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11 – Banner Alzheimer’s Institute, Phoenix, AZ
12 – National Institute for Neurological Disorders and Stroke
13 – Mount Sinai Medical Center, New York, NY
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Why do drug development programs fail?

Reason by phase

Development stage

% Failures

Preclinical
Phase I
Phase II
Phase III
Registration

Clinical safety
Efficacy
Formulation
Market potential
PK/Bioavailability
Strategic
Resources
Toxicology
COGS *
Unknown
Other

*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
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

<table>
<thead>
<tr>
<th>Consortium</th>
<th>Description</th>
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<tr>
<td>Coalition Against Major Diseases</td>
<td>Focusing on diseases of the brain</td>
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<td>Critical Path to TB Drug Regimens</td>
<td>Testing tuberculosis drug combinations</td>
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<td>Multiple Sclerosis Outcome Assessments Consortium</td>
<td>Measuring drug effectiveness in MS</td>
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<td>Polycystic Kidney Disease Consortium</td>
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<td>Electronic Patient-Reported Outcome Consortium</td>
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<td>Predictive Safety Testing Consortium</td>
<td>Drug safety</td>
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<td>Coalition For Accelerating Standards and Therapies</td>
<td>Data standards</td>
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- 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

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

A new in clinical trial simulation tool was created; endorsed by FDA & EMA.

First ever therapeutic-area CDISC user guide published.
### 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

www.cdisc.org/therapeutic
Data standards strive to elucidate the whole story.
Partnership with NINDS

NINDS Common Data Elements
Harmonizing Information. Streamlining Research.

CDEs > Parkinson's Disease > Data Standards

Parkinson's Disease

Data Standards Overview History and Acknowledgements References Updates Feedback and Suggestions

Organized into domains often used in clinical studies, data standards include:

- CDEs
- CRF Modules logically organize CDEs for data collection
- Guidelines to provide further information about the CDEs.
- Recommended Instruments spreadsheets with details (descriptions, scoring, references, etc.) for all recommended proprietary instruments/scales/tests. If proprietary instruments/scales/tests are made available for use, they are populated in the table below.

An overview of all Parkinson’s Disease (PD) CDE recommendations can be found in the PD CDE Highlight Summary document. For your reference, a zip file containing all the current PD CDE template CRF modules can be downloaded below.

Download PD CDE Recommendations
## 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

[www.cdisc.org/therapeutic](http://www.cdisc.org/therapeutic)
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*

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!

www.cdisc.org/therapeutic
The Big Picture....FDA will require data standards

Providing Regulatory Submissions In Electronic Format — Standardized Study Data

Guidance for Industry
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

Standards Directory

- **Foundational SDTM**
  www.cdisc.org/sdtm

- **Terminology**
  www.cdisc.org/terminology

- **NINDS Common Data Elements**
  www.commonelementdata.ninds.nih.gov

- **Therapeutic Area User Guides**
  www.cdisc.org/therapeutic

- **Published Controlled Terminology**
  www.cancer.gov/cancertopics/cancerlibrary/terminologyresources/cdisc