CDISC and Clinical Research Standards in the LHS

Learning Health System in Europe

24 September 2015, Brussels

Rebecca D. Kush, PhD, President and CEO, CDISC
CDISC Healthcare Link
Goal: Optimize the Process

Data conception

Healthcare Delivery
(e)Source Documents
EHR

(e)CRFs
Clinical Research

Automatic reconciliation

~1997
eSource Data Interchange (eSDI) Initiative

• **Purpose:** FDA initiative to facilitate the use of electronic technology in the context of existing regulations for the collection of eSource data in clinical research

• **Overarching Goals:**
  - To make it easier for physicians to conduct clinical research,
  - Collect data only once in an industry standard format for multiple downstream uses, and thereby
  - Improve data quality and patient safety

• **Product:**
  - eSDI Document
  - 12 requirements for eSource
  - Formed the basis for the Retrieve Form for Data Capture (RFD) Integration Profile
  - Available at [www.cdisc.org/eSDI-document](http://www.cdisc.org/eSDI-document)
09 June 2010
EMA/INS/GCP/454280/2010
GCP Inspectors Working Group (GCP IWG)
Date for coming into effect 01 August 2010

**Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials**

**References**
2. CDISC (Clinical Data Interchange Standards Consortium) Clinical Research *Glossary Version 8.0*, DECEMBER 2009
http://www.cdisc.org/stuff/contentmgr/files/0/be650811feb46f381f0af41ca40ade2e/misc/cdisc_2009_glossary.pdf.

**eSource** = data entered electronically first, i.e. EHRs, eDiaries....
ASTER (AE Reporting from EHRs)
30 Ambulatory care physicians at Harvard and Brigham and Women’s with Pfizer, CDISC, CRIX
Nov 08 – Jun 09, > 200 Reports Sent to FDA

Physician Reporting:
*91% of participating physicians had submitted no ADE reports in the prior year
*During the study, participants reported an average of approximately 5 reports in a 3 month time period
*All participants reported at least 1 AD
*Process: Time to report decreased from ~35 min to < 1 min

Source: Michael Ibara, Pfizer
The Value of Using Standards from the Start

2007 CDISC Business Case

2014 Business Case

Current Landscape 2014

- Study Complexity
- # Datapoints
- Data Management
- Time/Resources
- Cost of Research
The CDISC Vision: informing patient care and safety through higher quality medical research.

Mission: To develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare.
Synergistic Standards Available for Research in an LHS

Healthcare Delivery
- eSource Documents
- EHR

Medical Research
- Integration Profiles (e.g. RFD)
- eCRFs

eArchive at Clinical Site

CDISC Integrated Domain Group

IHE

CDISC ODM

CDASH Initiative
Basic Concepts of CDASH
Clinical Data Acquisition Standards Harmonization

• Minimal ‘core’ dataset for clinical research (meets global regulatory requirements) developed as an FDA Critical Path Opportunity

• Developed through a global consensus-based approach, with volunteers from around the world

• Standardize the questions/fields on case report forms (e.g. for research, public health)

• Collect data using standard CDISC controlled terminology that maps into the Study Data Tabulation Model (SDTM) for reporting of results-- to be required by 2016 by MHLW/PMDA and U.S. HHS/FDA
CDISC Operational Data Model

- Transport (XML) standard developed to carry case report form data or data in other forms
- Carries complete audit trail information (21CFR11), thus ensures provenance (traceability)
- Supports electronic signatures
- **Archives** electronic data without need to archive original system at sites
- Can automate generation of eCRFs
- Enables remote monitoring or auditing
- Facilitates exchange of data between different technologies

Annotated CRFs for CDASH

**Demographics**

<table>
<thead>
<tr>
<th>Field</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth Date</td>
<td>1980-01-01</td>
</tr>
<tr>
<td>Age</td>
<td>40</td>
</tr>
<tr>
<td>Race</td>
<td>BLACK OR AFRICAN AMERICAN</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>HISPANIC OR LATINO (with or without Hispanic)</td>
</tr>
</tbody>
</table>

ODM Form conformant with CDASH Demographics
ODM & Audit Trail (Provenance)

Who

Why

When

What
- Single, trusted, authoritative source for CDISC data standards
- Concepts, metadata, collections, relationships, value sets across the full spectrum of CDISC content
- Aligned with NCI Semantic Systems
- Can link research to healthcare concepts to support interoperability

SHARE

BRIDG, ISO21090
Protocol, CDASH
SDTM, ADaM
Terminologies

Facilitates Data Exchange

- Access to data standards
- Source to target mapping & traceability
- Transformation logic

Adapted from Source by Sue Dubman, Genzyme/Sanofi
CDISC- IHE Profiles for EHR-enabled Research

• make the connection
  ▪ Retrieve Form for Data-capture (RFD)

• auto-populate the eCRF
  ▪ Clinical Research Data (CRD)
  ▪ Drug Safety Content (DSC)
  ▪ Redaction Services
  ▪ Data Element Exchange (DEX)

• automate collaborative business processes
  ▪ Retrieve Process for Execution (RPE)
  ▪ Clinical Research Process Content (CRPC)
  ▪ Research Matching (RM)
Data Mining
(BIG DATA) vs
Form Capture
(small/precious data requiring high quality)
Swivel chair interoperability
EHR to Electronic Data Capture (CDASH) with IHE Retrieve Form for Data Capture (RFD)

See the key CRF video by Landen Bain on the CDISC Website.
Data Element Exchange (DEX), based on ISO 11179

Retrieve Metadata

(Metadata Source)  (Metadata Consumer)

Key-CRF: IMI Project with CDISC and PhUSE
Using SALUS Metadata Repository

Trying this with CDISC SHARE this year…
keyCRF
Other Projects and Initiatives

• American College of Cardiology – Population of registries using RFD

• FDA BAA Grant – for CDISC to support one or more standards-based implementation of EHR-enabled clinical research

• LHC – ESTEL – continue to build a framework for Learning Health Cycles to identify essential standards to support data sharing and the Learning Health System
Learning Health Community: Essential Standards to Enable Learning (ESTEL) Initiative

To define a parsimonious/essential/minimum core set of standards that could enable a standards-based yet flexible and scalable LHS in accordance with the following goals:

a) Ease the burden for any clinician to participate in a research study or other learning activity;

b) Increase the capacity for learning from data;

c) Obtain knowledge and results in an actionable form to contribute to building the LHS;

d) Ensure that the data obtained can be readily aggregated and/or compared; and

e) Ensure that the data uphold scientific integrity.
Strength *through collaboration.*
A Learning Health System Should…

Support the collection of high quality research data for Data Science.
What are the barriers and how can we break through them?
One Example…

• **Common Misperception**: These standards only work for interventional/regulated studies!

• **Proposed “Solution”**: Let’s develop NEW standards for OUR use!

• **Fact**: Consensus-based standards cited (IHE and CDISC) have proven to be useful and valuable for outcomes research, observational studies, registries, device studies, nutritional research, public health, safety reporting, outbreak surveillance AND regulated interventional research…around the world.
An industry initiative that successfully demonstrated clinical information interoperability between physician clinical systems (EHR) and pharmaceutical clinical trials systems based on open standards. - Duke Clinical Research Institute, CDISC, Novartis, Merck, J&J, Microsoft.

Next Step was the Development and Demonstration of an Integration Profile called Retrieve Form for Data Capture (RFD)

(Project Leader: Landen Bain, lbain@cdisc.org, CDISC Liaison to Healthcare)
Information from healthcare (private, aggregated) to enable research

Healthcare
- Quality healthcare
- Informed decisions
- Personalized medicine
- Patient safety and privacy
- Public health
- Improved therapies
- Efficiencies/reduced costs

Currently Inefficient
~17-year cycle

Research
- Discovery of new therapies
- Understanding diseases
- Testing/comparing therapies (CER)
- Assessing efficacy
- Monitoring safety
- Understanding responses (genomics, biomarkers)
- Public health/quality evaluations
- Post-marketing surveillance

Research findings to inform healthcare decisions
"In an era of increased transparency and data sharing and integrative analyses of data from multiple origins, data standards are essential to ensure accuracy, reproducibility and scientific integrity."

Michel Goldman, IMI