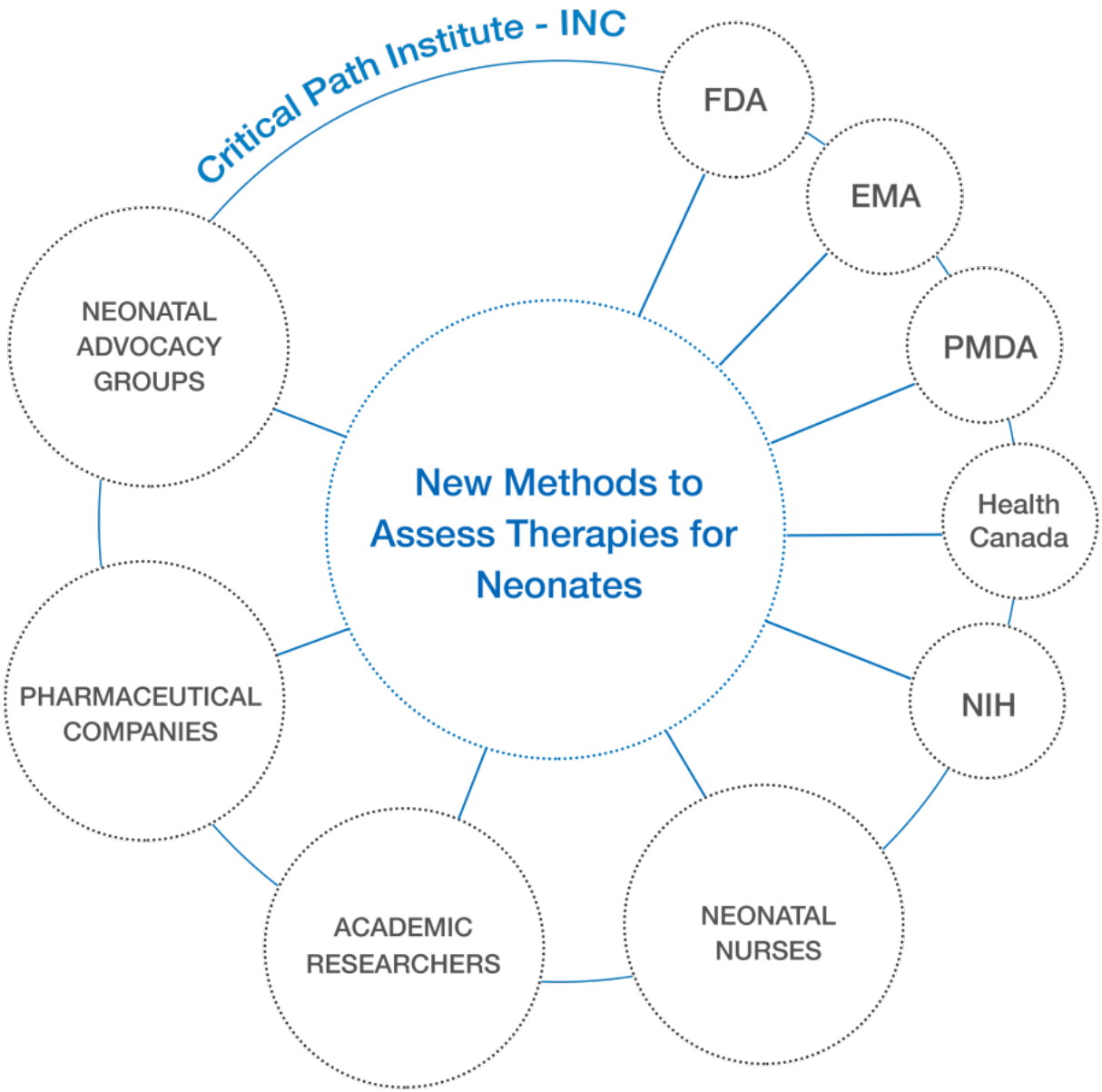
- Consortium will provide C-Path with recommendations to form a new non-profit organization.
- The new non-profit organization will provide the **sustainable infrastructure** needed to plan, start up, conduct, and close out pediatric clinical studies that deliver the **high-quality data** necessary for **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
- Jannsen
- Lilly
- Novartis
- Pfizer
- Sanofi
- Shire

Families/Advocacy

- Graham's Foundation
- March of Dimes

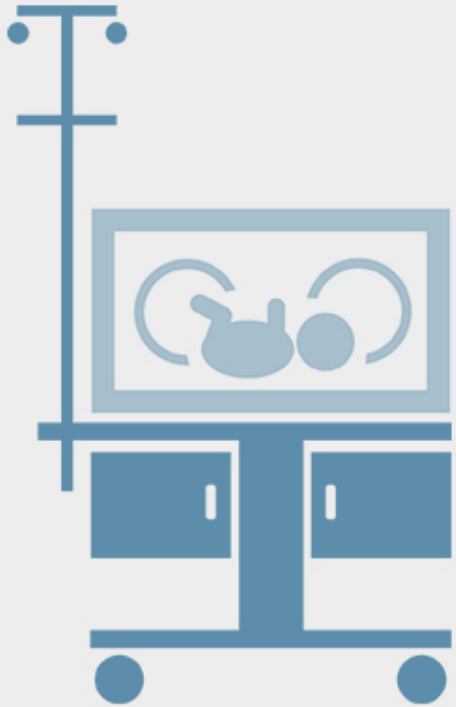
Prioritizing Initiatives to Address Unmet Needs

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.

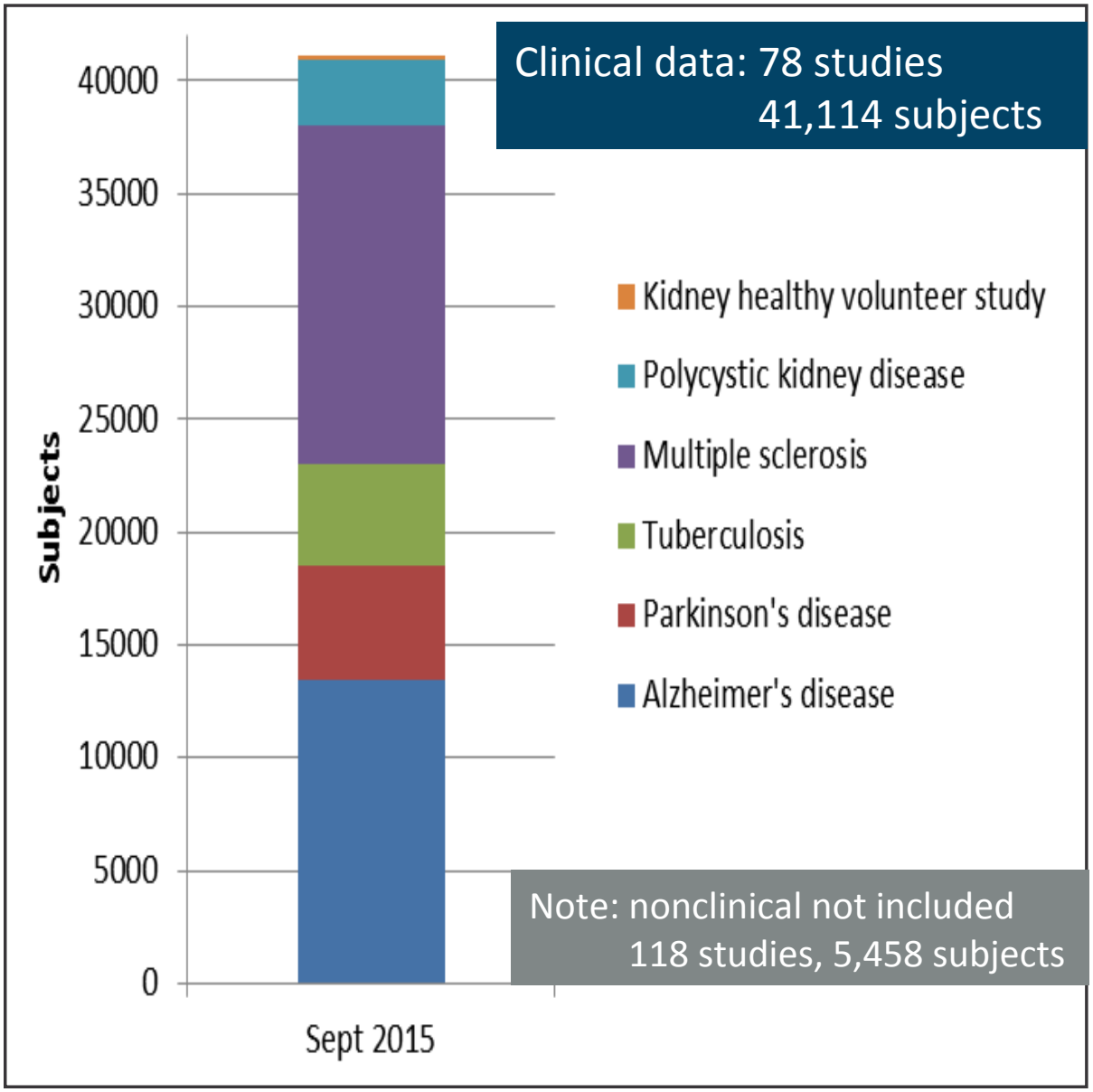
INC CRITICAL PATH INSTITUTE

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

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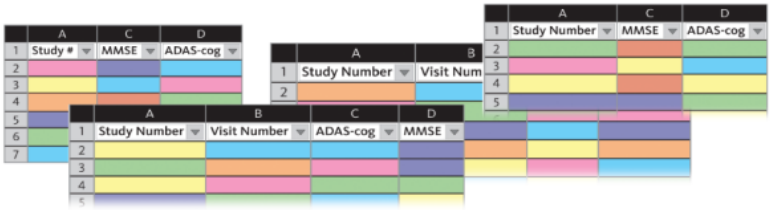
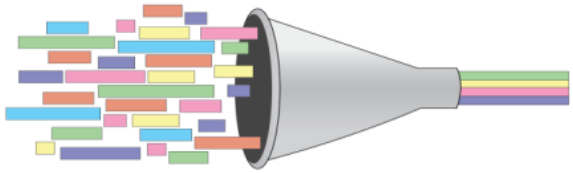
Start Point

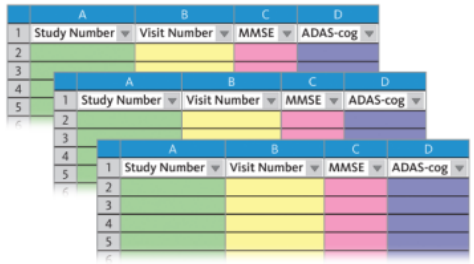
- Nine member companies agreed to share data from 24 Alzheimer's disease (AD) trials
- The data were not in a common format
- All data were remapped to the CDISC AD standard and pooled



Disparate Legacy Data



CDISC Data Standards



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

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

Changing the Paradigm in Drug Development

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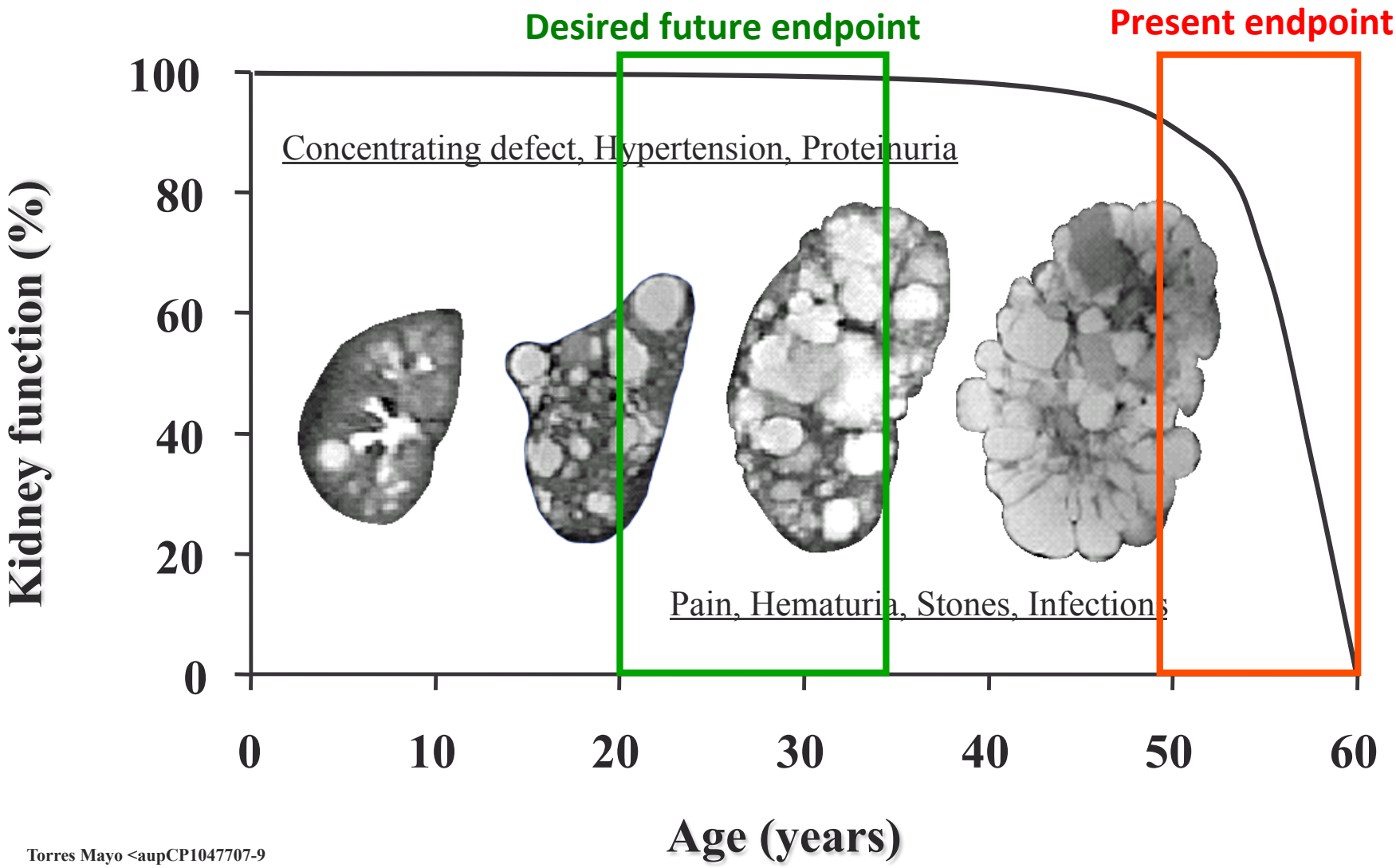
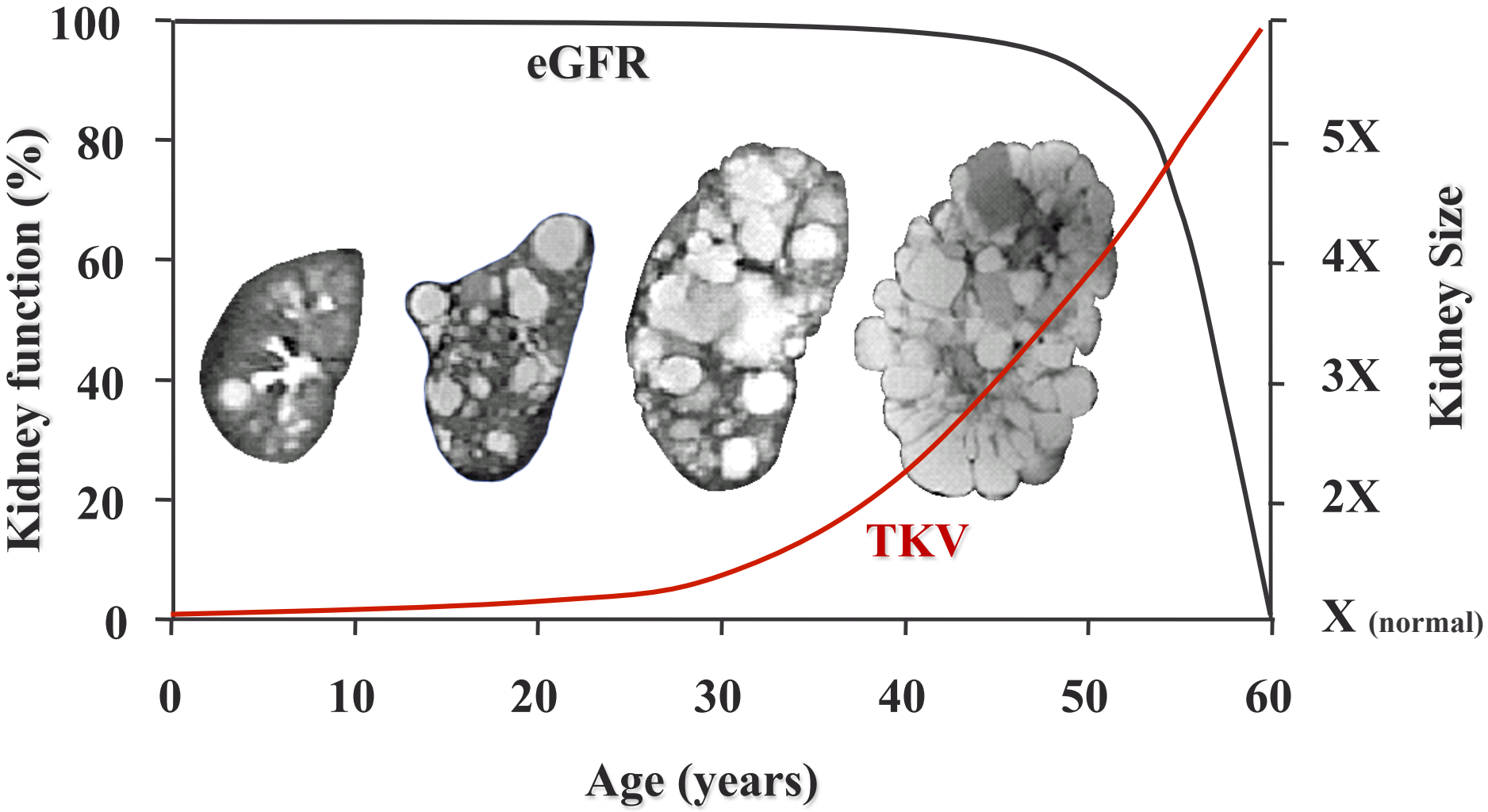
Progressive kidney enlargement in Autosomal Dominant Polycystic Kidney Disease (PKD)



Torres Mayo <aupCP1047707-9

Biomarkers for Polycystic Kidney Disease: Baseline TKV and Baseline eGFR



Torres Mayo <aupCP1047707-9

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

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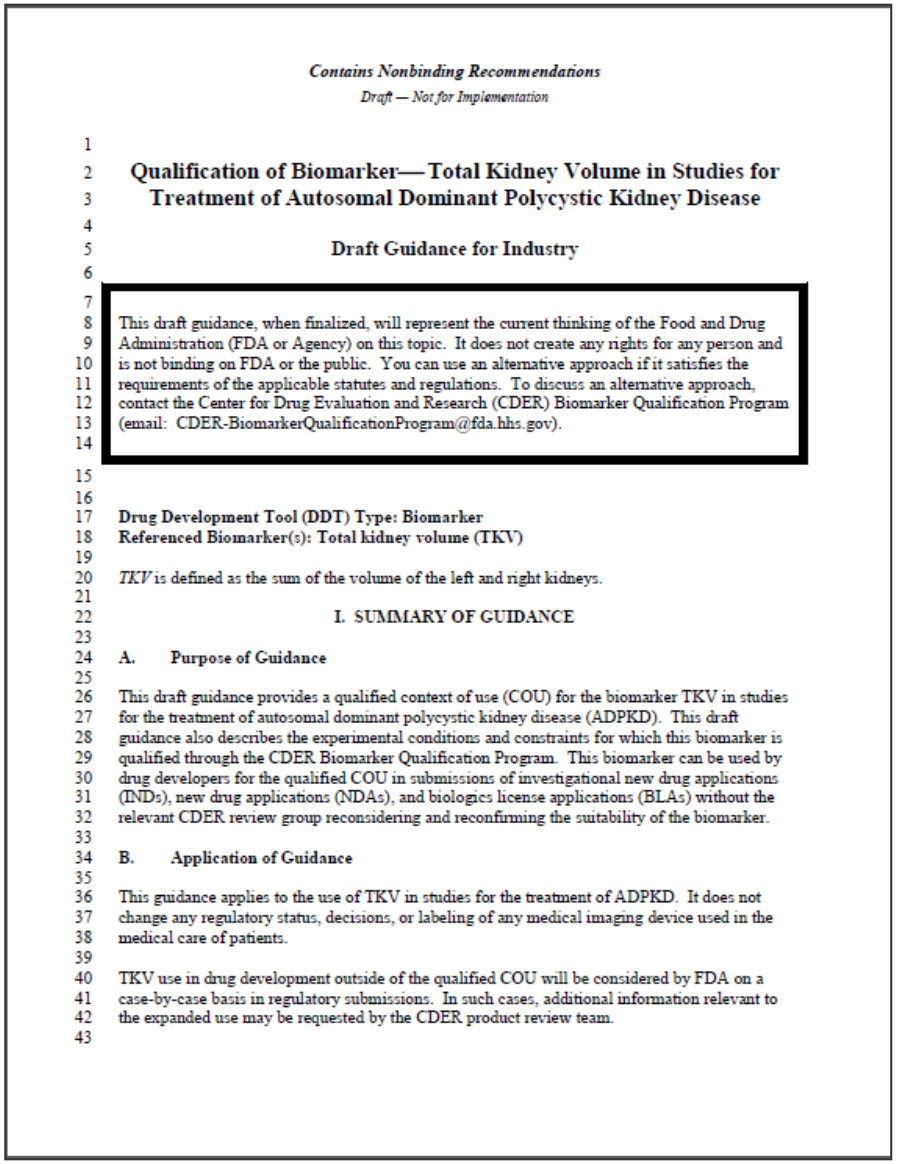
August 17, 2015

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).

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

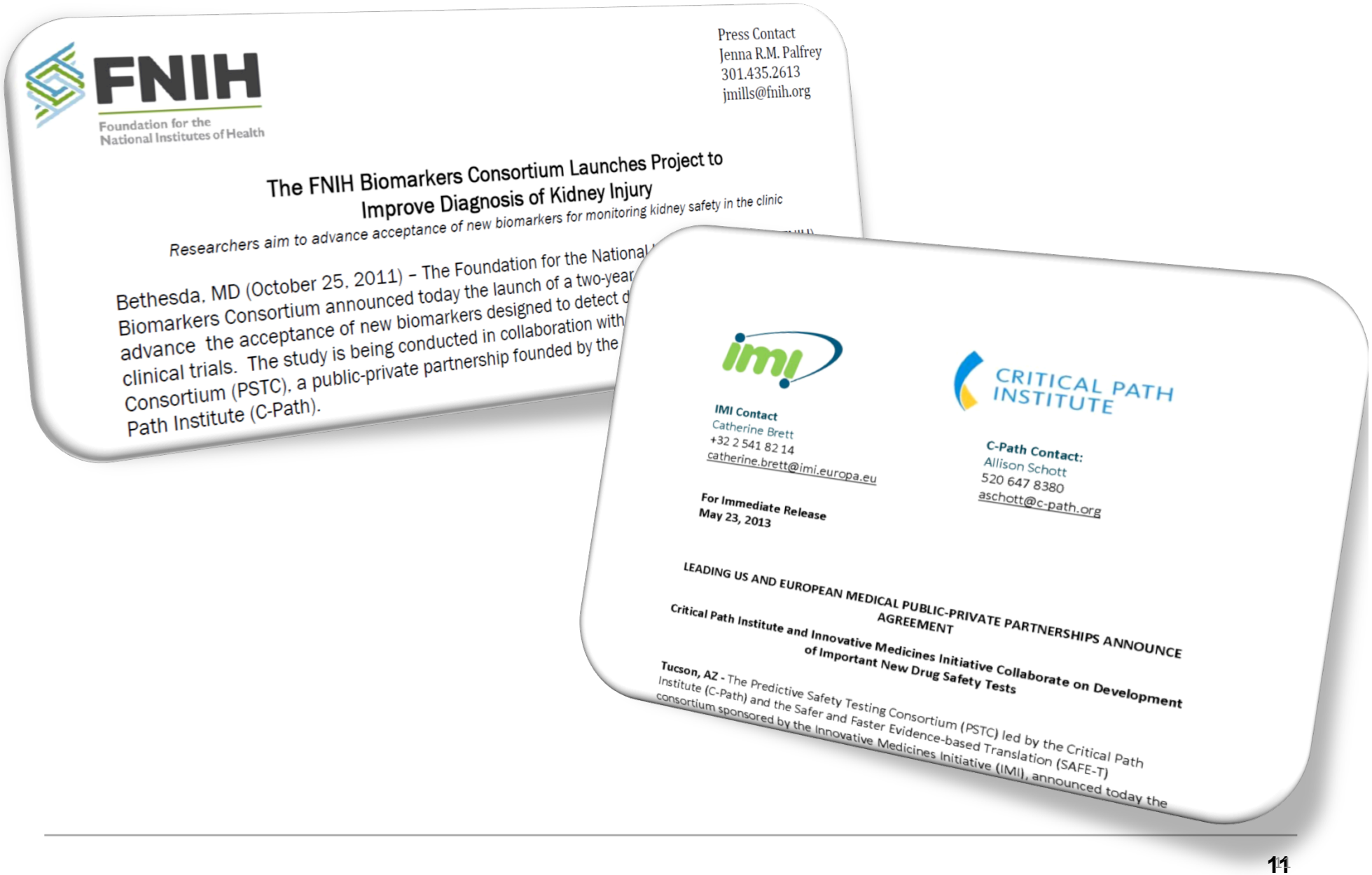
This draft guidance provides a qualified context of use (COU) for the biomarker TKV in studies for the treatment of autosomal dominant polycystic kidney disease (ADPKD). This draft guidance also describes the experimental conditions and constraints for which this biomarker is qualified through the CDER 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



Thank You

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