LOINC in Regulated Clinical Research

Lab LOINC Steering Committee Meeting
08 June 2017

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Asst Prof, Duncan Comprehensive Cancer Center, Baylor College of Medicine
Clinical Data Interchange Standards Consortium (CDISC)

<table>
<thead>
<tr>
<th>Drivers</th>
<th>CDISC Team &amp; Volunteers</th>
<th>SHARE Ecosystem</th>
</tr>
</thead>
<tbody>
<tr>
<td>REGULATION</td>
<td>NEW SCIENTIFIC DISCOVERY</td>
<td><img src="SHARE-2.0.png" alt="" /></td>
</tr>
<tr>
<td>EHR, CLAIMS AND OTHER DATA SOURCES</td>
<td>CONSUMER-DRIVEN HEALTHCARE</td>
<td><img src="mRFD.png" alt="" /></td>
</tr>
</tbody>
</table>

- >435 organizational members
- Community consensus standards development for clinical & translational research
- Ongoing global research support in the Americas, Europe, Japan, China, India, Korea and other regions
  - Standards downloaded in 90+ countries

www.cdisc.org
CDISC Standards Required for Regulated Research in the US and Japan

FDA & Japan’s PMDA Require CDISC Standards, China’s CFDA and EMA Recommend CDISC Standards
...and Used for Non-Regulated Research in the U.S.

- Controlled Terminologies in NCI EVS, BRIDG model, SHARE metadata

- Adopted CDISC standards for FDA submissions, pharmacovigilance, and meta-analyses

- NINDS CDEs used in Parkinson’s and TBI TAs for FDA submissions

- CDE contributors to Schizophrenia TA, Future CDE alignment to PTS TA

- Part of C-Path Polycystic Kidney Disease TA consortium

- Pediatric terminologies developed with NCI EVS and CDISC
As Well as the EU and Asia

- Vaccines Standard Training on collection, modeling and aggregation standards for interoperability
- Standards Starter Pack Curation pipeline to TransMART
- Use of standardized data for research sourced from multiple EHRs
- Mobile patient reported outcomes (PRO)
- Data sharing recommendations
- Infectious Diseases - field research data collection and aggregation support
CDISC Standards Do NOT Dictate Research Questions or Conduct

CDISC Standards in the Clinical Research Process

CDISC Standards improve and maintain consistent DATA QUALITY and improve TRACEABILITY across the research value chain.
They DO Support Major Functions Common to All Translational & Clinical Research

Providing Common Structure & Terminology for:

- Data Collection
- Data Aggregation (Tabulation)
- Data Analysis
- Data Transfer
# TA-Specific Extensions Include

<table>
<thead>
<tr>
<th>Oncology</th>
<th>Infectious Diseases</th>
<th>Mental &amp; Behavioral Disorders</th>
<th>CV</th>
<th>Neurology</th>
<th>Chronic Respiratory Diseases</th>
<th>Auto-immune Diseases</th>
<th>Endocrinology</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer v1</td>
<td>Tuberculosis v1, Tuberculosis v2, <em>Gates</em></td>
<td>Schizophrenia <em>FDA</em></td>
<td>Dyslipidemia v1</td>
<td>Parkinson’s Disease v1</td>
<td>Asthma v1</td>
<td>Rheumatoid Arthritis v1</td>
<td>Polycystic Disease v1</td>
<td>University of Rochester</td>
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<tr>
<td>Prostate Cancer v1 <em>FDA</em></td>
<td>Influenza v1</td>
<td>Alzheimer’s v1, v2</td>
<td>CV Endpoints v1 <em>FDA</em></td>
<td>Multiple Sclerosis v1 <em>MS Society</em></td>
<td>COPD v1</td>
<td></td>
<td>Diabetes v1</td>
<td>*Solid Organ (Kidney Transplant) v1 <em>FDA</em></td>
</tr>
<tr>
<td>Colorectal Cancer v1 <em>FDA</em></td>
<td>Hepatitis C, v1 <em>FDA</em></td>
<td>Parkinson’s v1</td>
<td>CV Imaging v1</td>
<td>Duchenne Muscular Dystrophy v1</td>
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<td>Diabetic Kidney Disease v1</td>
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<td>Lung Cancer v1 <em>FDA</em></td>
<td>Virology v1, v2 <em>FDA</em></td>
<td>Traumatic Brain Injury v1 <em>One Mind</em></td>
<td>QT Studies v1</td>
<td>Huntington’s Disease v1</td>
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<td>Malaria v1 <em>Gates / WWARN</em></td>
<td>Major Depressive Disorder v1 <em>FDA</em></td>
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<td><em>Parkinson’s v2</em></td>
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<td>Ebola v1</td>
<td>Post Traumatic Stress Disorder v1 <em>Cohen Veterans Bioscience</em></td>
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<td>Vaccines v1</td>
<td>Bi-Polar v1</td>
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<tr>
<td>HIV v1 <em>NIAID &amp; FDA</em></td>
<td>General Anxiety Disorder v1</td>
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<tr>
<td>CDAD <em>FDA</em></td>
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</table>

**Bold** - ongoing

**Planned**
### March 2018 Mandate for LOINC Submissions

<table>
<thead>
<tr>
<th>Part</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Component</td>
<td><strong>Analyte</strong> - The substance or entity being measured or observed.</td>
</tr>
<tr>
<td>Property</td>
<td>The characteristic or attribute of the analyte.</td>
</tr>
<tr>
<td>Time</td>
<td>The interval of time over which an observation was made.</td>
</tr>
<tr>
<td>System</td>
<td><strong>Specimen</strong> - The specimen or thing upon which the observation was made.</td>
</tr>
<tr>
<td>Scale</td>
<td>How the observation value is quantified or expressed: quantitative, ordinal, nominal.</td>
</tr>
<tr>
<td>Method</td>
<td><strong>Assay Method</strong> - high-level classification of how the observation was made. Only needed when the technique affects the clinical interpretation of the results.</td>
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</table>
Laboratories in Clinical Research

Standard of Care, Central Lab

Research Lab, Local Laboratories
# CDISC Variables Mappings to LOINC Dimensions

<table>
<thead>
<tr>
<th>Part</th>
<th>What is this in CDISC standards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Component</td>
<td>LBTEST/CD + others</td>
</tr>
<tr>
<td>Property</td>
<td>Does not exist yet</td>
</tr>
<tr>
<td>Time</td>
<td>MULTIPLE: Various Timing Variables</td>
</tr>
<tr>
<td>System</td>
<td>SPEC+LOC</td>
</tr>
<tr>
<td>Scale</td>
<td>Does not exist yet</td>
</tr>
<tr>
<td>Method</td>
<td>METHOD + other things</td>
</tr>
</tbody>
</table>

Discrete variable, LBLOINC
Is your organization currently collecting LOINCs from any source?

- Yes: 18%
- No: 54%
- Not Sure: 19%
- What is LOINC?: 9%

N=155

Percentage of clinical research studies collecting LOINCs:

- Few (>2-5%): 24%
- Very few (< 1-2%): 9%
- Many (>15-50%): 14%
- Some (>5-15%): 29%
- Not Sure: 24%

N=22

Does your company store and/or use LOINCs today?

- Yes: 25%
- No: 44%
- Not Sure: 31%

N=105
CDISC LOINC Survey Positives

Useful Where Received

• “We welcome the LOINC mandate since it will help ensure a more precise description of the collected assay, and it is hoped that local labs will be able to provide these codes directly.”

• “As an academic institution, we feel committed to LOINC for it's wide adaption, it's open governance process, it's free availability and it's coherence to healthcare standards as HL7 CDA. “

• “For studies where we receive LOINCs from a central lab, I would much prefer to use them. The problem is with academic labs and other local labs..”
CDISC LOINC Survey Concerns

Availability & Realm Specificity

• “…we have asked central labs to provide LOINC codes and were told that they were not available.”
• “We have tried to get labs to provide LOINC codes for years, but they NEVER provide them…since we never get them we have never incorporated them into our analyses.”
• “New tests are developed and applied and complexity increases. I foresee the challenge that a LOINC standard is not enabled to cover these various and new test code needs?”
• “…the bulk of the issues with this guidance will lie with the lab vendors we work with in providing the data. Unfortunately, as we work with labs around the world (and many labs are global) and this is a U.S. mandate, it is likely that the adoption rate may be slower than needed.”
• “LOINC terminology is more clinically-oriented and US centric. As a global company, we receive lab data from all over the world and some of the laboratories are smaller local lab vendors who do not assign LOINC codes to their lab tests.”
CDISC LOINC Survey Concerns

Inconsistency / Lack of Clarity

• “It is my understanding that there is inconsistent use of LOINC among vendors which may make implementation difficult.”

• “If guidelines become available, they need to be very clear to enable distinction between very similar analytes. Very clear!”

• “We would also like to understand it there is a regulatory expectation that the LOINC codes would be needed for analysis as opposed to just living in SDTM.”

• “The various requirements being placed on industry are increasing every quarter. Much of this work falls to programmers ...[who] have limited knowledge of labs for example. These LOINC codes may be very clear to those who use them regularly, but for SAS programmers they are just another research project that we would have to try to figure out.”
CDISC LOINC Survey Concerns

Non-Clinical/Pre-Clinical Data

• “I am concerned about how the LOINC requirement impacts nonclinical data. It seems that the LOINCs do not take into account animal parameters and so I am concerned as to how these will be applied to our studies. Are there plans to include the LOINCs in SEND datasets or will another submission format be required?”

Low General Preparedness

• “This email was the first that I have heard of LOINCS.”
• “…dealt with LOINC coding, but only as the recipient of already mapped data. In our experience, very few companies are working with LOINC, and most are generally unprepared for incorporating it into their processes.”
FDA/CDISC/Regenstrief/NIH LOINC Working Group

• Convened to review sponsors’ concerns and make recommendations to FDA on how to best support the coming mandate
• Membership from CDISC, FDA, NIH and Regenstrief
• F2F meetings and teleconferences
• Related activity, CDISC Labs Team: Central Labs Task Force
  ▪ Quintiles and Covance/LabCorp, seeking members from Quest
  ▪ Creating a map of most common standard of care LOINCs used in clinical research
  ▪ Estimated that ~2,000 codes represent ~90% of labs
  ▪ Map document to be cross-posted on Regenstrief & CDISC site
Draft WG Recommendations

- LOINC codes should be required for human subjects only, though LOINC codes for animal studies should be encouraged.
- LOINC submissions should not have a status of deprecated, trial or discouraged.
- LOINC codes should be provided, wherever they are available to sponsors.
- LOINC codes for the subset of the most common labs utilized as standard of care are required where they are available.
  - Initially, LOINC codes for other labs should not be required to allow the community and regulatory officials to adapt to the new requirement. LOINC codes for other labs should be accepted by FDA, but not required.
- Missing required LOINC codes should be noted within an electronic submissions Study Data Reviewers Guide.
- Submitters must still submit all lab data in CDISC format.
Next Steps

• LOINC WG is internally reviewing the draft recommendations document now
  ▪ Feedback due 16 June 2017

• Document to be finalized with all members’ comments, then submitted to FDA for consideration

• LOINC WG to finalize Communication Plan

• Once recommendations are accepted by the FDA, LOINC WG Communication Plan to be enacted to inform community
<table>
<thead>
<tr>
<th>What</th>
<th>When</th>
<th>To Whom</th>
<th>How</th>
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</thead>
<tbody>
<tr>
<td>White Paper</td>
<td>One-time</td>
<td>All CDISC &amp; LOINC Listserv Members</td>
<td>Publication [TBD – By Whom, Where]</td>
</tr>
<tr>
<td>Joint Statement</td>
<td>One-time</td>
<td>All Stakeholders’ Communities</td>
<td>Release on Stakeholder Websites, Email blasts to the Listserv, and Other Channels as Deemed Appropriate by Stakeholders</td>
</tr>
<tr>
<td>Web Post</td>
<td>One-time</td>
<td>CDISC Linked In Members</td>
<td>Linked-In Post by LB &amp; BN Cross-Posted to CDISC Linked-In Groups</td>
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<tr>
<td></td>
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<td>Link from the CDISC Website</td>
</tr>
<tr>
<td>Newsletter</td>
<td>One-time alert, then monthly reminders from Jan-May 2018</td>
<td>All CDISC Listserv Members</td>
<td>e-Newsletter with Link to White Paper &amp; Educational Resources</td>
</tr>
<tr>
<td>Collaboration Update on Websites</td>
<td>One-time</td>
<td>Update CDISC &amp; LOINC Websites to Name Each Other as Collaborative SDOs?</td>
<td>Websites</td>
</tr>
<tr>
<td>Update at Lab LOINC Committee Meeting</td>
<td>June &amp; December</td>
<td>Attendees of the Committee Meeting</td>
<td>Presentation (F2F in Indianapolis or via webex)</td>
</tr>
<tr>
<td>Updated Joint Webinar</td>
<td>After Pilot Details Final</td>
<td>All Stakeholders’ Communities, Where Appropriate</td>
<td>Post to CDISC and Regenstrief websites</td>
</tr>
</tbody>
</table>
Questions?

• Standards
• SHARE Exports & API
• Education
• Updates, News
• Events
• Webinars
• Becoming a Member