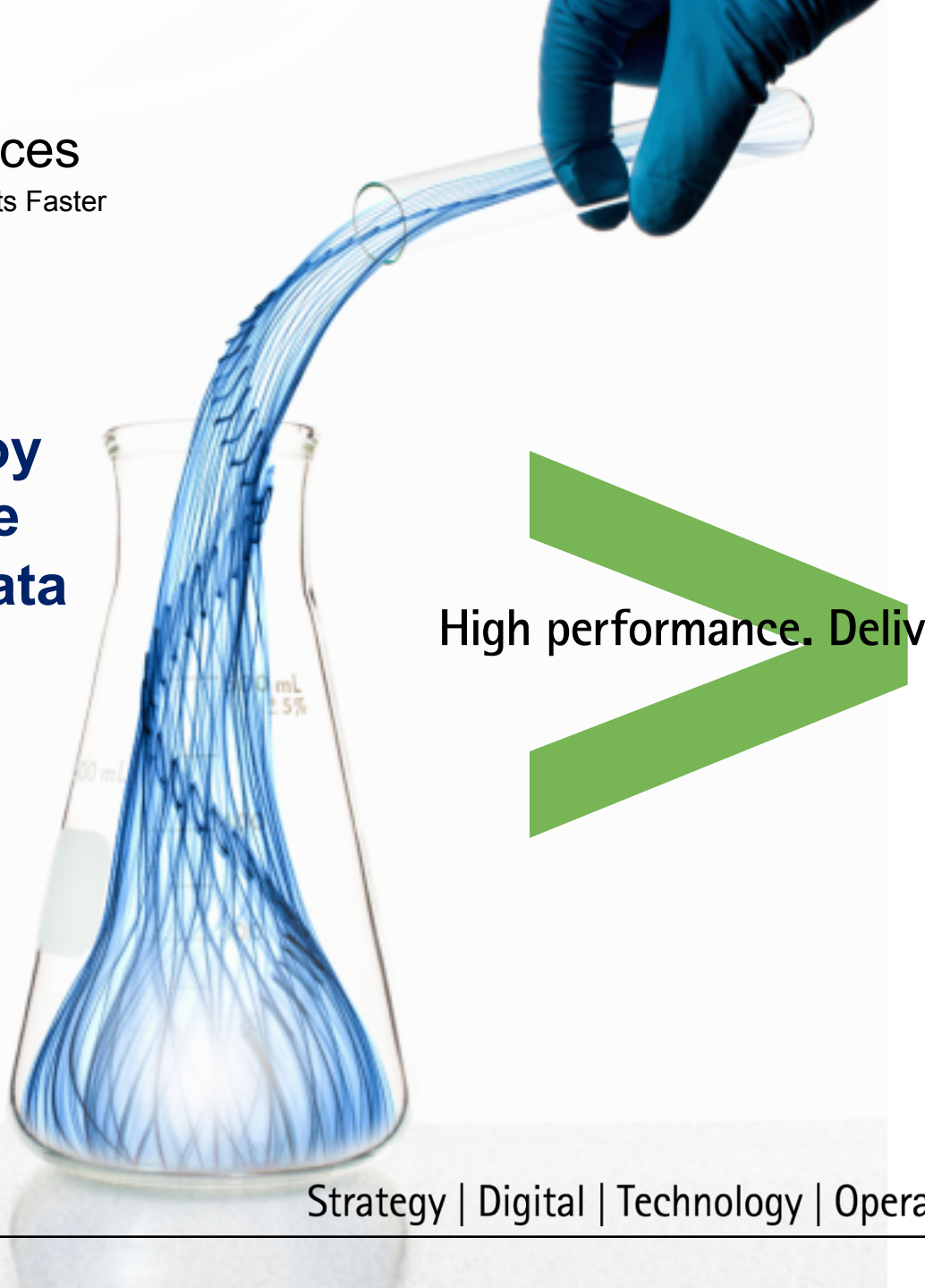
Life Sciences

Accelerated R&D Services

The Science of Getting Products to Patients Faster



Tools to Plan, Deploy & Document the Use of FDA Endorsed Data Standards

PhUSE Philly SDE
16 July 2015

High performance. Delivered.

accenture

Strategy | Digital | Technology | Operations

Goal for This Presentation

Get to know these four tools

- Study Data Standardization Plan
- Study Data Reviewer's Guide
- Analysis Data Reviewer's Guide
- Legacy Data Conversion Plan & Report

Food & Drug Administration Safety & Innovation Act (FDASIA)

Food and Drug Administration Safety and Innovation Act (FDASIA)

The Food and Drug Administration Safety and Innovation Act (FDASIA), signed into law on July 9, 2012, expands the FDA's authorities and strengthens the agency's ability to safeguard and advance public health by:

- **Giving the authority to collect user fees** from industry to fund reviews of innovator drugs, medical devices, generic drugs and biosimilar biological products;
- **Promoting innovation** to speed patient access to safe and effective products;
- **Increasing stakeholder involvement** in FDA processes; and
- **Enhancing the safety of the drug supply chain.**

To help the public keep track of the agency's progress on these and other provisions, we've established a 3-year implementation plan, which is planned to be updated on a monthly basis.

User Fees

FDASIA includes the fifth authorization of the Prescription Drug User Fee Act (PDUFA), first enacted in 1992, and the third authorization of the Medical Device User Fee Act (MDUFA), first enacted in 2002. Both programs have provided steady and reliable funding to maintain and support a staff of trained reviewers who must determine whether a proposed new product is safe and effective for patients within a certain time period. The new user fee programs for generic drugs and biosimilar biological products build on the successes of these two established user fee programs.

- Prescription drug provisions (PDUFA V)
- Medical device provisions (MDUFA III)
- Generic Drug User Fee Amendments of 2012 (GDUFA)
- Biosimilar User Fee Act (BsUFA)

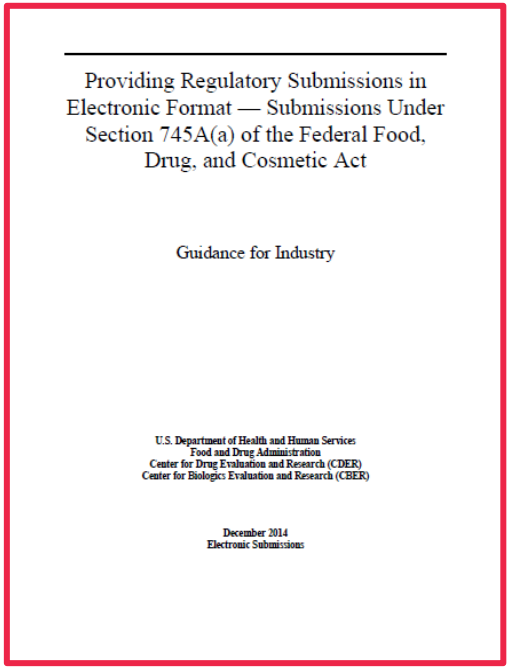
Prescriptions Drug User Fee Act (PDUFA) V

PDUFA V
Information Technology/Informatics Plan
FY 2013 – FY 2017

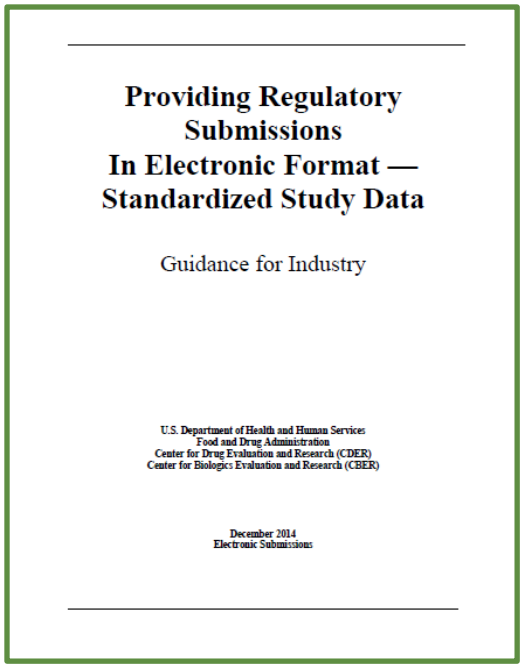
September 2014

Objective(s)	Milestones	FY13 Q1	FY13 Q2	FY13 Q3	FY13 Q4	FY14 Q1	FY14 Q2	FY14 Q3	FY14 Q4	FY15 Q1	FY15 Q2	FY15 Q3	FY15 Q4
Objective 1: Require the electronic submission of data in standardized formats.	**Milestone 1.1:** Publish final guidance requiring regulatory submissions in electronic format — Submissions Under Section 745A(a).										▼		
	Milestone1.2: Publish final guidance requiring regulatory submissions in electronic format — Standardized Study Data.										▼		
	Milestone 1.3: Publish final Data Standards Catalog.										▼		
	Milestone 1.4: Publish final Study Data Technical Conformance Guide.										▼		
	Milestone 1.5: Publish therapeutic area standards Initiative Project plan, v2.0, for public comment.							▼					
	Milestone 1.6: Require NDA, certain BLA, and ANDA submissions of data in standardized formats.											✸	

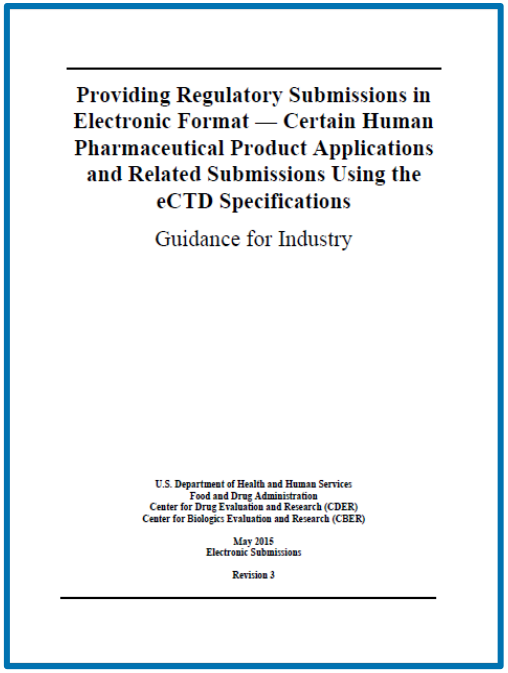
Binding Guidance Documents



Guidance for Industry:
Providing Regulatory Submissions in Electronic Format – Submissions Under Section 745A (a) of the Federal Food Drug, and Cosmetic Act

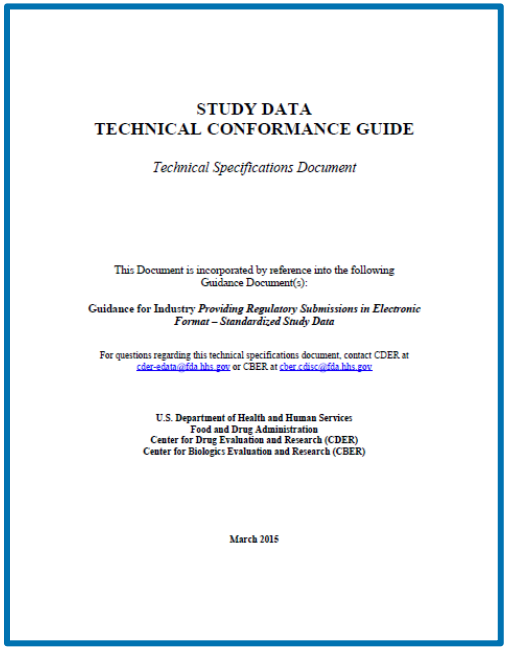


Guidance for Industry:
Providing Regulatory Submissions in Electronic Format – Standardized Study Data



Guidance for Industry:
Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

Companion Documents



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*

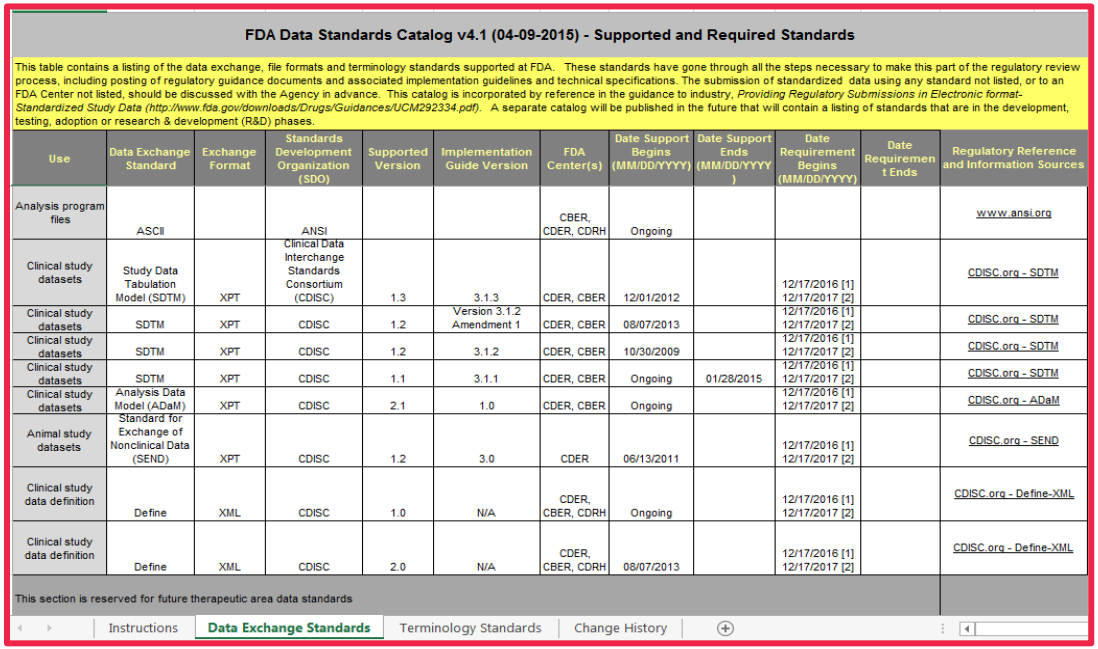
For questions regarding this technical specifications document, contact CDER at cder-edata@fda.hhs.gov or CBER at cber.cdisc@fda.hhs.gov

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)

March 2015

Study Data Technical Conformance Guide

Technical Specifications Document



FDA Data Standards Catalog v4.1 (04-09-2015) - Supported and Required Standards

This table contains a listing of the data exchange, file formats and terminology standards supported at FDA. These standards have gone through all the steps necessary to make this part of the regulatory review process, including posting of regulatory guidance documents and associated implementation guidelines and technical specifications. The submission of standardized data using any standard not listed, or to an FDA Center not listed, should be discussed with the Agency in advance. This catalog is incorporated by reference in the guidance to industry, *Providing Regulatory Submissions in Electronic format-Standardized Study Data (http://www.fda.gov/downloads/Drugs/Guidances/UCM292334.pdf)*. A separate catalog will be published in the future that will contain a listing of standards that are in the development, testing, adoption or research & development (R&D) phases.

Use	Data Exchange Standard	Exchange Format	Standards Development Organization (SDO)	Supported Version	Implementation Guide Version	FDA Center(s)	Date Support Begins (MM/DD/YYYY)	Date Support Ends (MM/DD/YYYY)	Date Requirement Begins (MM/DD/YYYY)	Date Requirement Ends	Regulatory Reference and Information Sources
Analysis program files	ASCII		ANSI			CBER, CDER, CDRH	Ongoing				www.ansi.org
Clinical study datasets	Study Data Tabulation Model (SDTM)	XPT	Clinical Data Interchange Standards Consortium (CDISC)	1.3	3.1.3	CDER, CBER	12/01/2012		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.2	Version 3.1.2 Amendment 1	CDER, CBER	08/07/2013		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.2	3.1.2	CDER, CBER	10/30/2009		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.1	3.1.1	CDER, CBER	Ongoing	01/28/2015	12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	Analysis Data Model (ADaM)	XPT	CDISC	2.1	1.0	CDER, CBER	Ongoing		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - ADaM
Animal study datasets	Standard for Exchange of Nonclinical Data (SEND)	XPT	CDISC	1.2	3.0	CDER	06/13/2011		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SEND
Clinical study data definition	Define	XML	CDISC	1.0	N/A	CDER, CBER, CDRH	Ongoing		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - Define-XML
Clinical study data definition	Define	XML	CDISC	2.0	N/A	CDER, CBER, CDRH	08/07/2013		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - Define-XML
This section is reserved for future therapeutic area data standards											

Instructions | Data Exchange Standards | Terminology Standards | Change History

Data Standards Catalog

Guidance for Industry
Submissions Under 745A(a)

- Binding guidance is coming (and, BTW, its here…)
  - Requirement to submit electronically based on eCTD specifications (finalized May 5, 2015)
  - Requirement to initiate trials based on FDA recognized data standards (finalized December 17, 2014)
- Waiver criteria will be articulated in individual guidances
- Scope of submission types
  - NDAs, ANDAs, BLAs, INDs
- Out of scope
  - Non-commercial INDs
  - BLA/device combos designed to test/screen blood donations

Guidance for Industry
Human Pharmaceutical Product Applications
Using eCTD Specifications

- Reiterates scope of submission types that must follow this guidance
- Submission of data and related documentation
  - Highlights sections of eCTD (3,4,5) where data can be included in a submission
  - Reinforces appropriate use of study tagging files to identify type and role of data
  - Calls out to the Standardized Study Data guidance document for information about submitting clinical and non-clinical data
- Useful appendix of additional resources & guidance documents related to utilizing eCTD

Guidance for Industry
Standardized Study Data

- Clarifies…
  - When you will be required to initiate studies based on FDA recognized data standards
    - 24 months – NDAs, ANDAs, BLAs (clinical studies)
    - 36 months – INDs (non-clinical studies)
  - VERY high level summary of
    - Study data exchange formats
    - Study data exchange standards
    - Terminology

Data Standards Catalog
Data Exchange Standards

FDA Data Standards Catalog v4.1 (04-09-2015) - Supported and Required Standards

This table contains a listing of the data exchange, file formats and terminology standards supported at FDA. These standards have gone through all the steps necessary to make this part of the regulatory review process, including posting of regulatory guidance documents and associated implementation guidelines and technical specifications. The submission of standardized data using any standard not listed, or to an FDA Center not listed, should be discussed with the Agency in advance. This catalog is incorporated by reference in the guidance to industry, *Providing Regulatory Submissions in Electronic format- Standardized Study Data (http://www.fda.gov/downloads/Drugs/Guidances/UCM292334.pdf)*. A separate catalog will be published in the future that will contain a listing of standards that are in the development, testing, adoption or research & development (R&D) phases.

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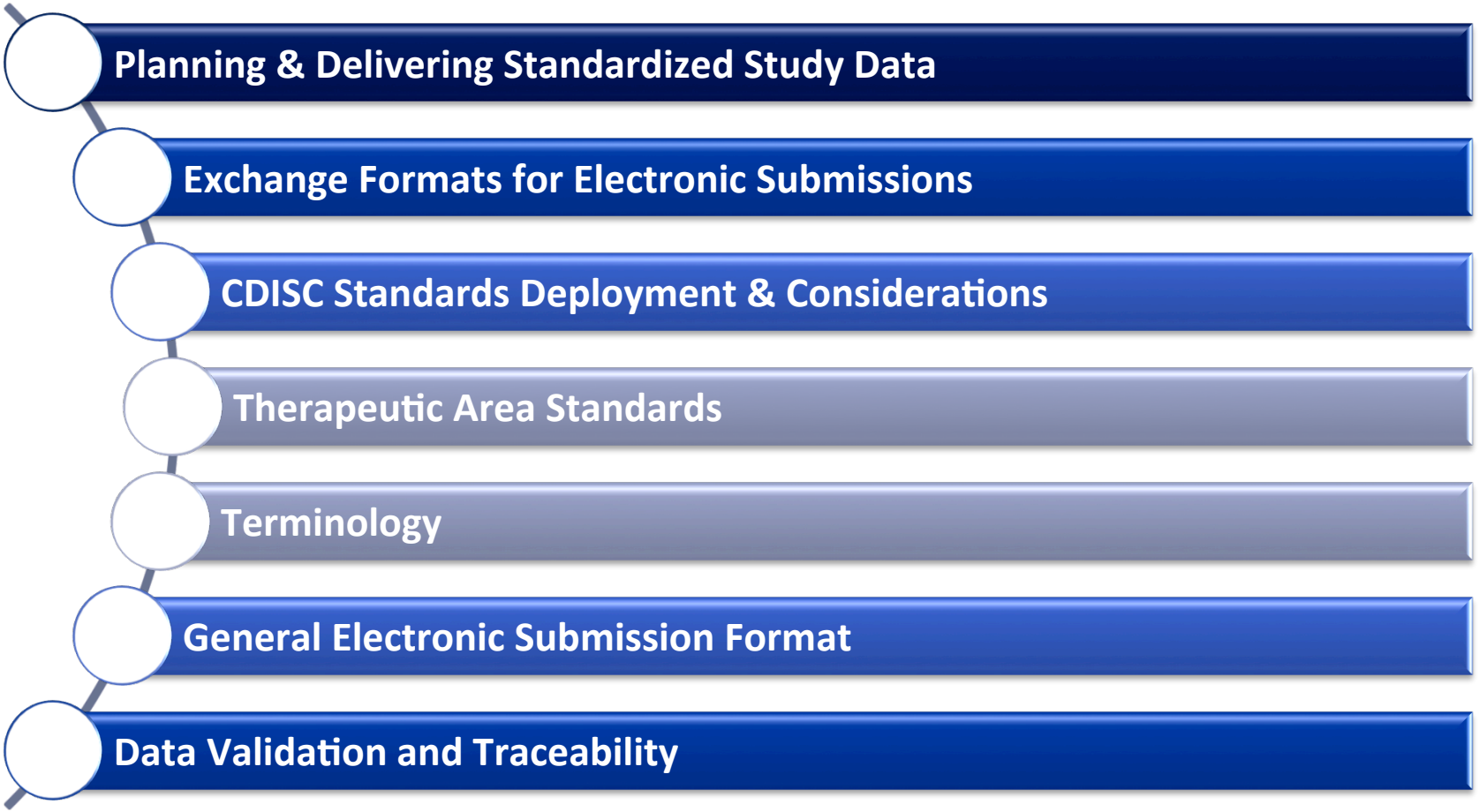
Clinical study datasets	SDTM	XPT	CDISC	1.2	Version 3.1.2 Amendment 1	CDER, CBER	08/07/2013		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.2	3.1.2	CDER, CBER	10/30/2009		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.1	3.1.1	CDER, CBER	Ongoing	01/28/2015	12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	Analysis Data Model (ADaM)	XPT	CDISC	2.1	1.0	CDER, CBER	Ongoing		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - ADaM
Animal study datasets	Standard for Exchange of Nonclinical Data (SEND)	XPT	CDISC	1.2	3.0	CDER	06/13/2011		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SEND
Clinical study data definition	Define	XML	CDISC	1.0	N/A	CDER, CBER, CDRH	Ongoing		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - Define-XML
Clinical study data definition	Define	XML	CDISC	2.0	N/A	CDER, CBER, CDRH	08/07/2013		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - Define-XML

Study Data Technical Conformance Guide Organization



Study Data Technical Conformance Guide
Section 2: Study Data Standardization Plan

- Content
  - List of planned studies
  - Study Phase
  - Study Design
  - Planned used of standards
  - Justification for not using standards

(Study Data TCG, Section 2.1, list below 1st paragraph)

- Development & Maintenance
  - Prepare & include as part of IND
  - Discuss as early as Pre-IND
  - Update / submit as additional studies are planned

(Study Data TCG, Section 2.1, 1st & 3rd paragraphs)

NOTE: No required frequency of providing plan updates is specified, but implication is that it is your responsibility to keep FDA informed if you don't want surprises

Study Data Technical Conformance Guide
Section 2: Study Data Standardization Plan

- Recommendations for preparation… (Study Data TCG, Section 2.1, 2nd paragraph)

  http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm

3. **Study Data Technical Conformance Guide v2.2.** Click here to access the Guide. This Guide provides technical specifications, recommendations, and general considerations on how to submit standardized electronic study data.

   3a. Recommendations for Preparing a Study Data Standardization Plan (click here)

4. **Study Data Validation Rules**

   4a. FDA Specific SEND Validation Rules

CDER / CBER
Study Data Standardization Plan Recommendations

ABC Pharma Company

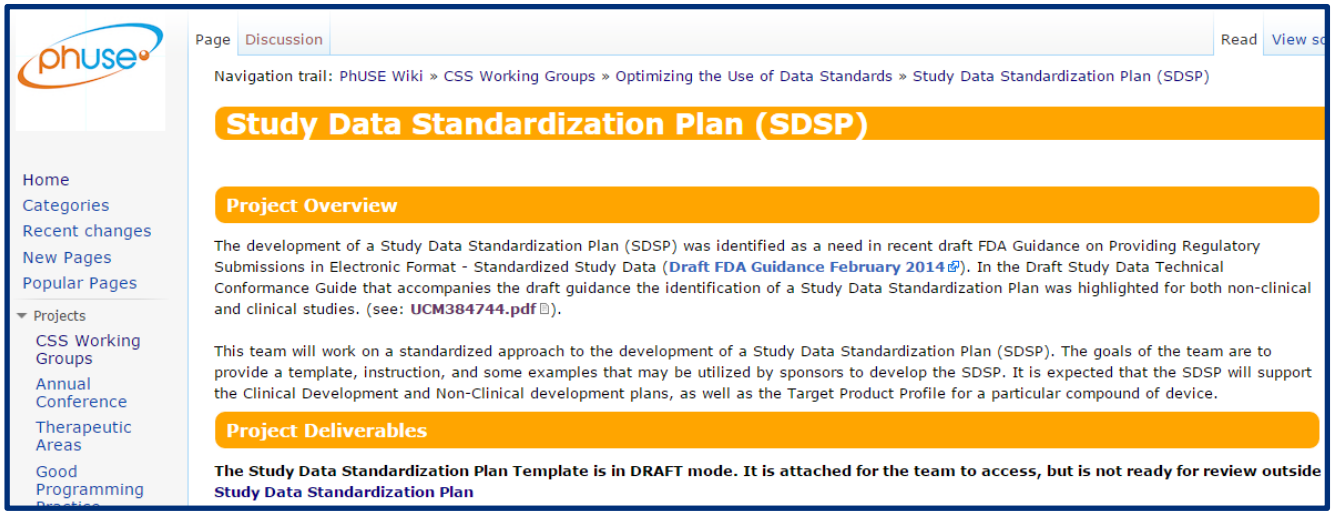
Study Data Standardization Plan

1. General Sponsor Information

Name of Product	SuperDrug
Indication(s)	Hypertension
IND	054321
Sponsor Name	ABC Pharma
Sponsor Contact	Joe Smith
Sponsor Contact Email	Joe.Smith@abcpharma.com

Study Data Standardization Plan
PhUSE Resources

http://www.phusewiki.org/wiki/index.php?title=Study_Data_Standardization_Plan_(SDSP)



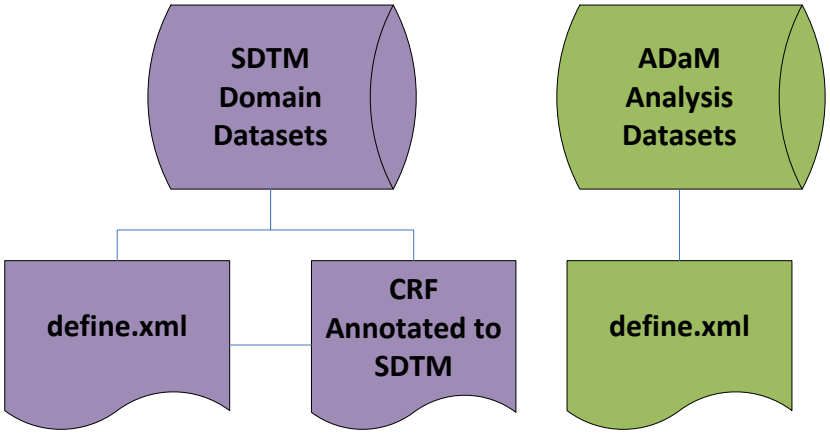
- Objectives w/ timelines
- Team members
- Meeting minutes

and…

- A template

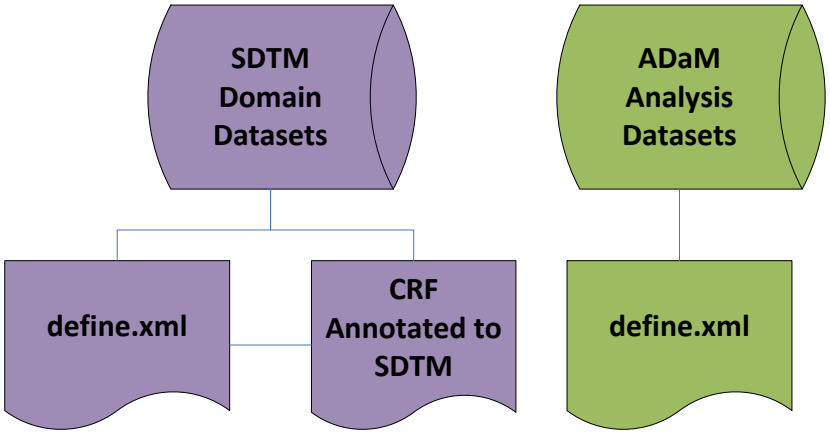
Scope of Standardized Study Data Requirement

- Tabulation datasets for clinical and non-clinical studies
- Analysis datasets for clinical studies
  - Study Data TCG, Section 4.1, 2nd paragraph



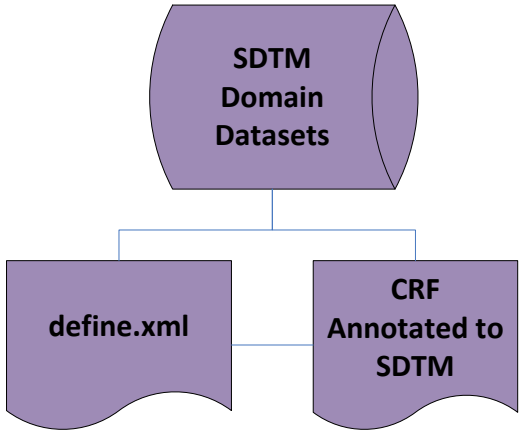
Specific Standards

- CDISC SDTM w/ SDTM IG for clinical tabulation datasets
- CDISC SDTM w/ SEND IG for non-clinical tabulation datasets
- CDISC ADaM w/ ADaM IG for clinical analysis datasets
  - Study Data TCG, Sections 4.1.1-3.1



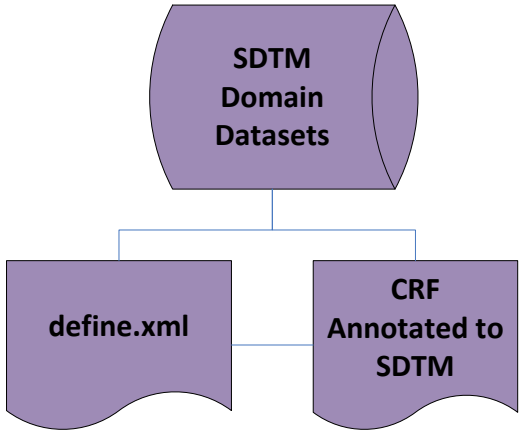
Tabulation Submission Data Package

- SDTM domain datasets
  - Prepared based on the SDTM IG (Study Data TCG, Section 4.1.1.1) for clinical data
  - Prepared based on the SEND IG (Study Data TCG, Section 4.1.3.1) for non-clinical data
  - Delivered as SAS transport (XPT) files (Study Data TCG, Section 3.3.1)



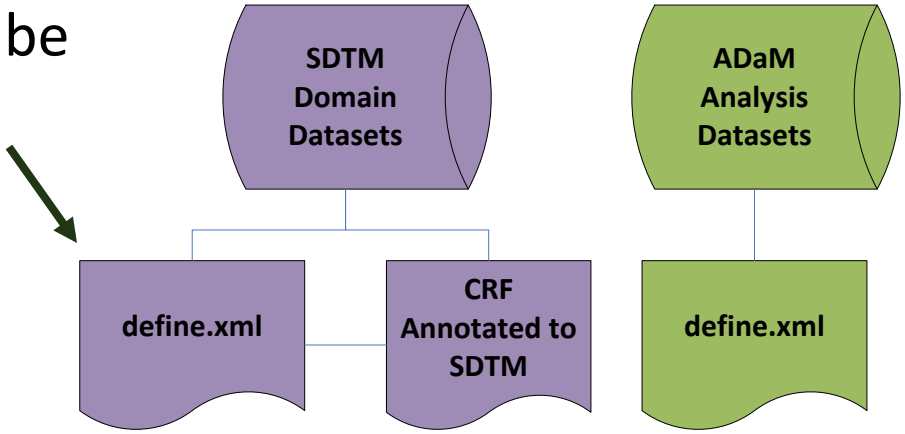
Tabulation Submission Data Package

- A data definition file in define.xml format (Study Data TCG, Section 4.1.4.5)
- A blank case report form (CRF) annotated to the tabulation data for clinical studies (Study Data TCG, Section 4.1.4.6)
- A Study Data Reviewer's Guide (Study Data TCG, Section 2.2)



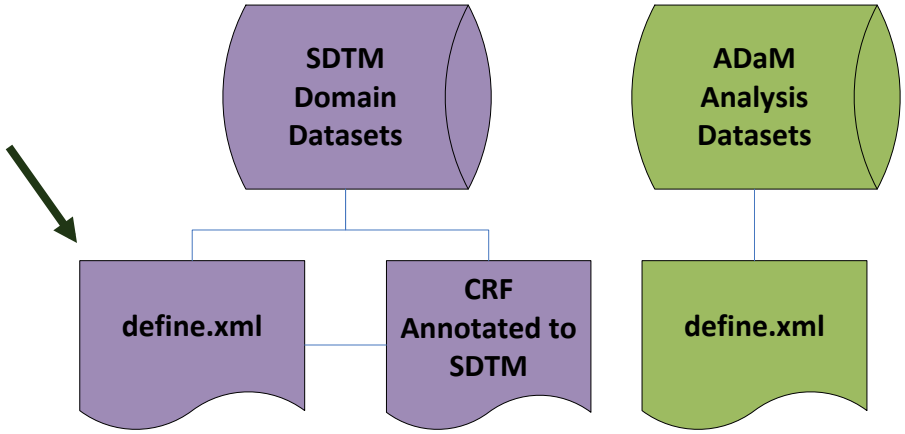
Study Data Technical Conformance Guide
Section 2: Study Data Reviewer's Guide

- Describe any special considerations or directions that may facilitate an FDA reviewer's use of the submitted data
- Help the reviewer understand the relationship between the study report and the case report tabulation data
  - Study Data TCG, Section 2.2, 1st paragraph
- The Study Data TCG does not define a specific template for the Study Data Reviewer's Guide, but an example of a Study Data Reviewer's Guide, including a template, completion guidelines and examples, can be found on the PhUSE website (Study Data TCG, footnote #11 at bottom of Page 4)



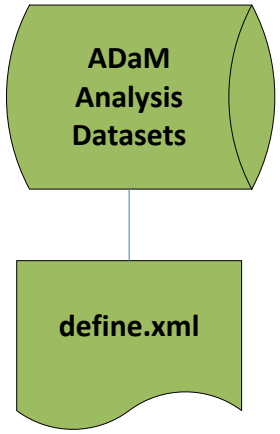
Study Data Technical Conformance Guide
Section 2: Study Data Reviewer's Guide

- If submitting to CBER you need to continue to prepare the Data Interpretation and Validation Report (DIVR). It should be incorporated into the Study Data Reviewer's Guide. Information on the DIVR can be found at http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/ucm209137.htm (Study Data TCG, Footnote #11 on bottom of Page 4)



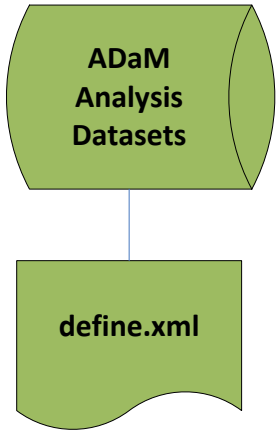
Analysis Submission Data Package

- Analysis datasets
  - Prepared based on the ADaM IG (Study Data TCG, Section 4.1.2.1, also Standardized Study Data, Section II.C.2) as well as other necessary analysis datasets (Study Data TCG, Section 4.1.2.2)
  - Delivered as SAS transport (XPT) files (Study Data TCG, Section 3.3.1, also Standardized Study Data, Section II.C.1)



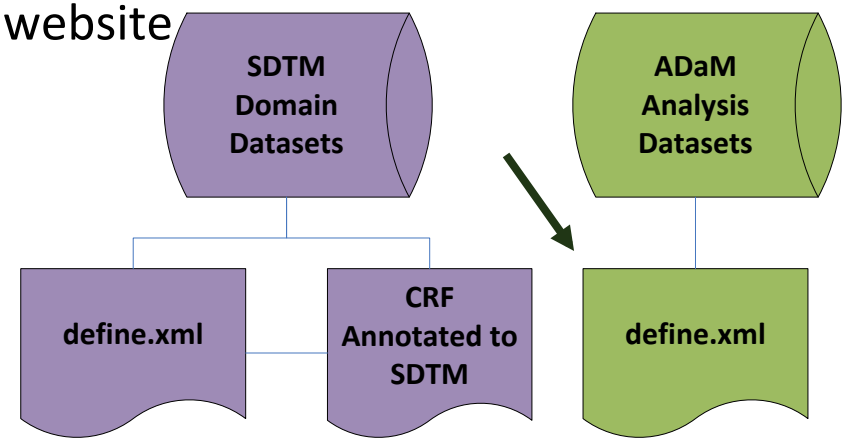
Analysis Submission Data Package

- A data definition file in define.xml format (Study Data TCG, Section 4.1.4.5)
- An Analysis Data Reviewer's Guide (Study Data TCG, Section 2.3)
- Software programs used to create all of the analysis datasets as well as software programs used to create tables & figures for primary & secondary endpoints (Study Data TCG, Section 4.1.2.8)



Study Data Technical Conformance Guide
Section 2: Analysis Data Reviewer's Guide

- Provides the FDA reviewers with context for analysis datasets and terminology
- Purposefully duplicates limited information found in other submission documents in order to provide FDA reviewers with a single point of orientation to the analysis datasets
  - (Study Data TCG, Section 2.3, 1st paragraph)
- The Study Data TCG does not define a specific template for the Analysis Data Reviewer's Guide, but an example of an Analysis Data Reviewer's Guide, including a template, completion guidelines and examples, can be found on the PhUSE website
  - (Study Data TCG, footnote #13 at bottom of page 5)



Study Data Technical Conformance Guide
Section 8: Traceability & Legacy Data Conversion

- Traceability is important
  (Study Data TCG, Section 8.3.1, 1st paragraph)
- For a period of time, as sponsors move from legacy data collection to the use of FDA endorsed data standards, you might have to perform legacy data conversion
  (Study Data TCG, Section 8.3.1, 3rd paragraph)
- Traceability can be difficult if not impossible to establish when performing legacy data conversion
  (Study Data TCG, Section 8.3.1, 2nd paragraph)

Study Data Technical Conformance Guide
Section 8: Traceability & Legacy Data Conversion

In order to mitigate risk associated with legacy data conversion, sponsors should:

- Prepare and submit a Legacy Data Conversion Plan & Report (Study Data TCG, Section 8.3.2.2, item #1 under the 1st paragraph)
  - A template with completion guidelines and examples is under development by PhUSE as part of the PhUSE/FDA CSS Working Groups Initiative and should be available by the end of 2015.
- Incorporate the Legacy Data Conversion Plan & Report into the Study Data Reviewer's Guide in order to record significant data issues, clarification and explanations of traceability (Study Data TCG, Section 8.3.2.2, item #3 under the 1st paragraph)
- Prepare and submit a CRF annotated to the legacy source data (Study Data TCG, Section 8.3.2.2, item #2 under the 1st paragraph)
- Prepare and submit the legacy data (Study Data TCG, Sections 8.3.2, 1st paragraph, and 8.3.2.2, item #4 under the 1st paragraph)

Opportunity Following This Presentation

Continue your education on these four tools

- Study Data Standardization Plan
- Study Data Reviewer's Guide
- Analysis Data Reviewer's Guide
- Legacy Data Conversion Plan & Report

http://www.phusewiki.org/wiki/index.php?title=Optimizing_the_Use_of_Data_Standards

Life Sciences

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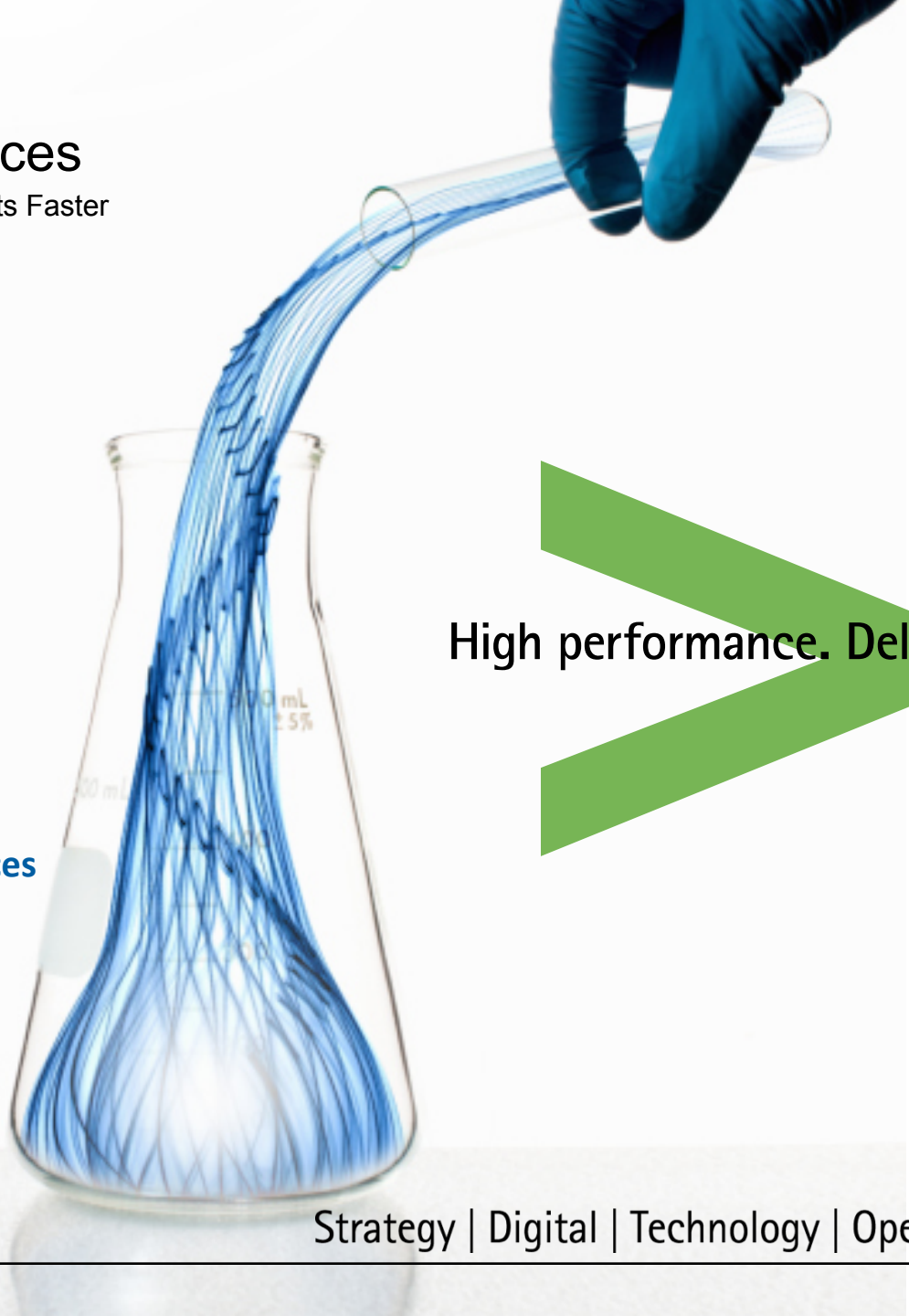


Thank you!

High performance. Delivered.

For further information:

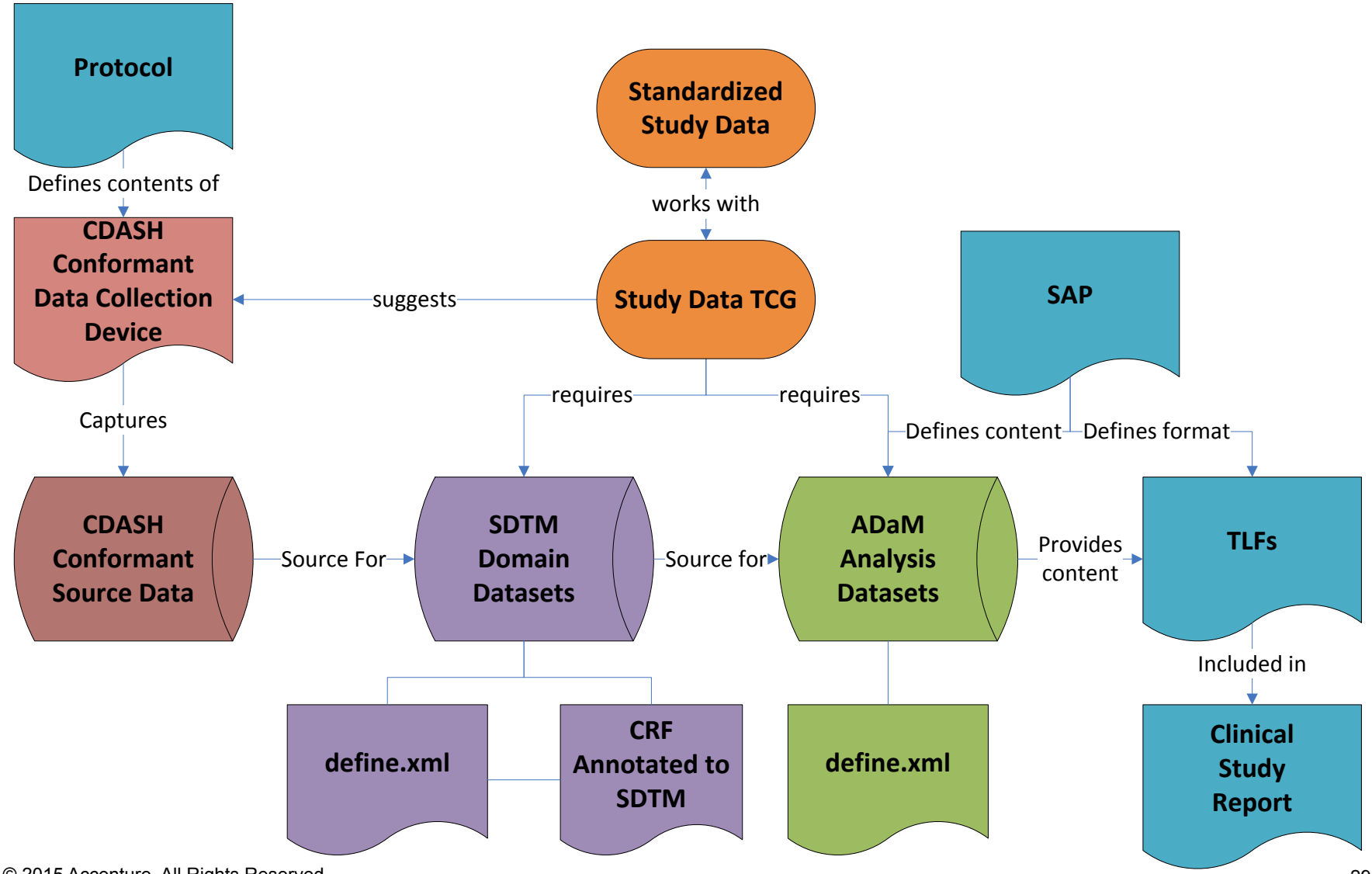
David C. Izard
Clinical Data Consulting Lead
Accenture Accelerated R&D Services
1160 Swedesford Road
Berwyn, PA 19312
m: (484) 467-0193
david.c.izard@accenture.com

accenture

Strategy | Digital | Technology | Operations

Backup Slides

Clinical Data Flow



Study Data Technical Conformance Guide
Key Messages