SEND Development Update
(and how can PhUSE help?)

Overview of current work in SEND

- Not details
- Just a flavor of the work in progress & challenges
- If any of these topics spark interest or thoughts related to your data challenges, speak up!

Priorities for 2018 & Beyond

- Respond to Fit For Use (FFU) pilot, especially PCPP and MAMI
- Prepare for SENDIGv3.1 mandate
  - Safety Pharm Proof Of Concept (POC) Pilot
  - CoDEx v1.0 for SENDIGv3.1
  - Fill CT Gaps (including CDISC cross team CT issues)
  - SENDIGv3.1 Safety Pharm clarifications
- Conformance Rules: Publish SENDIGv3.0 this year
- 2018 Releases?
  - Planning for the CDISC November annual release
  - SENDIG for Dermal Ocular Toxicity (tentative)
  - SENDIG for Animal Rule (TAUG-like project)
- CBER support (IS Domain and Biodistribution)
- Improved Example data

CDISC Priorities (lots of change!)

- Support for teams (Team Liaisons, new tools)
- Governance across standards (GGG)
- Standards Development Process emphasis: cadence and communication
  - External facing: Known Issues, Work in Progress, Principles
  - Internal process: Cadence of development, versioning, supplements (CoDEx), supplemental IGs, etc.
  - Clean up: migrating off of old collaboration tools
- Volunteer Engagement
- Volunteer Policies and Hour tracking

SEND Standards Development Status

Stage of Development	Scoping (Stage 0)	Development (Stage 1 and 2)	Internal Review (Stage 3a)	Prep for Public Review (Stage 3a)	Public Review (Stage 3b)	Resolving Public Review Comments (Stage 3b)	Prep for Publication (Stage 3b)	Published (include date of publication per the CDISC website) (Stage 3b)	Published Status (Provisional or Final)
SENDIG-DART v1.1								COMPLETE 11 Dec 2017	Final
SENDIG-AR v1 (Animal Rule)	COMPLETE	ONGOING (March 2018)							
SENDIG-Genotoxicity v1	COMPLETE	ONGOING							
SENDIG v 3.0 Rules	COMPLETE	ONGOING							
SENDIG-Dermal Ocular v1	COMPLETE	ONGOING							
SENDIG-DARTv1.2	ONGOING								
SENDIG v3.x (CCB, MAMI, PCPP, FFU, CBER)	ONGOING								
SENDIG v3.2 (NV)*	ONGOING								
CoDEx for SENDIG v3.1									
TF and TUMOR.xpt	ONGOING	ONGOING							

DART

- SENDIG-DART v1.1 published by CDISC (not in FDA data standards catalog)
- Charter for Proof of Concept (POC) piloting approved.
- POC pilot supports use of v1.1, data assembled are being reviewed
  - V1.1 scope, Embryo-Fetal Developmental (EFD) Toxicity studies
  - POC study, EFD Tox in Rats with prenatal evaluations (Non-TK)
- Target release (v1.2?) to add examples to existing domains for Juvenile Tox studies, and recommended updates per POC pilot results
- Future development: Fertility, Postnatal development, Multi-generational studies
- Challenges: prioritization for EFD Tox Fit for Use, resources and SMEs for supplemental docs (e.g., conformance rules, CoDEx, etc.)

Animal Rule (SENDIG – AR)

- Implementation (or User) Guide for Animal Rule Studies
- Animal Rule studies use animal model when it is not feasible nor ethical to use human trials (e.g. Anthrax, Radiation, etc.)
- New domains include those to describe the challenge agent (e.g. Anthrax)
- This is intended to support studies where study treatment (medical countermeasure) is given prior to exposure to challenge agent as well as those with post-exposure study treatment.
- Also to support Natural History studies (those used to develop the model for efficacy studies using data on the natural history of the disease or condition in the selected animal species compared and contrasted with the same in humans)

Genetic Toxicology

- Modeling the standard battery of nonclinical studies in support of genetic toxicology assessments in both in vivo(micronucleus and comet) and in vitro(Ames and micronucleus)
- Challenges in identifying subjects (e.g. cell cultures, bacterial cultures, samples from animals not on this study, test kits, etc.)
- Assessed the gaps in LB variables and concepts
- Defined two new domains GT (in vitro) and GV (in vivo)
- Methods

Conformance Rules

- Conformance Rules are required to be created for any new IG before CDISC will publish that IG
- The first set of SEND Conformance Rules will be for SENDIGv3.0
- Status: intend to publish SEND Conformance Rules for SENDIGv3.0 this year
- The SEND Conformance Rules for SENDIGv3.0 will serve as a springboard to creating Conformance Rules for other SENDIG versions (SENDIGv3.1, DARTv1.1)

Dermal Ocular Toxicology

- Modeling nonclinical studies in support of dermal and ocular assessments
- Challenges in trial designs
- Recommending Trial Look up table
- Methods

PCPP – a thorough review

- Updates to the PC and PP domains based on industry feedback and input from FDA in the 'Fit for use'.
- Have improved recommendations around date/time – when to use actual and when to use calculated or nominal
- How to properly group PC records with their associated PP records. (e.g. using --TPTREF and VISITDY) and the proper use of PCELTM
- Updates on how to represent when measurement is outside limits of quantitation (upper and lower limits)
- Baseline flags, definition and varied use between PC and PP
- Provided specific feedback to FDA and writing updates for future versions of SENDIG
- Plan to produce improved examples for SENDIGv3.0 to improve implementation
- Have posted wording of recommended changes to PhUSE to share approach and also receive feedback, will post improved examples to share via PhUSE. Feedback is important!

MA/MI - – a thorough review

- Updates to the MI domain based on defined use cases from industry and input from FDA in the 'Fit for use'.
- Ensure that PDF presentation of microscopic data is reproducible from SEND data, that additional tests and data end points can be handled, and that confirmatory relationships with data entries in other domains can be made apparent.
- Definition and use of: MITEST, Specimen condition
- Review result variable qualifiers (RESLOC, RSANTREG, RSDIR, RSLAT, RSPORTOT)
- Assessments based on microscopic findings in multiple organs (e.g. sexual maturity based on reproductive organ findings)
- Additional F2F topics: Need for new CT? How to recreate incidence tables in reports?

Safety Pharmacology

- New NV domain, created for CNS tests
  - Includes FOBs, motor activity, rotorod, water maze passive avoidance tests
  - Draft completed, publication schedule pending
- New CV and RE Domains are complete and in SENDIGv3.1
  - EG also augmented for 3.1 to better support safety pharmacology studies
  - Currently included in FDA data standards catalog as an accepted standard
- Proof of Concept pilot (CDISC safety pharm subteam members only) for use of SENDIGv3.1 for continuous monitoring cardiovascular and respiratory studies
  - Focus on Latin-Squared and Rising Dose study designs

CoDEx for SENDIGv3.1

- Team of SMEs who will define which data endpoints can be confidently exchanged.
- Helpful supplement to a published IG (as with CoDEx for SENDIGv3.0)
- Challenge – need leader!

Controlled Terminology

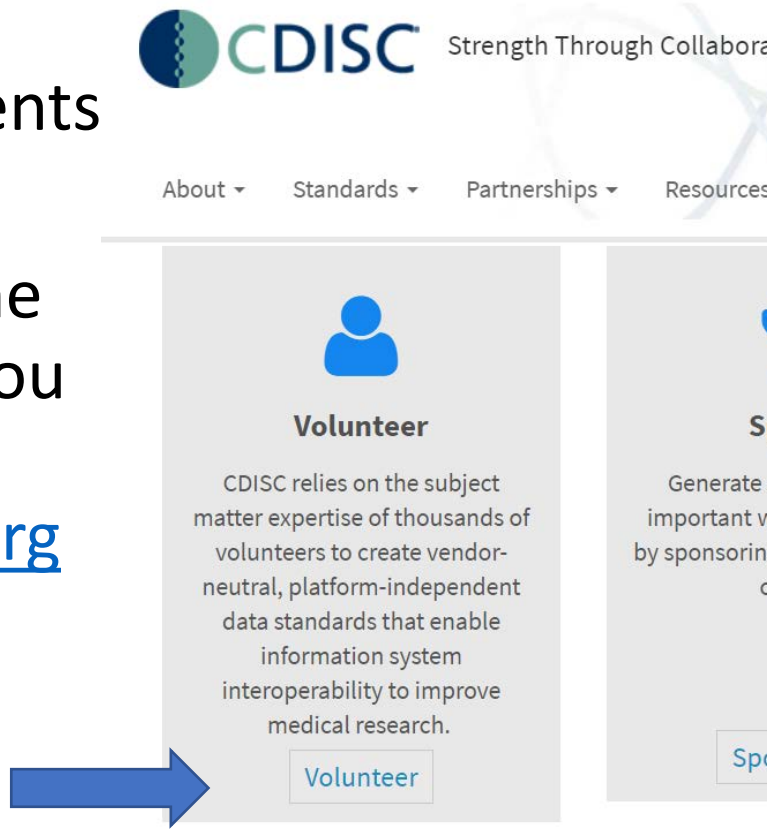
- Example of challenges:
  - When codelists are restructured into new lists and terms are deprecated (e.g. PKUNIT), previously published IGs can become misaligned
  - Managing backward compatibility (e.g. VSTEST codes, VSRESU, etc.)
  - Multiple code lists for one variable (Separate code lists for clinical vs. nonclinical)
- Sub-team working on CT for tumor combinations

Tumor Findings

- Improvements to tf.xpt
- Assessment of utility of tf.xpt to replace tumor.xpt in the future
- Relatively new team working with the biostatisticians from FDA

How can PhUSE help?

- Continue to provide feedback on postings from CDISC teams
- Continue to provide early assessments of industry issues with use cases
- Help us direct volunteer SMEs to the right subteams in SEND. For now, you do this by asking them to choose "Volunteer" button at www.cdisc.org



Questions?

- Bill Houser (SEND Team Leader, william.houser@bms.com)
- Lou Ann Kramer (CDISC team liaison, lkramer@cdisc.org)
- In the future, we hope to have a public facing site that contains sub-team details as on the SEND wiki (https://wiki.cdisc.org/display/SEND/SEND+Home)