CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

LOINC in Regulated Clinical Research

Lab LOINC Steeringg Committee Meeting
08 June 2017

Lauren Becnel, Ph.D.
VP, Biomedical Informatics & Alliances, CDISC
Asst Prof, Duncan Comprehensive Cancer Center, Baylor College of Medicine

Clinical Data Interchange Standards Consortium (CDISC)

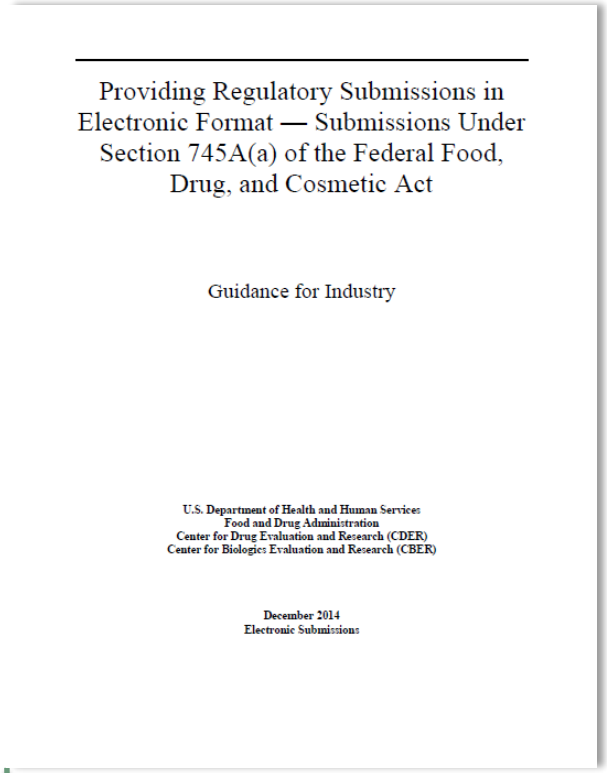
- >435 organizational members
- Community consensus standards development for clinical & translational research

- 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

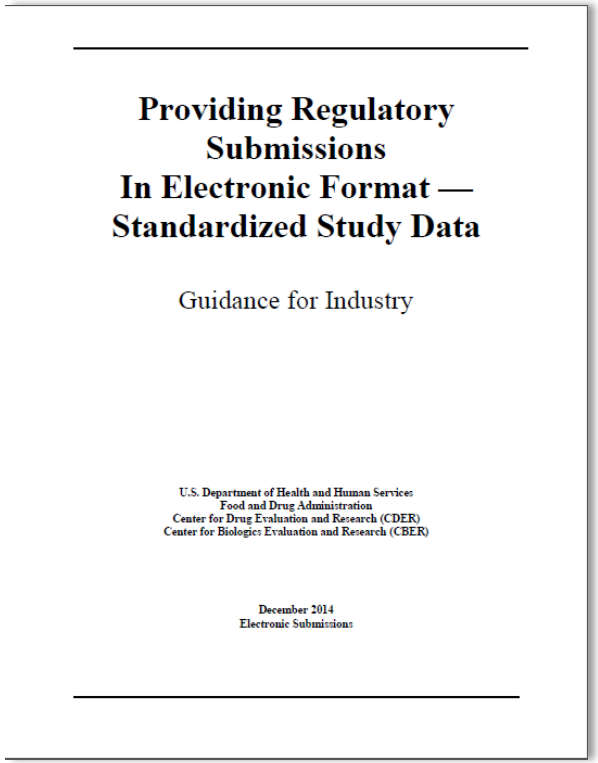


Providing Regulatory Submissions in Electronic Format — Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2014
Electronic Submissions



Providing Regulatory Submissions In Electronic Format — Standardized Study Data

Guidance for Industry

U.S. Department of Health and Human Services
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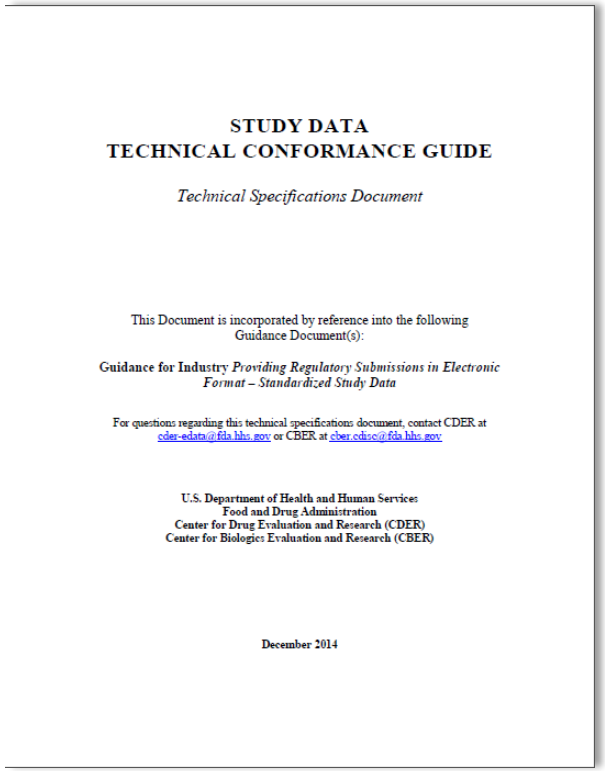


STUDY DATA TECHNICAL CONFORMANCE GUIDE

Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

Guidance for Industry *Providing Regulatory Submissions in Electronic Format – Standardized Study Data*

For questions regarding this technical specifications document, contact CDER at cder-edata@fda.hhs.gov or CBER at cber.cdisc@fda.hhs.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2014

…and Used for Non-Regulated Research in the U.S.

Controlled Terminologies in NCI EVS, BRIDG model, SHARE metadata

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

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

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

TRANSFoRm

Mobile patient reported outcomes (PRO)

eTRIKS

Standards Starter Pack Curation pipeline to TransMART

CORBEL

Data sharing recommendations

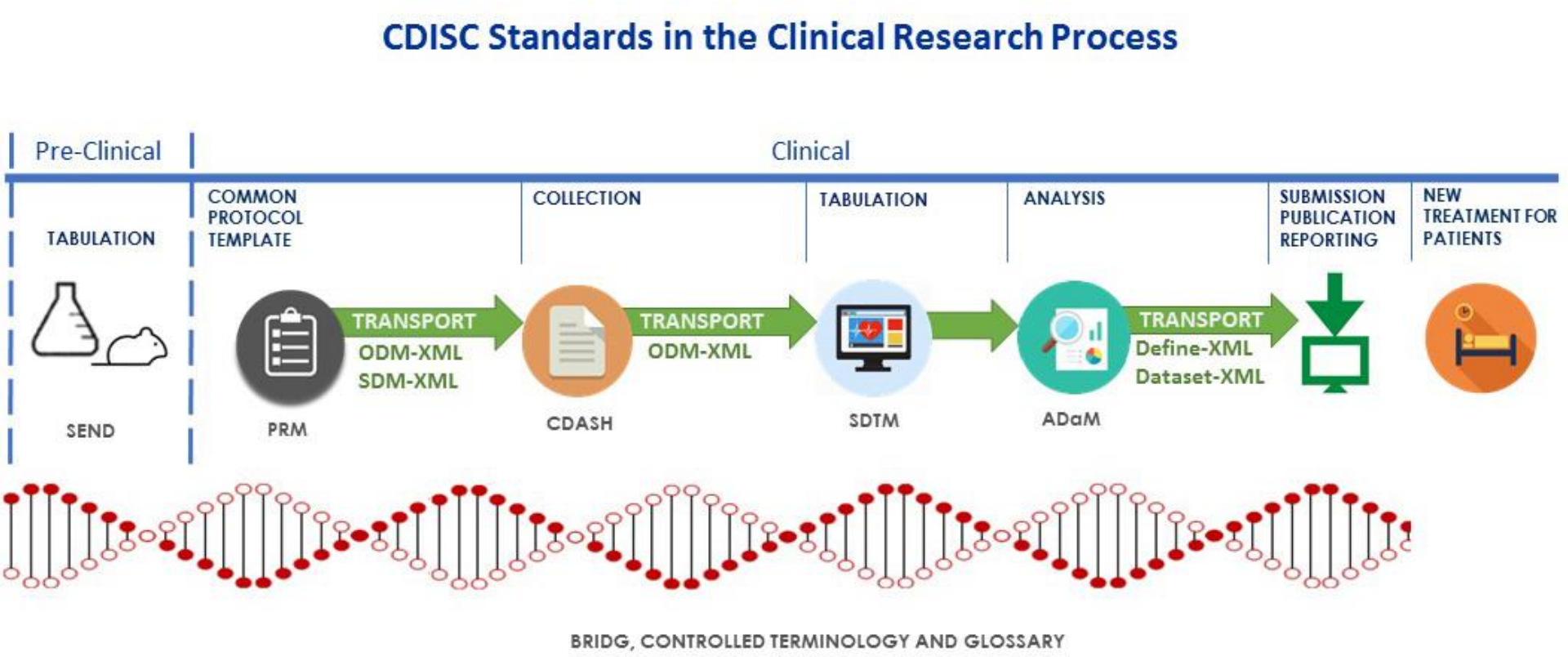
EHR4CR

Use of standardized data for research sourced from multiple EHRs

UNIVERSITY OF OXFORD

Infectious Diseases - field research data collection and aggregation support

CDISC Standards Do NOT Dictate Research Questions or Conduct



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

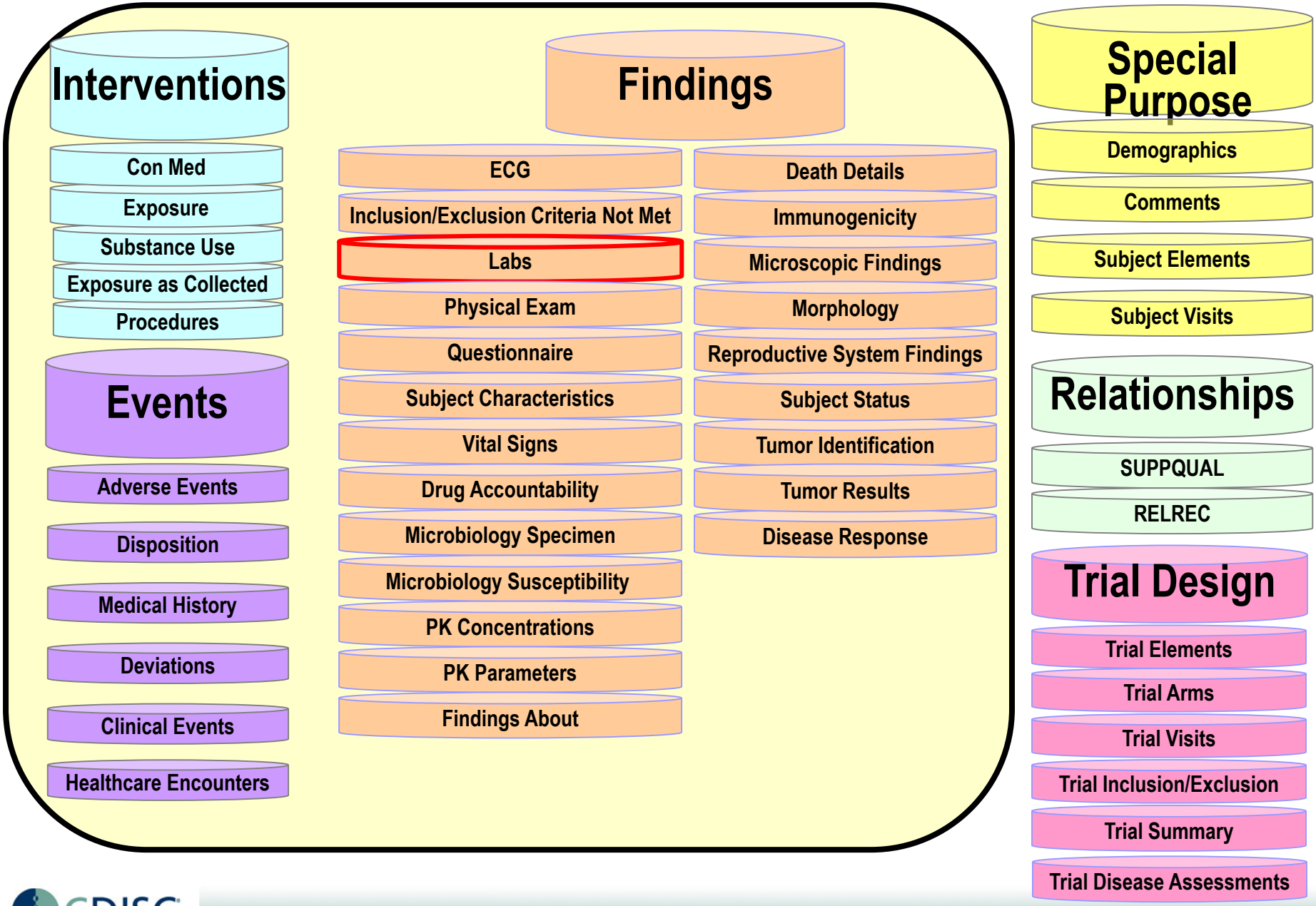
Data Transfer

TA-Specific Extensions Include

Oncology	Infectious Diseases	Mental & Behavioral Disorders	CV	Neurology	Chronic Respiratory Diseases	Auto-immune Diseases	Endocrinology	Other
Breast Cancer v1	Tuberculosis v1 Tuberculosis v2, *Gates*	Schizophrenia *FDA*	Dyslipidemia v1	Parkinson's Disease v1	Asthma v1	Rheumatoid Arthritis v1	Polycystic Disease v1 University of Rochester	Pain v1 *University of Rochester*
Prostate Cancer v1 FDA	Influenza v1	Alzheimer's v1, v2	CV Endpoints v1 *FDA*	Multiple Sclerosis v1 *MS Society*	COPD v1		Diabetes v1	*Solid Organ (Kidney Transplant) v1* FDA
Colorectal Cancer v1 FDA	Hepatitis C, v1 *FDA*	Parkinson's v1	CV Imaging v1	**Duchenne Muscular Dystrophy v1**			Diabetic Kidney Disease v1	
Lung Cancer v1 FDA	Virology v1, v2 *FDA*	Traumatic Brain Injury v1 *One Mind*	QT Studies v1	**Huntington's Disease v1**				
	Malaria v1 Gates / WWARN	Major Depressive Disorder v1 FDA		***Parkinson's v2***				
	Ebola v1	Post Traumatic Stress Disorder v1 Cohen Veterans Bioscience						
	Vaccines v1	Bi-Polar v1						
	HIV v1 **NIAID & FDA**	General Anxiety Disorder v1						
	CDAD **FDA**							
4	9	8	4	5	2	1	3	2

Bold - ongoing
Planned

How to Tabulate Your Data for Reporting: SDTM

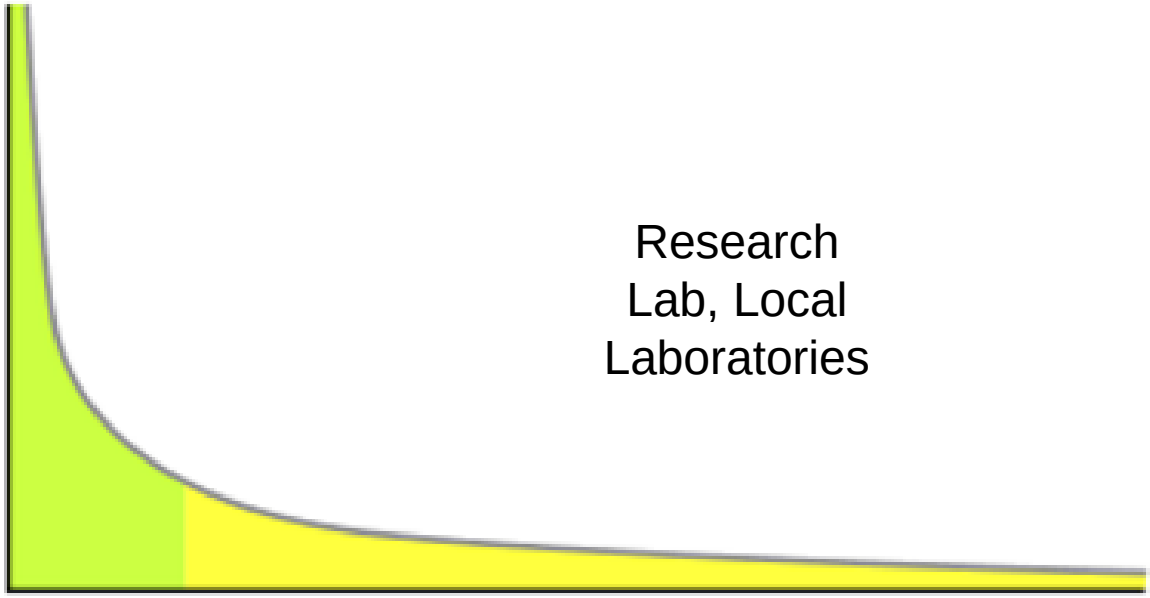


March 2018 Mandate for LOINC Submissions

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

Laboratories in Clinical Research

Standard of Care, Central Lab



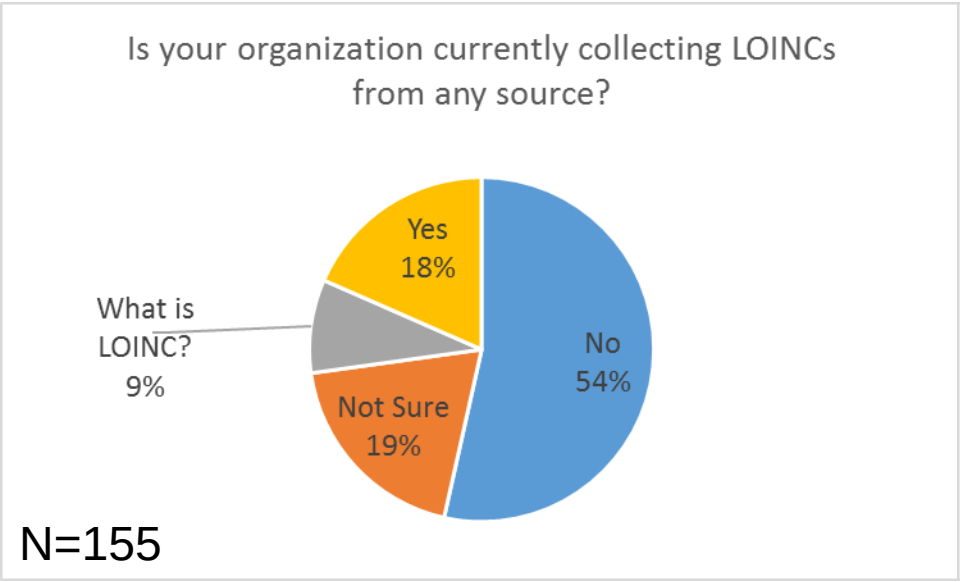
Research Lab, Local Laboratories

CDISC Variables Mappings to LOINC Dimensions

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

Discrete variable, LBLOINC

CDISC LOINC Survey Data



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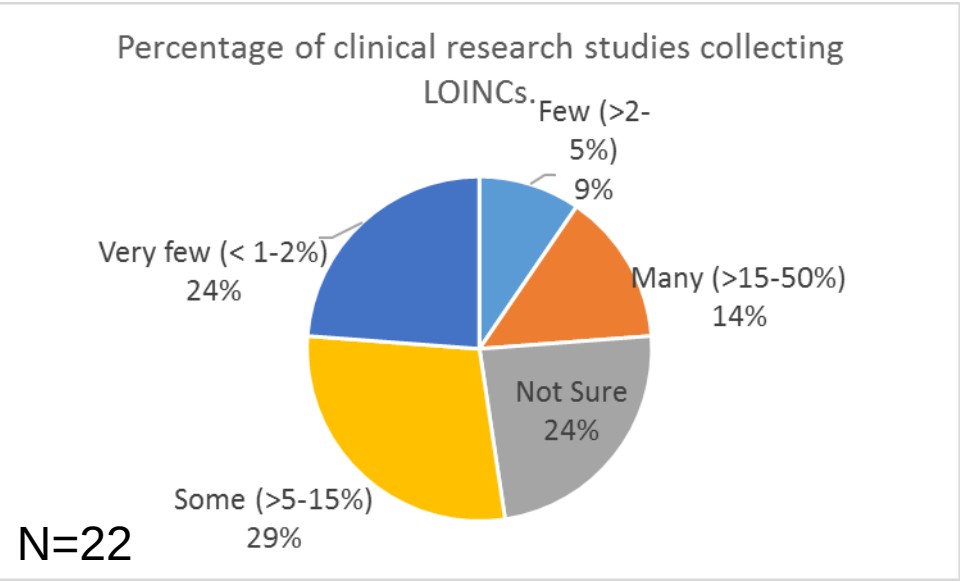

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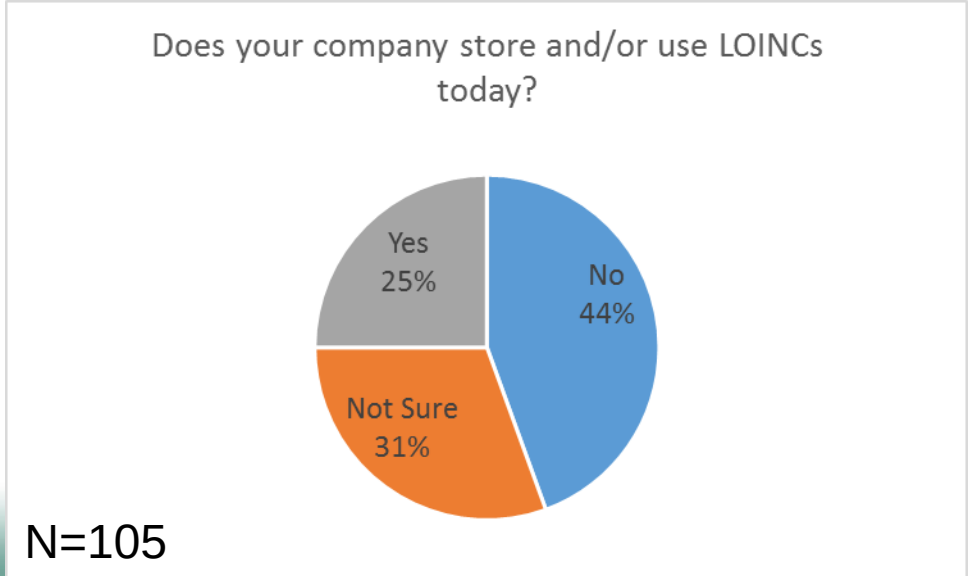

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CDISC LOINC Survey Positives

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 distinguishment 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 LOINCs 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 LOINCs 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

What	When	To Whom	How
White Paper	One-time	All CDISC & LOINC Listserv Members	Publication [TBD – By Whom, Where]
Joint Statement	One-time	All Stakeholders' Communities	Release on Stakeholder Websites, Email blasts to the Listserv, and Other Channels as Deemed Appropriate by Stakeholders
Web Post	One-time	CDISC Linked In Members	Linked-In Post by LB & BN Cross-Posted to CDISC Linked-In Groups Link from the CDISC Website
Newsletter	One-time alert, then monthly reminders from Jan-May 2018	All CDISC Listserv Members	e-Newsletter with Link to White Paper & Educational Resources
Collaboration Update on Websites	One-time	Update CDISC & LOINC Websites to Name Each Other as Collaborative SDOs?	Websites
Update at Lab LOINC Committee Meeting	June & December	Attendees of the Committee Meeting	Presentation (F2F in Indianapolis or via webex)
Updated Joint Webinar	After Pilot Details Final	All Stakeholders' Communities, Where Appropriate	Post to CDISC and Regenstrief websites

Questions?

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