Alzheimer's Disease Therapeutic-area Standards Development

A collaborative effort between CDISC and the Critical Path Institute

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collaborate · innovate · accelerate

Overview

Background: Critical Path Institute and the Coalition Against Major Diseases (CAMD)

Process for Alzheimer's disease data standards development

Current progress

Next steps

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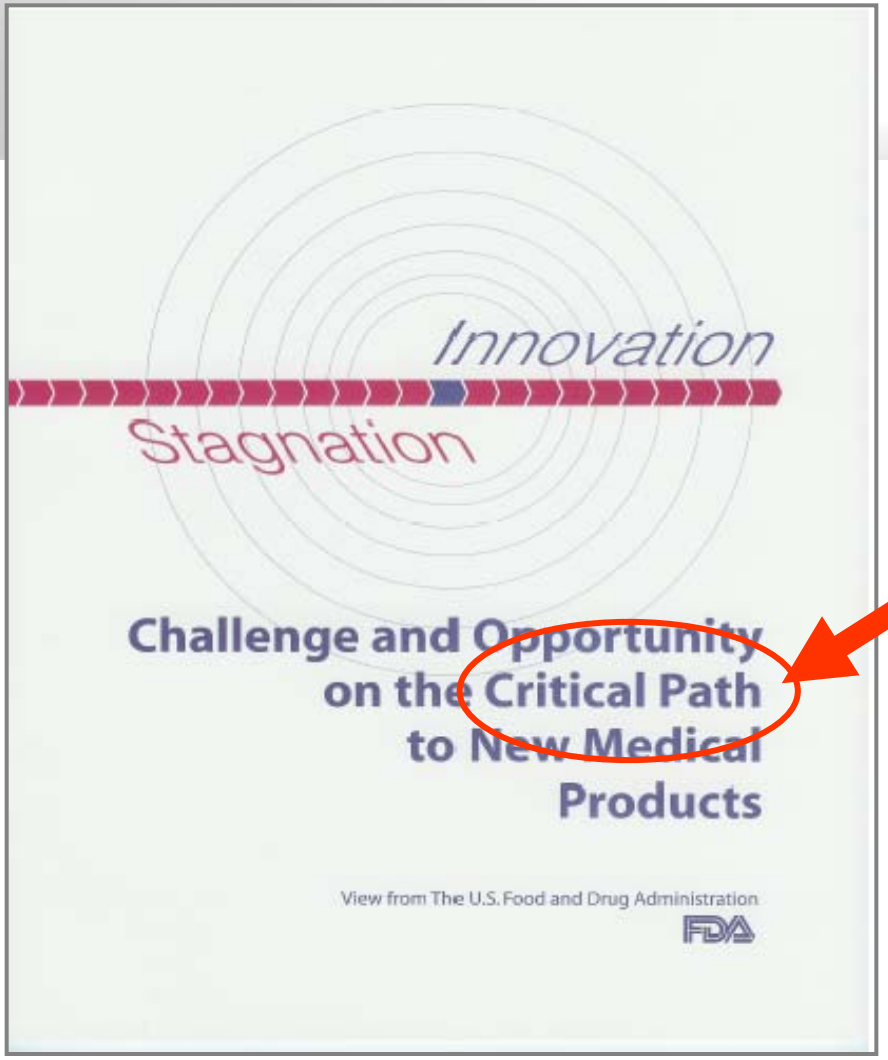
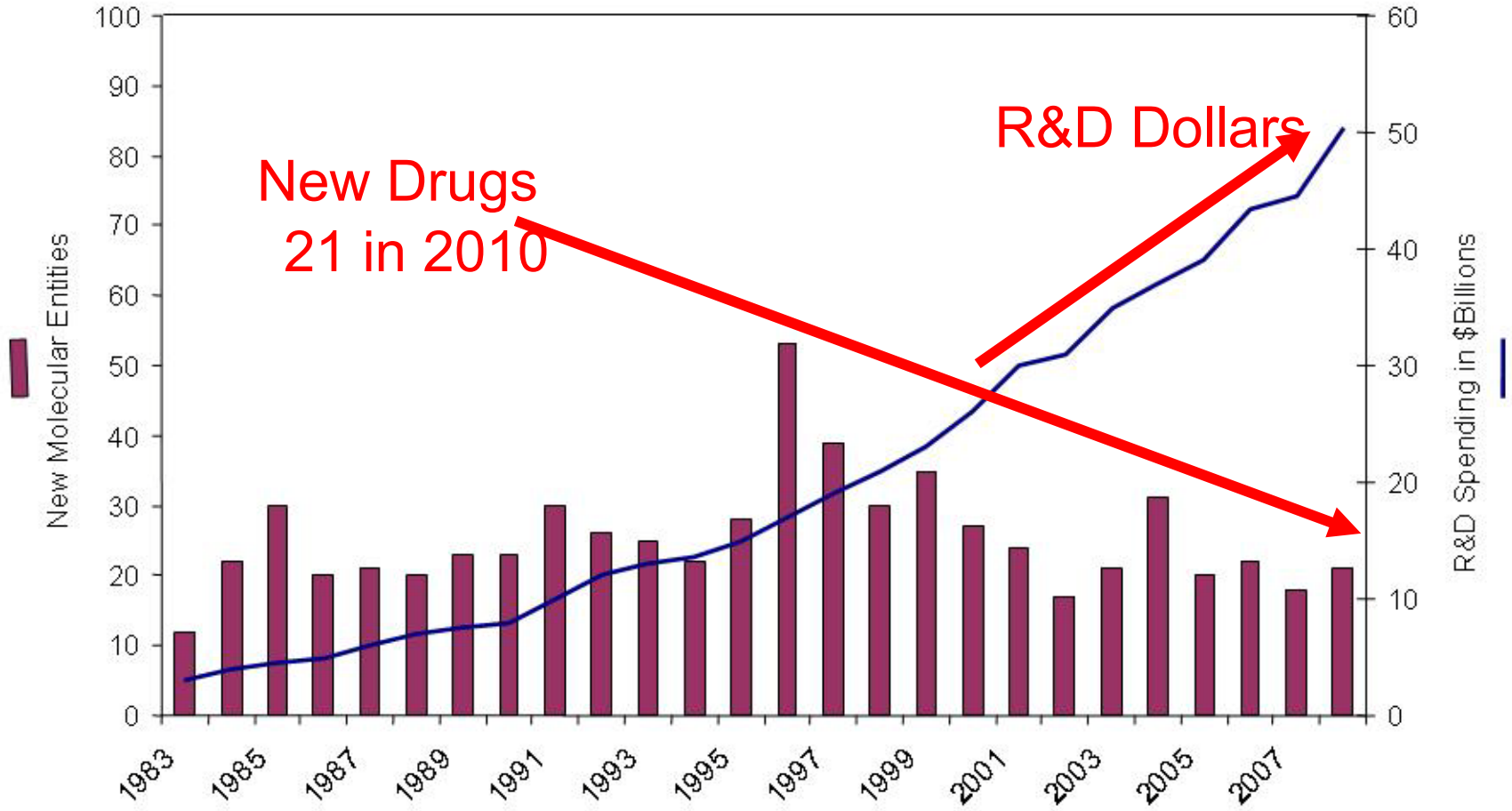


R&D Expenditures Increasing; New Drugs Not Increasing



CDISC and C-Path

C-Path Mission:

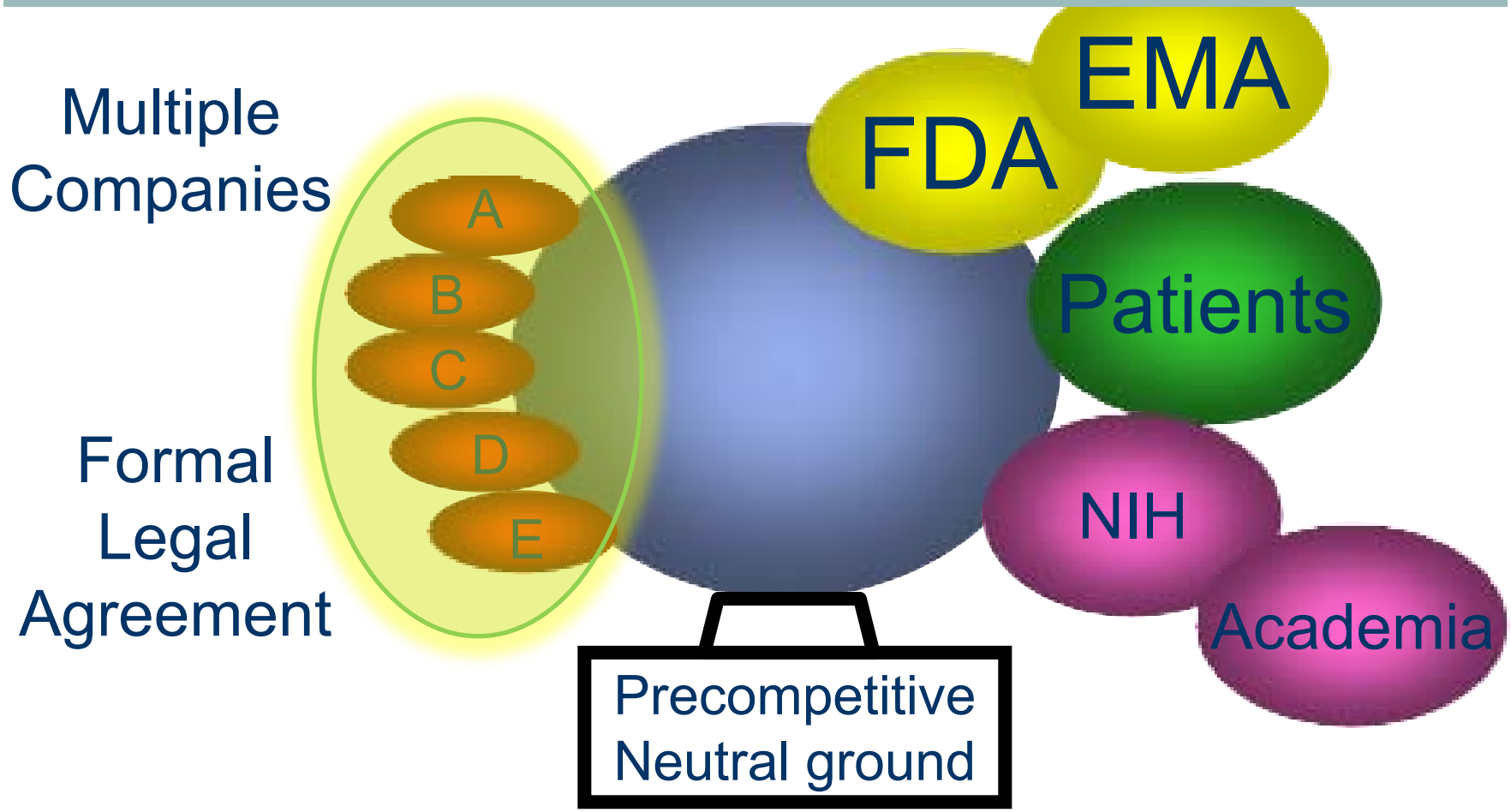
To create innovative collaborations in regulatory science that enable the most efficient and safe medical product development.

CDISC Mission:

To develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare

C-Path Consortia Model

Critical Path Institute (C-Path) has developed a consortium structure that provides a unique neutral, precompetitive environment to increase collaborative efforts for drug development



Current C-Path Consortia

Predictive Safety Testing Consortium (PSTC)

DRUG SAFETY

Patient-Reported Outcome (PRO) Consortium

DRUG EFFICACY

Coalition Against Major Diseases (CAMD)

UNDERSTANDING DISEASE

Polycystic Kidney Disease Consortium (PKD)

IMAGING BIOMARKERS

Critical Path to TB Drug Regimens (CPTR)

COMBINATION DEVELOPMENT PARADIGM

Coalition Against Major Diseases (CAMD)

Public-private partnership

170 scientists from EU/ US/ Japanese regulatory authorities, device/diagnostic pharmaceutical/CRO industry and academia

CAMD Goals

Create public databases of pooled clinical trials data

Advance drug development- create "tools"

- *Biomarkers* "qualified" for use in drug development
- *Quantitative disease models* "accepted for use" in drug development

Initial Focus: Alzheimer's and Parkinson's

CAMD Members and Partners

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Industry

- Abbott
- Astrazeneca
- BMS
- Eisai
- Forrest
- GSK
- J&J
- Lilly
- Novartis
- Orion
- Pfizer
- Roche
- sanofi-aventis
- Teva

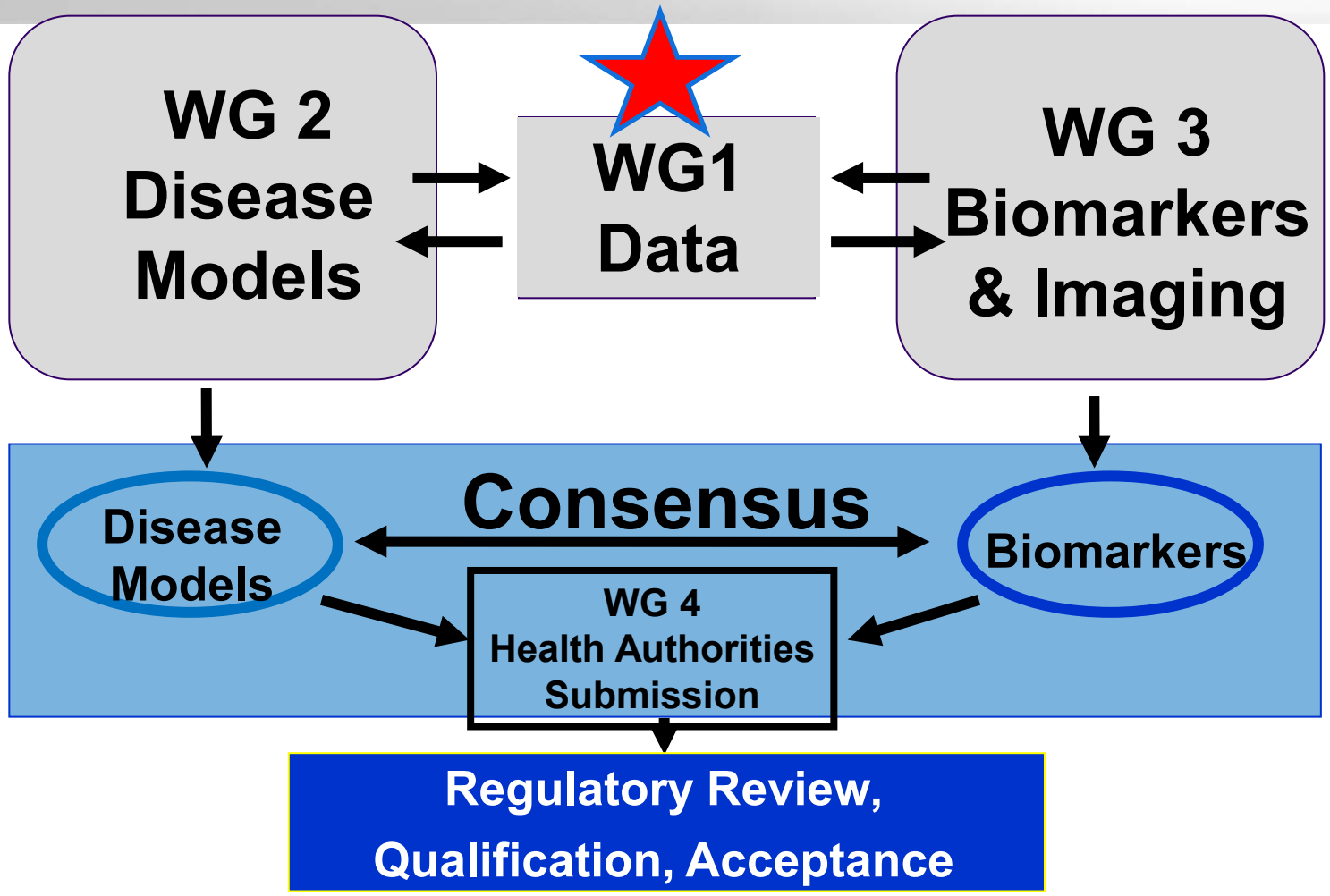
Government

- FDA
- EMA
- NIA
- NINDS

Patients

- Alliance for Aging Research
- Alzheimer's Association
- Alzheimer's Foundation
- Michael J. Fox Foundation
- National Health Council
- Parkinson's Action Network

CAMD Process Overview



Data Standards & Integration Workgroup Mission

To work with CAMD membership and CDISC teams to model *requested data elements* in CDISC Study Data Tabulation Model (SDTM)

To work with membership to map legacy data from source to new target SDTM format

To provide other CAMD workgroups with a pooled, integrated database of AD and PD subject-level data for analysis

Data Standards & Integration Workgroup Philosophy

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- Make use of existing SDTM domains and controlled terminology when possible
- Create new domains and request new terminology through existing CDISC processes when necessary
- Disseminate the work in an implementation guide when we're done

Workgroup Scope

Question:

How do we model disparate sources of legacy data in an SDTM database that can be used for creating analyses in support of CAMD goals?

Workgroup Scope

NOT in scope:

- We do not propose how to score rating scales/questionnaires
- We do not propose which scales/ labs/ any other type of data *should* be collected in AD studies nor which version of a scale or assay should be used

Simply stated: if you collect it, we show how to fit it into SDTM

Requested AD Data

- Demography
- ADAS-Cog
- MMSE
- AVLT
- ApoE genetic status
- Memantine use
- AChEi use
- Height/Weight
- Status/severity at start
- Status/severity at end
- Missed visits
- Time on disease
- Hippocampal volume
- Total brain volume
- CSF Tau
- CSF aBeta

Standards Development Process

Representative aCRFs requested from all data contributors

- Publically-available CRFs also reviewed

Requested SDTM experts from members to volunteer on workgroup

- Non-member participation (via CDA) ultimately necessary

Biweekly webinars, one-on-one calls, one two-day face-to-face meeting

Requested AD Data

Demography DM
ADAS-Cog QS
MMSE QS
AVLT QS
ApoE genetic status SC
Memantine use CM
AChEi use CM
Height/Weight VS

~~Status/severity at start~~ Derived
~~Status/severity at end~~ Derived
Missed visits SV
~~Time on disease~~ Derived
Hippocampal volume OM/DU*
Total brain volume OM/DU*
CSF Tau LB
CSF aBeta LB

***Draft Proposal. New SDTM domains required**

AD Standards Development Process

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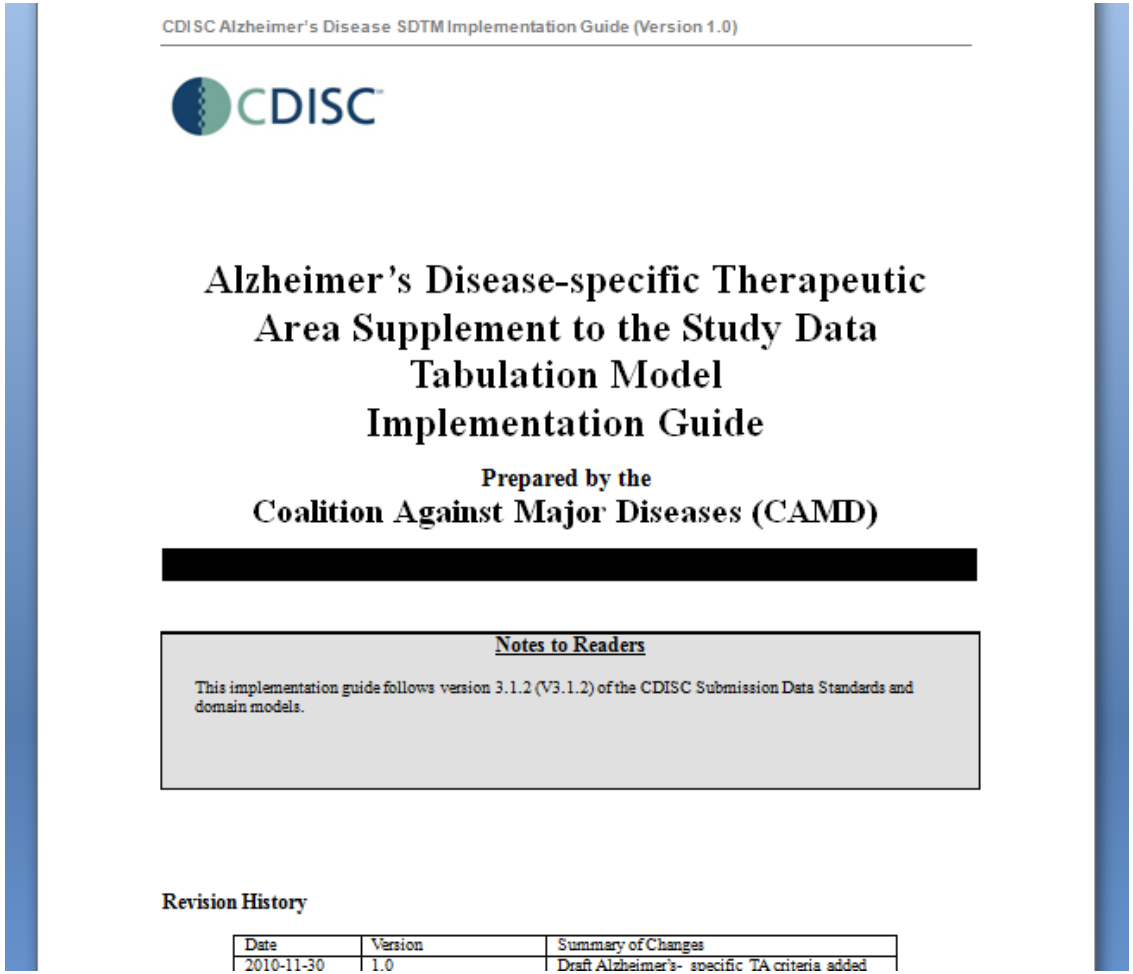
Start-to-finish > 1 year

- From kickoff meeting to initial data transformation
- >2 years from kickoff to user guide review
- Majority of time: ADAS-Cog

Multiple iterations required

- Late-comers' CRFs created need for minor tweaks
- Many feedback sessions with clinical scientists required

Alzheimer's Data Users' Guide



CDISC Alzheimer's Disease SDTM Implementation Guide (Version 1.0)

CDISC

Alzheimer's Disease-specific Therapeutic Area Supplement to the Study Data Tabulation Model Implementation Guide

Prepared by the
Coalition Against Major Diseases (CAMD)

Notes to Readers

This implementation guide follows version 3.1.2 (V3.1.2) of the CDISC Submission Data Standards and domain models.

Revision History

Date	Version	Summary of Changes
2010-11-30	1.0	Draft Alzheimer's- specific TA criteria added

Alzheimer's Data Users' Guide

- Follows structure and format of the SDTM Implementation Guide
- Shows explicitly how to model AD data in SDTM format, with references to SDTM/IG
- Posted for public review December 27, 2010
  - Received/responded to ~150 comments

The Alzheimer's Data Standard v1.0

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- 3 questionnaires modeled into QS domain of SDTM
  - Proposed controlled terminology for ~170 QSTEST/QSTESTCD values
- 3 LBTEST/TESTCDs for CSF labs
- Medical History and genotype terminology
- Two draft imaging domains new to SDTM
  - Includes ~15 proposed new TEST/TESTCD

Current Status

- Minor changes to terminology to follow QS Sub-team conventions for QSTEST and QSTESTCD

- CDISC requesting permission to show representative scales from their publishers
  - Explicit denial from publishers of MMSE
  - Other responses still pending

AD Data Standard In Use for CAMD

CAMD database currently houses AD/MCI data on ~4,000 subjects in common SDTM format

- 10 trials from 6 pharmaceutical companies

One academic study (ADCS Homocysteine) just transformed, final QC

11 more industry trials currently in QC

Lessons Learned

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Active participation from clinical scientists is vital to the development process

Questionnaires in the public domain vary wildly in content and implementation due to end-user edits

Legacy data is often at odds with ultimate prospective standards

Mapping data to draft standards is problematic

Lessons Learned

- A well-defined process for developing future therapeutic-area standards is needed
  - Where do you start?
  - When do you call it done?
  - What does the end deliverable look like?

Next Steps

- Publish AD user guide on CDISC website so the standards can be implemented industry-wide (CDISC lead)
  - Copyright issues with CRFs
- Expand current guide with additional questionnaires, imaging parameters, biomarkers relevant to AD, etc
    - CDR-SB, NPI, etc
- Move into additional disease areas
  - Parkinson's, MS, etc?

Thank You!

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