Science For A Better Life

CDISC Intrachange 2013

30.07. - 01.08.2013 Silver Spring

German User Group Meeting, 24-Sep-2013

Melanie Füllbeck

Intrachange Agenda

30.07.2013

- Technical Plan, Roadmap
- Study Data Standards at FDA
- Cross-team Sessions:
  - FDA-CDISC Submission Issues
  - Integrated Standards from Study Planning through Execution
  - Discussing the impact of Therapeutic Area Standards projects on CDISC Foundational teams

31.07.2013

- CDISC Standards Development Process, SHARE and Tools for Teams
- Cross-team Sessions:
  - SDTM Governance - Integrating SEND, Drug Trials, Devices

31.07.2013 (cont.)

- Validation Conformance Requirements; Interaction with PhUSE CSS
- Education and Tools for Teams

01.08.2013

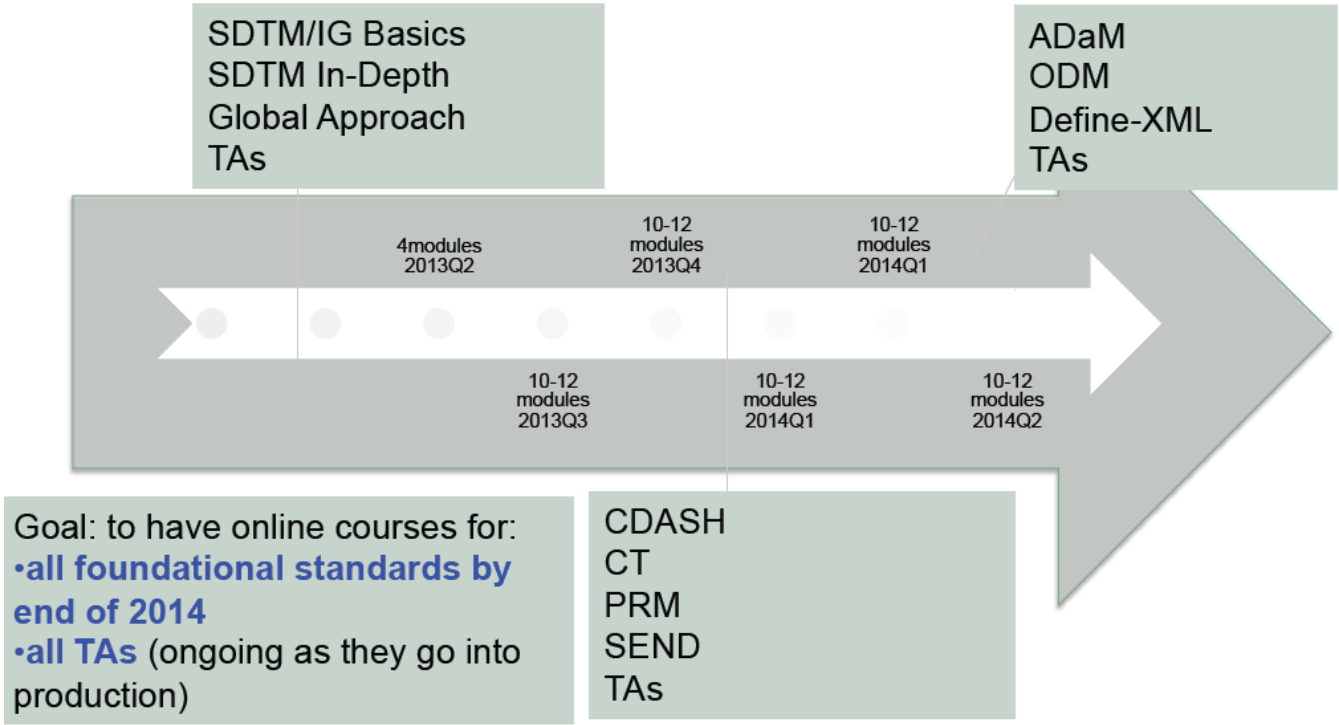
- Cross-team Sessions:
  - Managing Questionnaires from Protocol to Analysis
  - Drug Exposure from Protocol to Analysis
  - Integrated Metadata: Using Define-XML for full submissions

On all Days:

- Individual Team Meetings: ADaM, SDS, SEND, CDASH, XML Tech, Protocol, QS

Technical Plan/Roadmap

Proposed Online Course Release Schedule



Source: Presentation - W. Kubick, Intrachange 2013

Collaboration Tools

- Portal Enhancements:
  - Comprehensive list of standards documents that are currently under development
  - Contact list of who is working on what
  - Detailed instruction on sharepoint functionalities (check-in and check-out)

- Launch of online training campus:
  - General Training webinars
  - Training on what to expect as a project team member

Collaboration Tools

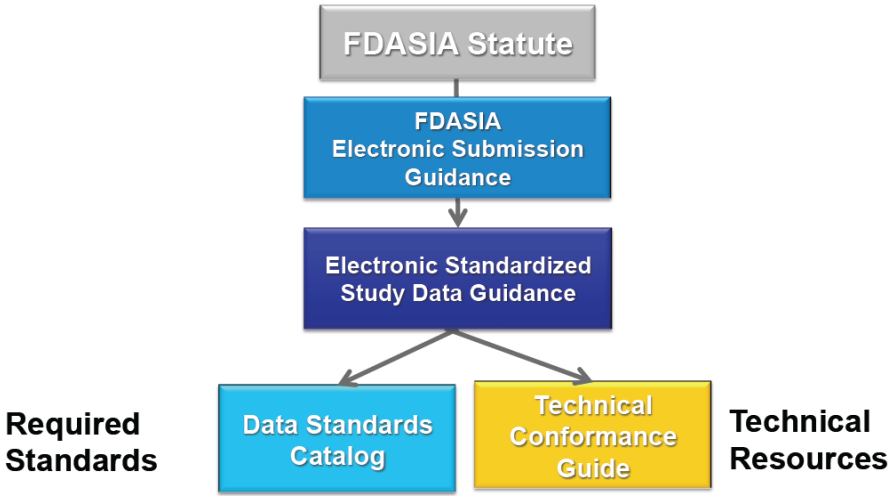
- Issue Tracking
  - Jira (http://jira.cdisc.org)
  - Plan to begin evaluation in conjunction with Confluence
  - Can also be utilized for action items and decision register

- Document Collaboration
  - Confluence (http://wiki.cdisc.org)
  - Any comments/issues identified with documents posted on Confluence linked directly with issue tracking in Jira

- Both are currently in a testing phase (CDISC sub-team)

Study Data Standards at FDA

- In 2012 the FDA received 662 study datasets per week, up to 10GB in size
- 43% of effort in a review is spent on data management and primary analysis
- Guidance on the standards and format of electronic submission
  - Binding: 24 month after issuance of final guidance: For NDA and BLA submissions, efficacy/labeling/manufacturing supplements and amendments, and all other new NDA submissions
- Periodic releases of final guidance



Adapted from Source by Ron Fitzmartin, FDA

NDA: New Drug Application, BLA: Biologics License Application, FDASIA: FDA Saftey and Innovation Act

FDA-CDISC Submission Issues

- Industry would like feedback on submissions
  - CDISC can improve implementation advice
  - Sponsors learn what they can improve
- Clear communication of FDA expectations
  - Template for communication
  - Let reviewers know data are SDTM/ADaM based
- Validation challenges
  - Need feedback to improve
  - Understand that validation checks do not rule the data
  - Poor implementations can still be compliant

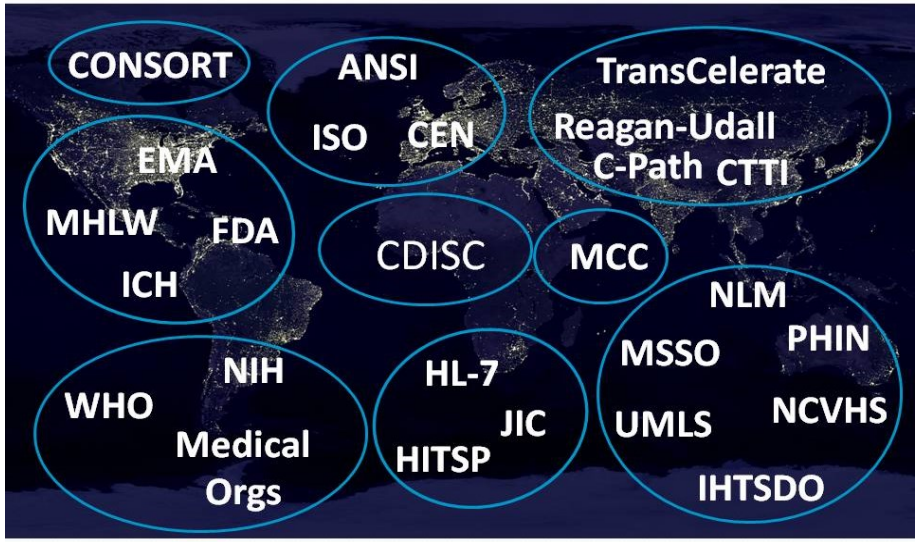
Validation Conformance Requirements

- CDISC teams own/drive validation requirements for their standard(s)
  - Currently: discrepancies between rule definitions and implementation at vendor
  - Validation requirements definition will be integrated in standard development process
  - Validation/Conformance Rule document needs to be documented after new releases

- FDA-PhUSE Data Quality Working Group will provide common place for finding all of the Validation/Conformance Rules for a standard and will support governance process
  - http://www.phusewiki.org/wiki/index.php?title=Data_Validation_and_Quality_Assessment

Integrated Standards from Study Planning through Execution

- High-level picture of standards that impact CDISC and that CDISC impacts



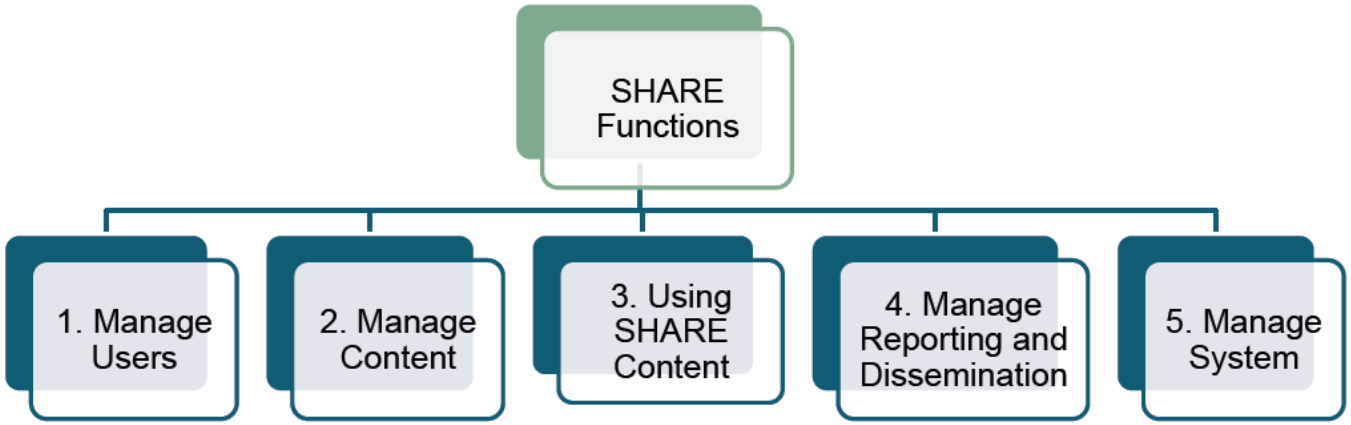
Source: XT2 Summary, Gary Walker and Kit Howard, Intrachange 2013

CONSORT: Consolidated Standards of Reporting Trials (CONSORT Statement)
EMA: European Medicines Agency
MHLW: Ministry of Health, Labour, and Welfare
FDA: Food and Drug Administration
ICH: International Conference on Harmonisation
NIH: National Institute of Health
WHO: World Health Organisation
ANSI: American National Standards Institute
ISO: International Organizaion for Standardization
HL-7: Health Level 7
JIC: Joint Initiative Council
HITSP: Healthcare Information Technology Standards Panel
CTTI: Clinical Trials Transformation Initiative
NLM: National Library of Medicine
MSSO: Maintenance and Support Service Organization
UMLS: Unified Medical Language System
IHTSDO: International Health Terminology Standards Development Organisation
NCVHS: National Committee on Vital and Health Statistics
PHIN: Public Health Information Network

- List will be completed
- Relationships will be defined (both direction)
- Define expectations among CDISC standards
- Identify gaps
  - What is needed to address the gaps?
  - Determine and develop solutions (Process…)
- Determine to which degree SHARE could be a backbone for this

SHARE(Shared Health and Clinical Research Electronic Library)

SHARE Top-Level Functions



- Manage User Roles
- Manage User Profiles
- Manage Password
- Manage User Dashboard

- Development templates
- Manage Work Items/ work in progress
- Manage Standard Objects
- Manage Audit Trail
- Version control
- Associations, links, references
- Value sets, codelists

- Search, Browse, Compare, Reconcile
- Impact analysis
- Import
- Export
- Print
- API integration

- Send Notifications to users re object changes
- Manage listserv

- Manage SHARE MDR Framework Components
- Monitor User Activity
- Maintain Metrics
- Manage System Availability

Source: Presentation - W. Kubick, Intrachange 2013

SHARE

SHARE MDR Framework

A Versioned Standard is comprised of a set of Operational Collections and associated variables and rules for a specific use case (e.g., SDTM, CDASH)

An Operational Collection is a grouping of Research Concepts. There may be additional rules between objects within the Operational Collection. An Operational Collection may be analogous with a SDTM Domain, a CRF, an ADaM data set, or a similar level of operational structure.

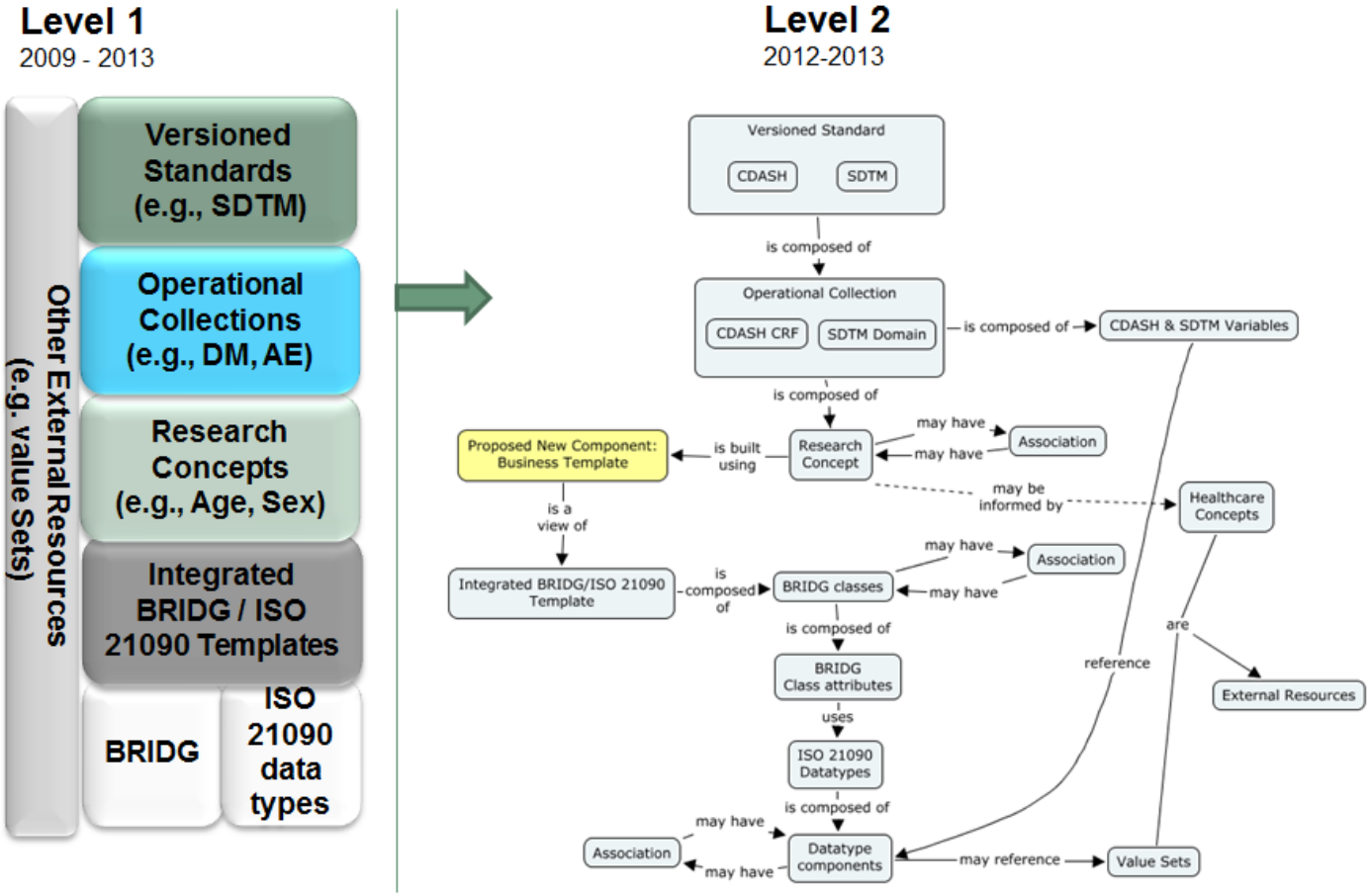
Basic elements that are the foundation for the content described in the SHARE repository. A Research Concept defines one or more related pieces of clinical data, which is developed using an Integrated BRIDG / ISO 21090 Template.

Integrated BRIDG / ISO 21090 Templates use BRIDG classes and relationships to fashion small re-usable patterns that are commonly needed in clinical research

BRIDG is the foundation model for SHARE that provides classes, attributes and associations use to creates core building blocks.

Source: Presentation - S. Hume, Intrachange 2013

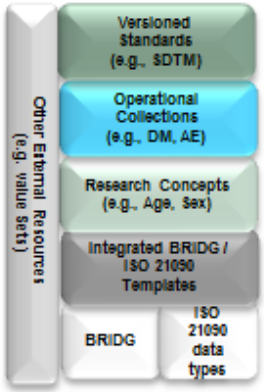
SHARE



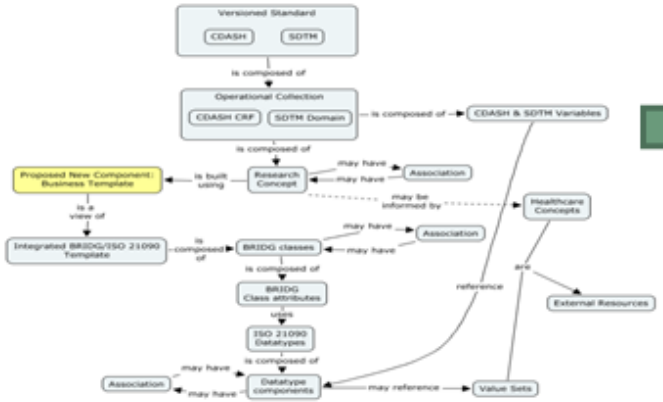
Source: Presentation - J. Evans, Intrachange 2013

SHARE

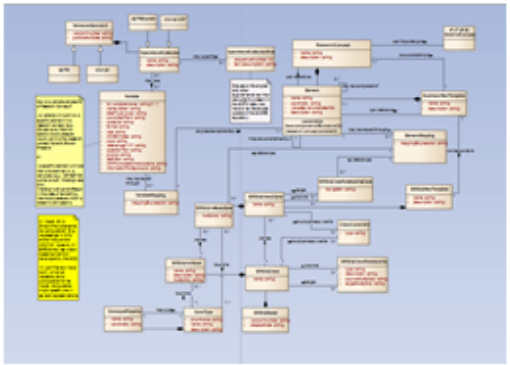
Framework Level 1
2009 - 2013



Framework Level 2
2012-2013



Logical Model
2013



Source: Presentation - J. Evans, Intrachange 2013

→ Deployment is planned for Q1 2014

CFAST (Coalition for Accelerating Standards and Therapies)

CFAST Program Overview – July 2013

Therapeutic Area Standards Under Development

		Coordinating Organization(s)	Stage 0	Stage 1	Stage 2	Stage 3a	Stage 3b	Stage 3c	Issues
		Project Manager	Scoping & Input	Concept Modeling	Standards Development	Internal Review	Public Review	Publication	
Alzheimer's V1.1	●	CPATH/CDISC Jon Neville	Jan	Mar	Jun	*Jul*	*Sep*	*Q313*	
Asthma V1	●	CDISC Rhonda Facile	Jan	Mar	Jun	*Jul*	*Sep*	*Q413*	
Cardiovascular Endpoints V1	●	CDISC/DCRI Amy Palmer	Jun	*Jul*	*Aug*			*Q114*	
Multiple Sclerosis V1	●	CPATH/CDISC Bess Leroy	May	*Aug*	*Jul*			*Q114*	*Concept modeling done prior to standards development step.*
Diabetes V1	●	TCB/CDISC Rachael Zirkle	Mar	*Jun*	*Aug*			*Q114*	
QT Studies V1	●	TCB/CDISC John Owen	*Jul*	*Sep*				*Q214*	
Traumatic Brain Injury V1		CDISC TBD	*Aug*					*Q214*	
Hepatitis C V1		TBD	*Sep*					*Q314*	
Schizophrenia V1		CDISC/DCRI Amy Palmer	*Oct*					*Q314*	
Oncology		TBD	*Oct*						*SAC working to define scope and deliverables.*

Project Status: ● On track ○ At risk ● Critical issues ▭ Stage ongoing ▭ Stage completed *Italics = Projected*

Published Therapeutic Area Standards

Alzheimer's Disease V 1 - Final	Polycystic Kidney Disease V1- Provisional
Pain V1 - Provisional	Tuberculosis V1 - Provisional
Parkinson's Disease V1 - Provisional	Virology V1 - Provisional

Source: Presentation - W. Kubick, Intrachange 2013

CFAST - Deliverables

1. Mindmap visualization of disease area clinical concepts
2. Essential **core** data elements of the disease
3. Definitions
4. Data types (simple & ISO 21090)
5. BRIDG and SDTM mappings
6. SDTM domains and examples
7. Minimum value sets (from code lists)
8. User/Implementation Guide
9. Standard CDASH CRFs with SDTM annotations, as appropriate

More detailed & rigorous development process

- quality checks and gates
  - 3 review cycles
  - SRC final approval

New roles & team organization

- New roles: scoping expert, concept modelers, metadata analyst, clinical experts
- That collaborate with established CDISC teams:
  Terminology, SDS, CDASH, ADaM teams

Questionnaires Sub-Team

- QS Supplement Quarterly Delivery Schedule
  - Approximately 6-10 per quarter
- On the CDISC new term request page a link to the new questionnaire implementation request form is available
- Backlog of 31 questionnaires
  - Backlog needs to be cleared with the help of volunteers
  - A WebEx to train volunteers is planned

CDASH

- CDASH Model to be drafted in Q4 2013
  - Explains what CDASH standard is and how companies can implement themselves

- CDASH Terminology Guidance internal review Q1 2014
  - Develop CRF completion instructions for code lists
  - Goal is to provide terminology guidance for 15-20 codelists in the next CDASH update

- PK Domain → eventually with next CDASH release

- CDASH Device CRFs
  - Volunteers needed

CDASH

- CDASH v1.2 internal review in Q1 2014
  - SDTM 3.1.3 domains
  - Terminology guidance
  - Changes from CDASH v1.1 (comments)
  - PK domain (?)
  - Oncology CRFs (?)

- CDASH v2.0 internal review in Q3 2014
  - SDTM 3.1.4 domains

- CDASH UG 2.0 internal review in Q4 2014

SDS Team

- Clear guidance on preparing proposals for new domains
- Clear guidance on development process (milestones…)
- Ongoing consistency checks
  - E.g. Governance of SDTM separated from IG

- Goal is to have more frequent IG releases
  - Domains become available as soon as they are finished
  - Provisional domains could be tested by the user community: Rules are needed → after SRC approval

- Transparency of comment handling
  - Public Comment Tracker

SDS Team

- SDTM 3.1.4
  - Release as portfolio
  - Domains are inserted in the observation class in alphabetical order
  - Consistent sections within each domain
  - Some domains are released as topic sets (PP/PC, MB/MS, EX/EC)

- CT checks for 3.1.4
- Release: Q4 2013 ?

- 2014 and beyond:
  - Timing variables
  - USUBJID/SUBJID clarifications in DM (proposal in internal review)
  - SUPPQUAL, FA
  - Synchronizing with other teams/initiatives
    - CDISC Teams (CDASH, ADaM, SEND….)
    - TA Projects
    - Other External Teams (PhUSE Validation/Conformance)

SDS Team

- SDTM 3.1.4
  - Release as portfolio
  - Domains are inserted within the observation class in alphabetical order
  - Consistent sections within each domain
  - Some domains are released as topic sets (PP/PC, MB/MS, EX/EC)

SDTM 1.4	SDTM IG 3.1.4
SDTM 1.3	SDTMIG 3.1.3
New Device variables	Death Details (DD)
New EX variables	Exposure as Collected (EC) and EX enhancements
Associated Person IG	Healthcare Encounters (HO)
	Immunogenicity domains (IS/SR)
	Microscopic Findings (MI)
	Morphology (MO)
	Procedures (PR)
	Reproductive System Findings (RP)
	Subject Status (SS)
	Associated Person IG (AP IG)
	Virology User Guide (VR, VF, VP)
	Trial Disease Assessments (TD)

SDS Team

SDTM 1.5	SDTM IG 3.1.5
SDTM 1.4	SDTMIG 3.1.4
SDTM Timing Variables	Cardiovascular (CV)
	Lesion Attributes (LA)
	Nervous System (NV)
	Respiratory Measurements (RE)
	Urinary System (UR)
	FA Model Clarification
	SUPPQUAL - Supplemental Qualifiers Public Proposal
	Updates to existing domains: PC, CM, QS

Science For A Better Life

Thank you!