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
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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

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

• 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

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

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

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)*
The Role of Public Private Partnerships

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

Coalition Against Major Diseases

Accelerating the development and review of medical products for neurodegenerative diseases.

Access to AD data available to qualified researchers
Model endorsed by FDA and EMA

The Coalition Against Major Diseases (CAMD) is a public-private-partnership aimed at creating new tools and methods that can be applied to increase the efficiency of the development process of new treatments for Alzheimer’s disease (AD) and Parkinson’s disease (PD).
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

Consistent data structure

Everything in its place, a place for everything

Utility of data

Represent data using smallest usable elements of information

Data Integrity

Do not alter the meaning of the data

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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Access to AD data available to qualified researchers

Model endorsed by FDA and EMA
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.
June 12, 2013

Dear Dr. Stevenson:

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 context, and with the concerns 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
- Sensitivity of competing trial designs to assumptions about the types of expected treatment effects (time to maximal effect, effect that increase or decrease over time)
- Determination of the most appropriate data analytic methods for novel trial designs

FDA Assessment

Quantitative disease-modeling tools are potentially useful tools to represent the true course of clinical outcomes, placebo effects, drug pharmacokinetic 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 sources (e.g., derived from literature, the AD Neuroimaging Initiative (ADNI), and CAMD database) were used to build the current model and describe longitudinal changes in ADAS-Cog.

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

EMA qualification opinion on CAMD CTS tool. 2013
The Role of Public Private Partnerships

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