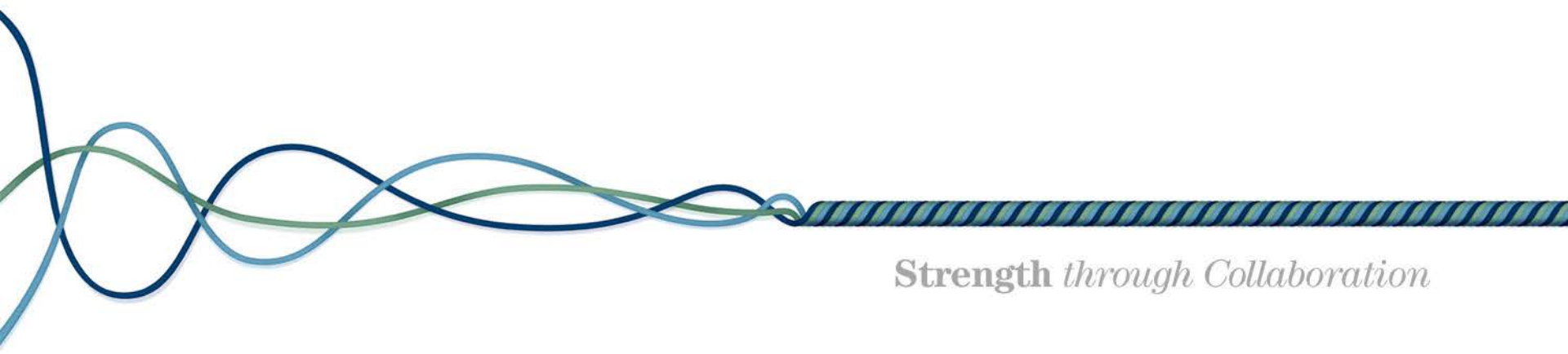
CDISC Public Webinar – Standards Updates and Additions

1 FEB 2017



Agenda

- Vaccines TA Public Review
  - John Owen, Project Manager, CDISC
  - Bess LeRoy, Metadata Engineer, CDISC
  - Cedric Davister, System Owner, GSK
- CDISC Online Education & Event Updates
  - John Ezzell, CDISC

Question & Answer

- ‘Panelist’: Question

OR

- ‘Presentation’: Question

Examples:

Fred: What are some best practices for the Assessing SDTM Conformance?

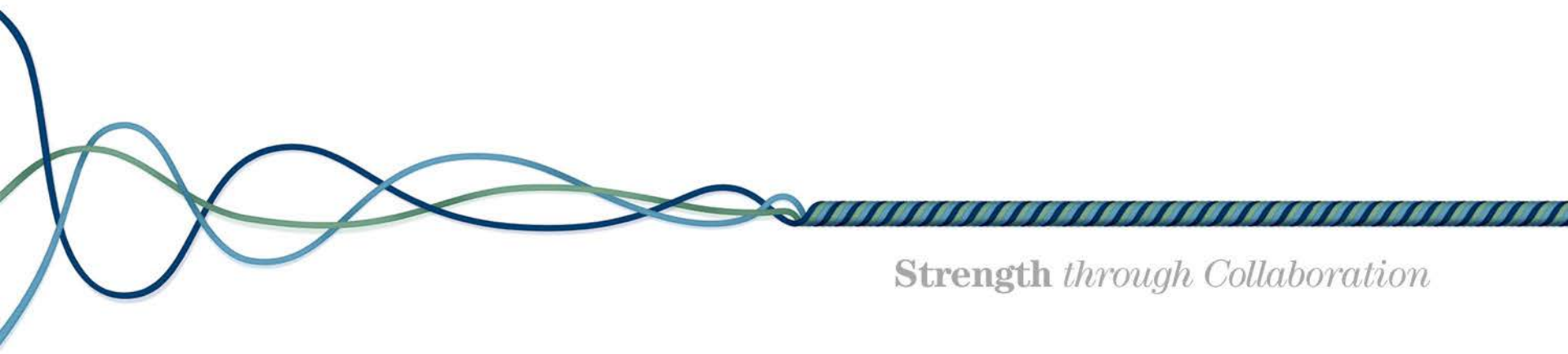
OR

CDISC: When can we start registering for the US Interchange?

CDISC Public Webinar-
Vaccines Therapeutic Area User Guide

1st February 2017

10am CDT



AGENDA

- Team Collaboration (John Owen)
- Vaccines Project Update (John Owen)
- Introduction to Vaccines (John Owen)
- Vaccines TAUG Overview (Bess LeRoy)
  - Sections
  - Domains
  - Variables
  - Non-Standard Variables
  - Controlled Terminology
- Public Review Information (John Owen)
- Q&A

We would like to thank our sponsors

& our Team Collaboration

Vaccines TAUG Development Team

Vaccines TAUG Development Team

Core Team Members

Name	Institution/Organization
Cedric Davister - Team Lead	GlaxoSmithKline Vaccines
Frances M. Acton	Merck&Co
Xavier Cornen	SanofiPasteur-MSD
Pamela Freese	Pfizer
John Ginis	Pfizer
Audrey Hagenbach	Sanofi-Pasteur
Geert Hannink	GlaxoSmithKline Vaccines
Christian Hoppe	Vienna Vaccine Safety Initiative (ViVI)
Ragini Khedoe	GlaxoSmithKline Vaccines
Veronique Long	Sanofi-Pasteur
Dave O'Riordan	GlaxoSmithKline Vaccines
Deborah Paletta	Business&Decision Life Sciences
John Perez	Pfizer

Name	Institution/Organization
Barbara Rath	Vienna Vaccine Safety Initiative (ViVI)
Magali Savoy	Sanofi-Pasteur
Ramana Setty	Sanofi-Pasteur
Olive Yuan	Johnson & Johnson
Elodie Zaworski	Sanofi-Pasteur
Brenda Baldwin	FDA - CBER, Liaison
Kirk Prutzman	FDA - CBER, Liaison
Former Members	
Anne-Sophie Bekx	Business&Decision Life Sciences
Karin Botilde	GlaxoSmithKline Vaccines
Joan Lippincott	Merck&Co
Lauren Shinaberry	Business&Decision Life Sciences

CDISC Core Team Members

Name	Institution/Organization
Paul Houston - Team Lead	CDISC
John Owen - Team Lead	CDISC
Dorina Bratfalean	CDISC
Bess LeRoy	CDISC
Diane Wold	CDISC

Vaccines Project Update

Stage 0	Stage 1	Stage 2	Stage 3a	Stage 3b	Stage 3c	Stage 4
Scoping & Planning	Identification/ Modeling of Research Concepts	Development of Draft Standards	Internal Review	Public Review	Public Release	Maintenance & Education

- TAUG submitted to SRC for approval to publish for public review (2nd January 2017)
- SRC comments addressed and final approval to release for public review due w/c 6th February 2017
- Vaccines will use a 30-day public review period.
- Anticipated review comments closing date 10th March 2017
- Vaccines team will then address public review comments and re-submit the TAUG to SRC for approval to publish on the CDSIC website
- Anticipated public release Mid April 2017 (dependant on number/complexity of public review comments received)

Introduction to Vaccines

- *Vaccines* are preparations containing antigenic substances capable of inducing a specific and active immunity against the disease or infection.

- Such immunity may then result in the lack of spread of that disease or infection

- *Reactogenicity* refers to the property of a substance to produce an expected or common adverse reaction when introduced into the body. In vaccine studies

Introduction to Vaccines – cont'd

- Reactogenicity is typically caused by an immunologic response to the vaccine under study and may include things like fever, rash, or redness at the site of administration.

- Reactogenicity generally describes immediate short-term reactions to vaccines, not long term sequelae.

- V1.0 of the Vaccines TAUG concentrates on representing reactogenicity events data using SDTM v1.4 and the SDTMIG v3.2.

Overview of TAUG Content

•**Section 1**, Introduction, provides an overall introduction to the purpose and goals of the Therapeutic Area Data Standards User Guide for Vaccines.

•**Section 2,** Overview, provides some general information on vaccines trials and in particular reactogenicity events.

•**Section 3**, Case Description, provides background information about the type of study that the examples are based on.

•**Section 4**, Trial Design, provides examples used to support the modelling of Reactogenicity Safety Assessments.

Overview of TAUG Content

•**Section 5**, Vaccine Administration, provides examples used to support the modelling of Reactogenicity Safety Assessments.

•**Section 6,** Reactogenicity Safety Assessments, provides examples of modelling reactogenicity data using different data collection methods.

•**Section 7**, Relating Records, provides information on how domains used in these examples can be linked.

•**Section 8**, Appendices, provide additional background material and describe other supplemental material relevant to Vaccines.

Known Issues
Representation of Planned Assessment Period

- TAUG uses the variables --STINT (Planned Start of Assessment Interval) and –ENINT (Planned End of Assessment Interval)
  - --STINT and --ENINT were originally developed for use in describing the time interval covered by pharmacokinetic parameters such as area under the curve
  - Cannot be used for point in time measurements such as temperature
- Should the examples use --EVLINT (Evaluation Interval) instead (e.g., -PT24H)?

Known Issues
Representation of Maximum Temperature

- If subjects take their temperature multiple times throughout the day, often they are asked to record only their maximum temperature.

- Should the concept of maximum be pre-coordinated in VSTESTCD/VSTEST with temperature or should this concept be represented in a separate variable?

Known Issues
Representation of Occurrence and Severity

- The representation of the occurrence and severity of an event in SDTM is dependent on the type of data collected. If data is collected for the entirety of an event, the variables CEOCCUR and CESEV are used.

- If data is collected for a part of the event, the data are represented as findings about the event, using the FATESTs "Occurrence Indicator" and "Severity/Intensity". This modeling decision is based on recommendations from an SDS sub-team looking at best practices at representing occurrence data.

Known Issues
Linking variables

- This guide uses the variables FOCID and TAETORD to help link data across domains. We are looking for feedback on this approach.

Case Description

- A hypothetical trial was used as the basis for examples in this user guide
  - Parallel design
  - Comparator-controlled vaccine trial
  - Two co-administered vaccines
  - Both vaccines administered on two different occasions
- Data were collected at three visits,
  - Vaccines administered during Visit 1 and Visit 2
  - A third visit at the end of a 3-month follow-up period
- Case Design was chosen since it can easily be extrapolated to more vaccines and/or more vaccination occasions. It can also be easily simplified to a single vaccine and/or a single administration occasion.

Case Description

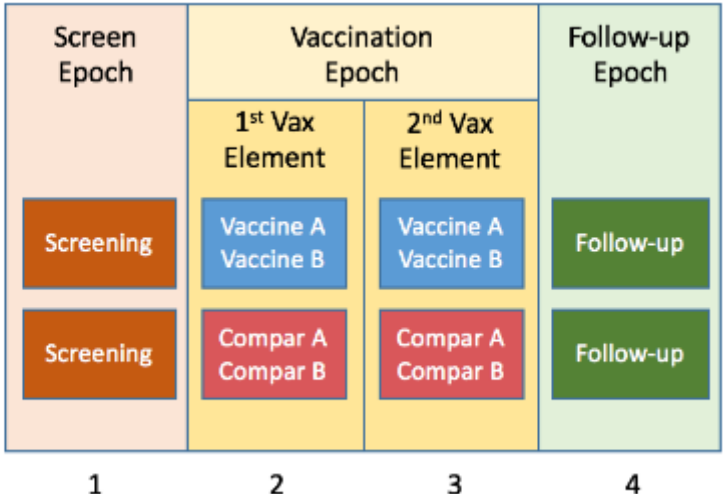
- Data on reactogenicity events was collected via a reactogenicity collection form (e.g., a subject diary) for a pre-defined observation period of 3 days starting on the day of each vaccine's administration.
- Reactogenicity Data were collected for
  - **Vomiting**, the number of vomiting episodes experienced during the day was recorded on each day (0 in case of no vomiting).
  - **Fever**, the temperature was recorded on each day, whether or not fever occurred. One value was reported per day. If several assessments were performed during the day, the maximum value observed during the day was reported.
  - **Redness at administration sites**, the largest diameter of the redness spot was reported on each day.

Case Description

- Post 3-day Data on reactogenicity events also collected until resolution or end of study
  - End date of the event
  - Maximum value of the measure
    - Number of vomiting episodes
    - Intensity
    - Temperature
    - Largest diameter of redness
- Investigator-recorded data about reactogenicity events included
  - Action taken
  - Resolution
  - Relationship to vaccination.

Trial Design

- Highlights the use the SDTM variable TAETORD



ta.xpt

Row	STUDYID	DOMAIN	ARMCD	ARM	TAETORD	ETCD	ELEMENT	TABRANCH	EPOCH
1	ABC	TA	VAXAB	Vaccine A Vaccine B	1	SCRN	Screening	Randomized to Vaccine A and B	SCREENING
2	ABC	TA	VAXAB	Vaccine A Vaccine B	2	VAXAB	Vaccine A and B		VACCINATION AND OBSERVATION
3	ABC	TA	VAXAB	Vaccine A Vaccine B	3	VAXAB	Vaccine A and B		VACCINATION AND OBSERVATION
4	ABC	TA	VAXAB	Vaccine A Vaccine B	4	FLLW	Follow-up		FOLLOW-UP
5	ABC	TA	COMPAB	Compar A Compar B	1	SCRN	Screening	Randomized to Comparator A and B	SCREENING
6	ABC	TA	COMPAB	Compar A Compar B	2	COMPAB	Compar A and Compar B		VACCINATION AND OBSERVATION
7	ABC	TA	COMPAB	Compar A Compar B	3	COMPAB	Compar A and Compar B		VACCINATION AND OBSERVATION
8	ABC	TA	COMPAB	Compar A Compar B	4	FLLW	Follow-up		FOLLOW-UP

Vaccine Administration

- Highlights the use the SDTM variable FOCID
  - It is expected to be standard for use in human clinical trials in the next version of the SDTMIG
  - For this guide FOCID is represented as a non-standard variable

Variable	Variable Label	Type	Description
FOCID	Focus of Study-Specific Interest	Char	Identification of a focus of study-specific interest on or within a subject or specimen as called out in the protocol for which a measurement, test, or examination was performed, such as a drug application site, e.g., "Injection site 1", "Biopsy site 1", "Treated site 1", or a more specific focus, e.g., "OD" (right eye) or "Upper left quadrant of the back". The value in this variable should have inherent semantic meaning.

Vaccine Administration

FOCID Value	Description of FOCID Value
SITE1A	Administration site at which vaccine/comparator A was applied at the first vaccination occasion
SITE1B	Administration site at which vaccine/comparator B was applied at the first vaccination occasion
SITE2A	Administration site at which vaccine/comparator A was applied at the second vaccination occasion
SITE2B	Administration site at which vaccine/comparator B was applied at the second vaccination occasion

Vaccine Administration

ex.xpt

Row	STUDYID	DOMAIN	USUBJID	EXSEQ	EXTRT	EXCAT	EXDOSE	EXDOSU	EXDOSFRM	EXROUTE	EXLOC	EXLAT
1	ABC	EX	ABC-1001	1	VACCINE A	STUDY VACCINE	0.5	mL	INJECTION	INTRAMUSCULAR	ARM	LEFT
2	ABC	EX	ABC-1001	2	VACCINE B	STUDY VACCINE	0.5	mL	INJECTION	INTRAMUSCULAR	ARM	RIGHT
3	ABC	EX	ABC-1001	3	VACCINE A	STUDY VACCINE	0.5	mL	INJECTION	INTRAMUSCULAR	ARM	LEFT
4	ABC	EX	ABC-1001	4	VACCINE B	STUDY VACCINE	0.5	mL	INJECTION	INTRAMUSCULAR	ARM	RIGHT

EXDIR	VISITNUM	VISIT	TAETORD	EPOCH	EXSTDTC	EXENDTC	EXDY	FOCID
UPPER	1	VISIT 1	2	VACCINATION AND OBSERVATION	2015-01-10	2015-01-10	1	SITE1A
UPPER	1	VISIT 1	2	VACCINATION AND OBSERVATION	2015-01-10	2015-01-10	1	SITE1B
UPPER	2	VISIT 2	3	VACCINATION AND OBSERVATION	2015-01-31	2015-01-31	22	SITE2A
UPPER	2	VISIT 2	3	VACCINATION AND OBSERVATION	2015-01-31	2015-01-31	22	SITE2B

Reactogenicity Safety Assessments Domains used

- Vital Signs (VS): Daily temperature records
- Findings About (FA): Daily assessment of vomiting, fever, and redness
- Clinical Events (CE)/Adverse Events (AE): Events of vomiting, fever, and redness when described as a whole

Reactogenicity Safety Assessments Transcription of Diary Cards

Different studies often use different strategies when transcribing diary cards. The representation of three different strategies are shown in the guide.

- All of the daily assessments are transcribed from the daily card and a global event record is created only when a reactogenicity event occurred during the three-day assessment interval ***(flat model)***.
- A global record is created for each reactogenicity event that is assessed and the daily assessment records for an event are created only if the event occurred during the three-day assessment interval ***(nested model)***.
- A global record is created for each type of reactogenicity category that is assessed (i.e., systemic and site administration events). If an event occurred in one the categories, additional global records for all the events in that category are created. Daily assessment records for an event are created only if the event occurred during the three-day assessment interval ***(highly nested model)***.

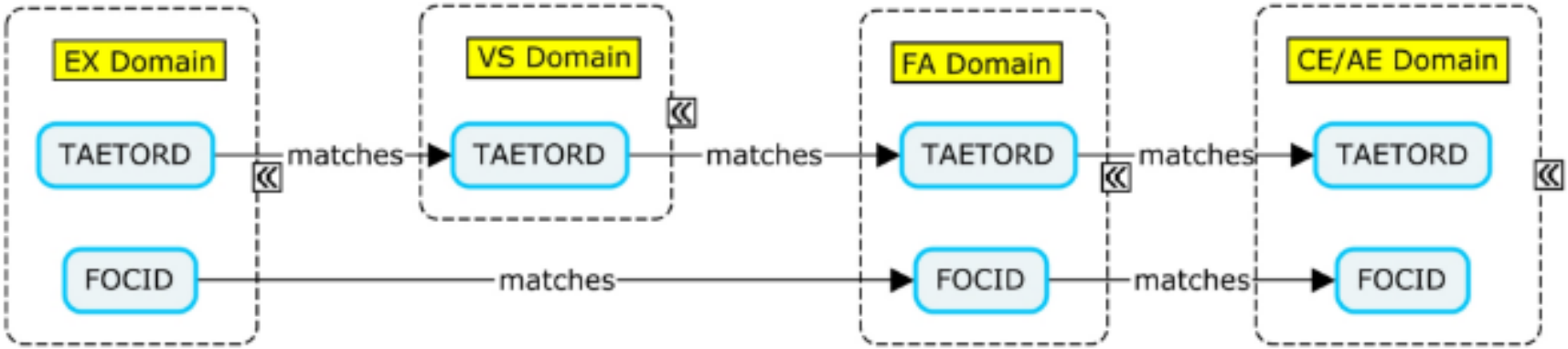
Reactogenicity Safety Assessments

- Representation of events that continue beyond the planned assessment period
  - Clinical Events
  - Adverse Events

- Representation of events when daily assessments are missing

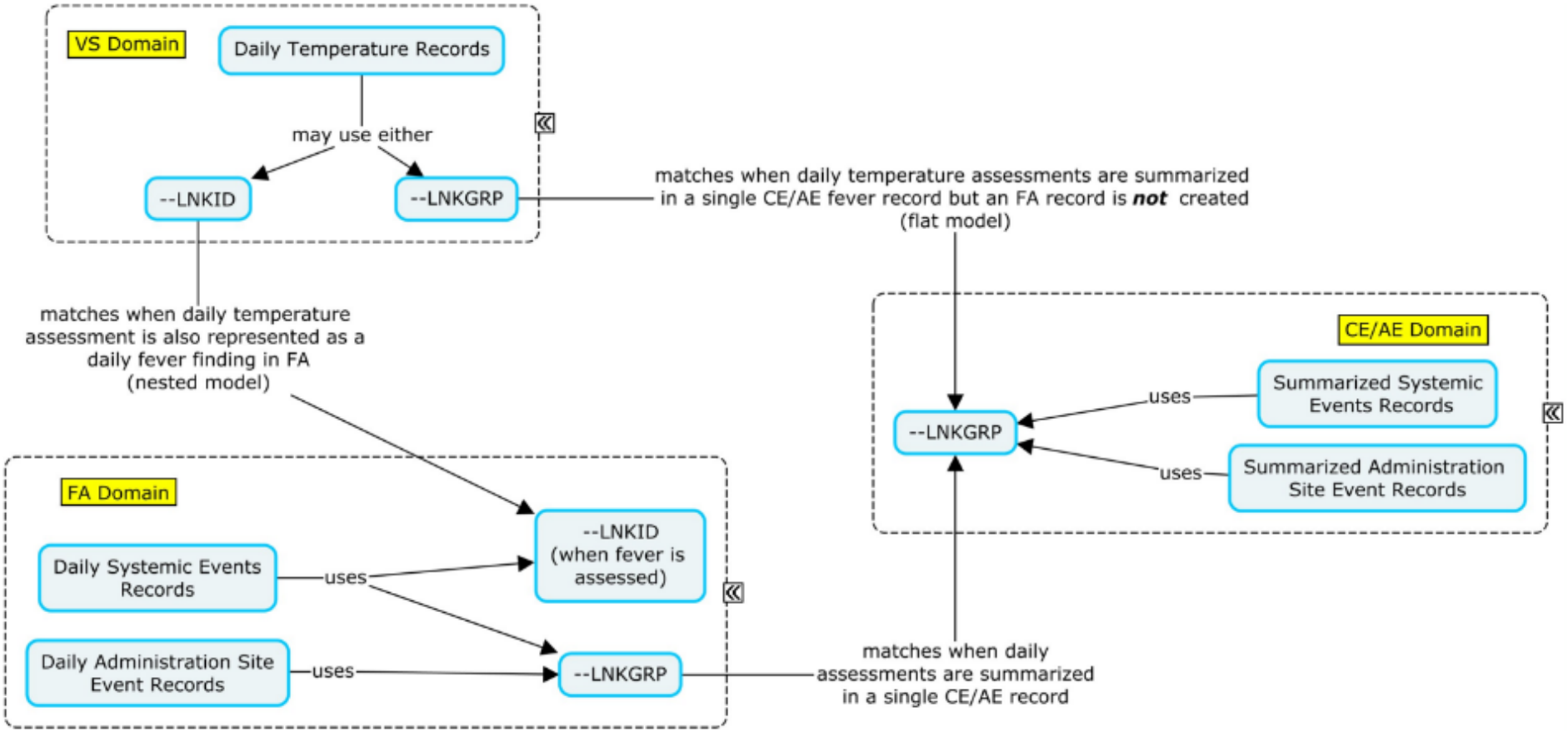
Relating Records

- FOCID and TAETORD
  - Allows data to be related across multiple domains on timing and location of administration



Relating Records

- --LNKGRP and --LNKID



Domains

- No new domains were submitted for this version of the TAUG
- The following Domains are referenced in the TAUG

Datasets	Description	Section in TA User Guide	Section Description
TA/TE/TV	Trial Arms/Elements/Visits	4 Ex 1	Trial Design
EX	Exposure	5 Ex 1	Vaccine Administration
VS	Vital Signs	6 Ex 1a, 1b, 1c	Reactogenicity Safety Assessments
FA	Findings About	6 Ex 1a, 1b, 1c 6 Ex 2 6 Ex 3	Reactogenicity Safety Assessments
CE	Clinical Events	6 Ex 1a, 1b, 1c 6 Ex 2 6 Ex 3	Reactogenicity Safety Assessments
AE	Adverse Events	6 Ex 3	Reactogenicity Safety Assessments

New Variables

- No new variables were submitted for approval to become SDTM variables for this user guide

Non-Standard Variables

- Note that FOCID is represented as a non-standard variable for this user guide
- It is expected to be a standard variable for use in human clinical trials in the next version of the SDTMIG

Parent Domain	Variable	Label	SAS Data Type	XML Data Type	Codelist/Controlled Terms	Role	Description	Comments
EX, CE, FA	FOCID	Focus of Study-Specific Interest	Char	text		Non-Standard Identifier	Identification of a focus of study-specific interest on or within a subject or specimen as called out in the protocol for which a measurement, test, or examination was performed, such as a drug application site	This is an anticipated new variable.

Controlled Terminology

- **EPOCH –** Requested extension of definition to include prevention

- **FATESTCD –** In development with the Vaccines team and NCI-EVS group

Public Review Information

- Review Package Contents (will be made available only on the CDISC WIKI)
  - Links/Instructions will be provided in the Public Review announcement email

- Reviewers are requested to make any comments directly via JIRA
  - Detailed instructions are provided on the TAUG-Vax WIKI page.
  - Wiki and JIRA use the same credentials, so if you can see the TAUG-Vax page in the WIKI, then you can use JIRA.

Public Review Information – cont.

TAUG-Vax compiled

- Allows review of entire document as a single document
- View is more prone to errors when entering comments into JIRA.

TAUG-Vax sections

- Allows review of each section separately
- Easy navigation between sections using navigation label at the bottom of the page
- Reviews can also jump back and forth between sections
- Tables, and tables representing datasets (including any attendant row captions or footnotes), are inside expandable sections. Clicking on an indented line “ > “reveal the content within.

Public Review Information – cont.

Vax Examples, Figures and Concept Maps

- Allows all the SDTM examples, figures and concept maps used in the TAUG-Vax to be viewed in 1 section.

Any technical issues with the use of the WIKI and JIRA please contact jowen@cdisc.org

Public Review Information – cont.

- Reading the TAUG-Vax in its entirety at least once before jumping to specific sections or examples
- Always check the Known Issues Section prior to review of the TAUG
- Comments can be entered direct into the WIKI TAUG
  - Creates a link between the TAUG and JIRA
  - Always check to make sure the project selected in JIRA is Vaccines
  - Ability to see comments from other reviewers (reduction in comment duplication)

Public Review Information – cont.

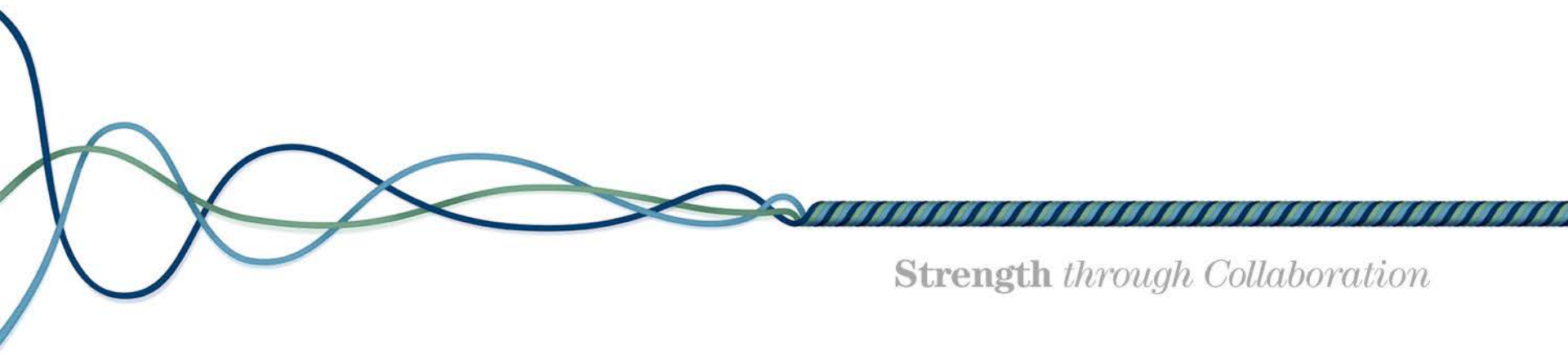
- Add scope suggestions for future versions

- **If you have no edits or comments to a page, c**lick 'Like' at the bottom of the page. This will help us determine who has read each page.

Q&A

CDISC Online Education & Event Updates

John Ezzell, CDISC



Upcoming Webinars

Topics	Presenters	Webinar Date
Results Level Metadata: What, How and Why	Jeffrey Abolafia, Rho, Frank DiIorio, CodeCrafters, Inc	16 FEB 2017, 11:00 AM EST
Some Considerations When Designing ADaM Datasets	Nate Freimark, Senior Director, Biometrics Operations Standards Group, Theorem Clinical Research	9 MAR 2017, 1100 AM EST

Webinar details and registration at www.cdisc.org/webinars

Regulation Update

- CDISC SDTM Standard
  - Now in regulation in US and Japan
  - Required format for all new clinical trial submissions
  - Visit cdisc.org/standards/foundational/sdtm for more information about SDTM

UPCOMING NORTH AMERICA PUBLIC COURSES

Location	Dates	Courses Offered:	Discount period ends:	Late fees kick(ed) in:	Host
Raleigh, NC	27 Feb – 3 Mar 2017	SDTM, CDASH, ADaM Primer, ADaM T&A	28 Nov 2016	28 Jan 2017	
Audubon, PA	3-7 Apr 2017	SDTM, CDASH, ADaM Primer, ADaM T&A, CT, Define-XML	3 Jan 2017	3 Mar 2017	
South San Francisco, CA	15-19 May 2017	SDTM, CDASH, ADaM Primer, ADaM T&A, Define-XML, Controlled Terminology	13 Feb 2017	15 Apr 2017	

Visit cdisc.org/public-courses for information on other CDISC Public Training events.

UPCOMING EUROPE PUBLIC COURSES

Location	Dates	Courses Offered:	Discount period ends	Late fees kick(ed) in:	Host
London, UK	24-28 Apr 2017	See web.	24 Feb 2017	24 Mar 2017	CDISC
Frankfurt, Germany	19-23 Jun 2017	SDTM, CDASH, Define-XML, ADaM Primer, ADaM T&A	20 Mar 2017	20 May 2017	CLINIPACE WORLDWIDE
Leiden, Netherlands	11-15 Sep 2017	SDTM, CDASH, Define-XML, ADaM Primer, ADaM T&A	12 Jun 2017	13 Aug 2017	OCS Consulting
Copenhagen, Denmark	2-10 Nov 2017	SEND, SDTM, ADaM Primer, ADaM T&A, Define-XML	2 Aug 2017	3 Oct 2017	SCUBED

Visit cdisc.org/public-courses for information on other CDISC Public Training events.

UPCOMING ASIA PUBLIC COURSES

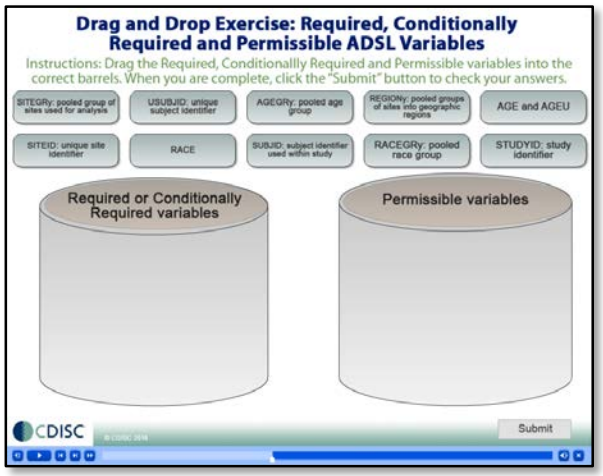
Location	Dates	Courses Offered	Discount period ends:	Late fees kick(ed) in:	Host
Tokyo, Japan	13-17 Mar 2017	SDTM, CDASH, ADaM Primer, ADaM T&A, Define-XML	11 Jan 2017	11 Feb 2017	Croit
Tokyo, Japan	5-9 Jun 2017	SDTM, CDASH, ADaM Primer, ADaM T&A, Define-XML, ODM	TBD	TBD	Croit

Visit cdisc.org/public-courses for information on other CDISC Public Training events.

CDISC Online Training Production Update

- Just Released
  - Mini-Training: EPOCH Variable
  - Define-XML Module 1: Introduction to Define-XML
  - Controlled Terminology Module 1: Overview of Terminology

Online Courses in Development
TA Alzheimer's
TA Vaccines
TA Prostate Cancer
TA Rheumatoid Arthritis
TA Pain
ADaM Modules 5-8



Any more questions?

Thank you for attending this webinar.

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Inform Patient Care & Safety Through Higher Quality Medical Research

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