DEVELOPMENT OF THERAPEUTIC AREA-SPECIFIC DATA STANDARDS FOR BRAIN DISEASES

Jon Neville, Critical Path Institute, Tucson AZ

CRITICAL PATH INSTITUTE
a decade of excellence

10 YEARS

Contributors

Jon Neville[1], Steve Kopko[2], Bess LeRoy[1], Mark Forrest Gordon[3], Susan De Santi[4], Andreas Jeromin[5], Ellen Mowry[6], Mark Austin[7], Patricia Cole[8], Ken Marek[9], Jerry Novak[10], Klaus Romero[1], Bob Stafford[1], Emily Hartley[1], Amy Palmer[2], Rhonda Facile[2], Kewei Chen[11], Adam Fleisher[11], Joanne Odenkirchen[12], Enrique Avilés[1], Fred Lublin[13], Eric Reiman[11], Geoffrey Manley[14], Lynn Hudson[1], Diane Stephenson[1]

AFFILIATIONS:

1 – Critical Path Institute, Tucson, AZ

2 – Clinical Data Interchange Standards Consortium, Austin, TX

3 – Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT

4 – Piramal Pharma Inc, Boston, MA

5 – Quanterix, Lexington, MA

6 – Johns Hopkins University School of Medicine, Baltimore, MD

7 – Ixico, London, UK

8 – Takeda Pharmaceuticals U.S.A., Inc., Deerfield, IL

9 – Institute for Neurodegenerative Disorders, New Haven, CT

10 – J&J PRD, Titusville, NJ

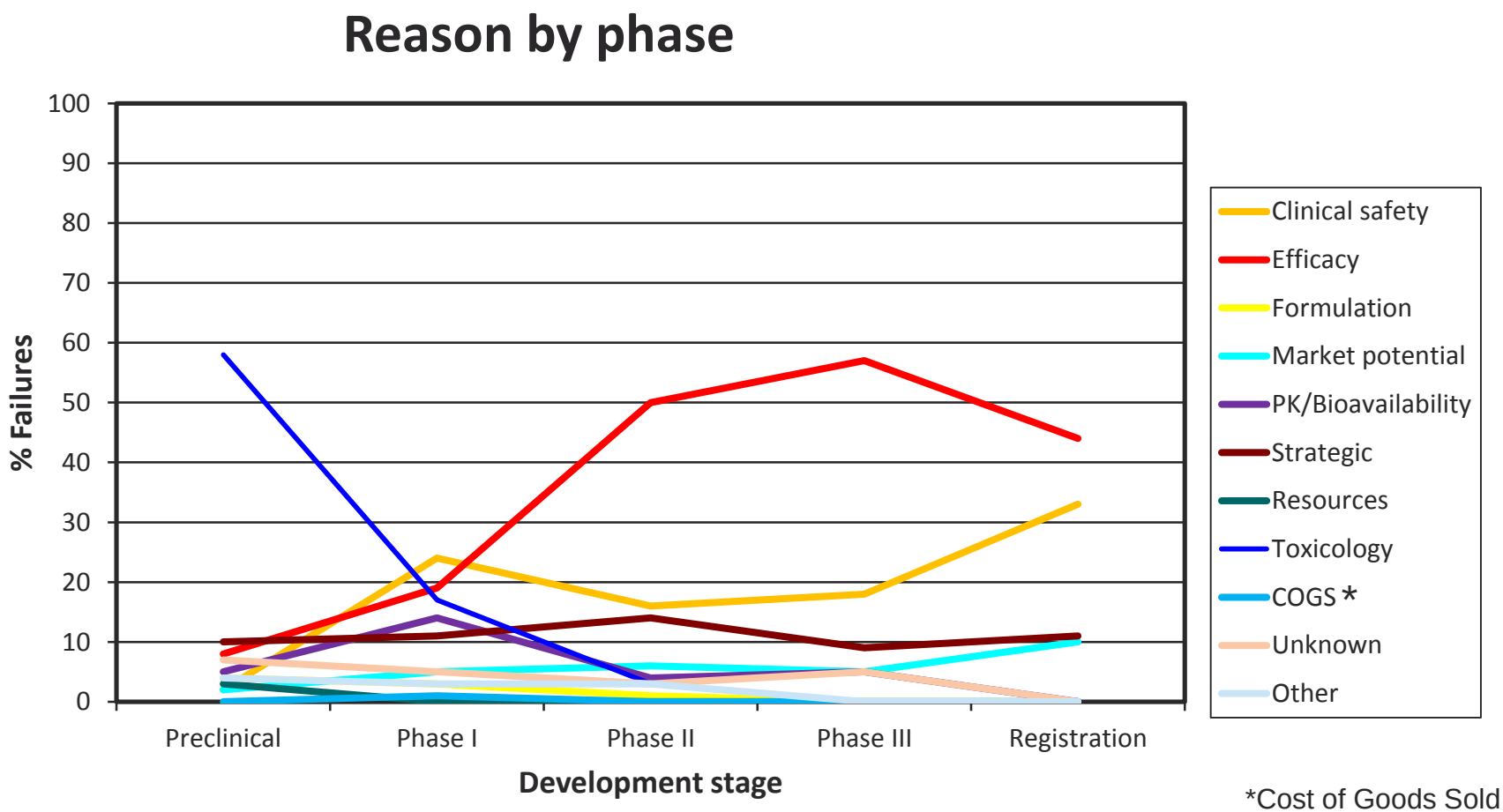
11 – Banner Alzheimer's Institute, Phoenix, AZ

12 – National Institute for Neurological Disorders and Stroke

13 – Mount Sinai Medical Center, New York, NY

14 – University of California, San Francisco, San Francisco, CA

Why do drug development programs fail?



*Cost of Goods Sold

FDA Data, 2010

Perspective for Brain Disorders

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

FDA's Critical Path Initiative

Memorandum of Understanding created between the FDA and C-Path in 2005

Critical Path Institute Consortia

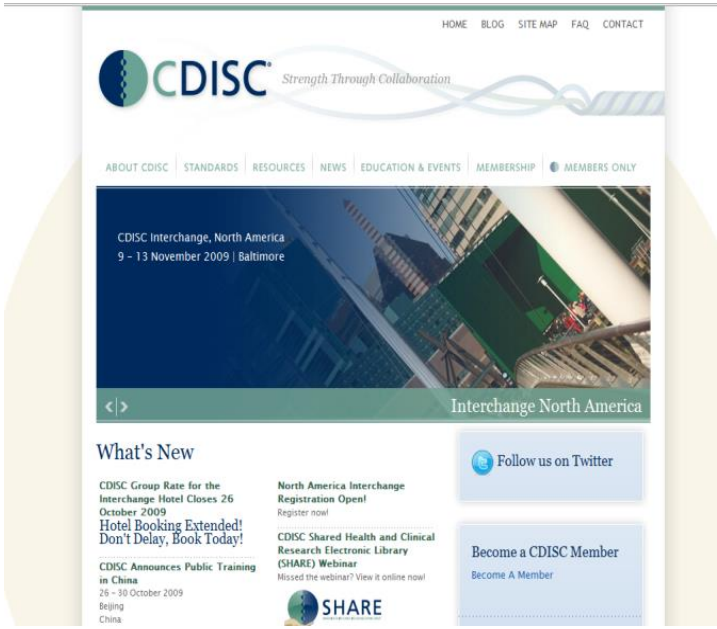
Eight global consortia collaborating with 1,300+ scientists and 61 companies

CAMD	**Coalition Against Major Diseases** Focusing on diseases of the brain
CPTR	**Critical Path to TB Drug Regimens** Testing tuberculosis drug combinations
CRITICAL PATH INSTITUTE MS National Multiple Sclerosis Society	**Multiple Sclerosis Outcome Assessments Consortium** Measuring drug effectiveness in MS
PKD CONSORTIUM CRITICAL PATH INSTITUTE	**Polycystic Kidney Disease Consortium** New imaging biomarkers
PRO CONSORTIUM CRITICAL PATH INSTITUTE ePRO CONSORTIUM CRITICAL PATH INSTITUTE	**Patient-Reported Outcome Consortium** Measuring drug effectiveness **Electronic Patient-Reported Outcome Consortium** Electronic capture of drug effectiveness
PSTC CRITICAL PATH INSTITUTE	**Predictive Safety Testing Consortium** Drug safety
CFAST	**Coalition For Accelerating Standards and Therapies** Data standards

- ✓ Biomarkers
- ✓ Clinical Outcome Assessment Instruments
- ✓ Clinical Trial Simulation Tools
- ✓ Data Standards
- ✓ In Vitro Tools

Clinical Data Interchange Standards Consortium (CDISC)

- **Global, open, multi-disciplinary, vendor-neutral non-profit standards developing organization (SDO)**
  - Founded in 1997; incorporated in 2000
  - > 300 organizational members
  - (academia, biopharma, service and technology providers, etc)
  - Works closely with other standards organizations (ISO, ANSI, HL7)
  - Standards downloaded in over 90 countries



www.cdisc.org

Established global industry standards to support the electronic acquisition, exchange, submission and archiving of data to streamline biomedical research (open via www.cdisc.org)

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CDISC specifies how to structure the data you have collected in a database, not what *should* be collected nor how to conduct clinical assessments or protocols

Coalition Against Major Diseases (CAMD)

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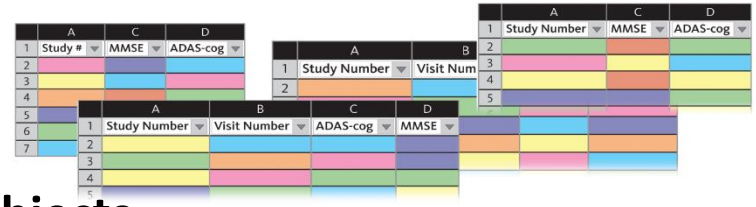
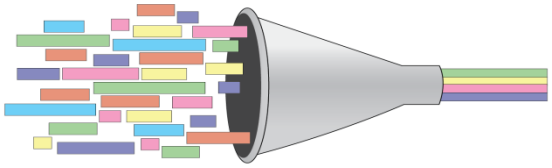
Starting Point

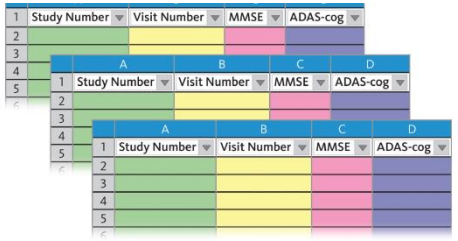
- Nine member companies agreed to share data from 24 trials; 6500 subjects
- The data were not in a common format
- The data needed to be combined in a consistent manner
- All data were remapped to the CDISC AD standard



Disparate Legacy Data



CDISC Data Standards



Integrated Data

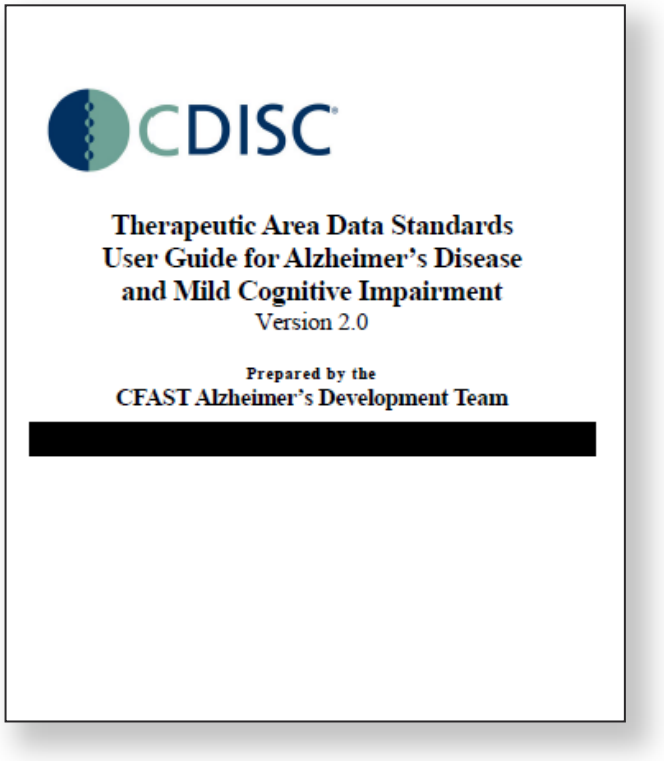
Results

- A new in clinical trial simulation tool was created; endorsed by FDA & EMA
- First ever therapeutic-area CDISC user guide published

Alzheimer's disease CDISC standard

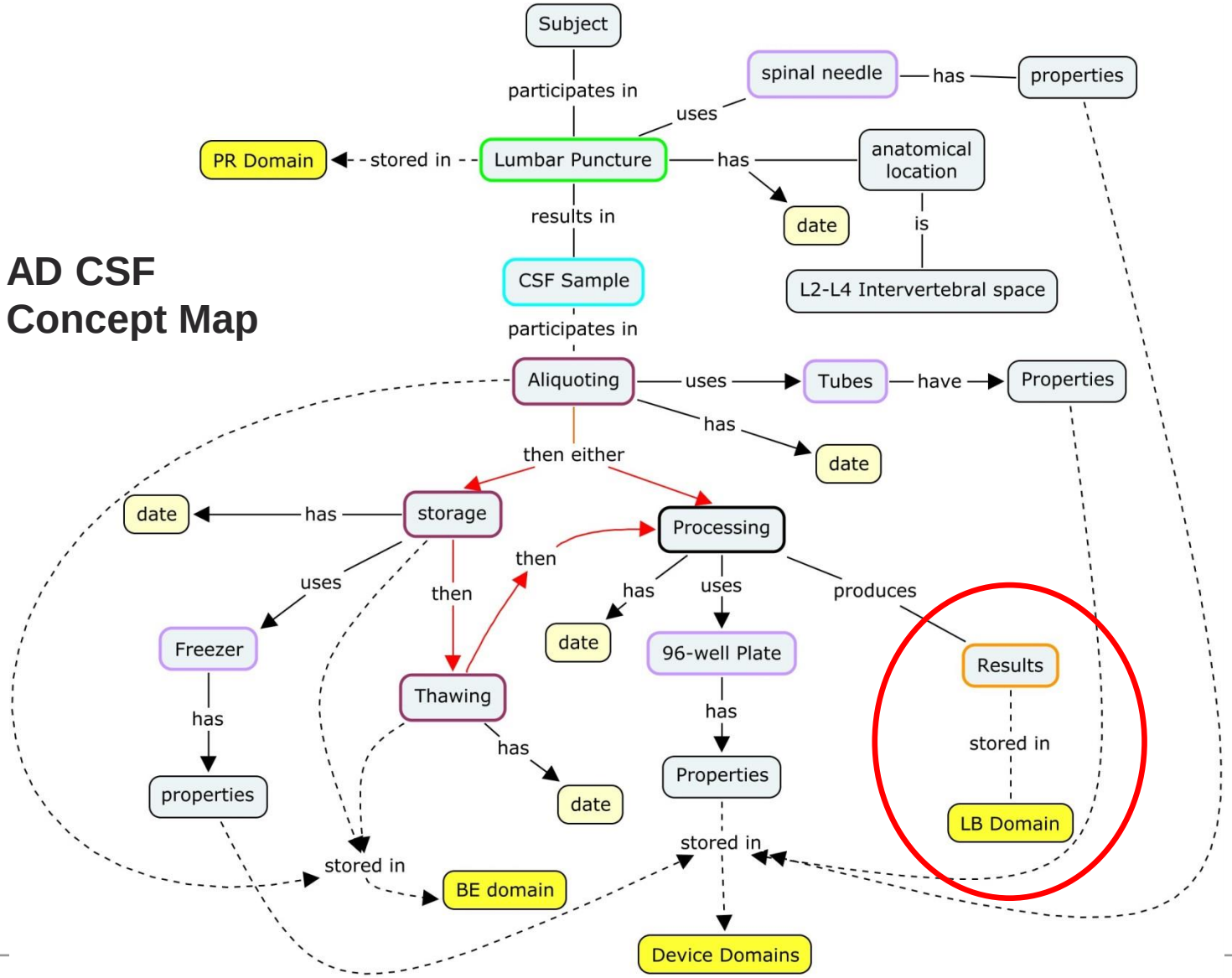
Concepts covered by the Alzheimer's CDISC User Guide
ApoE Genotype
Family History of AD
Volumetric MRI
PET, PET/CT (FDG, Florbetapir, PiB)
CSF Biomarkers and Sampling
Outcome Assessment Scales
ADAS-COG
CDR
AVLT
FAQ
Modified Hachinski
DAD
ADCS-ADL MCI
NPI
CGI
GDS

ADNI Alzheimer's Disease Neuroimaging Initiative

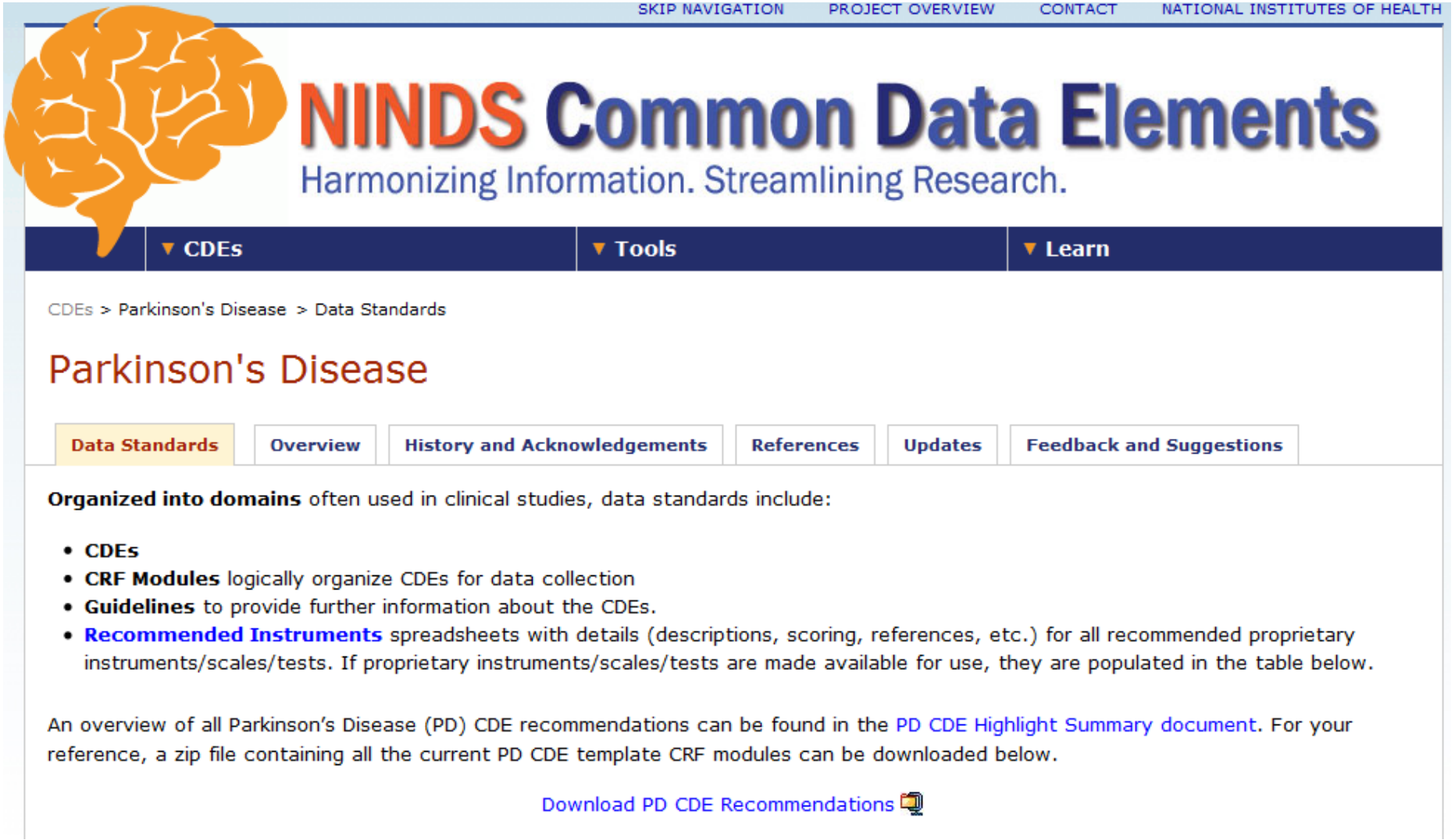


www.cdisc.org/therapeutic

Data standards strive to elucidate the whole story



Partnership with NINDS



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What's covered in the CDISC Parkinson's Disease Data Standard?

SDTM PD Therapeutic Area Supplement (new)

- UPDRS/ MDS-UPDRS
- Imaging: MRI, PET/SPECT
- Deep Brain Stimulation
- Neuropathology
- Family History of PD

Concepts Covered: Multiple Sclerosis v1.0

- **23 outcome assessment scales**
- **Disease course and characteristics**
- **Relapse**
- **OCT (Retinal Nerve Fiber Layer Thickness)**
- **Visually Evoked Potential (VEP)**
- **Visual acuity**

V2.0 in process; will include imaging

National Multiple Sclerosis Society

www.cdisc.org/therapeutic

Traumatic Brain Injury Draft User Guide Content

- **Glasgow Outcome Scale - Extended (GOS-E)**
- **Rey Auditory Verbal Learning Test (RAVLT)**
- **Glasgow Coma Scale (GCS)**
- **Disability Rating Scale (DRS)**
- **Expanded Disability Rating Scale - Postacute Interview (E-DRS-PI)**
- **Rand-36 (public domain version of the SF-36)**
- **Rivermead Postconcussive Symptom Questionnaire (RPQ)**
- **Trail Making Test (TMT)**

>35 instruments in total are in process, some pending copyright approval

- **TBI history**
- **Imaging**
- **Pupil measurements and reactivity**
- **Second insults and complications**

The TBI User Guide will be available for public comment in June!

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The Big Picture….FDA will require data standards

CAMD AD CSF Letter of Support

DEPARTMENT OF HEALTH & HUMAN SERVICES — PUBLIC HEALTH SERVICE

Food and Drug Administration
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993

Date: February 26, 2015

We encourage the inclusion of these exploratory CSF biomarkers in clinical trials to evaluate their clinical utility for identifying patients likely to show clinical progression of their MCI symptoms for the purpose of clinical trial enrichment. We consider data collection on this biomarker to be exploratory in nature. When including these biomarkers in clinical trials, sponsors are encouraged to employ consensus AD CDISC[2] standards for data harmonization. We believe that sharing and integrating data across trials can foster an accelerated path for AD drug development programs. If sponsors intend to include analyses of these biomarkers to support regulatory decision making for a given IND drug development program, they should prospectively discuss with the Division of Neurology Products in CDER.

Janet Woodcock, M.D.

Director, CDER

U.S. Food and Drug Administration

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/ucm434382.htm

Standards Directory

Foundational SDTM

www.cdisc.org/sdtm

Terminology

www.cdisc.org/terminology

Therapeutic Area User Guides

www.cdisc.org/therapeutic

NINDS Common Data Elements

www.commondataelements.ninds.nih.gov

Published Controlled Terminology

www.cancer.gov/cancertopics/cancerlibrary/terminologyresources/cdisc