Institute of Medicine

Large Simple Trials and Knowledge Generation in a Learning Health System

Infrastructure Needs: Getting to Comparable, Computable Data

Rebecca Kush, PhD, President and CEO, CDISC
The Problem

Site research processes require multiple systems and lots of paper…

And, where is the electronic health record (EHR)?
What ‘infrastructure’ is available to streamline research studies now?

- eSource Data Interchange (eSDI) Document
- Data Interchange Standards
  - Continuity of Care Document (CCD) – C32
  - CDISC CDASH and ODM
- Integration Profiles (IHE and CDISC) to improve workflow from EHRs to EDC/CTMS
- Interoperability Specification #158 (ANSI and HHS/(ONC): core standard dataset from EHRs
- Regulatory eSource Guidance (FDA and EMA)
- Increasing EHR Adoption – Meaningful Use Incentives
- A Challenge by FDA, ONC and CDISC…….
Optimizing the Research Process

Healthcare Delivery

(e)Source Documents
EHR

data conception

auto reconciliation

~1997

Clinical Research

(e)CRFs
Kush, Rebecca Daniels w/ Bleicher, Paul, Kubick, Wayne, Kush, Stephen, Marks, Ronald, Raymond, Stephen, Tardiff, Barbara

CDISC 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)
CDISC Global Standards – Research from Planning through Analysis/Reporting
CDISC CDASH Initiative
Initiated 2006
V1 Published October 2008
= Core Minimum Dataset Common Across Research Protocols

• Adverse Events (AE)
• Concomitant Medication (CM)
• Demographics (DM)
• Subject Characteristics (SC)
• Inclusion/Exclusion Criteria (IE)
• Medical History (MH)
• Substance Use (SU)
• Physical Exam (PE)
• Vital Signs (VS), Disposition (DS)
• Drug Accountability (DA)
• Exposure (EX)
• Protocol Deviations (DV)
• Comments (CO)
• Lab (LB), ECG (EG)

18 Domains
(including common timing and variable tables)
ODM & Audit Trail

Who
- UserRef
- LocationRef

Why
- ReasonForChange
- Source

When
- DateTimeStamp
- CryptoBindingManifest
- MeasurementUnitRef
- Annotation
- Comment
- Flag

What
- ItemData
- Signature
- SignatureRef
- DateTimeStamp
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.

Led to:

**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)*
EHR Clinical Research Priority Value/Use Case

• With support/encouragement from HHS/ONC and others, ANSI convened an EHR Clinical Research Value Case Workgroup for prioritization of clinical research use cases.

• Initial Prioritized Value Case: Identify a common set of core research data elements that can readily be exchanged between EHRs and clinical research systems to support global clinical research.

• Anticipated to provide a foundation for future use cases:
  • Patient eligibility and recruitment
  • Pharmacogenomics and biomarkers
  • Safety reporting
  • Compliance reporting

• Long-term objective: Create an infrastructure through which health care advances clinical research which, in turn, informs clinical care.
EHR Clinical Research Workgroup Members

- Jonathan Andrus - SCDM
- Robert Annechiarico - Duke Comprehensive Cancer Center
- Kate Blenner – Faster Cures
- Kenneth Buetow – NCI
- Christopher Chute – Mayo Clinic, CTSA
- Perry Cohen - Parkinson Pipeline Project
- Elaine Collier – NCRR
- Kevin Coonan – Harvard, HL7, Dana Farber
- Timothy Cromwell - VA
- Jeffrey David - HIMSS
- Peggy Devine - Cancer Information and Support Network
- *Gregory Downing - HHS
- Paul Harris - Vanderbilt University, CTSA
- Steven Hirschfeld – NICHD
- Charles Jaffe – HL7
- Michael Kahn – AMIA, Colorado Children’s
- Linda King – eClinical Forum, PhRMA
- Judith Kramer – Duke, CTTI
- *Rebecca Kush - CDISC
- David Leventhal – ASTER, Pfizer
- Nikolay Lipskiy - CDC
- Armando Oliva - FDA
- Rachel Richesson – USF
- John Speakman – NCI
- Gary Walker - ACRO

*Co-chairs
Contributors to HITSP EHR Clinical Research Initiative

- Abbott
- Accenture
- Biogen Idec
- Boehringer Ingelheim Pharmaceuticals, Inc.
- Cleveland Clinical and Translational Science Collaborative at Case Western Reserve University
  - Case Western Reserve University
  - Cleveland Clinic
  - MetroHealth System
  - University Hospitals
- Critical Path Institute
- CWR
- Digital Infuzion
- Duke University
  - Duke Comprehensive Cancer Center
  - Duke Clinical Research Institute
- Eli Lilly
- Genetic Alliance
- Genentech
- GlaxoSmithKline
- Greenway Medical Technologies
- HP
- Anonymous
- JSS Medical Research Inc.
- McDougall Scientific Ltd.
- Medidata Solutions Worldwide
- MedXview
Contributors to HITSP EHR Clinical Research Initiative (2)

- Nextrials, Inc.
- Numoda Corporation
- Outcome
- Partners HealthCare
- Perceptive Informatics
- PharmaNet Development Group, Inc.
- Pfizer
- Phoenix Data Systems, a division of Bio-Imaging Technologies
- Quintiles
- Schering Plough Research Institute
- Target Health Inc.

**Government Agencies**
- Eunice Kennedy Shriver National Institute of Child Health and Human Development
- National Cancer Institute
- National Center for Research Resources
- Office of the National Coordinator for Health Information Technology
- Department of Veterans Affairs,
- The Assistant Secretary of Planning and Evaluation, Department of Health and Human Services.
Patient Value: Quality of Healthcare, Safety

Site Research Archive

EHR
De-identified Continuity of Care Doc (CCDA)->CRD

RFD
Study Sponsor EDC DB
Research Results, eSubmission Standard Formats

Reviewers (Regulators, Sponsor, Others)

HITSP Interoperability Specification # 158

Produces a standard core research dataset; Enables 21CFR11-compliant interoperability and eSource
Integrating Workflow: EHRs and Clinical Research, Quality, Safety and Public Health

H1N1 Outbreak Reports to CDC (+ bio-surveillance demo)

ASTER Project @ Harvard to FDA: AE Reporting 34 min to < 1 min and rate increased dramatically & Hamamatsu Med School CPOE and EMR to PMDA in Japan

EHR4CR in Europe (IMI Project) & Prof. Park Med Services w/ Greenway EHR Georgia, U.S.

Possibility to Harmonize Value Sets between Quality Measures and Research IHE-QRPH

IHE-CDISC Retrieve Form for Data Capture (RFD) = key common workflow integration profile (easy for EHRs to implement)
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
Study Sponsor
(e.g. ARO, CRO, Vendor, Principal Investigator, federal agencies...)

Care and/or Research Site
(Healthcare Location, Investigator, Site Personnel)

CDASH: Std. Common Research Dataset (+)
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/cdictoc_2009_glossary.pdf.
Capturing source data electronically should help to:

- Eliminate unnecessary duplication of data
- Reduce the possibility for transcription errors
- Encourage entering source data during a subject’s visit
- Eliminate transcribing source data before entering the data into an electronic data capture system
- Promote real-time data access for review
- Ensure the accuracy and completeness of the data
CDISC’s Healthcare Link

Existing profiles

• Representing and sharing a clinical research protocol for its execution:
  ▪ Retrieve Process for Execution (RPE)
  ▪ Clinical Research Process Content (CRPC)

• Representing and sharing clinical research documentation such as an eCRF or adverse event reporting form, to be pre-populated by existing clinical data in EHRs:
  ▪ Retrieve Form for Data Capture (RFD)
  ▪ Clinical Research Document (CRD)
  ▪ Drug Safety Content (DSC)
  ▪ Redaction Service Profile (RSP)

• Addressing confidentiality and security aspects
  ▪ Consistent Time (CT)
  ▪ Cross-Enterprise User Assertion (XUA)
  ▪ Audit Trail Node Authentication (ATNA)

Newly approved (Oct 2012) profiles to be developed

▪ Data Element Exchange
▪ Research Matching (identification of eligible patients)
▪ CRD – Patient Authored Note
Do you have EHR Technology that meets the new Certified EHR Technology definition for Meaningful Use **Stage 1**?

**START HERE**

1. Do you have a 2014 Edition Complete EHR for the Ambulatory (EPs) or Inpatient (EHs/CAHs) Setting?

   - Yes
     - FP
     - EP
     - No
     - EH/CAH

2. Is your EHR technology certified to the following certification criteria required to meet the **Base EHR definition**? § 170.314:
   - (a)(1),(3)&(5-8) – CPOE/Demogfrx/ProbList/MedList/MedAllergyList/CDS
   - (b)(1),(2)&(7) – TOC/Data Port
   - (c)(1)-3 – CQMS
   - (d)(1)-8 – P&S

   - Yes
     - EP
     - No
     - EH/CAH

   - EP
     - No
     - EH/CAH

3A. Is your EHR technology certified to the following certification criteria to support the **MU1 EP Core Objectives** you seek to meet and for which you cannot meet a MU exclusion? § 170.314:
   - (a)(2) – DD/DA
   - (a)(4) – Vitals
   - (a)(11) – Smoking
   - (b)(3) – eRx
   - (e)(1) – VDTx3
   - (e)(2) – Clinical Sum

   - Yes
     - EP
     - No
     - EH/CAH

4A. Is your EHR technology certified to the following certification criteria to support the **MU1 EP Menu Objectives** you seek to meet? § 170.314:
   - (a)(10) – RxFormulary
   - (a)(14) – Pt List
   - (a)(15) – Pt Edu
   - (b)(4) – ClinInfoRec
   - (b)(5) – Incorp Lab
   - (b)(6) – Immz Info
   - (b)(7) – Immz Tx
   - (b)(8) – Syn Surv

   - Yes
     - EP
     - No
     - EH/CAH

2B. Do you have EHR technology that has been:
   - Certified to ≥ 9 CQMs
     - ≥ 6 from CMS’ recommended core set
     - Address ≥ 3 domains from the set selected by CMS for EPs?

   - Yes
     - EP
     - No
     - EH/CAH

3B. Is your EHR technology certified to the following certification criteria to support the **MU1 EH/CAH Core Objectives** you seek to meet and for which you cannot meet a MU exclusion? § 170.314:
   - (a)(2) – DD/DA
   - (a)(4) – Vitals
   - (a)(11) – Smoking
   - (b)(3) – eRx
   - (e)(1) – VDTx3

   - Yes
     - EP
     - No
     - EH/CAH

4B. Is your EHR technology certified to the following certification criteria to support the **MU1 EH/CAH Menu Objectives** you seek to meet? § 170.314:
   - (a)(10) – RxFormulary
   - (a)(14) – Pt List
   - (a)(15) – Pt Edu
   - (a)(16) – AD
   - (b)(4) – ClinInfoRec
   - (b)(5) – Incorp Lab
   - (b)(6) – Immz Info
   - (b)(7) – Immz Tx
   - (b)(8) – Syn Surv

   - Yes
     - EP
     - No
     - EH/CAH

Note: To meet the CEHRT definition, EHR technology will need to have been certified to:
- Automated numerator recording (170.314(g)(1)) or Automated measure calculation (170.314(g)(2));
- Safety-enhanced design (170.314(g)(3)); and
- Quality management system (170.314(g)(4))
CDISC, HHS/ONC and FDA Issue Challenge: Regulated Clinical Research Study using EHRs

August 6, 2012

Austin, TX – 7 August 2012 – CDISC, HHS/ONC and FDA issued a ‘challenge’ to use EHRs for regulated clinical research during a Session on 26 June at the Annual DIA meeting in Philadelphia. Specifically, clinical research study sponsors were challenged to use at least two different electronic health record systems at different sites to conduct a multi-site, multi-visit, standards-based regulated clinical research study. The panelists at DIA spoke on the feasibility of this challenge, based upon technology and data standards and processes that have been developed over the past decade. Despite the potential and demonstrated benefits of this approach, the clinical research industry has not yet embraced these new methods and standards to conduct clinical research studies.
Capabilities with Available (Core) Data Standards and Integration Profiles/Interoperability Specifications (Standards-inspired Innovation)

- Dramatic reduction in time and effort for clinicians to report core data for safety, research, public health
- Can accommodate eDiaries, patient-entered data and multiple sites with various data collection methods
- Improved data quality
- Data can be more readily aggregated and analyzed or queried
- Extensible; paves the way for more complex research and clinical genomics for personalized healthcare
- Easily implemented by vendors; endorsed by EHRA

What will it take for sponsors to broadly adopt this approach?
Research findings to inform healthcare decisions

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

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

CDISC
CDISC is more than Standards!

Enablers

- Quality Improvement
- Process Redesign
- Standards-inspired Innovation

Resources
- Speed
- Workflow Integration
- Resource Savings

Strength through collaboration