WITH STANDARDS – UNLOCK THE POWER OF DATA

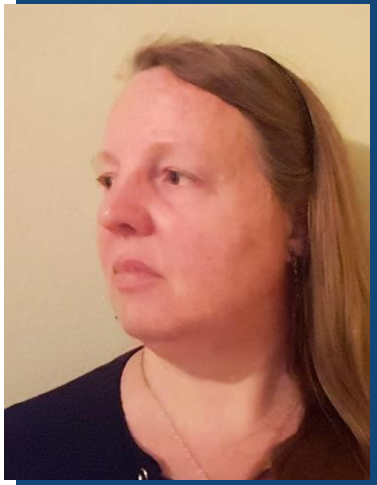
cdisc

2022
JAPAN
INTERCHANGE
13-14 JUNE | VIRTUAL EVENT

The DRAGON Project and the CDISC Observational Studies Document

Kit Howard, CDISC
Jon Neville, CDISC

Meet the Speakers



Kit Howard

Title: Senior Director, Standards Development and Education

Organization: CDISC

Kit Howard spent much of the past 30 years developing data and process standards for clinical trials. She started volunteering with CDISC in 2007, and is now Senior Director of Standards Development and Education for CDISC, co-leads CDISC's Medical Device standards development, and is an authorized CDISC instructor. Kit earned her graduate degree from the University of Michigan's School of Public Health in Clinical Research Design and Statistical Analysis.

Jon Neville

Title: Senior Standards Developer

Organization: CDISC

Jon Neville is Senior Standards Developer at CDISC, where he has worked for almost 5 years. He has over 12 years' experience with both implementing and developing CDISC standards. He has led, co-led, or otherwise participated in many CDISC therapeutic-area data standards projects. He is currently co-leading CDISC's Biomedical Concept Development team. Mr. Neville also serves on the CDISC Global Governance Group (GGG), and the SDS sub-teams for Genomics.

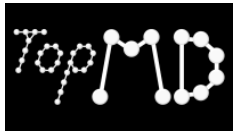
Agenda

1. The DRAGON Project
2. CDISC Considerations and Examples Document for Observational Study Data

RapiD and SecuRe AI enhAnced DiaGnosis, Precision Medicine and Patient EmpOwerment Centered Decision Support System for Coronavirus PaNdemics

DRAGON Partners

Data
Artificial Intelligence Modeling
App Development
Project Management
Data Standards
More



DRAGON

Data Harmonization for Artificial Intelligence (AI) Modelling

COVID User Guide v2.0 Imaging Guide

Recommendations and Considerations for Using CDISC Standards with Observational Studies

Goal: Gathering Information

Admission information

Evaluation Data

Patient arrives

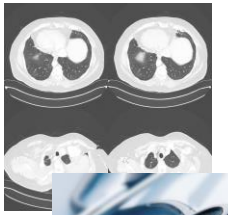
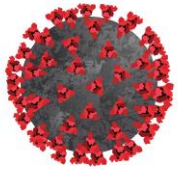


Image files

Clinical Observations

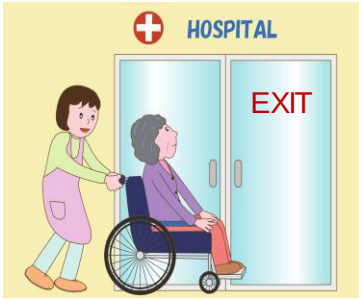
Test Results

Goal: Providing a Prediction

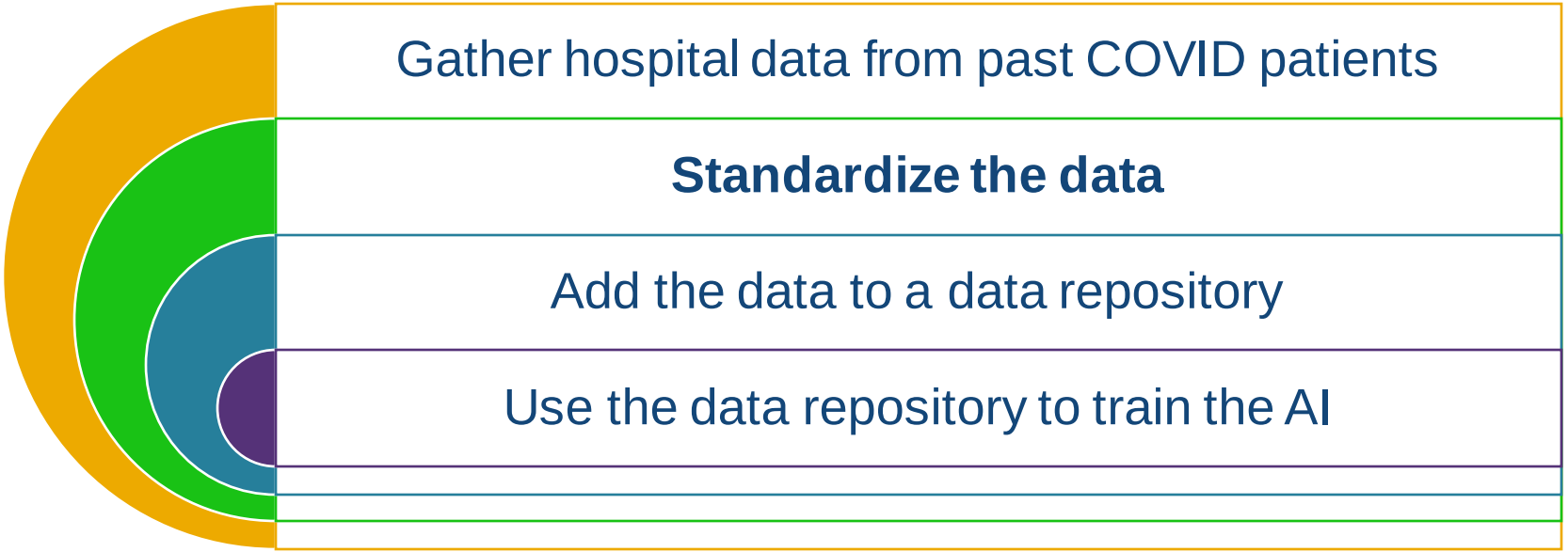


Diagnosis

Prognosis (predicted outcome)



How Can We Do This?



CDISC's Approach?

List of clinical concepts important for DRAGON analyses

- Demographics
- Vital Signs
- Labs
- Comorbidities
- COVID-19 Symptoms
- Medications
- Pregnancy

- Supplemental Oxygen
- Procedures
- Hospitalizations
- Smoking History
- Essential Worker Status
- Death

CDISC Mapping Tool

- Organized by Domain, referencing CDASH & SDTM
- Shows DRAGON Concept(s) represented in that domain
- Shows example(s) of what a conformant SDTM dataset would look like
- Adjusts many CDASH and SDTM requirements to accommodate EHR data

Microbiology Specimen

A findings domain that represents non-host organisms identified including bacteria, viruses, parasites, protozoa and fungi.

Variable		Units		Explanation	STDM Domain	Notes
COVID-19 proven by PCR		yes / no	y /n	If the COVID-19 diagnosis was proven by PCR	Microbiology Specimen (MB)	In CDISC, this item is not handled as Yes/No, rather as Positive/Negative as shown below

DRAGON Concept

Represented as SDTM

Row 1: Shows a subject whose endotracheal fluid sample tested positive for SARS-CoV-2 by qRT-PCR
Row 2: Shows a subject whose swabbed sample tested negative for SARS-CoV-2 by qRT-PCR
Row 3: Shows a subject whose infection was not confirmed by PCR

STUDYID	DOMAIN	USUBJID	MBSEQ	MBREFID	MBTESTCD	MBTEST	MBTSTDTL	MBORRES	MBSTRESC	MBSTAT	M
DRAGON	MB	DRAGON-[siteID]-001	1	SP001	SARSCOV2	Severe Acute Resp Syndrome Coronavirus 2	DETECTION	POSITIVE	POSITIVE		E
DRAGON	MB	DRAGON-[siteID]-002	1	SP131	SARSCOV2	Severe Acute Resp Syndrome Coronavirus 2	DETECTION	NEGATIVE	NEGATIVE		S
DRAGON	MB	DRAGON-[siteID]-003	1	SP067	SARSCOV2	Severe Acute Resp Syndrome Coronavirus 2	DETECTION			NOT DONE	

MH Examples - Dx and Symptoms | LB | LB Examples | RP | RP Examples | SC | SC Examples | MB | MB Examples | SU | SU

Mapping Tool (cont)

- Provides ability to map partner data to CDISC variables

Microbiology Specimen (MB)

Study, Site and Patient/Subject/Participant Identificatic

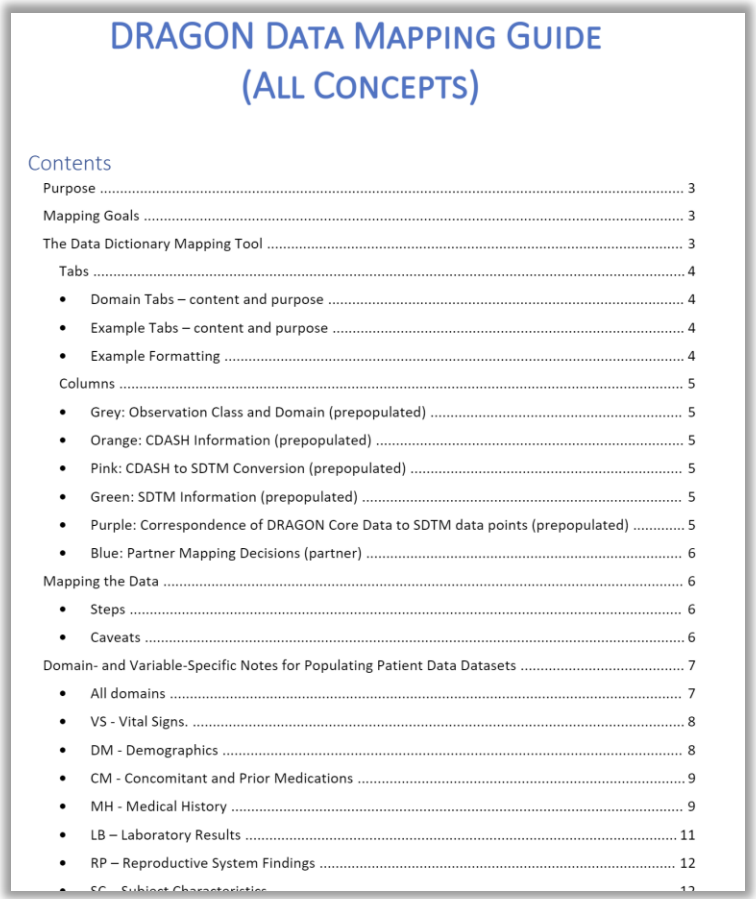
No personnally identifiable information should be included (e.g., nam

Observation Class	Domain	CDASHIG Variable	ner Original Variable Name (if no variable, leave null)	Partner Original Variable Label	Partner Original Controlled Terminology (Code List)	Partner's SDT Algorithm (in n
Findings	MB	MBTEST				
Findings	MB	MBTSTDTL				
Findings	MB	MBORRES				
Findings	MB	MBORRESU				

LB | LB Examples | RP | RP Examples | SC | SC Examples | MB | MB Examples | SU | SU Examples | PR | PR Examples | H

Data Mapping Guide

- Orients partner sites to using the mapping tool
- Provides more detailed domain- and variable-level notes / rules for DRAGON
- Provides steps and cautions to guide accurate mapping results



DRAGON DATA MAPPING GUIDE
(ALL CONCEPTS)

Contents

Data entry templates

Some partners cannot export data and are entering data manually

Lab Core Tests ("Blood Gas Deviation")

Core Fields Record structure: one record per test result per time point per

NOTE: the number of tests per patient is unknown; 8 rows per subject w

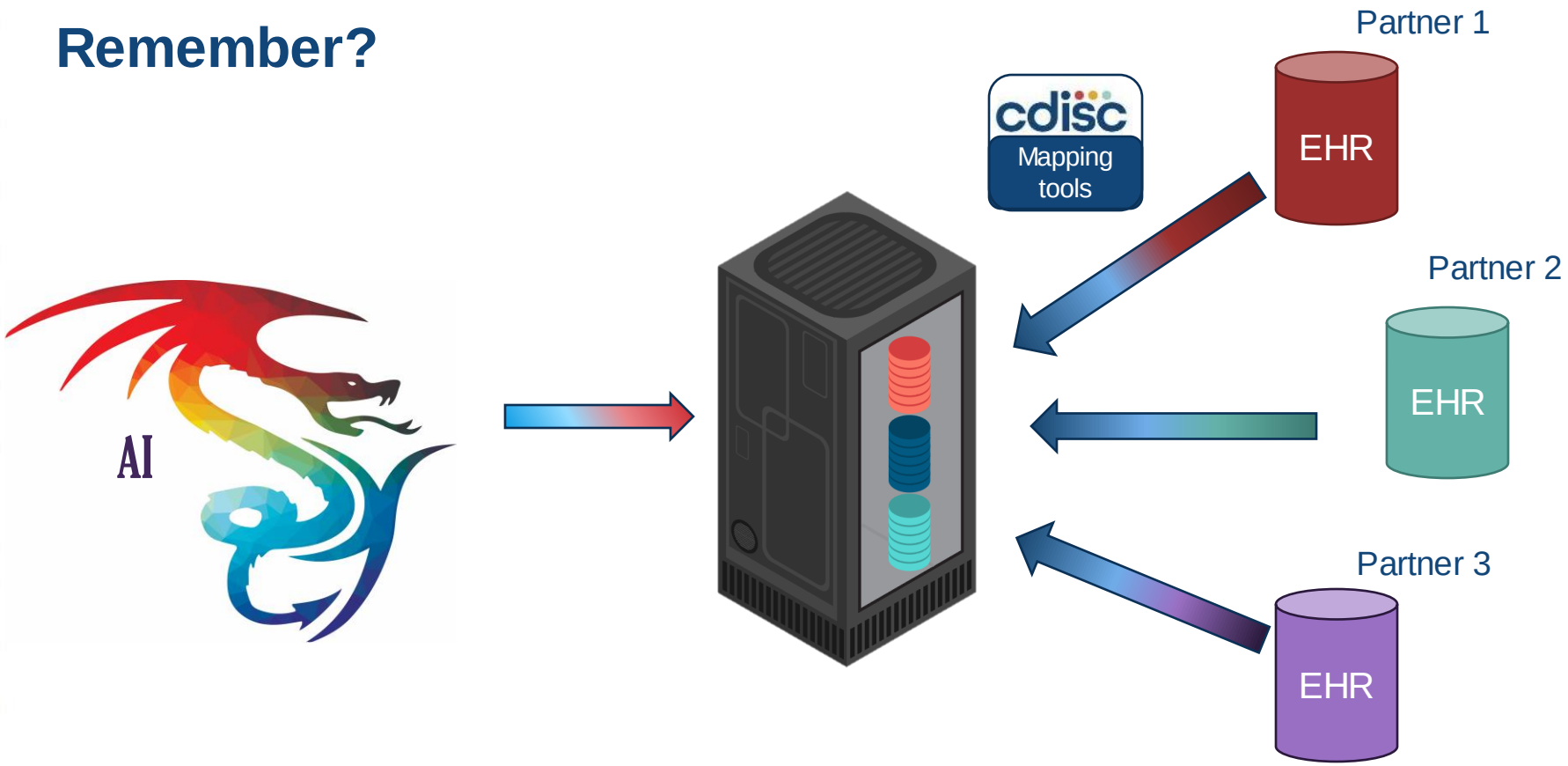
The conversion factor for converting kPa to mmHg has been included in

	STUDY	DOMAIN	USUBJID	LBTEST	LBCAT	LBORRES	LBORRESU	LBORNRLO
	[Project]	*Domain*	*Patient ID*	*Name of the Measurement*	*Category of lab test*	*Original Result of the Measurement*	*Original Result Unit*	*Lower limit of norm range original resul*
Codelist/Contro	-	*DOMAIN C66734*	-	*C67153 VSTEST*			*C66770 VSRESU*	
Validation Data	DRAGON	LB	DRAGON-YOURSITE-PSEUDOID	PARTIAL PRESSURE OXYGEN	BLOOD GAS PANEL	75	kPa	
Validation Data	DRAGON	LB	DRAGON-YOURSITE-PSEUDOID	PARTIAL PRESSURE OXYGEN	BLOOD GAS PANEL	109	kPa	
Patient Data	DRAGON	LB	DRAGON-YOURSITE-PSEUDOID01	PARTIAL PRESSURE OXYGEN	BLOOD GAS PANEL		kPa	
Patient Data	DRAGON	LB	DRAGON-YOURSITE-PSEUDOID01	PARTIAL PRESSURE OXYGEN	BLOOD GAS PANEL		kPa	
Patient Data	DRAGON	LB	DRAGON-YOURSITE-PSEUDOID01	PARTIAL PRESSURE OXYGEN	BLOOD GAS PANEL		kPa	
Patient Data	DRAGON	LB	DRAGON-YOURSITE-PSEUDOID01	PARTIAL PRESSURE OXYGEN	BLOOD GAS PANEL		kPa	
Patient Data	DRAGON	LB	DRAGON-YOURSITE-PSEUDOID01	PARTIAL PRESSURE OXYGEN	BLOOD GAS PANEL		kPa	
Patient Data	DRAGON	LB	DRAGON-YOURSITE-PSEUDOID01	PARTIAL PRESSURE OXYGEN	BLOOD GAS PANEL		kPa	
Patient Data	DRAGON	LB	DRAGON-YOURSITE-PSEUDOID01	PARTIAL PRESSURE OXYGEN	BLOOD GAS PANEL		kPa	

VS Entry Core | CM Entry Core | LB Entry Core | LB Entry Non-Core | SC Entry Core | RP Repro Sys | MB Microbiology | SU S

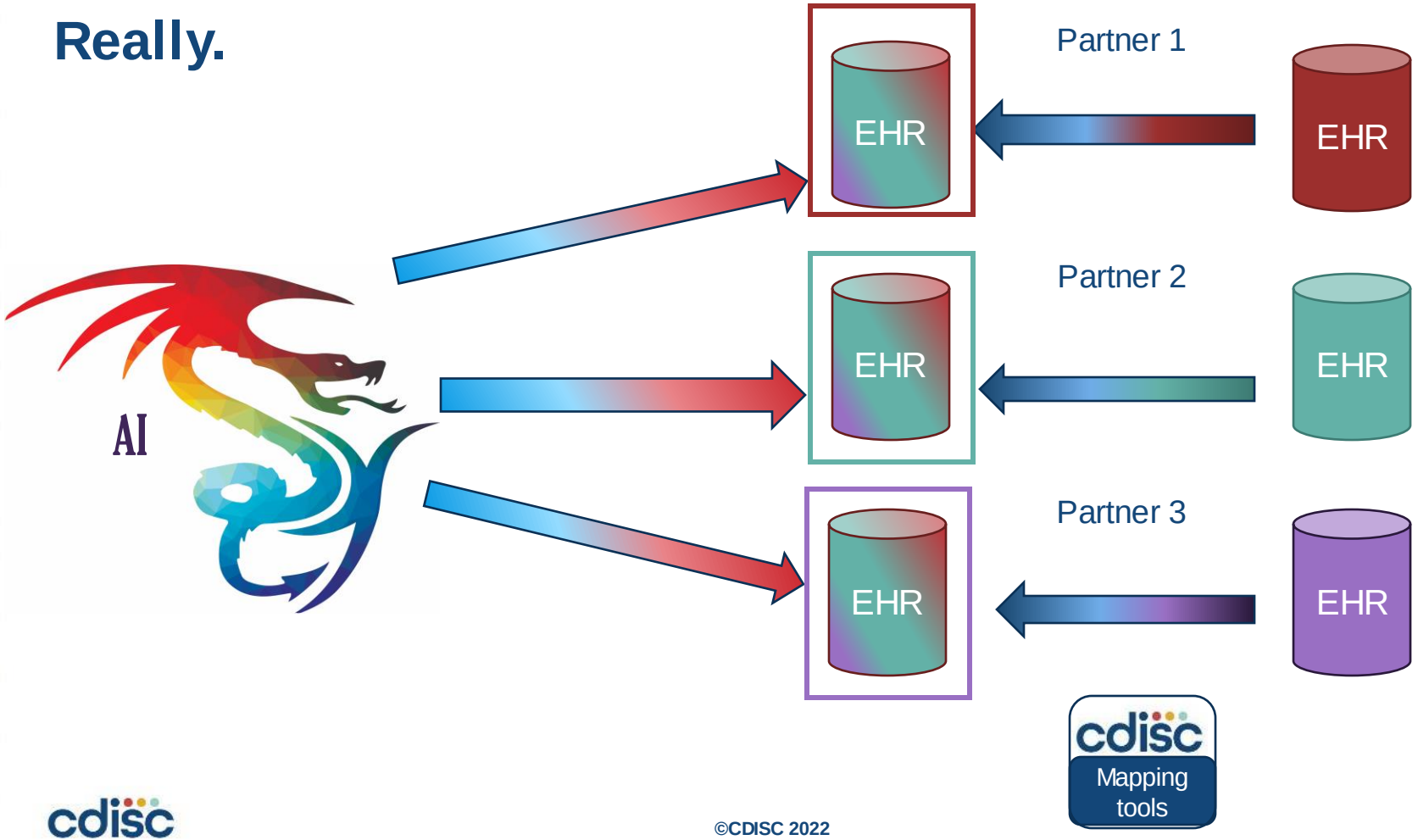
Simple, right?

Remember?



EHR: Electronic Health Record = patients' healthcare data

Really.



Actually… Really.

Access data

Update model

Keep ONLY the model

Data

Partner 1

EHR

EHR

cdisc Mapping tools

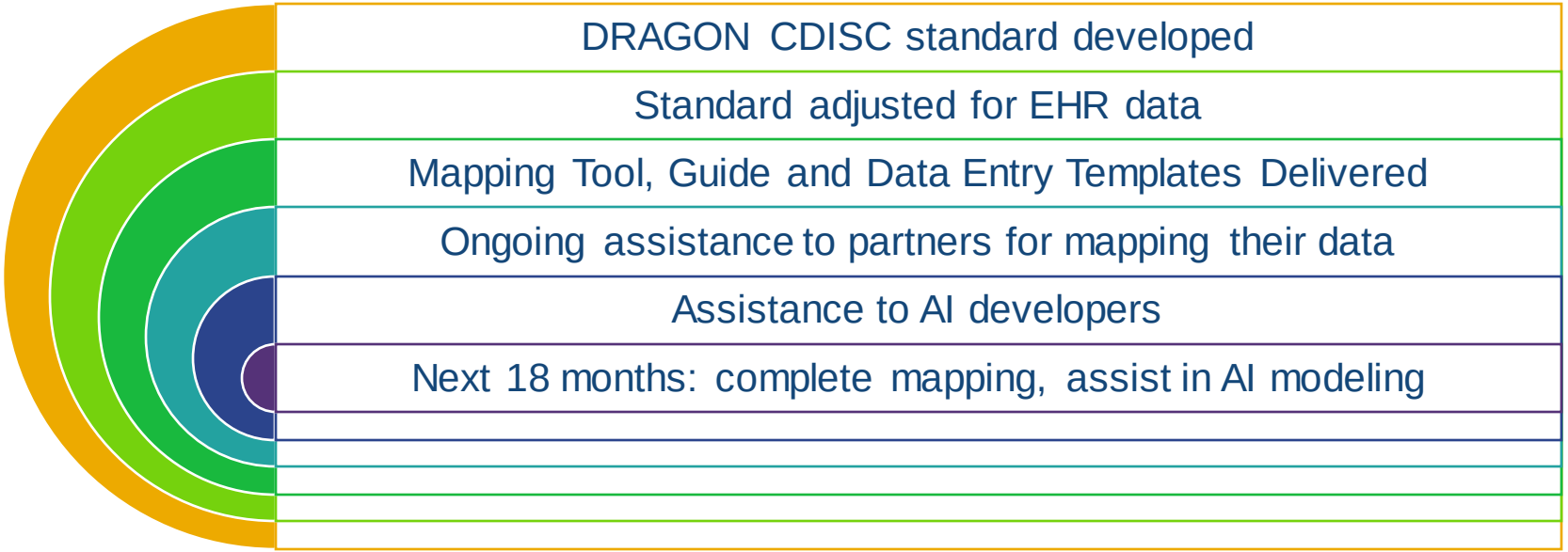
Partner 2

EHR

EHR

Go to the next site

Progress



Using SDTM in Observational Studies: Considerations and Examples Document

Announcing a new standards development project

Overview of Key Points

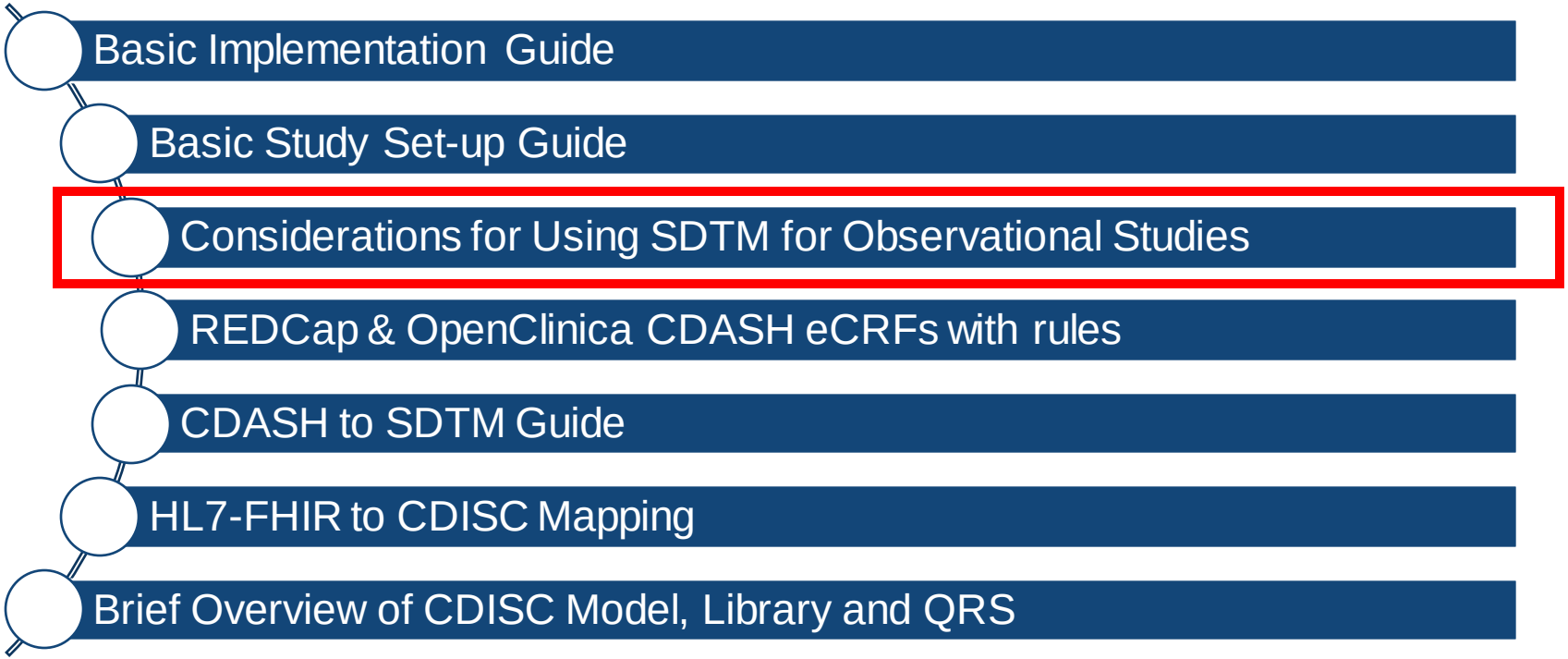
With funding from the IMI DRAGON project, CDISC is launching a new project to develop a document that will guide users in the implementation of SDTM for observational studies data.

Today we are just announcing and offering a chance to participate.
We plan to kick off in a couple weeks (date TBD)

We have formed a team (though it is not too late participate!)

We are considering holding a separate development call for the Japanese team members at a time that works for Japan so that you're not on the phone in the middle of the night

Proposed CDISC Suite of RWD Guides and Resources



RWD Resources Draft Timeline

Phase 1

Instantiate eCRFs:

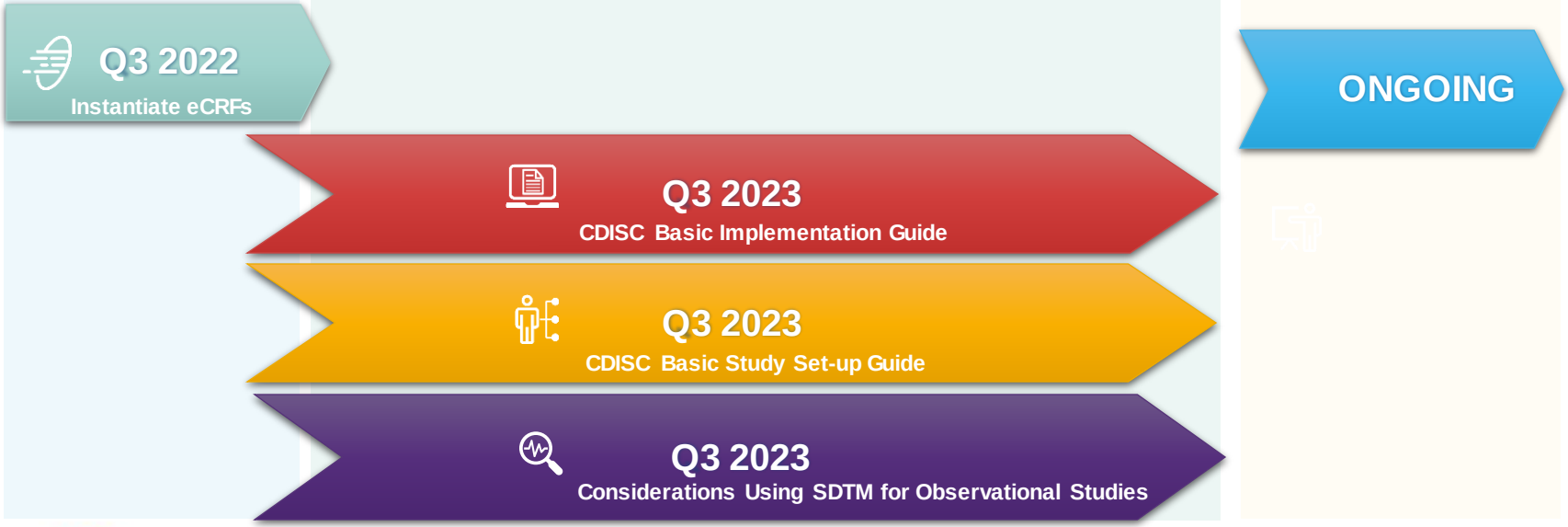
- CDISC eCRF Portal
- OpenClinica
- REDCap

Phase 2

- Develop CDISC Basic Implementation Guides, Basic Study Set-up and Considerations for Observational Data
- Review of draft guides (EAB), follow CDISC Standards Development Process
- Develop Educational Content > Publish as Ready
- Publish on Microsites > Publish as Ready

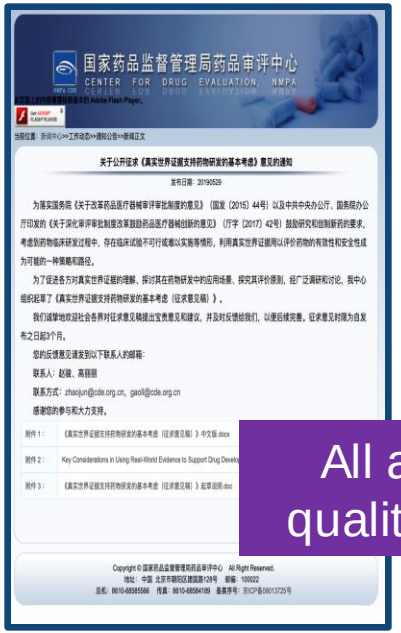
Ongoing

- Review
- Community Feedback
- Curation & Maintenance
- Communications



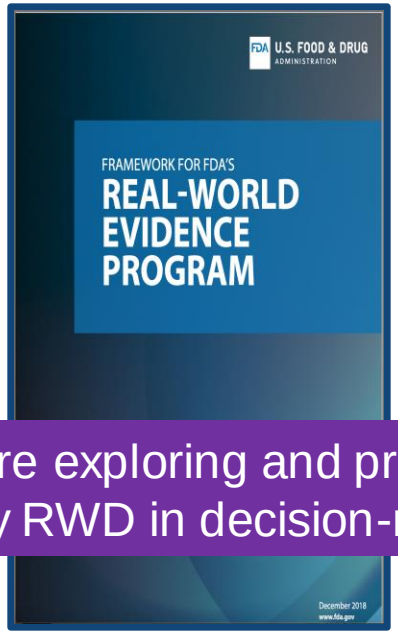
RWD and the Regulatory Environment

China's NMPA



http://www.cde.org.cn/news.do?method=largeInfo&id=23a2b4cbe0807fe2

US FDA

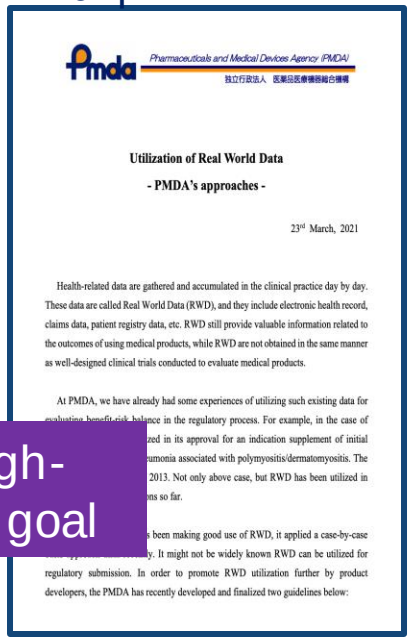


https://www.fda.gov/media/120060/download

EU EMA

https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/ema-regulatory-science-2025-strategic-reflection_en.pdf

Japan's PMDA



https://www.pmda.go.jp/english/about-pmda/0004.pdf

All are exploring and promoting the use of high-quality RWD in decision-making as a strategic goal

What will the observational data document contain?

Discuss common issues encountered when implementing SDTM for observational data

Develop implementation strategies that address these issues.

Illustrate these strategies in examples

- Reuse existing standards; create new domains and variables only if necessary

Discover and develop new concepts as needed, with examples

Adjust conformance rules to better fit these data

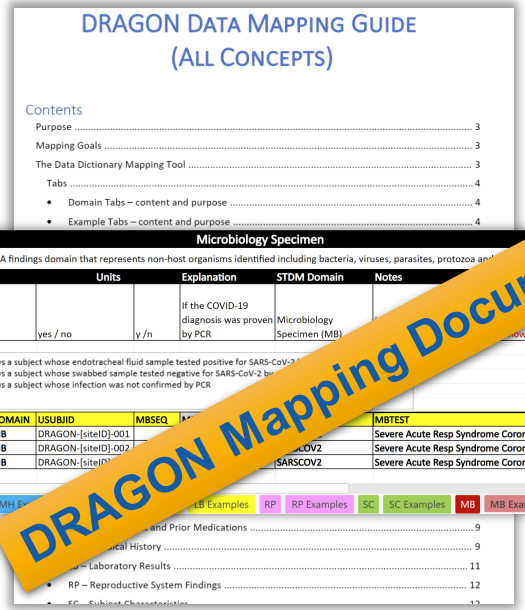
- New conformance rules as needed
- *Remove* irrelevant conformance rules from validation checks of observational studies.

Resulting document will be CDISC-endorsed by going through development process.

What will be identified in scoping?

- What types of studies will we accommodate, and how are these studies designed?
- What are the common issues encountered while using SDTM for observational research data?
- What domains/variables/conformance rules are not relevant?
- New concepts, if any, for which will have to develop implementation strategies

Relevant Resources


DRAGON Data Mapping Guide
(All Concepts)

Contents

Purpose 3
Mapping Goals 3
The Data Dictionary Mapping Tool 3
Tabs 4
- Domain Tabs – content and purpose 4
- Example Tabs – content and purpose 4

Microbiology Specimen

A findings domain that represents non-host organisms identified including bacteria, viruses, parasites, protozoa and

Variable		Units		Explanation	STDM Domain	Notes
COVID-19 proven by PCR		yes / no	y /n	If the COVID-19 diagnosis was proven by PCR	Microbiology Specimen (MB)	

Row 1: Shows a subject whose endotracheal fluid sample tested positive for SARS-CoV-2
Row 2: Shows a subject whose swabbed sample tested negative for SARS-CoV-2 by
Row 3: Shows a subject whose infection was not confirmed by PCR

STUDYID	DOMAIN	USUBJID	MBSEQ	MBTEST	MBTSTDTL	MBORRES	MBSTRESC	MBSTAT
DRAGON	MB	DRAGON-[siteID]-001		Severe Acute Resp Syndrome Coronavirus 2	DETECTION	POSITIVE	POSITIVE	
DRAGON	MB	DRAGON-[siteID]-002		Severe Acute Resp Syndrome Coronavirus 2	DETECTION	NEGATIVE	NEGATIVE	
DRAGON	MB	DRAGON-[siteID]		Severe Acute Resp Syndrome Coronavirus 2	DETECTION			NOT DONE

MH Examples | LB Examples | RP | RP Examples | SC | SC Examples | MB | MB Examples | SU

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ical History 9
– Laboratory Results 11
- RP – Reproductive System Findings 12


PhUSE US Connect 2019

Paper SI08

Considerations for Using CDISC Standards in Observational Studies

Jon Neville, CDISC, Austin, TX, USA
Bess LeRoy, CDISC, Austin, TX, USA

ABSTRACT

INTRODUCTION

OBSERVATIONAL D

DRAGON Mapping Documents

Phuse Publications

Examples of conformance issues discussed in PHUSE Paper

Conformance Rule	Flag Type	Challenge Presented
Demographics (DM) dataset must be included in every submission.	Error	Inclusion of the dataset should not present a problem. However, some required/expected variables will not be available (See table 2 below)
Adverse Events (AE) dataset should be included in every submission.	Warning	Depending on study type, these data may not be available
Lab Test Results (LB) dataset should be included in every submission.	Warning	Depending on study type, these data may not be available
Vital Signs (VS) dataset should be included in every submission.	Warning	Depending on study type, these data may not be available
Exposure (EX) dataset should be included in every submission.	Warning	Observational studies are not interventional studies. As such, exposure data will not be relevant.
Disposition (DS) dataset should be included in every submission.	Warning	Subjects won't likely meet formal milestones, nor will they have formal study completion/withdrawal dates.
Subject Elements (SE) dataset should be included in every submission.	Warning	Trial arms and elements are not relevant to observational research. Therefore, neither are subjects' progression through these.
Trial Arms (TA) dataset should be included in every submission.	Warning	Observational studies do not have rigid study designs with planned arms.
Trial Elements (TE) dataset should be included in every submission.	Warning	Without trials arms there are no elements to describe.
Trial Summary (TS) dataset must be included in every submission.	Error	Observational studies are not trials, but investigators could possibly create study parameters to describe here. It would require new controlled terminology and could be burdensome if it were considered a "required" dataset in observational research.

Examples of required/expected variables that may not be relevant to observational data

Variable(s)	Domain	Core	Challenge Presented
RFSTDTC / RFENDTC	DM	Expected	Study reference periods will not always be relevant. Defining these dates can be challenging. Sometimes dates will be missing altogether.
RFXTSDTC / RFXENDTC	DM	Expected	Observational research does not include regimented exposure to a protocol-defined drug. Phase IV studies / Post-marketing surveillance could possibly provide these
SITEID	DM	Required	Observational research includes observations from across healthcare and clinical settings. These will likely vary and not be available in the data anyway
ARM / ARMCD ACTARM / ACTARMCD	DM	Required	There are no arms to describe in observational research.
VISITNUM	Multiple	Sometimes Required	The concept of "visit" may not be relevant in observational research
EPOCH	Multiple	Sometimes Required	Use cases for observational research have not been explored. Existing controlled terminology is specific to clinical trials

Other Problems we could address

- Handling missing data (imputation of missing dates, etc.)
- Analysis considerations*
- Other topics we discover in scoping

*We do not plan to include ADaM in v1.0, but knowing how analyses may be done in observational research could help upstream SDTM modeling. Also, some imputations may best be handled in ADaM, which was discussed in the PHUSE white paper

What have we done so far?

Identified team members

Sent a survey to team members:

- What types of non-interventional studies have you worked with?
- What are the biggest challenges you have experienced when using CDISC standards in observational studies?
- Have you used a model/standard besides SDTM to submit the data to regulatory agencies? In what ways was this easier or more difficult than SDTM?
- What aspects of the CDISC trial design model have and have not worked well for observational data?
- Regarding medications data, how have you handled missing dosing information?
- Have you attempted to create define files for observational study data, and if so, how did you approach define style sheets?
- Have you encountered any issues with CDISC metadata (e.g., origin of data that was imputed whereas CDISC considers it collected)? If so, how did you handle this?

Draft Timeline and Progress

31 May 2022	☑ Develop Survey (experience trying to use CDISC standards in observational studies, and the issues encountered while doing so)
06 Jun 2022 - 30 Jun 2022	☑ Send out a survey to team members - 2 week timeline ☐ Compile results ☐ Schedule kick-off call 3rd week of June **Kick-off Call** 1. Introduce project, scope, timeline 2. Determine meeting time 3. Q&A
Jul - Aug 2022	**Scoping** - **Observational Study (non-interventional studies) Guide v1** • Study types, study design - prospective • Domains and variables that would not be used • Concept identification • Conformance rules - separate set of rules, add and remove based on study type
Aug - Sep 2022	**Identification of Concepts**
Oct - Mar 2023	Development - Considerations and Examples for using SDTM for Observational Data/Studies (need to make sure we are clear what we mean i.e., will not include mapping FHIR etc)
Apr - May 2023	**Internal Review**
Jun - Aug 2023	**Public Review**
Sep 2023	**Publication**

Next Step, date TBD

Thank You!

If you are interested in participating in the observational studies guide document development please contact Alana St Clair or Jon Neville soon!

astclair@cdisc.org

jneville@cdisc.org