Understanding the Role of Public-Private Partnerships to De-risk the Development Process and to Facilitate Data Sharing

Therapeutic Development for Nervous System Disorders in the Absence of Predictive Animal Models of Disease: A Workshop

September 12–13, 2016

John Michael Sauer, PhD

Executive Director, Predictive Safety Testing Consortium

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a decade of excellence

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Why are there so many failures in neuroscience drug development?

Well, it's very hard

Neuroscience drug require unique characteristics from a chemical design standpoint, poorly characterized disease processes, dearth of biomarkers, there is a lack of predictive animal models of disease, and so on…

Thus, new drug discovery and development tools and strategies need to be developed in order to help drive the development of drugs for nervous system disorders

The Role of Public Private Partnerships

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A **public-private partnership** is a contractual arrangement between a **public** agency (such as the FDA, public universities and scientific institutes) and a **private** sector entity (such as pharmaceutical companies). Through this agreement, the skills and assets of each sector (**public** and **private**) are shared in delivering a service or facility for the use of the general **public**.

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- **Critical Path Institute (C-Path)**
- **Innovative Medicines Initiative (IMI)**
- **Foundation for the National Institute of Health Biomarker's Consortium (FNIH BC)**

FasterCures Consortia-pedia (http://consortiapedia.fastercures.org/)

Currently 49 Active Consortia

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Critical Path Institute (C-Path)

Independent 501(c)3 founded in 2005 "… to foster development of new evaluation tools to inform medical product development"

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

C-Path: A Public Private Partnership

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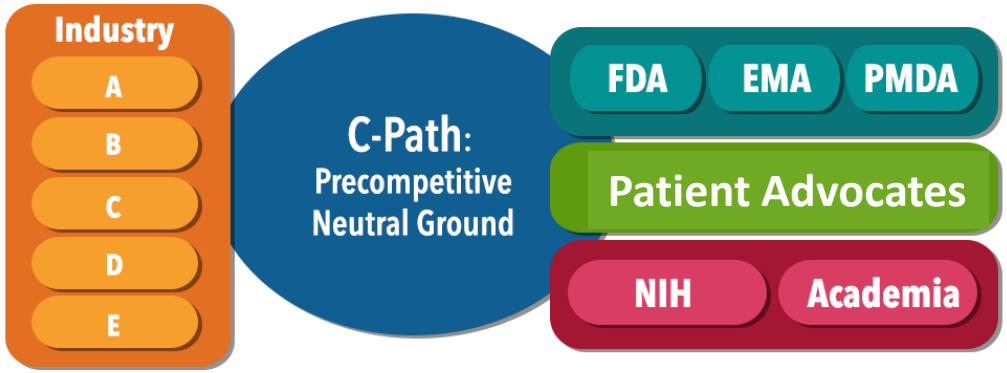
- Act as a trusted, neutral third party

- Convene scientific consortia of industry, academia, and government for sharing of data/expertise
  - ✓ The best science
  - ✓ The broadest experience
  - ✓ Active consensus building
  - ✓ Shared risk and costs

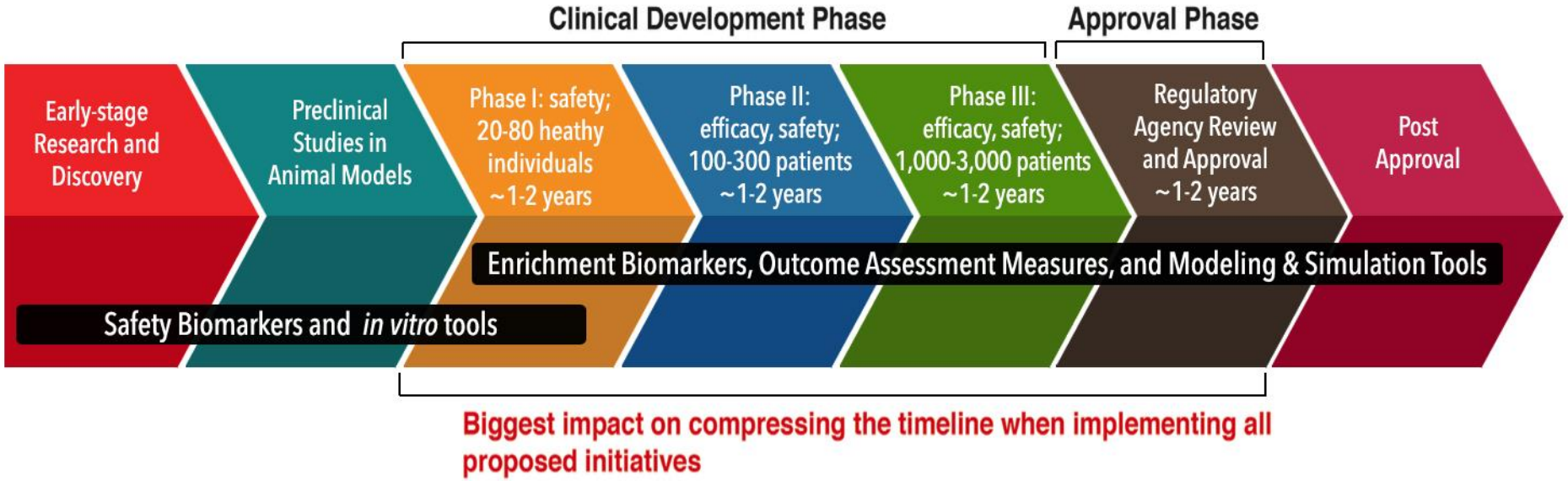


- Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products

- Official regulatory endorsement of novel methodologies and drug development tools

Shared Learning Can Shorten the Timeline

- ✓ Data Standardization and Sharing
- ✓ Biomarker Development and Qualification
- ✓ *In vitro* and *in vivo* tool development
- ✓ Outcome Assessment Measures
- ✓ Modeling and Simulation Tools



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

C-Path Consortia

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Twelve global consortia collaborating with 1,450+ scientists and 84 organizations

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

Duchenne Regulatory Science Consortium
Duchenne Muscular Dystrophy

International Neonatal Consortium
Neonatal clinical trials

Multiple Sclerosis Outcome Assessments Consortium
Drug Effectiveness in MS

Polycystic Kidney Disease Outcomes Consortium
New imaging biomarker for PKD

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

The Role of Public Private Partnerships

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Precompetitive collaborations among stakeholders (pharmaceutical companies, academics, and government institutes including the FDA) can be a mechanism for solving many of the issues discussed by creating new drug development tools for neuroscience.

De-risk the Development Process (tool development)

- Development and validation of predictive models
- Development (and regulatory qualification) of biomarkers and clinical outcome assessment tools

Nonclinical and Clinical Data Sharing

Facilitate alignment with health authorities

- Regulatory qualification and endorsement

This is not about the co-development of drugs, but rather a collaboration to create and validate tools to drive the drug development process

The Role of Public Private Partnerships

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De-risk the Development Process (tool development)

- Development and validation of predictive models
- Development (and regulatory qualification) of biomarkers and clinical outcome assessment tools - move the levers
  - Better dose selection
  - Better signal detection
  - Better target selection (validation)

- Gain general acceptance of approaches (including regulators)
- Resource sharing (resources and knowledge)

Michael J Fox: LRRK-2 example on potential pulmonary toxicity associated with kinase inhibitors (Todd Sherer)

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Nonclinical and Clinical Data Sharing

Types of Data that can be Shared

In vitro data

Animal model data

Clinical data

- Placebo arm data
- Natural history disease (longitudinal) data
- Biomarker data sharing (placebo and active arms)
- Sharing of failed trial data (placebo and active arms)

Data to construct computational models

C-Path's Coalition Against Major Diseases

Data Sharing

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CODR Database

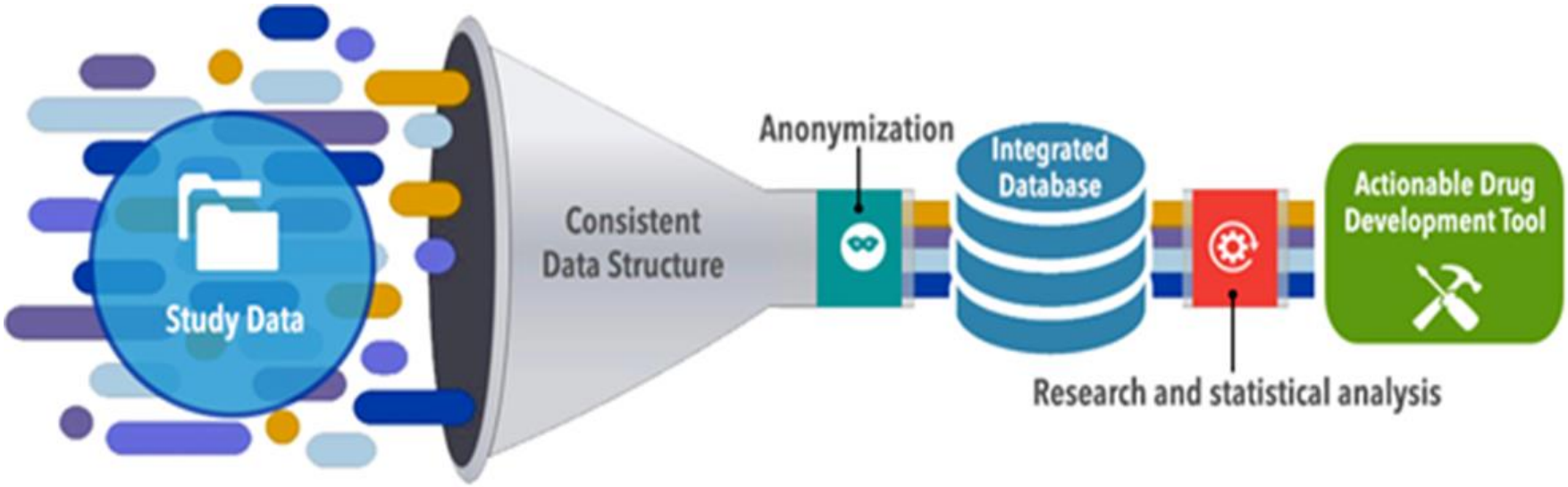
Critical Path Institute (C-Path) Online Data Repository (CODR): Coalition Against Major Diseases (CAMD) Alzheimer's Disease Database

What is in this database:

- 9 members of CAMD remapped and contributed patient-level, placebo-arm data from 6,500 patients across 24 clinical trials of AD and MCI.
- The database contains, but is not limited to, demographic information, APOE4 genotype, concomitant medications and cognitive scales (MMSE and ADAS-Cog).
- All data has been remapped to a common data standard (CDISC SDTM v3.1.2) such that all the data can be analyzed across all studies.
- It is openly available to CAMD members, as well as to external qualified researchers who submit, and are approved for, a request for access.
- All data are fully de-identified.

Database is accessible to any qualified investigator

C-Path Data Mapping and Integration Process



Data as contributed

Master Standardized Datasets

Analysis Datasets

Data Sharing – Key Success Factors

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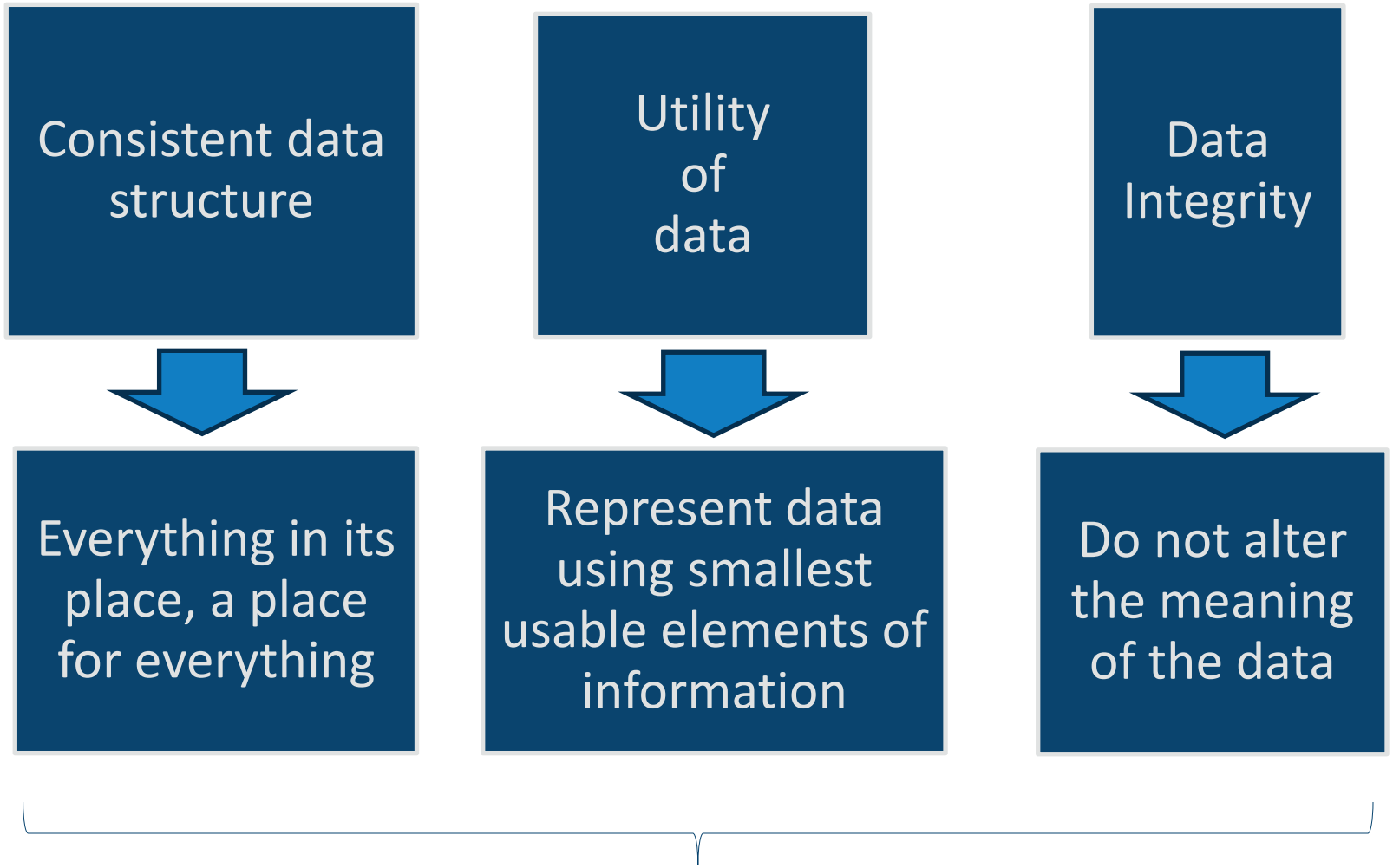

CDISC clinical data standards provide this capability

C-Path's Coalition Against Major Diseases

Alzheimer's Disease Clinical Trial Simulation Tool

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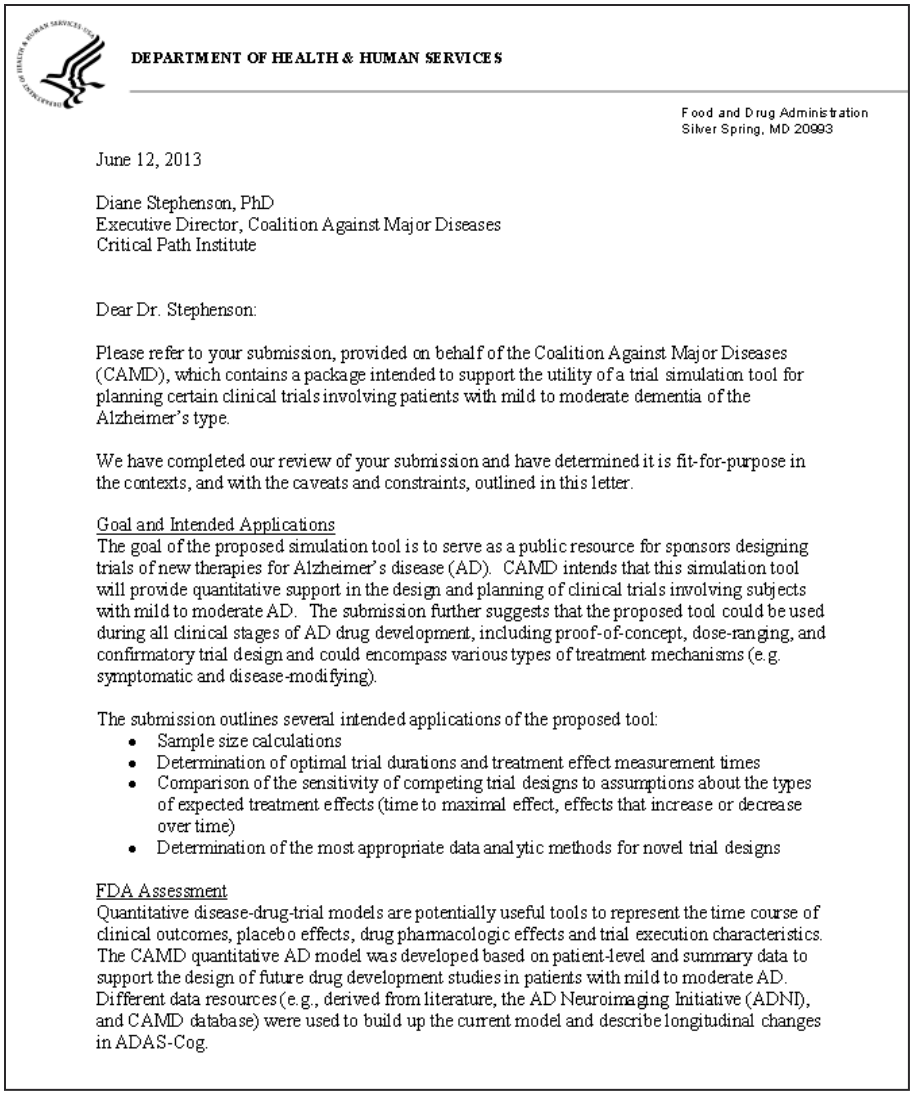
Alzheimer's Disease Clinical Trial Simulation Tool

What the tool is:
A clinical trial simulation tool to help optimize clinical trial design for mild and moderate AD, using ADAS-cog as the primary cognitive endpoint

What is it based on:
A drug-disease-trial model that describes disease progression, drug effects, dropout rates, placebo effect, and relevant sources of variability

The trial simulation tool is endorsed by FDA and EMA

2013 CAMD Modeling Regulatory Decisions



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

June 12, 2013

Diane Stephenson, PhD
Executive Director, Coalition Against Major Diseases
Critical Path Institute

Dear Dr. Stephenson:

Please refer to your submission, provided on behalf of the Coalition Against Major Diseases (CAMD), which contains a package intended to support the utility of a trial simulation tool for planning certain clinical trials involving patients with mild to moderate dementia of the Alzheimer's type.

We have completed our review of your submission and have determined it is fit-for-purpose in the contexts, and with the caveats and constraints, outlined in this letter.

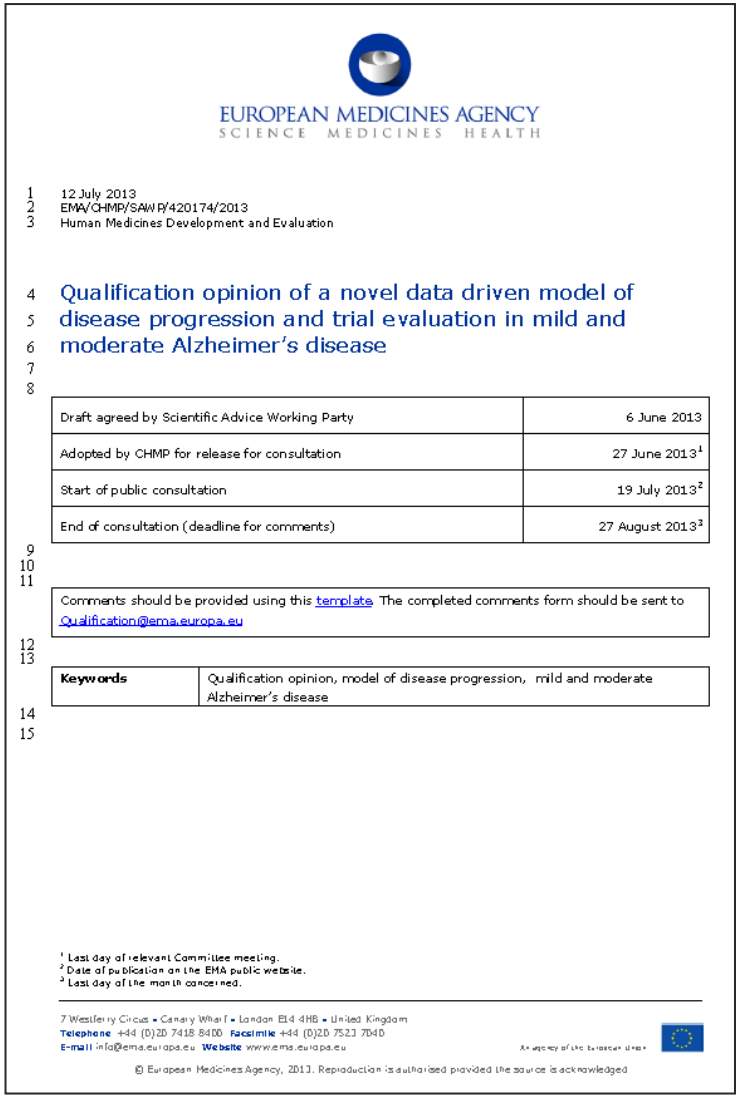
Goal and Intended Applications
The goal of the proposed simulation tool is to serve as a public resource for sponsors designing trials of new therapies for Alzheimer's disease (AD). CAMD intends that this simulation tool will provide quantitative support in the design and planning of clinical trials involving subjects with mild to moderate AD. The submission further suggests that the proposed tool could be used during all clinical stages of AD drug development, including proof-of-concept, dose-ranging, and confirmatory trial design and could encompass various types of treatment mechanisms (e.g. symptomatic and disease-modifying).

The submission outlines several intended applications of the proposed tool:

- Sample size calculations
- Determination of optimal trial durations and treatment effect measurement times
- Comparison of the sensitivity of competing trial designs to assumptions about the types of expected treatment effects (time to maximal effect, effects that increase or decrease over time)
- Determination of the most appropriate data analytic methods for novel trial designs

FDA Assessment
Quantitative disease-drug-trial models are potentially useful tools to represent the time course of clinical outcomes, placebo effects, drug pharmacologic effects and trial execution characteristics. The CAMD quantitative AD model was developed based on patient-level and summary data to support the design of future drug development studies in patients with mild to moderate AD. Different data resources (e.g., derived from literature, the AD Neuroimaging Initiative (ADNI), and CAMD database) were used to build up the current model and describe longitudinal changes in ADAS-Cog.

FDA fit-for-purpose decision on CAMD CTS tool. 2013



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

12 July 2013
EMA/CHMP/SAWP/420174/2013
Human Medicines Development and Evaluation

Qualification opinion of a novel data driven model of disease progression and trial evaluation in mild and moderate Alzheimer's disease

Draft agreed by Scientific Advice Working Party	6 June 2013
Adopted by CHMP for release for consultation	27 June 2013[1]
Start of public consultation	19 July 2013[2]
End of consultation (deadline for comments)	27 August 2013[3]

Comments should be provided using this template. The completed comments form should be sent to Qualification@ema.europa.eu

Keywords	Qualification opinion, model of disease progression, mild and moderate Alzheimer's disease

[1] Last day of relevant Committee meeting.
[2] Date of publication on the EMA public website.
[3] Last day of the month concerned.

7 Westferry Circus ▪ Canary Wharf ▪ London E14 4HB ▪ United Kingdom
Telephone +44 (0)20 7418 8400 Facsimile +44 (0)20 7523 7040
E-mail info@ema.europa.eu Website www.ema.europa.eu
An agency of the European Union

EMA qualification opinion on CAMD CTS tool. 2013

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Facilitate Alignment with Health Authorities

Gain general acceptance of approaches, including FDA, EMA and PMDA

Some consortium objectives will be discovery in nature

Other consortium objectives will have regulatory objectives

Very few consortia have regulatory experience and capability

Summary

The Public Private Partnership Consortia approach offers a pathway for collaboration across the diverse stakeholders involved in the discovery and development of neuroscience therapies

The conscience science approach allows all stakeholders to work towards a common goal and on what is important

Precompetitive consortia can allow for:

1. The development of tools to de-risk the development process
2. Mechanism for “safe” nonclinical and clinical data sharing
3. Facilitate alignment with health authorities