

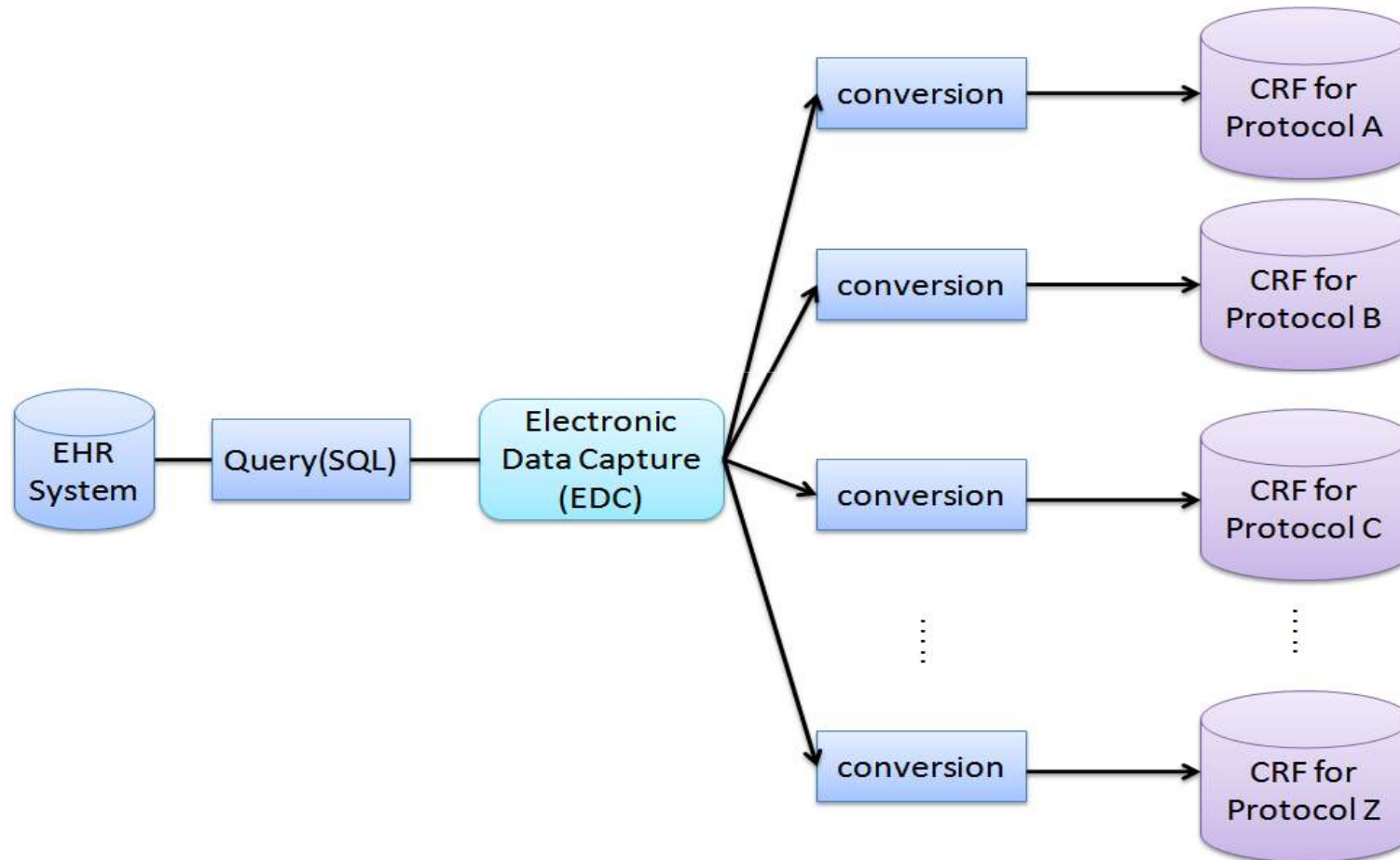
The Study of Standard-Based Electronic Case Report Form Design System

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National Yang-Ming University

Presenter: Chun-Chiao Huang

Date :2009/05/08

Challenge for Direct Data Capture



FDA's Critical Path Opportunity List(#45)

- Consensus on Standards for CRFs
 - Improve efficiency and accuracy for data collection

CDISC

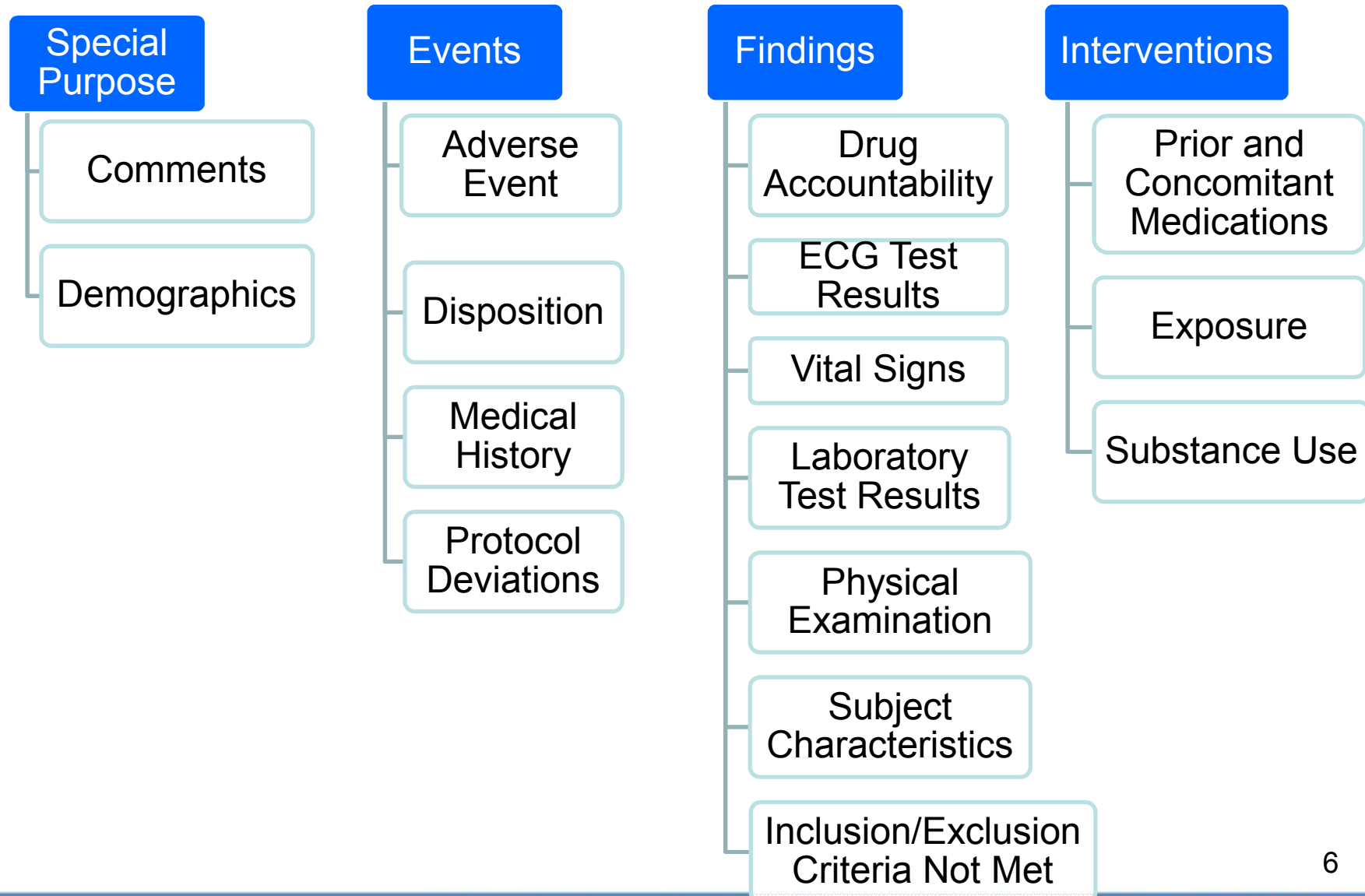
- Clinical Data Standards Interchange Consortium (CDISC)
 - Develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare



Clinical Data Acquisition Standards Harmonization (CDASH)

- Defines consensus-based CRF content standard
 - Speeding up initiation of new trials
 - Minimizing the need of customization for EDC systems

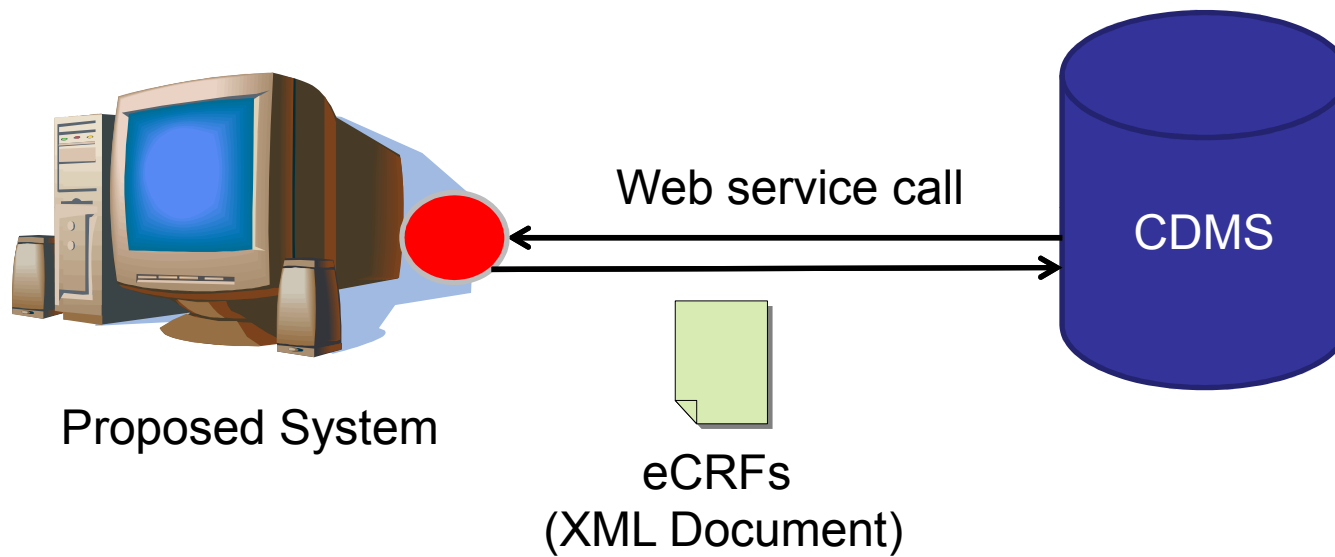
CDASH for Interoperability



Aims

- Building a system to facilitate researchers establishing CDASH-based eCRF

System Scope



CDMS : Clinical Data Management System

Result

Import Forms from Existing Template

Question MGMT | Template Design | 123 您好 登出

Template List

- My Workspace
- CDASH Template**
- Screening for Lung Cancer
- Cardiovascular Study
- Tuberculosis Study

New Template (Click to Edit): 2009/04/05 17:21:18

Assemble your template

Select	Form Title
<input checked="" type="checkbox"/>	Adverse Event
<input checked="" type="checkbox"/>	Common Identifier
<input checked="" type="checkbox"/>	Common Timing Variables
<input checked="" type="checkbox"/>	Prior and Concomitant Medications
<input checked="" type="checkbox"/>	Demographics
<input checked="" type="checkbox"/>	Disposition
<input checked="" type="checkbox"/>	Drug Accountability
<input checked="" type="checkbox"/>	ECG Test Results
<input checked="" type="checkbox"/>	Exposure
<input checked="" type="checkbox"/>	Inclusion / Exclusion Criteria Not Met
<input checked="" type="checkbox"/>	Laboratory Test Results
<input checked="" type="checkbox"/>	Medical History
<input checked="" type="checkbox"/>	Physical Examination
<input checked="" type="checkbox"/>	Protocol Deviations
<input checked="" type="checkbox"/>	Subject Characteristics
<input type="checkbox"/>	Substance Use
<input checked="" type="checkbox"/>	Vital Signs

Add to Template | Preview | Complete

Detail View of Template

Question MGMT Template Design 123 您好

Screening for Lung Cancer i

- Vital Signs
- Drug Accountability
- Demographics
- Exposure
- Inclusion / Exclusion Criteri
- Adverse Event
- Common Timing Variables
- Disposition
- Laboratory Test Results
- Prior and Concomitant Medi
- Medical History
- Physical Examination
- Common Identifier

Form List

Add Form

Form Name	Questions under this form	Delete
Vital Signs	Preview	
Drug Accountability	Preview	
Demographics	Preview	
Exposure	Preview	
Inclusion / Exclusion Criteria Not Met	Prex Start Date End Date Dose Amount Dose Unit Study Treatment Identification Number(e.g., Lot Number)	
Adverse Event	Prex Study Treatment Name Dose Adjusted? Reason for Dose Adjustment	
Common Timing Variables	Prex Frequency Route	
Disposition	Prex Formulation Duration of Interruption Duration of Interruption - units	
Laboratory Test Results	Prex Body Location Total Volume Administered Total Volume Administered Unit	
Prior and Concomitant Medications	Prex Flow Rate Flow Rate Unit	
Medical History	Prex Planned Time Point Did subject complete full course of study med?	
Physical Examination	Prex Planned Dose Planned Dose Unit	
Common Identifier	Prex	

Detail View of Form

Question MGMT Template Design 123 您好

Screening for Lung Cancer i

- Vital Signs
- Drug Accountability
- Demographics
- Exposure**
 - Start Date
 - End Date
 - Dose Amount
 - Dose Unit
 - Study Treatment Ident
 - Study Treatment Name
 - Dose Adjusted?
 - Reason for Dose Adjus
 - Frequency
 - Route
 - Formulation
 - Duration of Interruption
 - Duration of Interruption
 - Body Location
 - Total Volume Administ
 - Total Volume Administ
 - Flow Rate

Exposure

Add Question

Question Text	Display Order	Edit	Delete
Start Date	Move up Move down		
End Date	Move up Move down		
Dose Amount	Move up Move down		
Dose Unit	Move up Move down		
Study Treatment Identification Number(e.g., Lot Number)	Move up Move down		
Study Treatment Name	Move up Move down		
Dose Adjusted?	Move up Move down		
Reason for Dose Adjustment	Move up Move down		
Frequency	Move up Move down		
Route	Move up Move down		
Formulation	Move up Move down		
Duration of Interruption	Move up Move down		
Duration of Interruption - units	Move up Move down		
Body Location	Move up Move down		
Total Volume Administered	Move up Move down		
Total Volume Administered Unit	Move up Move down		
Flow Rate	Move up Move down		
Flow Rate Unit	Move up Move down		
Planned Time Point	Move up Move down		
Did subject complete full course of study med?	Move up Move down		

Discussion and Conclusion

- CDASH-based eCRFs + EDC system
→improving efficiency and accuracy
- CDASH focuses on safety data domain

Contribution

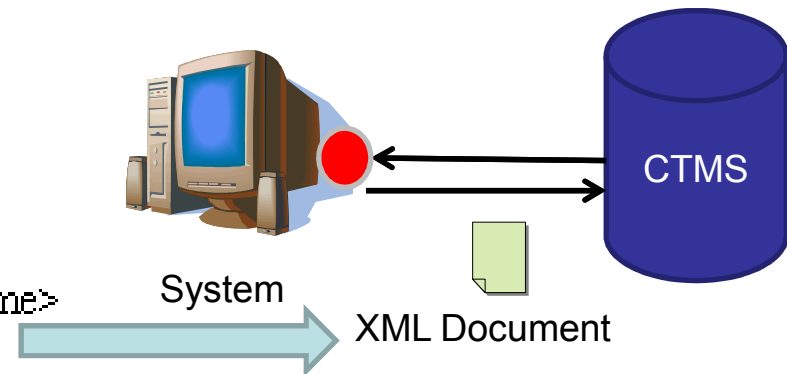
- Direct benefit
 - Speed up creation of CDASH-based eCRFs
 - Enhance the interoperability
- Indirect benefits
 - Minimize customization for EDC system
 - Painless in submission of CRF data to FDA

Thanks for Your Listening!

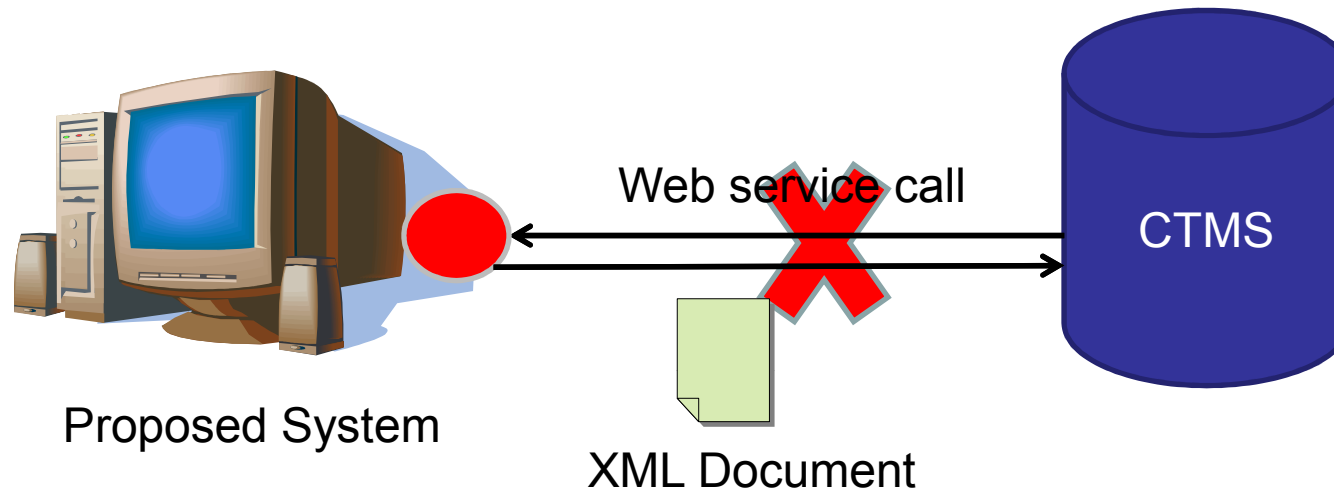
Backup Slides

Structure of eCRF Template

```
<eCRFTemplate>
  <templateName>CDASH Template</templateName>
  <body>
    <form>
      <title>Demographics</title>
      <question>
        <text>Date of Birth</text>
        <type>Date</type>
        <variableName>BRTHDAT</variableName>
        <isRequired>True</isRequired>
      </question>
      ....(other questions under this form)
    </form>
    ....(other forms under this template)
  </body>
</eCRFTemplate>
```



Limitation



- The overall usefulness of this system is limited to save time from creation of standard-based CRF

Standards Related to This Study

- Study Data Tabulation Model (SDTM)
 - Standard for the submission of CRF data to FDA
- Terminology
 - Distributed as part of NCI's Enterprise Vocabulary Service (EVS)
- Clinical Data Acquisition Standards Harmonization (CDASH)

FDA's Critical Path Opportunity List(#44)

- Development of Data Standards
 - Differences in data archiving convention across sponsors and trials
 - FDA Reviewers
 - Creates opportunities for confusion and error
 - Benefits
 - Enabling the creation of shared data repositories
 - Providing comparing and aggregating information across the NCI's clinical trial
 - Improving the efficiency and accuracy of the routine review

EDC Adoption Rate

- 27-30% of clinical trials

The Future Vision of Electronic Health Records as eSource for Clinical Research.
The eClinical Forum and PhRMA EDC Task Group, March 3 2006.

- 45% of clinical trials

EDC Adoption in Clinical Trials: A 2008 Analysis
CenterWatch survey in *Bio-IT World*, 2008

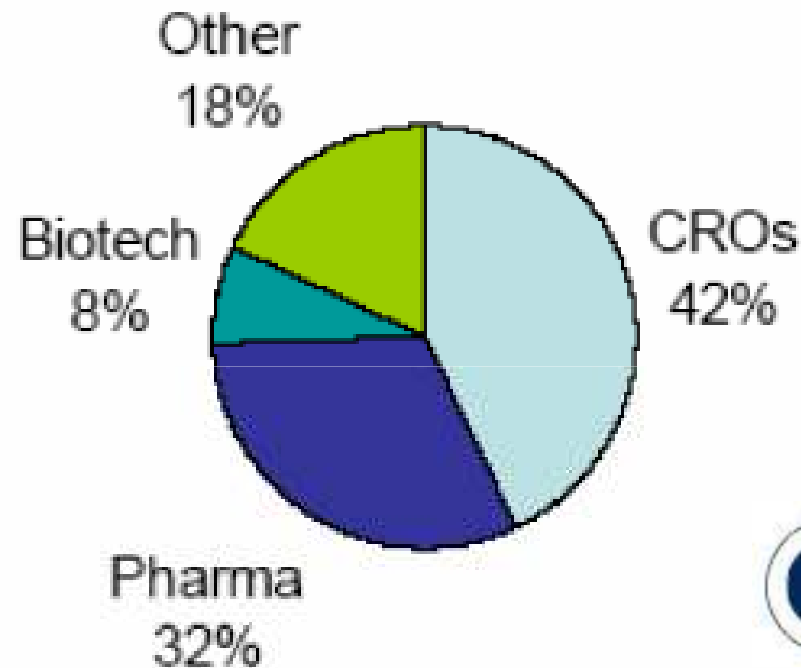
Openclinica

	Proposed System	Openclinica
CDASH-based eCRF Template	✓	✓
Free	✓	✗
Uncoupled with CTMS	✓	✗

Standard CRF of CaBIG

- **Round 1:**
 - Demography Documents
- **Round 2:**
 - Adverse Events Documents
 - Baseline Assessment Documents
 - Participant Enrollment/Registration Documents
 - Participant Identification Documents
 - Protocol Deviations Documents

Participants in the CDASH Initiative



Others = Academic Research Organizations, Government (NIH, NCI), Hospitals, Universities, and Military

Participating Companies, Agencies and Institutions (1)

1. Abbott
2. Accenture
3. Accovion GmbH
4. AdvaMed
5. American Medical Informatics Association (AMIA)
6. Amgen
7. ArisGlobal, LLC
8. Association of Clinical Research Organizations (ACRO)
9. Association of Clinical Research Professionals (ACRP)
10. Astellas
11. AstraZeneca
12. Bausch & Lomb
13. Baxter
14. Baylor College of Medicine
15. Biogen Idec
16. Biopharma Data Services
17. Biotechnology Industry Organization (BIO)
18. Boehringer Ingelheim
19. Boston Scientific Corporation
20. Bristol-Myers Squibb
21. Brown University
42. Enzon Pharmaceuticals, Inc.
43. Ethicon (Johnson & Johnson)
44. Exelixis
45. Fast Track Systems
46. Food and Drug Administration (FDA)
47. Formedix Inc.
48. Forest Laboratories, Inc.
49. Genentech, Inc.
50. Genzyme Corp.
51. Gilead Colorado, Inc.
52. GlaxoSmithKline
53. Global Research Services, LLC
54. Harvard Clinical Research Institute
55. Health Decisions
56. HealthRoad Co. Ltd,
57. ICON Clinical Research
58. ImClone Systems Incorporated
59. Insmmed Incorporated
60. InterMune, Inc.
61. Johnson & Johnson
62. Kai Research

Participating Companies, Agencies and Institutions (2)

23. Cambridge Cognition
24. CEDRA
25. Cephalon
26. Cleveland Clinic (CCF)
27. Clinical Data Interchange Standards Consortium (CDISC)
28. Clinical Research Forum
29. CliniPharma Consulting
30. Cognizant Technology Solutions
31. Commitum AB
32. Covidien (formerly Tyco Healthcare/Mallinckrodt)
33. Critical Path Institute
34. CSS Informatics
35. CV Therapeutics
36. Daedalus Software, Inc
37. DataLabs
38. DataScene
39. Duke Clinical Research Institute (DCRI)
40. Eisai Global Clinical Development
41. Eli Lilly and Company
42. Kestrel Consultants
43. Kos Pharmaceuticals, Inc.
44. Lab Connect LLC
45. Medidata
46. Medifacts
47. Merck & Company
48. Millennium Pharmaceuticals, Inc.
49. National Institutes of Health (NIH)
 - Clinical Research Policy Analysis and Coordination Program
 - National Cancer Institute (NCI); caBIG
 - National Cancer Institute - Center for Bioinformatics
 - National Center for Research Resources (NCRRR)
 - National Institute of Child Health and Human Development (NICHD)
 - National Library of Medicine (NLM)
 - NCI Cancer Therapy Evaluation Program
 - NCI Enterprise Vocabulary Service
 - NIH Office of Biotechnology Activities (OBA)
50. Nextrials, Inc.
51. Nounsware Company
52. Novartis Pharmaceuticals Corporation

Participating Companies, Agencies and Institutions (3)

75. Octagon Research Solutions
76. Ofni Systems Inc.
77. Omnicare
78. Oracle Health Sciences
79. Organon
80. Othera Pharmaceuticals, Inc
81. PAREXEL International
82. Percipenz
83. Pfizer, Inc.
84. Pharmaceutical Research and Manufacturers Association (PhRMA)
85. PharmaNet, Inc
86. Phoenix Data Systems
87. PHT Corp
88. PPD, Inc.
89. PRA International
90. Procter & Gamble
91. PTC Therapeutics
92. QIMR
93. Quintiles Transnational
94. Regeneron
95. Rho Inc.
96. RTI International
97. Schering-Plough Corporation
98. Schwarz BioSciences
99. Society for Clinical Data Management (SCDM)
100. SpaceLabs Healthcare
101. Statistics & Data Corporation
102. Stellar Systems
103. Synteract, Inc
104. TAKE Solutions Inc.
105. Takeda Global Research & Development Centre (Europe) Ltd.
106. Teva Neuroscience
107. The University of Texas Health Science Center at Houston
108. Tyco Healthcare Mallinckrodt
109. UCB Pharma SA
110. University of California, Irvine
111. University of Pennsylvania School of Medicine
112. University of Utah Health Science Center
113. Wake Forest University Baptist Medical Center
114. Westat Inc.
115. Wyeth Inc.
116. ZymoGenetics

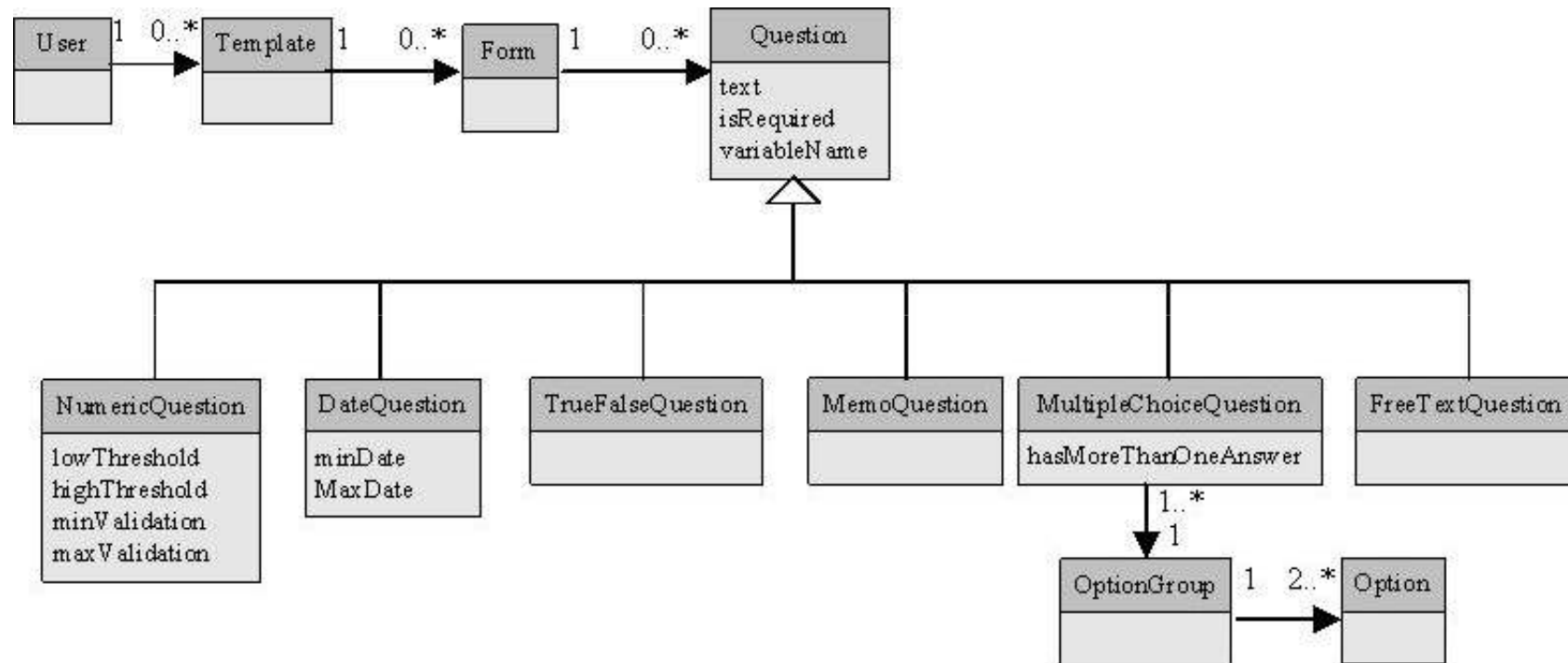
Benefits

- will provide a standardized mechanism for comparing and aggregating information across the NCI's clinical trial portfolio
- a harmonized CRF library will improve the efficiency and accuracy of the routine review of safety, efficacy, and administrative data from ongoing NCI-funded clinical trials. Finally, by reducing the time spent in developing a data collection strategy per trial, this core library will allow for faster initiation of new trials; thus, speeding the process of delivering new and improved treatments to patients.

System Design Requirements

- Web-based architecture
- In-house reusable and domain-specific eCRF library
- Public eCRF library
- Intuitive and user-friendly interfaces

Class Diagram



BRIDG Model

- Semantic foundation for all data interchange specifications in HL7, CDISC, the NCI, and caBIG

The BRIDG Project: A Technical Report.
J Am Med Inform Assoc, 2008; 15: 130-137

- Difference between BRIDG model and CDASH model
 - The BRIDG model copes with the interoperability issues between clinical trial management systems
 - The CDASH model deals with the interoperability issues between clinical trial management systems and EHR systems

