Coalition Against Major Diseases (CAMD)

CDISC French User Group – February 2011

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Agenda

- Coalition Against Major Diseases (CAMD)
- Data workgroup
- Difficulties
- Outcomes
- Conclusion

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CAMD – Goal

- **Coalition Against Major Diseases (=CAMD) launched in February 2008 by the Critical Path Institute (C-Path)**

- **GOAL**
  - **To develop new knowledge and models that will enable faster development of innovative and effective therapies**
  - **Initial focus on neurodegenerative diseases with huge unmet medical need**
    - Alzheimer's disease
    - Parkinson's disease

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CAMD – Overview

Participants

- 15 biopharmaceutical companies
- Representatives from FDA, EMA, the National Institute of Neurological Disorders and Stroke (NINDS) and the National Institute on Aging (NIA) serving as advisors

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CAMD – Biopharmaceutical members

Abbott	Genentech Inc.
Alliance for Aging Research	GlaxoSmithKline
Alzheimer's Association	Johnson & Johnson
Alzheimer's Foundation of America	National Health Council
AstraZeneca Pharmaceuticals LP	Novartis Pharmaceutical Corporation
Bristol-Myers Squibb Company	Parkinson's Action Network
CHDI Foundation	Parkinson's Disease Foundation
Eli Lilly and Company	Pfizer, Inc.
F. Hoffmann La Roche Ltd	sanofi-aventis, US, Inc.
Forest Research Institute	

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CAMD – Organization

Workgroup 1: Data

- Provides a common data format and remapping rules for pooling disparate sources of clinical data
- Provides data management infrastructure
- Loads transferred data into shared CAMD database for use in Workgroups 2 and 3

Workgroup 2: Disease-Progression Modeling

- Develops models that can be used to inform the design of clinical trials to test drugs for AD and PD as efficiently as possible (use of simulations)
- Submits those models for review and possible qualification by FDA

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CAMD – Organization (cont'd)

Workgroup 3: Biomarker Evaluation

- Identifies biomarkers that have utility in advancing clinical drug development
- Submits appropriate package for qualification of use to the FDA

Workgroup 4 will be formed to assist in the creation of the dossiers for submission to the FDA

→ This presentation will focus on the Data WG for Alzheimer's disease (AD)

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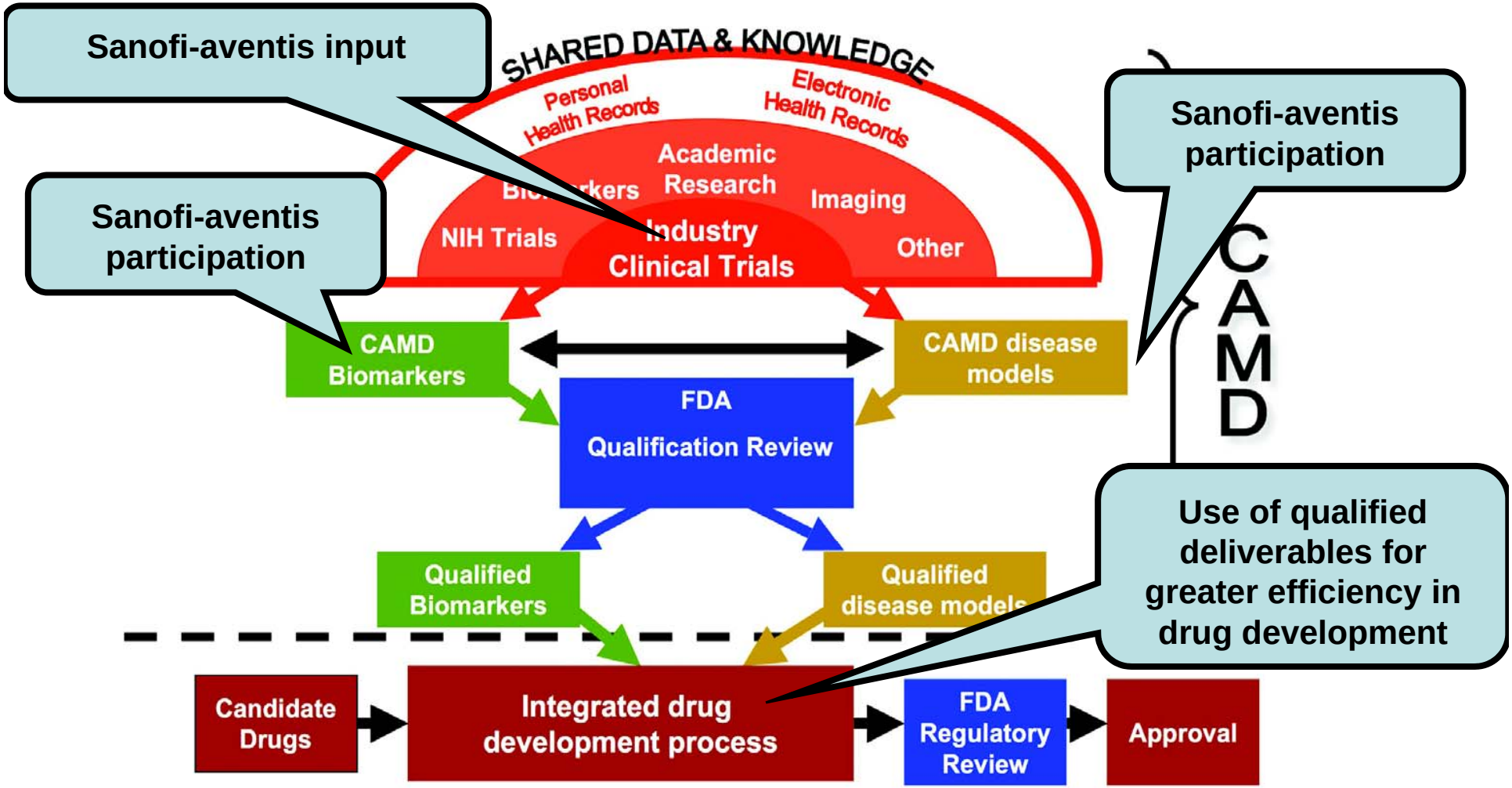
CAMD – Model



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Data WG – Sponsors contribution

- Each sponsor to identify trials for contribution
- Commitment to provide data
  - Placebo arm only
  - Following CDISC SDTM V3.1.2
- Supporting documentation required
  - Protocols
  - CDISC annotated CRFs
  - Webpage with secure access

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Data WG – Sanofi-aventis trials

- **Two Phase III studies in xaliproden program**
  - Randomized, multicenter, double-blind, placebo-controlled, 18-month study of the efficacy of xaliproden in patients with mild-to-moderate dementia of the Alzheimer's type
- **Large trials**
  - EFC2724: 719 patients in the placebo arm
  - EFC2946: 644 patients in the placebo arm
- **Long-term data**
  - Core study: 18-month treatment
  - For some patients having completed the planned 18-month treatment period, an optional double-blind extension phase was proposed (up to 31 months)
- **Biomarker: brain imaging (MRI data)**

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Data WG – Planned process

- Get consensus on initial data elements to be standardized → input from modeling workgroup (Aug 2009)
- Identify first round of trials to map (Oct 2009)
- Develop proposal of AD standards (Oct 2009)
- Submit proposed standards to CDISC and FDA (Oct 2009)
- Design and implement the database (Nov 2009)
- Initial sponsor data transformed and loaded on database (Q1 2010)

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Data WG – Domains requested

- CM Concomitant medications
- DM Demographics
- DS Disposition
- LB Laboratory results
- MH Medical history
- OM Organ measurement = MRI data
- QS Questionnaire data = efficacy assessments
  - ADAS-Cog
  - MMSE
- SC Subject characteristics = only ApoE genotyping
- SV Subject visit
- VS Vital signs

- SUPPDM (Other race), SUPPMH, SUPPSC

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Data WG process

- **Working document received from CAMD**
  - Define file = CDISC compliant + Core and CAMD expectation (few differences. eg STRESU in LB Exp in CDISC, Req in CAMD)
- **Deliverables :**
  - Validated mapped datasets
  - define (.xls) following CAMD specifications with sponsor specific rules (mostly derivation rules, eg age/scores, eg baseline definitions, reference start/end dates, handling of MD for score calculation).
    Needed for the modeling working group to pool the data

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Difficulties – Questionnaire (QS)

Patient's clinical assessment

- **ADAS-Cog (AD Assessment Scale – Cognitive)**
  - Several questions/tasks (success/failure or ordinal scales)
  - 13 to 15 items based on these results (word recall, commands, constructional praxis, delayed word recall, naming, ideational praxis, orientation, word recognition, remembering, language, word-finding, delayed word recall, concentration/distractibility + number cancellation, executive function maze, rarely included)
  - Several sub-scores and one global score
- **MMSE (Mini-Mental State Examination)**
  - 30 questions (success/failure)
  - 5 items based on these results (orientation, learning/memory/recall, attention/calculus, naming/understanding/language, praxis)
  - One global score

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Difficulties – Questionnaire (QS)

Differences in data collected

- **Variability in ADAS-Cog questionnaire itself**
  - 13 to 15 items
  - Number of trials for Word Recognition task (1 to 3) and words used
- **Variability in the level of data collection**
  - ADAS-Cog: 13-15 summary items, vs. summary items + each task
  - MMSE: 5 summary items, vs. each task (summary items derived)

Decision

- **Account for the maximum level of details (e.g. word capture)**
  → Individual tasks, all questions: optional if not collected
- **Provide the summary items as derived variables if not collected in the CRF (e.g. MMSE) with flag DRVFL=Y**
  → Summary items to be provided by all sponsors (derived if necessary)

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Difficulties – Questionnaire (QS)

Should derived gloval score and sub-scores be provided?

- Different ADAS-Cog score definition (11-item or more)
- Different ADAS-Cog sub-scores available
- Different sponsor derivation rules, especially for missing data

Decision

- **Not to be provided for ADAS-Cog**
  → Derived by Modeling Workgroup to ensure homogeneity
- **Total score to be provided for MMSE, with flag DRVFL=Y**
  → Collected by some sponsors

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Difficulties – Questionnaire (QS)

Variability in QS for mapping

- Different order of items (QSSPID)
- Different terminology (QSTESTCD & QSTEST)

Decision

- QS order and terminology for QSTESTCD,QSTEST, QSCAT and QSSCAT homogenized by CAMD

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Difficulties – Organ measurement (OM)

- MRI data: new Brain Measurement domain?
- New CDISC domain & terminology: Organ Measurement (OM)?
- Not in first transfer (last specifications prepared)

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Difficulties – Dictionaries

- WHODRUG dictionary requested for CM
- MedDRA for AE : coding in mixed case

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Difficulties – mapping of MH

- Three types of medical History
  - AD History and onset of cognitive symptoms
  - General Medical history
  - Family History
- CAMD defined controlled terminology MHCAT
  - MHCAT : “PRIMARY DIAGNOSIS,” and “GENERAL.”, “FAMILY HISTORY”

MHCAT	MHSCAT	MHTERM	MHDECOD	MHSTDTC
PRIMARY DIAGNOSIS		Mild Cognitive Impairment		2001-05
PRIMARY DIAGNOSIS		Alzheimer's Disease		2003-05

MHCAT	MHSCAT	MHTERM	MHDECOD	MHSTDTC
GENERAL		BLIND LEFT EYE	Blindness unilateral	1999-07-07
GENERAL		TRAUMATIC BRAIN INJURY	Traumatic brain injury	2005-03-28

MHCAT	MHSCAT	MHTERM	MHDECOD	MHSTDTC
FAMILY HISTORY	MOTHER	Angina		
	GRANDMOTHER	Unstable Angina		
	ANY RELATIVE	Myocardial Infarction		

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Difficulties – Other domains

- **Follow CDISC V3.1.2 standards and terminology**
  - **DSCAT, DSDECOD, LBTESTCD, LBTEST, LBSTRESU, VSTESTCD, VSTEST, VSSTRESU, etc.**
- **But…**
  - **CDISC terminology not available for all data**
    - E.g. LBCAT, LBSCAT, VSCAT, VSSCAT
  - **CDISC terminology not always exhaustive**
    - E.g. LBSTRESU, DSDECOD
- **When CDISC codelist not available or “extensible”, use sponsor-specific terminology**

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Difficulties – Conclusion

- **Variability between sponsors: standardization needed**
  → Not an easy task!

- **Impossible to homogenize all**
  - **Sponsor-specific terminology**
  - **Sponsor-specific derivation rules**
    - Reference start/end dates, baseline definitions, age calculation, handling of MD for score calculation, etc.
  - **To be provided in the Defines at time of data transfer (for future use by Modeling Workgroup)**

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Difficulties – Conclusion

- **Need time for workgroup members to map legacy data to CAMD standards, e.g. for sanofi-aventis**
  - From CDISC SDTM V3.1.1 to V3.1.2
  - To CAMD standardized terminology (with requested derivations)
  - Use of WebSDM to validate the data (CAMD used Open Cdisc)
- **Communication between workgroup members**
  - Many persons involved
  - Different continents
  - Bi-weekly meetings

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Outcomes – Sanofi-aventis data transfer

- **One of the first company to remap, upload data and pass the QC process**
- **Several transfers needed**
  - **From 05MAR2010 (meeting Q1 2010 target)**
    - Without MH (ongoing mapping discussions)
    - Without OM (specifications not completed yet)
  - **To 04MAY2010 (complete)**
- **Transfer package**
  - **Mapped SDTM (.XPT)**
  - **CAMD defines with sponsor specific rules (.XLS)**

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Outcomes – Shared and standard CAMD database

Currently more than 4000 AD patients (placebo)

- From 11 clinical trials from 7 pharmaceutical companies
- Following CDISC SDTM data standard
- As much standardization as possible between companies (though some heterogeneity remains)

Database publicly released on 11JUN2010

- Available for research (to design more efficient clinical trials of new treatment)

Will continue to expand

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Outcomes – Standards in AD

Alzheimer's Disease Standard Implementation Guide

- Consensus on use of CDISC standards for clinical data (ADAS-Cog) and other AD specific elements?
- Developed with CDISC and input from the FDA

Posted for public review

- http://www.cdisc.org/stuff/contentmgr/files/0/2356ae38ac190ab8ca4ae0b222392b37/misc/sdtmig_ad_final_for_public_review.doc
- Comments to cdiscreviewcomments@cdisc.org by 18FEB2011

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Conclusion

Unprecedented collaboration

Valuable deliverables to improve drug development in Alzheimer's disease

- Shared database available for research
- Data standards published and available to everyone once reviewed

What's next

- AD workgroups on Modeling and Biomarkers
- Parkinson's disease

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Thanks for your attention

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