



# Critical Path Institute

*Public Private Partnerships Enable Regulatory Science and Innovation*

**Diane Stephenson, Ph.D.**

**Executive Director, Critical Path for Parkinson's Consortium**

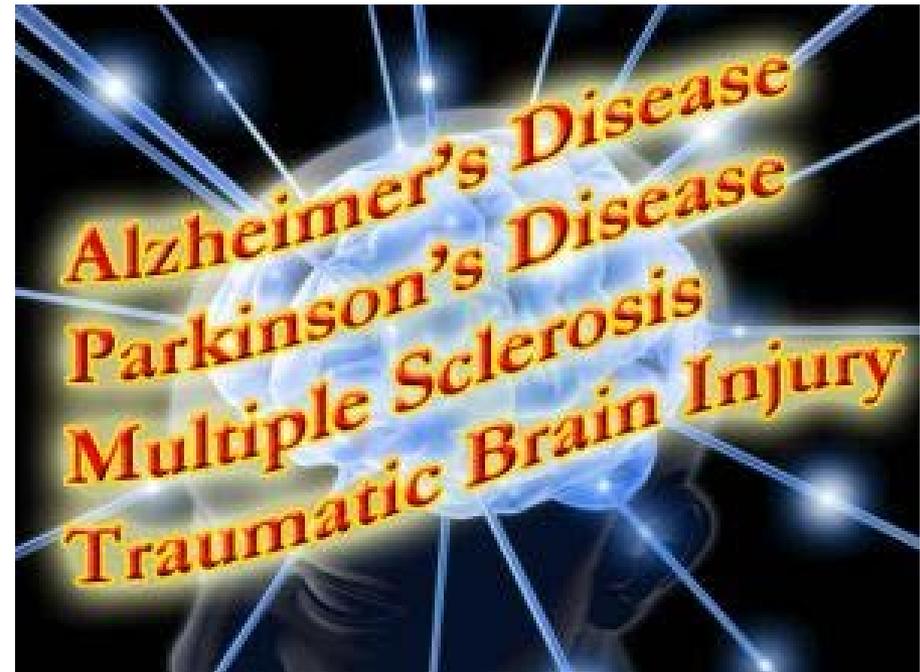


**CRITICAL PATH  
INSTITUTE**

a decade of excellence

**10  
YEARS**

- Failure rate of new therapies is exceedingly high for brain disorders
- Placebo effect is a challenge
- Outcome measures are blunt with high variability
- Biomarkers are an urgent need



***Regulatory Science has been identified as building block for enabling  
New Precision Medicine Initiative***



nature  
REVIEWS DRUG  
DISCOVERY

## The driving role of consortia on the critical path to innovative therapies

Janet Woodcock, Martha Brumfield, Dalvir Gill & Elias Zerhouni  
Nature Reviews Drug Discovery 13, 781 (2014)

## The Critical Path Institute: transforming competitors into collaborators

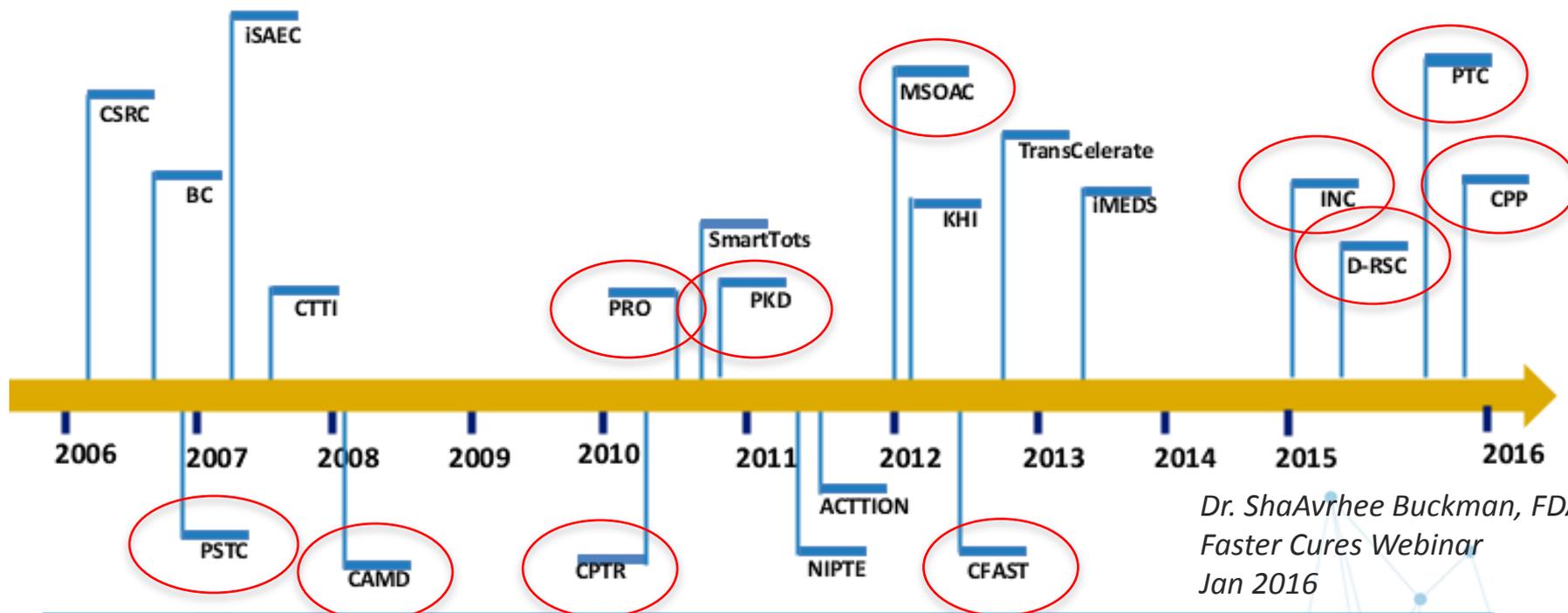
Martha Brumfield Nature Reviews Drug Discovery 13, 785-786 (2014)

## The Predictive Safety Testing Consortium and the Coalition Against Major Diseases

Diane Stephenson & John-Michael Sauer  
Nature Reviews Drug Discovery 13, 793-794 (2014)



## EXAMPLES OF CONSORTIA



*Dr. ShaAvrhee Buckman, FDA  
Faster Cures Webinar  
Jan 2016*

Cardiac Safety Research Consortium (CSRC), Biomarker Consortium (BC), Predictive Safety Testing Consortium (PSTC), Clinical Trials Transformation Initiative (CTTI), Coalition Against Major Disease Consortium (CAMD), Critical Path to TB Drug Regimens (CPTR) Consortium, Patient Reported Outcomes (PRO) Consortium, Polycystic Kidney Disease Outcomes (PKD) Consortium, National Institute for Pharmaceutical Technology and Education (NIPE), Analgesic Clinical Trial Translations, Innovations, Opportunities, and Networks Initiative (ACTTION), Multiple Sclerosis Outcome Assessments Consortium (MSOAC); Kidney Health Initiative (KHI), Coalition For Accelerating Standards and Therapies (CFAST), Innovation in Medical Evidence Development and Surveillance (IMEDS) Program, International Neonatal Consortium (INC), Duchenne-Regulatory Science Consortium (D-RSC), Pediatric Trials Consortium (PTC), Critical Path for Parkinson's Consortium (CPP).

# Critical Path for Parkinson's

*C-Path's Newest Consortium*



## 7 MAJOR PHARMA COMPANIES SIGN UP TO PARKINSON'S INITIATIVE



23 February 2016

**PARKINSON'S<sup>UK</sup>**  
CHANGE ATTITUDES.  
FIND A CURE.  
JOIN US.

**NINDS**

**Individual  
Advisors**



**Academic Experts**



**EUROPEAN MEDICINES AGENCY**  
SCIENCE MEDICINES HEALTH

[http://www.eurekalert.org/pub\\_releases/2016-02/pu-mpc022316.php](http://www.eurekalert.org/pub_releases/2016-02/pu-mpc022316.php)

# Critical Path Institute Consortia

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 Outcomes Assessment Consortium**



**Polycystic Kidney Disease Outcomes Consortium**



**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

# C-PATH REGULATORY SUCCESSES



AD clinical trial database

AD clinical trial simulation tool

EMA qualified AD biomarker

FDA letters of support - AD biomarkers



21 therapeutic area users guides, CDISC



FDA letter of support - PD biomarker



EMA qualified Hollow Fiber System for Tuberculosis

ReSeqTB data platform



Total Kidney Volume Imaging (TKV) biomarker qualified with EMA & FDA

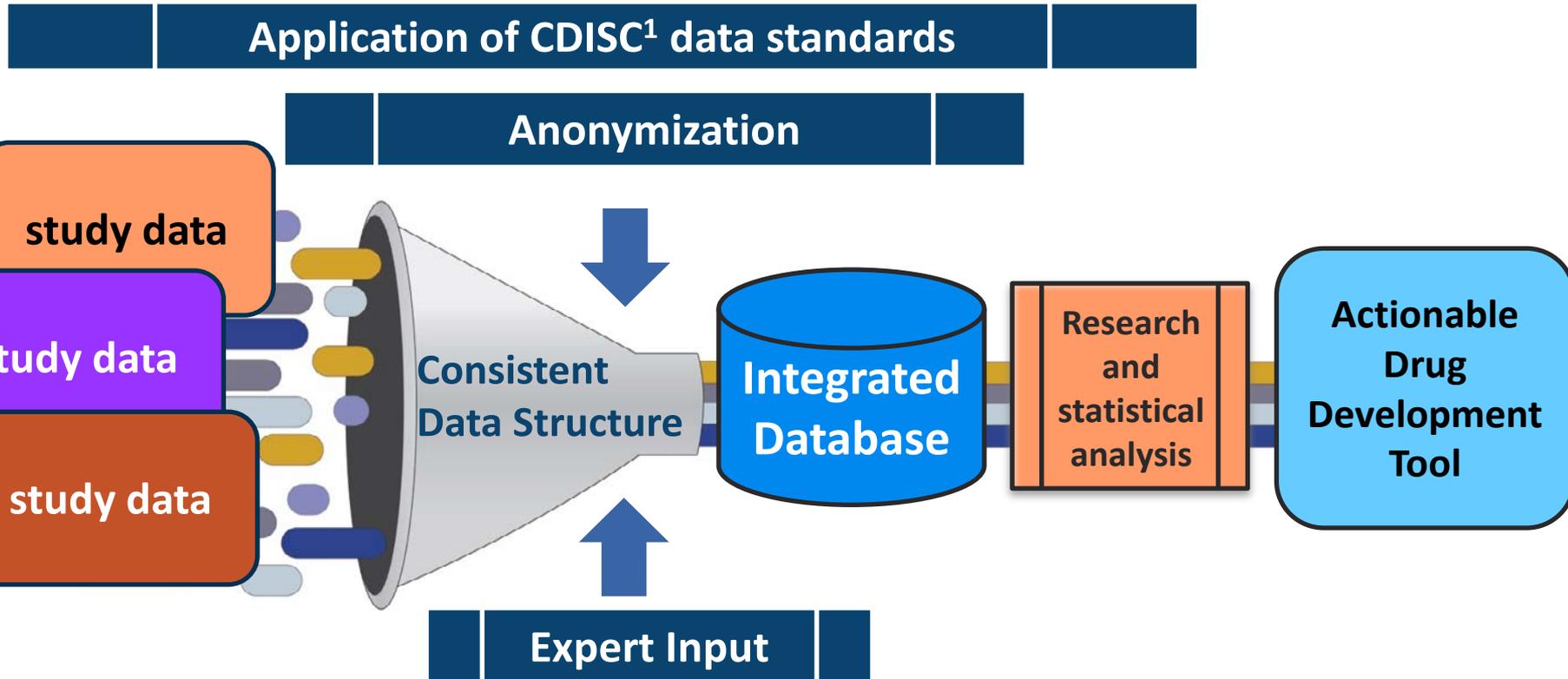
PKD clinical database



EMA/FDA/PMDA qualified non-clinical kidney safety biomarkers

FDA & EMA letters of support:  
- kidney biomarkers  
- skeletal muscle injury biomarkers

# C-Path Data Aggregation Approach



<sup>1</sup> CDISC: Clinical Data Interchange Standards Consortium, [www.cdisc.org](http://www.cdisc.org)

# Therapeutic Area Data Standards: *C-Path's Development Experience*



**USER GUIDES**

CDISC Alzheimer's disease SDTM User Guide (Version 1.0)



Alzheimer's Disease  
Area Supplement to the  
SDTM Model  
Guide



Parkinson's Disease T  
Area Supplement to the  
Tabulation Mo



Therapeutic Area Data Standards  
User Guide for Multiple Sclerosis  
Version 1.0  
Prepared by the

Coalition A

This User Guide follows vers

Revision History

Date	Vers
2010-11-30	1.0
2011-09-09	1.0



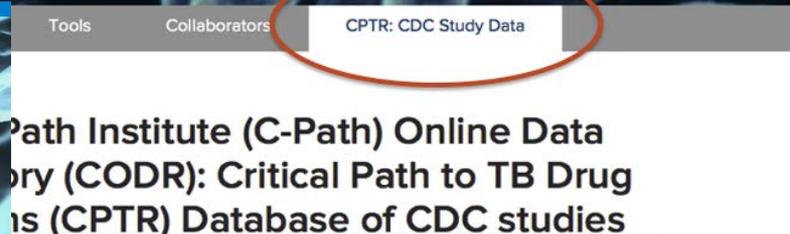
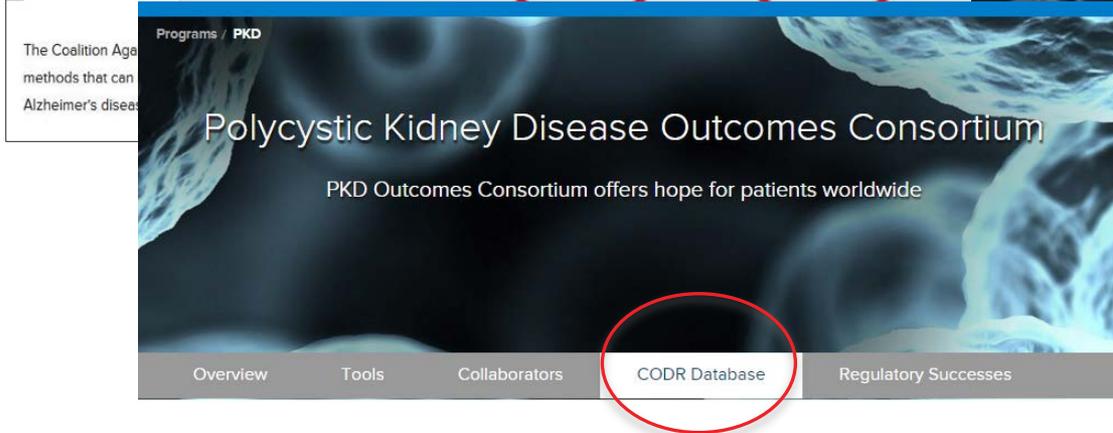
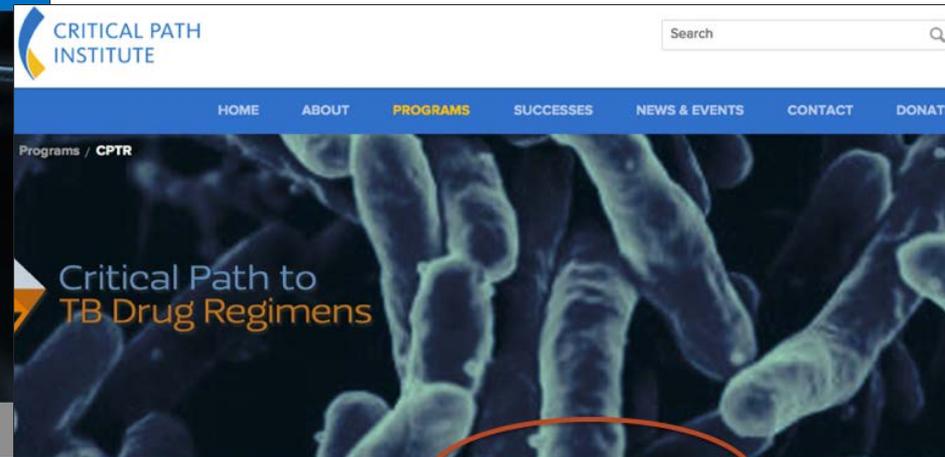
Therapeutic Area Data Standard  
User Guide for Alzheimer's Disease  
and Mild Cognitive Impairment  
Version 2.0  
Prepared by the  
CFAST Alzheimer's Development Team



Therapeutic Area Data Standards  
User Guide for Traumatic Brain Injury  
Version 1.0 (Draft)  
Prepared by the  
CFAST Traumatic Brain Injury Standards Team

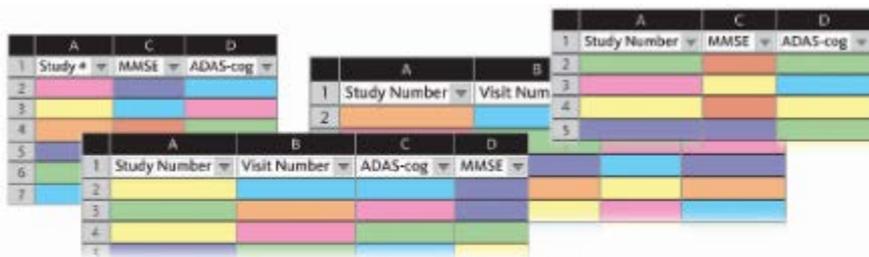
# C-Path Databases Accessible to Research Community

*Shared as allowed by data owner*

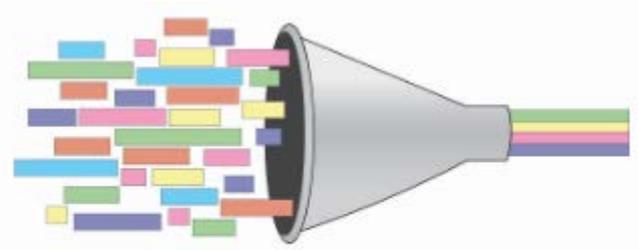


**Critical Path Institute (C-Path) Online Data Repository (CODR): Polycystic Kidney Disease Outcomes Consortium's Database**

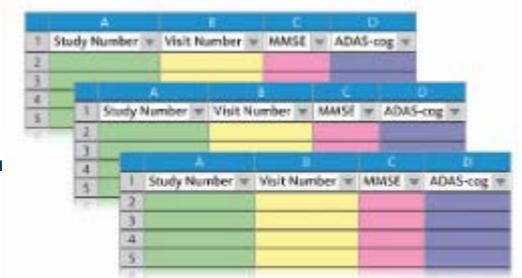
# C-Path CAMD Alzheimer's Disease Modeling & Simulation Tool



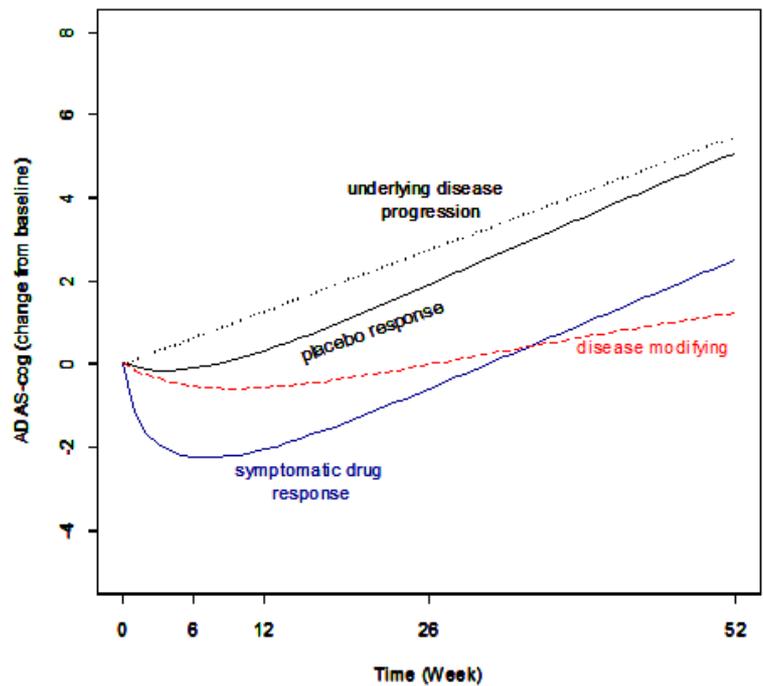
Mixed Legacy Data



Data Standards

Integrated Data



Deterioration



Romero K, Ito K, Rogers JA, Polhamus D, Qiu R, Stephenson D, Mohs R, Lalonde R, Sinha V, Wang Y, Brown D, Isaac M, Vamvakas S, Hemmings R, Pani L, Bain LJ, Corrigan B; [The future is now: model-based clinical trial design for Alzheimer's disease.. Clin Pharmacol Ther. 2015 97\(3\):210-4](#)

# CAMD AD Clinical Trial Simulation Tool: First Regulatory Endorsed Disease Model

## THE WALL STREET JOURNAL.

JOURNAL REPORTS: HEALTH CARE

### Simulators Help Build a Better Drug Trial

*Pharmaceutical firms start to use powerful computer programs to improve human testing*

By JONATHAN D. ROCKOFF

Nov. 17, 2013 4:07 p.m. ET



*“Model-based drug development was one of the goals defined in FDA’s 2004 Critical Path Initiative report, and this new tool sets the stage for applying new technologies to accelerating medical product development,”  
Janet Woodcock, FDA*

### Frequent Failure

Drug companies are looking to new tools to improve their odds in the development process because it’s currently such a long shot. The percentage of drugs in Phase I trials that advance to:

Phase II trials



Phase III trials



Application for government approval



Approval



Source: BioMedTracker data on more than 1,000 companies for 2003-12  
The Wall Street Journal

#### CAMD'S CLINICAL TRIAL SIMULATION TOOL FOR ALZHEIMER'S DISEASE

30

Organizations  
(non-academic)

58

Individuals

16

Academic  
Institutions

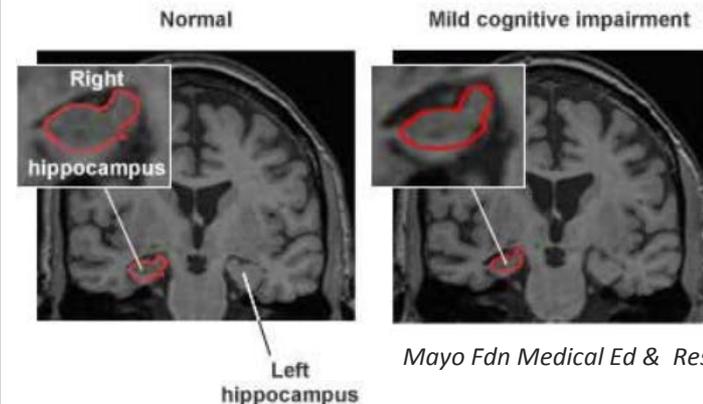
# C-Path Achieves First Imaging Biomarkers Qualified by Global Regulatory Agencies



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

17 November 2011  
EMA/CHMP/SAWP/809208/2011  
Committee for Medicinal Products for Human Use (CHMP)

Qualification opinion of low hippocampal volume (atrophy) by MRI for use in regulatory clinical trials - in pre-dementia stage of Alzheimer's disease



Mayo Fdn Medical Ed & Res

*Contains Nonbinding Recommendations*

*Draft — Not for Implementation*



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

06 November 2015  
EMA/CHMP/SAWP/473433/2015  
Product Development Scientific Support Department

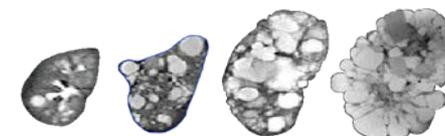
## Qualification opinion

Total Kidney Volume (TKV) as a prognostic biomarker for use in clinical trials evaluating patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD)

- 1
- 2
- 3
- 4
- 5
- 6

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

**Draft Guidance for Industry**



- Biomarker Standardization and Harmonization
- Sharing Biomarker data
- Define Regulatory Readiness



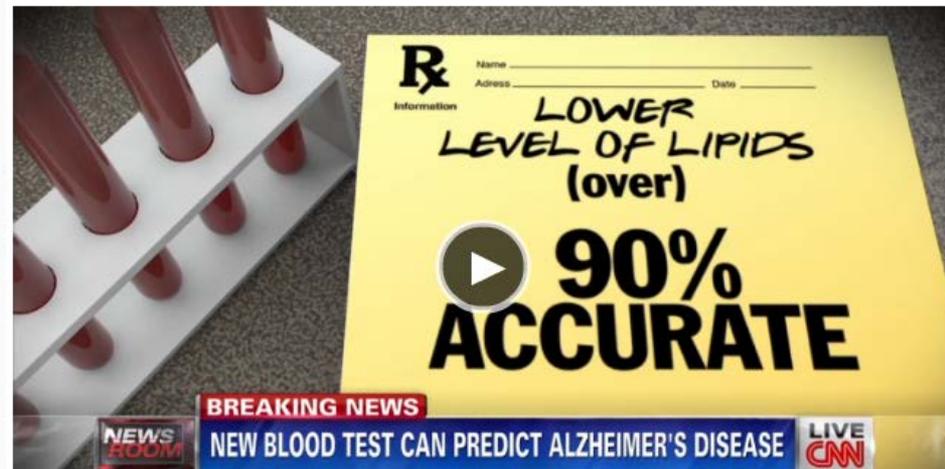
[http://www.cnn.com/2014/03/09/health/alzheimers-blood-test/index.html?hpt=hp\\_t2](http://www.cnn.com/2014/03/09/health/alzheimers-blood-test/index.html?hpt=hp_t2)

March 9, 2014

Mapstone et al, Nature Medicine  
Nat Med. 2014 Apr;20(4):415-8.

## Blood test predicts Alzheimer's disease

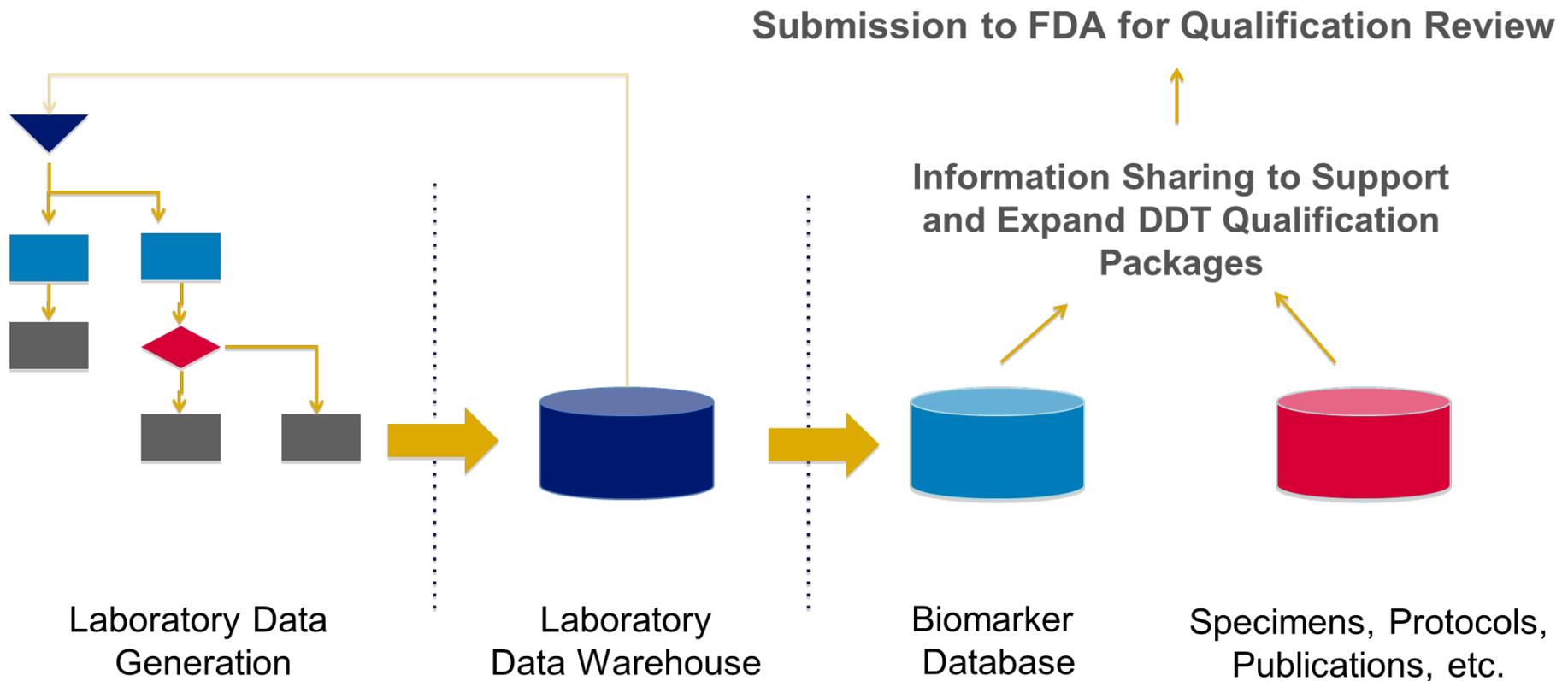
By Elizabeth Cohen, Senior Medical Correspondent  
updated 2:59 PM EDT, Sun March 9, 2014



# Success in the future:

*TBI / TED is on the right track!*

## APPROACH TO SHARING BIOMARKER DATA



## Traumatic Brain Injury Therapeutic Endpoints Development (TED) Initiative *2015-2016 Progress in Regulatory Science*

- CDISC TBI Therapeutic Area Consensus Clinical Data Standards
- Seed grants, *enabling regulatory readiness of biomarkers and outcome measures*
- Federal Register notifications
  - TED nominated biofluid biomarkers and imaging biomarkers in response to 2015 FDA call for novel biomarkers
  - Clinical Outcome Assessment Compendium
- FDA Commissioner's Fellow research project (CDRH)
- CPIM (Biomarkers for TBI)



Office of Translational Sciences  
**Critical Path  
Innovation Meeting**



# Thank You

**Ann Robbins, C-Path  
TED team**

**Geoff Manley, Amy Markowitz, Brian Fabian, UCSF  
Department of Defense**

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



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