accelerate

innovate

collaborate

Critical Path Institute Coalition Against Major Diseases (CAMD) Alzheimer's Clinical Trial Database

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Critical Path Institute

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What We Do

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DEVELOP "STANDARDS"

- **Measurement standards**
  - Molecular biomarkers for toxicity, efficacy and patient stratification
  - Imaging biomarkers for efficacy and stratification
  - Patient-, observer-, clinician- reported outcomes
- **Methods standards**
  - Disease models and clinical trial simulation tools
  - *In vitro* models
- **Data standards**
  - With CDISC, clinical data standards for therapeutic areas

ACQUIRE REGULATORY QUALIFICATION

- Recognition, endorsement for a given context of use

How We Do It

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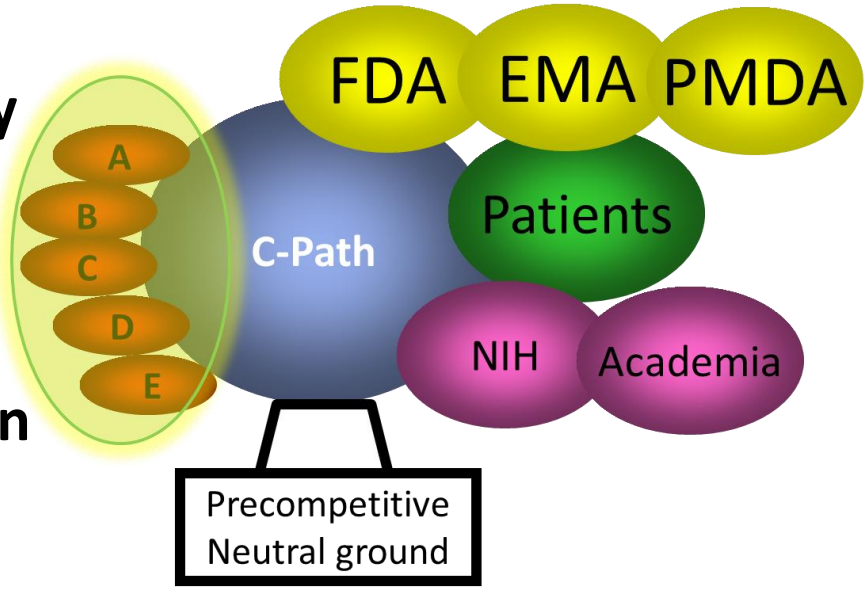
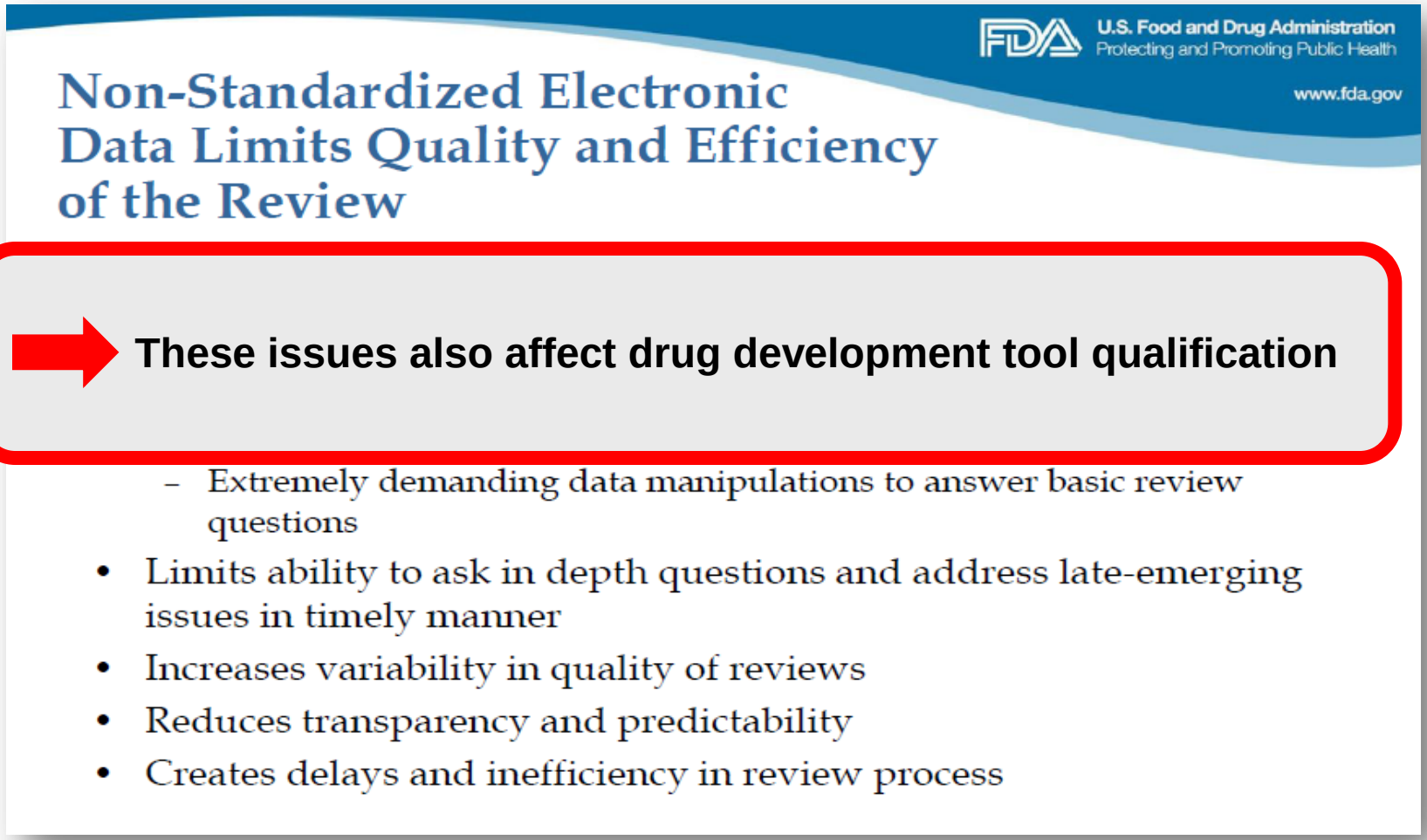
- Act as trusted neutral third party
- Convene consortia of industry, academia, and government for pre-competitive collaboration
  - The best science
  - Shared risk and costs



- Iteratively involve FDA in the development process
  - Regulatory participation, guidance
  - Official recognition through "qualification" of Drug Development Tools
    - DDTs = biomarkers, clinical outcome assessments, *(animal models)*

FDA Communicates Impact of Data Standards



Charles Cooper, Computational Science Center, CDER
Presented at CDISC European Interchange, April 18, 2012

Consortia Established

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Six global consortia collaborating with 1,000+ scientists and 41 companies

PSTC CRITICAL PATH INSTITUTE	Predictive Safety Testing Consortium **DRUG SAFETY**
PRO CONSORTIUM CRITICAL PATH INSTITUTE	Patient-Reported Outcome Consortium **DRUG EFFECTIVENESS**
ePRO CONSORTIUM CRITICAL PATH INSTITUTE	Electronic Patient-Reported Outcome Consortium **DRUG EFFECTIVENESS**
CAMD CRITICAL PATH INSTITUTE	Coalition Against Major Diseases **UNDERSTANDING DISEASES OF THE BRAIN**
PKD CONSORTIUM CRITICAL PATH INSTITUTE	Polycystic Kidney Disease Consortium **NEW IMAGING BIOMARKERS**
CPTR	Critical Path to TB Drug Regimens **TESTING DRUG COMBINATIONS**

FDA

- Biomarkers
- Patient Reported Outcome Instruments
- Disease Progression Models
- Data Standards

CDISC

CAMD: Tools to Advance Effective Treatments for Alzheimer's and Parkinson's Disease

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CAMD
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- Qualify biomarkers (FDA Draft Guidance 2010)
- Develop common data standards
- Create integrated databases of clinical trial data
- Develop "accepted for use" quantitative disease models

The first CDISC therapeutic area data standards were developed for Alzheimer's disease, published September 2011

Government/Regulatory participants	Industry members	Non-profit research members
National Institute on Aging	Eisai	Alzheimer's Association
National Institute of Neurological Disorders and Stroke	Johnson & Johnson	Alzheimer's Foundation of America
	Roche	The Michael J. Fox Foundation for Parkinson's Research
	Forest Laboratories, Inc.	National Health Council
	Lilly	US Against Alzheimer's
	SANOFI	
	Genentech, A Member of the Roche Group	
	Novartis	
	Teva	
	Takeda	

Nonmember participants: **Academic key opinion leaders, CROs**

CAMD Data Pooling: Building on Data Standards

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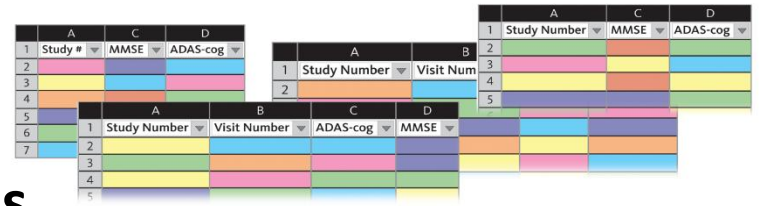
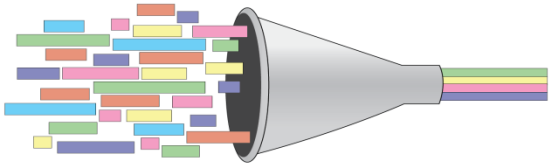
Start Point

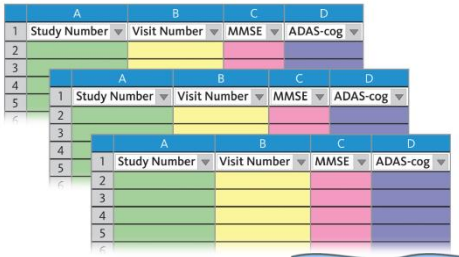
- Nine member companies agreed to share data from 22 trials
- The data were not in a common format
- The data needed to be combined in a consistent manner
- All data were remapped to the CDISC standard and pooled



Disparate Legacy Data



CDISC Data Standards



Result

- A new in silico modeling tool was created through the application of data standards and is under review by the FDA

Precompetitive Sharing of Alzheimer's Disease Control-Arm Trial Data

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- **Contributing organizations went through corporate approval procedures to share study data, de-identified for secondary use**

- **CAMD-AD data was subsequently de-identified further to HIPAA "Safe Harbor" requirements**

http://privacyruleandresearch.nih.gov/pr_08.asp

What Was Learned?
ADAS-Cog Variability

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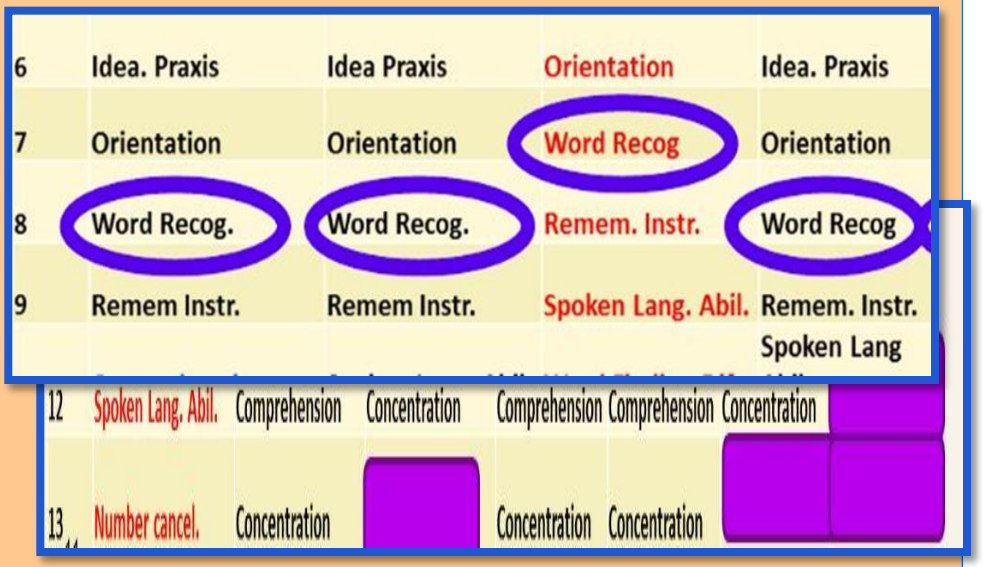
- Cognition tests are used to assess Alzheimer's patients
- Patients are asked to perform a set of tasks
  - Word recall
  - Follow a series of commands
  - Naming of objects
  - ….
- Different implementations of the test were found
  - Different number of questions
  - Different order of questions and tasks
  - Different scoring of same item
- These differences were identified and reconciled as a result of the Alzheimer's data standards and mapping project



Item 9	Remem Instr.	Remem Instr.	Ability	Remem. Instr.	Remem. Instr.	Ability	Comprehension
Item 10	Comprehension	Spoken Lang. Ability	Word Finding Difficulty	Spoken Lang Ability	Spoken Lang Ability	Word Finding Difficulty	Word Finding Difficulty
Item 11	Word Finding Difficulty	Word Finding Difficulty	Comprehension	Diff. Spont. Speech	Word Finding Difficulty	Comprehension	Remem. Instr.
Item 12	Spoken Lang. Ability	Comprehension	Concentration	Comprehension	Comprehension	Concentration	
Item 13	Number cancel.	Concentration		Concentration	Concentration		

Sources of Data for Building AD Model: Integration from Diverse Sources

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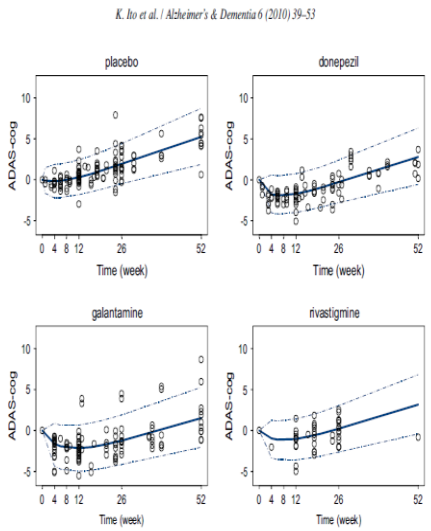
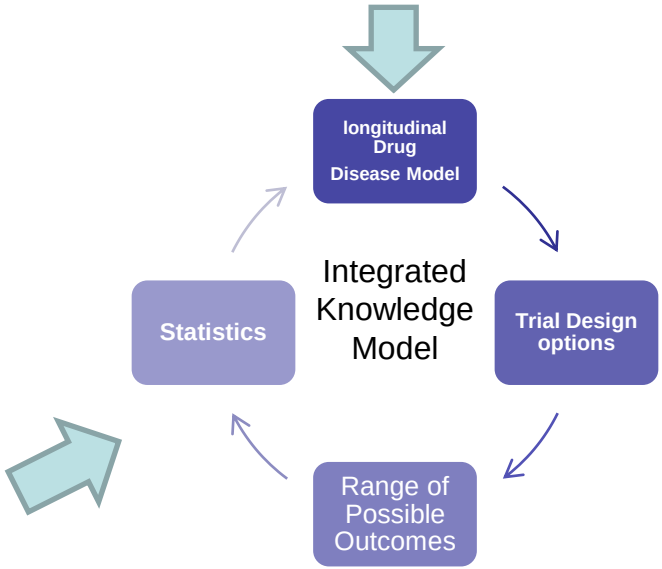


ADNI Defining Alzheimer's Disease

•Natural History
- Inter-patient variability
- Patient specific factors
- Imaging and CSF biomarkers



•Treatment Effect
- Estimate data on drug treatment effects (magnitude, onset, offset)
- 73 Trials (1990 to Present)
- Inter-study variability

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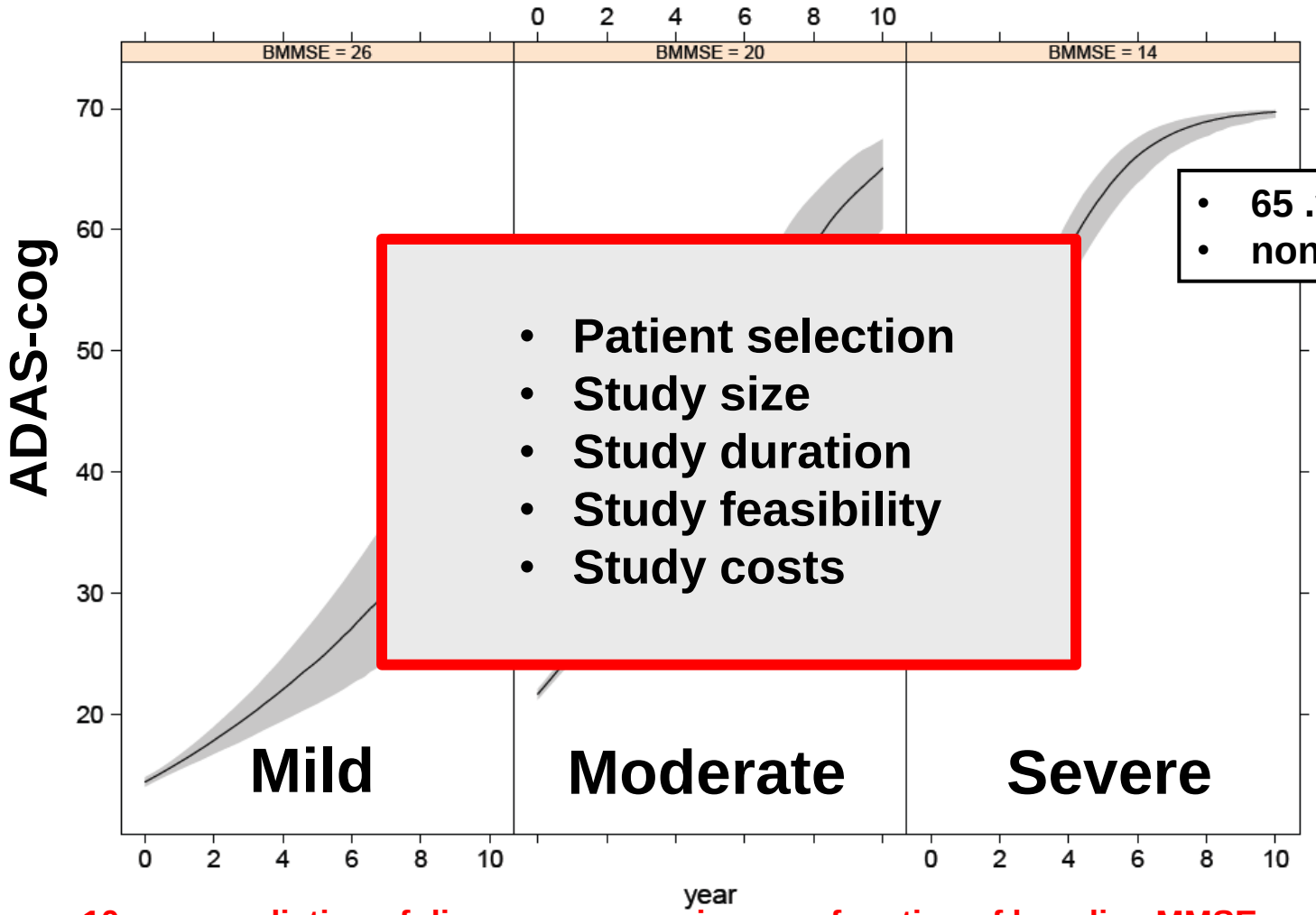
•Placebo Effect
- 9 trials, 3223 patients
- Inter-patient variability
- Patient Specific Factors

Model Allows for Accurate Quantitative Predictions of Defined Patient Populations



10 year prediction of disease progression as a function of baseline MMSE scores

Mean (line) and 90% Credible Intervals (gray shaded area)

Value Proposition

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Research goal→ shared data→ data standards → integrated database → new drug development tools

Approach used for AD is being applied in other project areas to support development of new drug development tools for:

- **Parkinson's Disease**
- **Polycystic Kidney Disease**
- **Tuberculosis**

The CAMD Data Challenge

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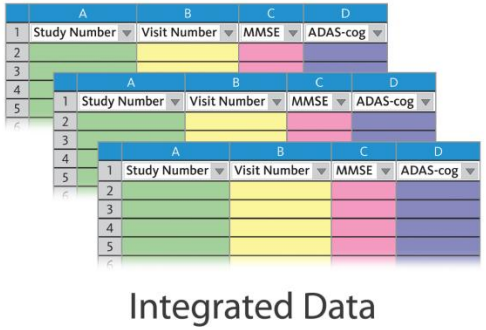
Key Insights Gained



- Legacy data conversion is resource intensive but worthwhile for specific projects
- Assurance is needed that a specific dataset will be useful in achieving research/regulatory qualification objectives
- Selectivity is beneficial: convert only the needed data
- New insights can be obtained from data converted to a common standard and aggregated to enable queries and analysis
- Addition of standardized data from other sources (prospective, retrospective) becomes simplified and expands the power and utility of a standardized data resource

Drug Development Pipeline: Applicability of Data Standards

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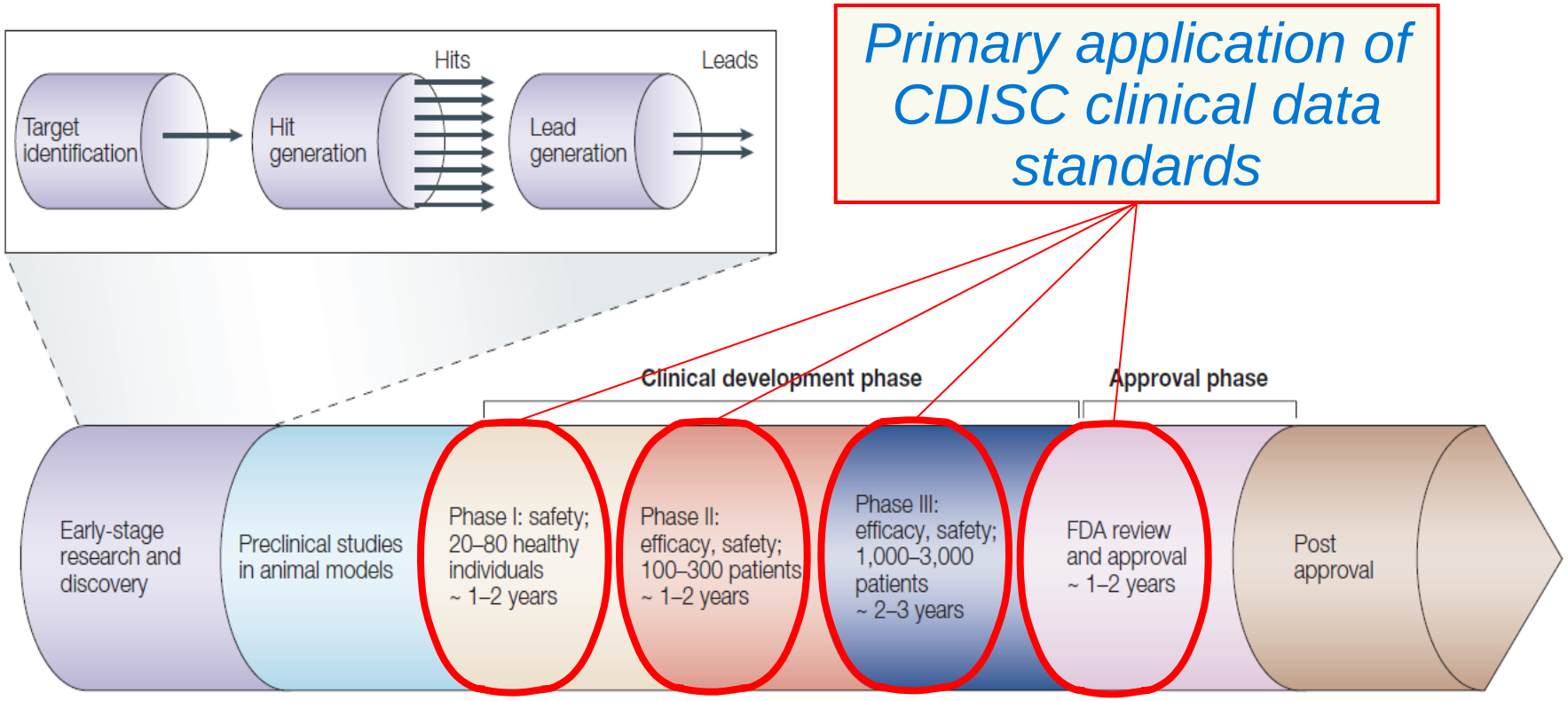

"A virtual space odyssey", Cath O'Driscoll (2004)
http://www.nature.com/horizon/chemicalspace/background/odyssey.html

FDA PDUFA V Goals 2013-2017

Clinical Terminology Standards (Section XII E pg 28):

Using a public process that allows for stakeholder input, FDA shall develop standardized clinical data terminology through o al D goal of completing clinical data terminology and detailed implementation guides by FY 2017.

FDA has defined specific goals for development and use of data standards

http://www.fda.gov/downloads/forindustry/userfees/prescriptiondruguserfee/ucm270412.pdf

FDA Priorities for Therapeutic Area Data Standards

Priority Disease/Domain Areas for Data Standardization

Tier 1		
Acne	Pain*	Schizophrenia
Alzheimer's Disease*	Parkinson's Disease*	Solid organ transplantation
Anti-diabetic agents*	Prevention of pregnancy	Treatment of Hepatitis C*
Crohn's Disease	Psoriasis	Treatment of postmenopausal osteoporosis
Infections of skin and/or subcutaneous tissue	QT Studies	Tuberculosis*
Oncology: time to efficacy event other than overall survival*	Rheumatoid arthritis	Urinary tract infections
Tier 2		
Addiction	Gastroesophageal reflux disease	Pneumonia
Anticonvulsants	Influenza	Prevention of HIV
Asthma	Irritable bowel syndrome	Treatment of HIV
Bipolar Disorder	Lipid-altering drug groups	Treatment of overactive bladder
Clostridium difficile colitis	Major depressive disorder	Treatment of vasomotor

Drugs

Home › Drugs › Development & Approval Process (Drugs) › Fo

- **Development & Approval Process (Drugs)**
- Forms & Submission Requirements
- Electronic Submissions to CDER
- CDER Data Standards Program
- Electronic Common Technical Document (eCTD)

Priority Therapeutic Areas for Development

An initial inventory of data standards needs, resulted in the identification of 57 therapeutic areas prioritized into three tiers[1]. Further standardization of clinical study data specific to these and other therapeutic areas will facilitate the evaluation of medical products. To identify the preliminary priority areas several factors were considered: (1) areas of particular need, (2) areas with existing data standardization projects underway, and (3) areas with greater drug development pipeline activity. We encourage interested stakeholders to engage in and, whenever possible, sponsor these data standardization efforts.

Priority Disease/Domain Areas for Data Standardization

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm287408.htm

CFAST = CDISC + C-PATH: Coalition for Accelerating Standards and Therapies

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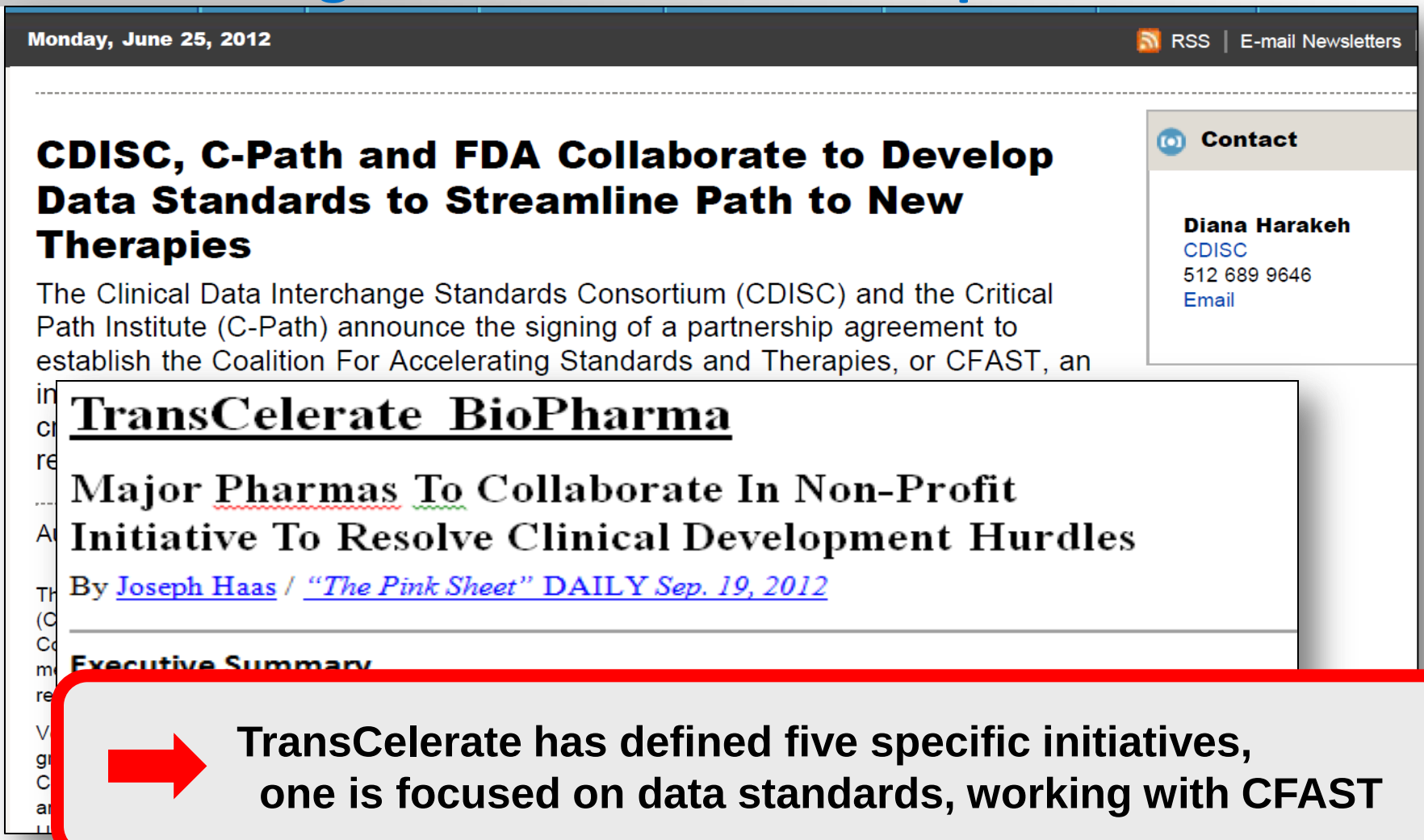

Monday, June 25, 2012

RSS | E-mail Newsletters

CDISC, C-Path and FDA Collaborate to Develop Data Standards to Streamline Path to New Therapies

The Clinical Data Interchange Standards Consortium (CDISC) and the Critical Path Institute (C-Path) announce the signing of a partnership agreement to establish the Coalition For Accelerating Standards and Therapies, or CFAST, an in
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re

Contact

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TransCelerate BioPharma

Major Pharmas To Collaborate In Non-Profit Initiative To Resolve Clinical Development Hurdles

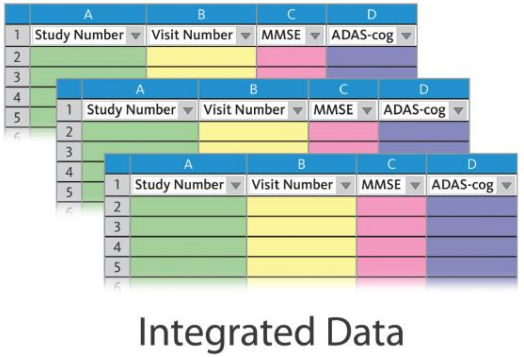
By Joseph Haas / *"The Pink Sheet" DAILY Sep. 19, 2012*

Executive Summary

TransCelerate has defined five specific initiatives, one is focused on data standards, working with CFAST

Sharing Clinical Research Data

Governance Considerations



Integrated Data

- Rules for developing the data standards themselves
  - Collaborative expert input and consensus
- Rules of the road for merging data
  - Use high value data
  - Use data standards that the FDA accepts
  - Use data standards end-end
- Rules for accessing data
  - Obtain broadest possible data use agreement
  - De-identify data to HIPAA “Safe Harbor” requirements
  - Use access controls appropriate to use objectives
- Rules for access to qualified drug development tools
  - Place DDTs in the public domain to maximize use

Recommended Best Practices

- Data standards: use standards *ab initio* if they are warranted by the intended use
- Database design
  - Fully define & document database architecture
  - Define use cases in advance
  - Invest in ease of use
- Data access
  - Develop a data use agreement template
  - Define access levels specific to each project
  - Perform an independent security review
  - De-identify datasets to HIPAA “Safe Harbor” requirements

http://privacyruleandresearch.nih.gov/pr_08.asp

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We want to thank the Food and Drug Administration and Science Foundation Arizona for their significant funding of our work.

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First CDISC Therapeutic Area Data Standard, Published Sept 2011

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COALITION AGAINST MAJOR DISEASES

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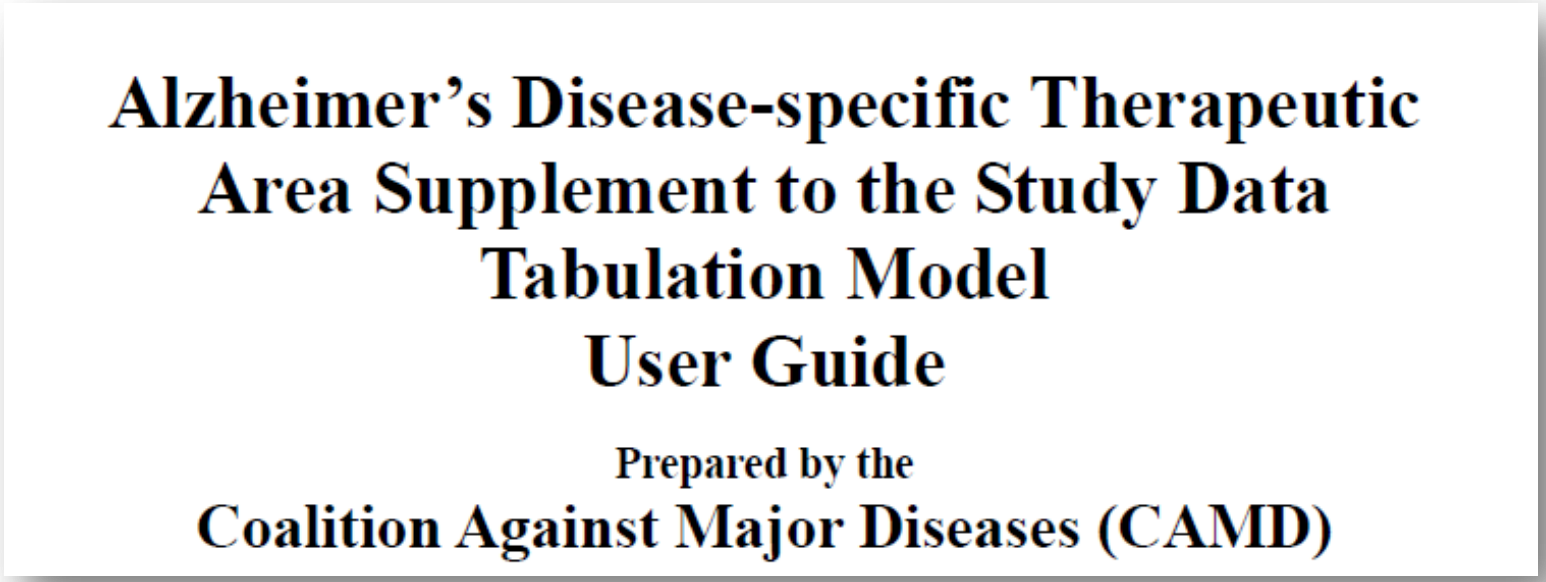

http://www.cdisc.org/stuff/contentmgr/files/0/464c32d97e58d1e0640c77ab2809f0ef/misc/sdtmug_alzheimer__s_2011_09_23_final_revised.pdf