



CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

# ***LOINC in Regulated Clinical Research***

***Lab LOINC Steering Committee Meeting  
08 June 2017***

**Lauren Becnel, Ph.D.**

**VP, Biomedical Informatics & Alliances, CDISC**

**Asst Prof, Duncan Comprehensive Cancer Center, Baylor College of Medicine**

A decorative graphic consisting of several overlapping, wavy lines in shades of blue and green, extending from the left side of the slide towards the right. At the end of these lines, there is a horizontal bar with a repeating diagonal hatched pattern in blue and green.

**Strength** *through Collaboration*

# Clinical Data Interchange Standards Consortium (CDISC)

## Drivers



REGULATION



NEW SCIENTIFIC  
DISCOVERY



EHR, CLAIMS AND  
OTHER DATA SOURCES

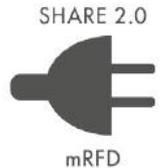
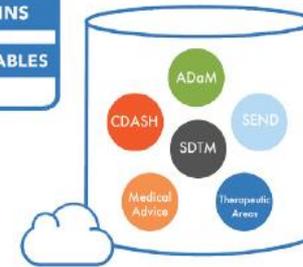
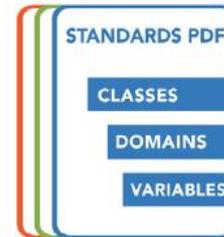


CONSUMER-DRIVEN  
HEALTHCARE

## CDISC Team & Volunteers



## SHARE Ecosystem



- >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](http://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  
Food and Drug Administration  
Center for Drug Evaluation and Research (CDER)  
Center for Biologics Evaluation and Research (CBER)

December 2014  
Electronic Submissions

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  
[cdcr-edata@fda.hhs.gov](mailto:cdcr-edata@fda.hhs.gov) or CBER at [cber.cdisc@fda.hhs.gov](mailto: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



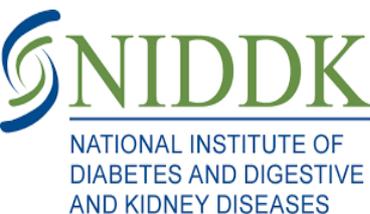
NINDS CDEs used in Parkinson's and TBI TAs for FDA submissions



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



Mobile patient  
reported outcomes  
(PRO)



Standards Starter Pack  
Curation pipeline to  
TransMART



Data sharing  
recommendations



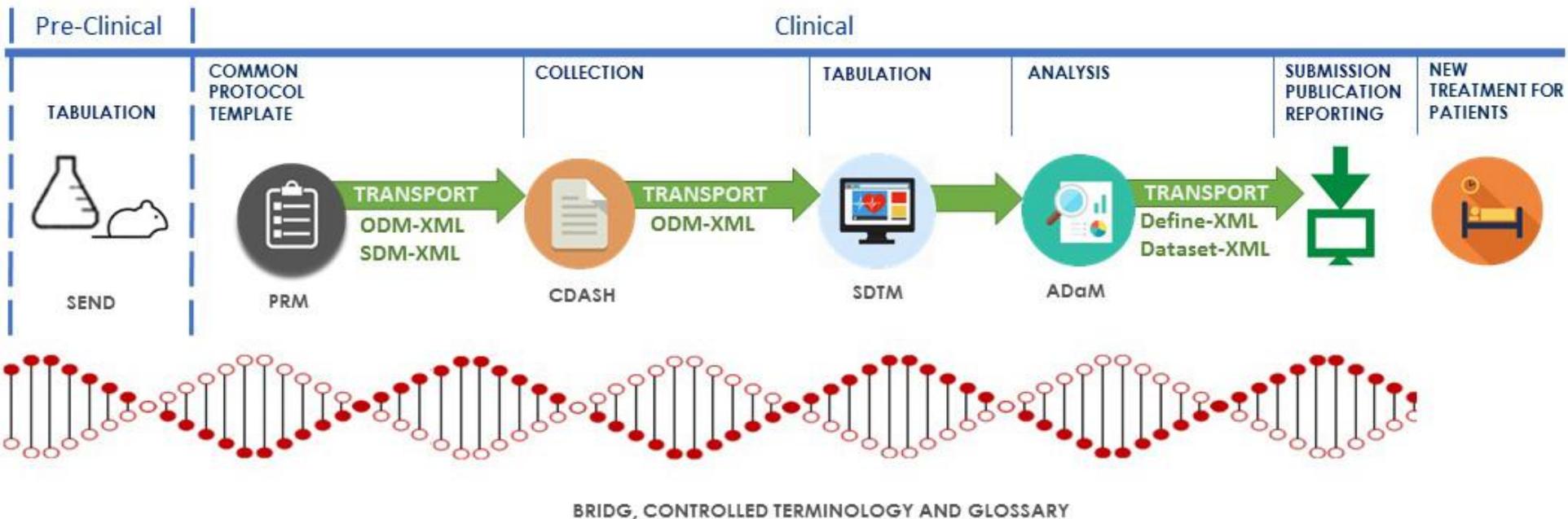
Use of standardized  
data for research  
sourced from multiple  
EHRs



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



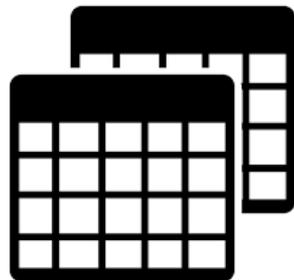
CDISC Standards improve and maintain consistent **DATA QUALITY** and improve **TRACEABILITY** across the research value chain

# They DO Support Major Functions Common to All Translational & Clinical Research

Providing Common Structure & Terminology for:



Data Collection



Data  
Aggregation  
(Tabulation)



Data Analysis



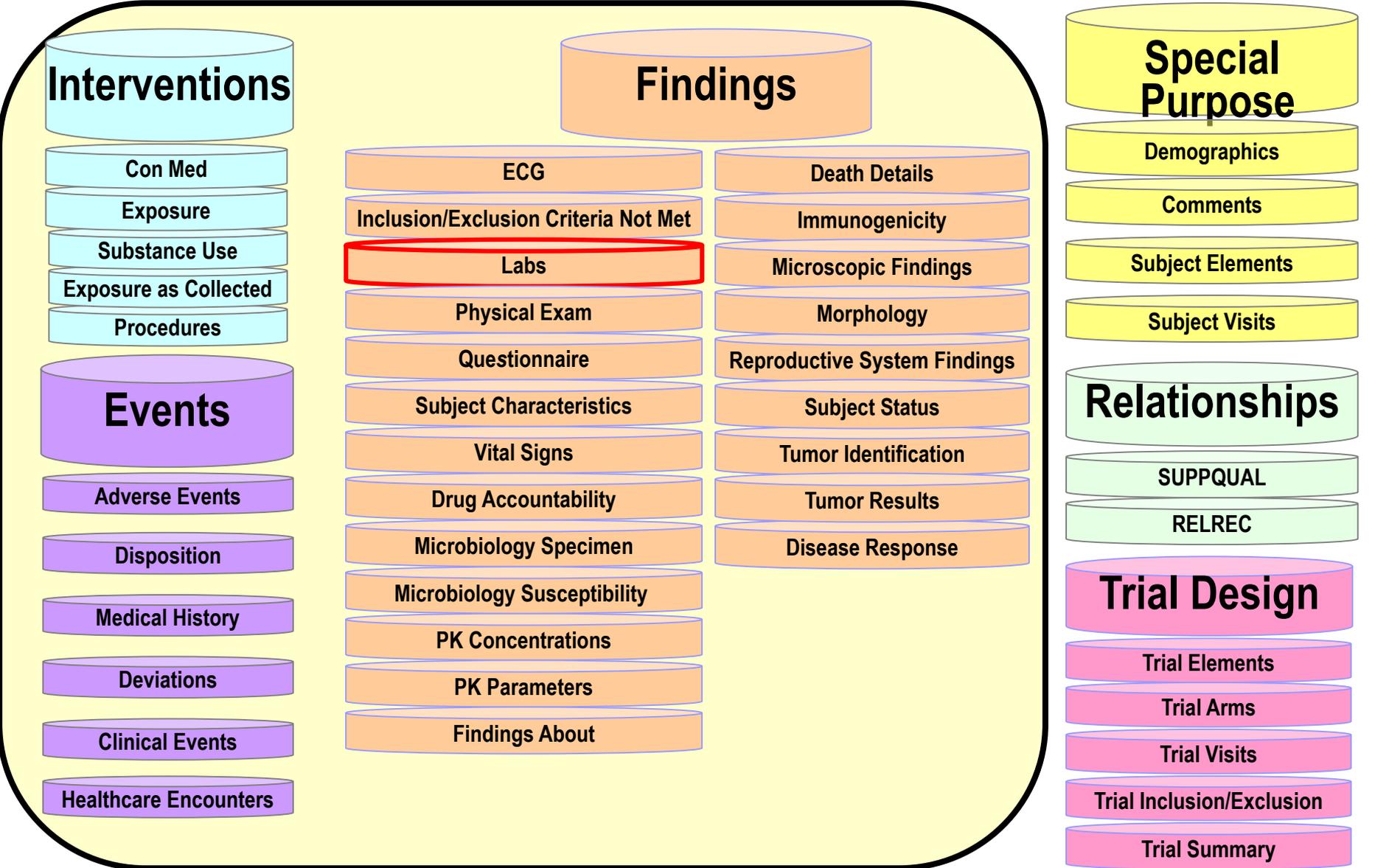
Data Transfer

# TA-Specific Extensions Include

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

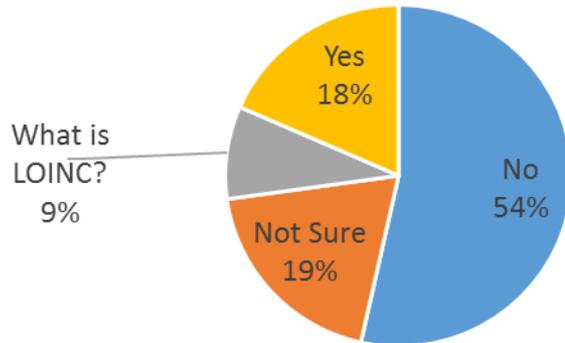
# CDISC Variables Mappings to LOINC Dimensions

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

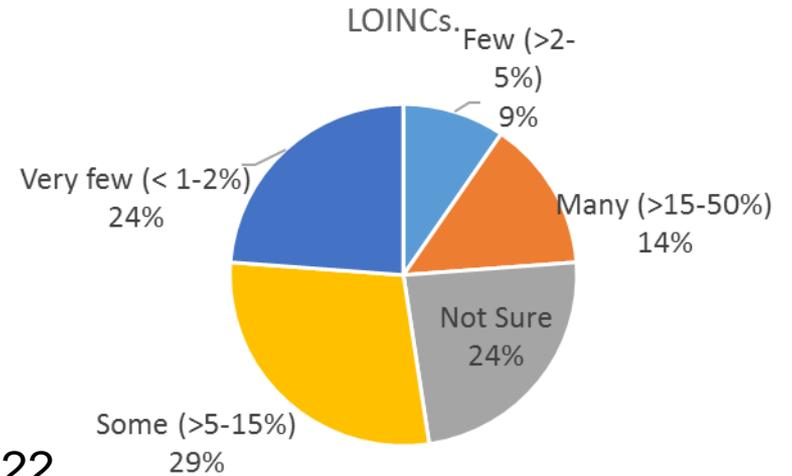
# CDISC LOINC Survey Data

Is your organization currently collecting LOINC<sup>s</sup> from any source?



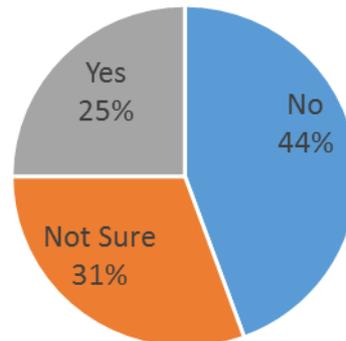
N=155

Percentage of clinical research studies collecting LOINC<sup>s</sup>.



N=22

Does your company store and/or use LOINC<sup>s</sup> today?



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 LOINC**s 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 **LOINC**s 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 LOINC**s in **SEND datasets** or will another submission format be required?”

## Low General Preparedness

- “This email was the **first that I have heard of LOINC**s.”
- “...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 LOINC codes 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

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