Electronic Submissions - The Requirement for Standardized Study Data

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FDA Webinar

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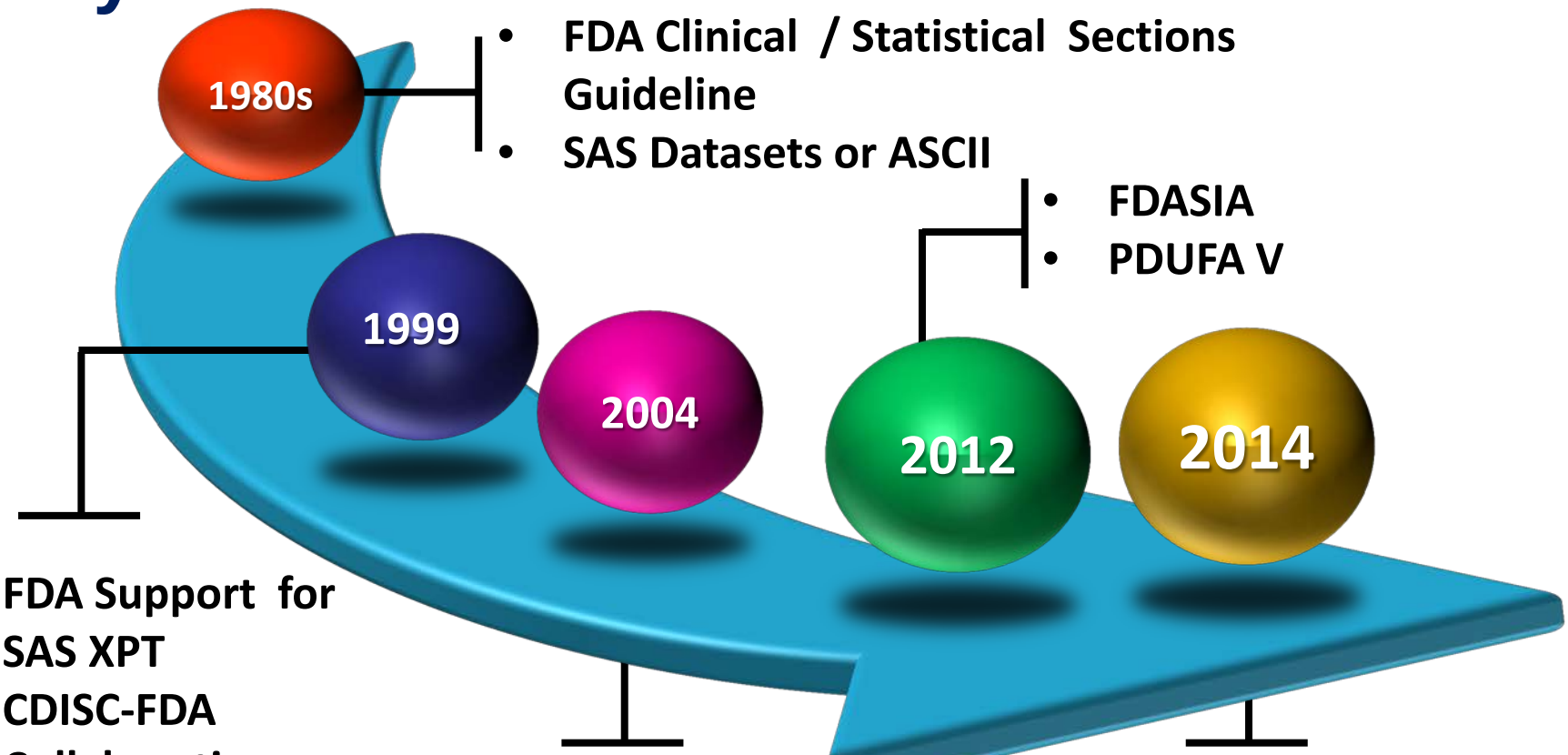
Path to Electronic Standardized Study Data



- FDA Clinical / Statistical Sections Guideline
- SAS Datasets or ASCII

- FDASIA
- PDUFA V

- FDA Support for SAS XPT
- CDISC-FDA Collaboration

- FDA Support for CDISC Submissions

- Final 745A(a) Guidance
- Final eStudy Data Guidance
- Tech Conformance Guide

Value Proposition for Study Data Standards

Predictability

CDISC

Traceability

Replication

Aggregation

Tools

Interchange

Data Quality
Transparency
Interoperability

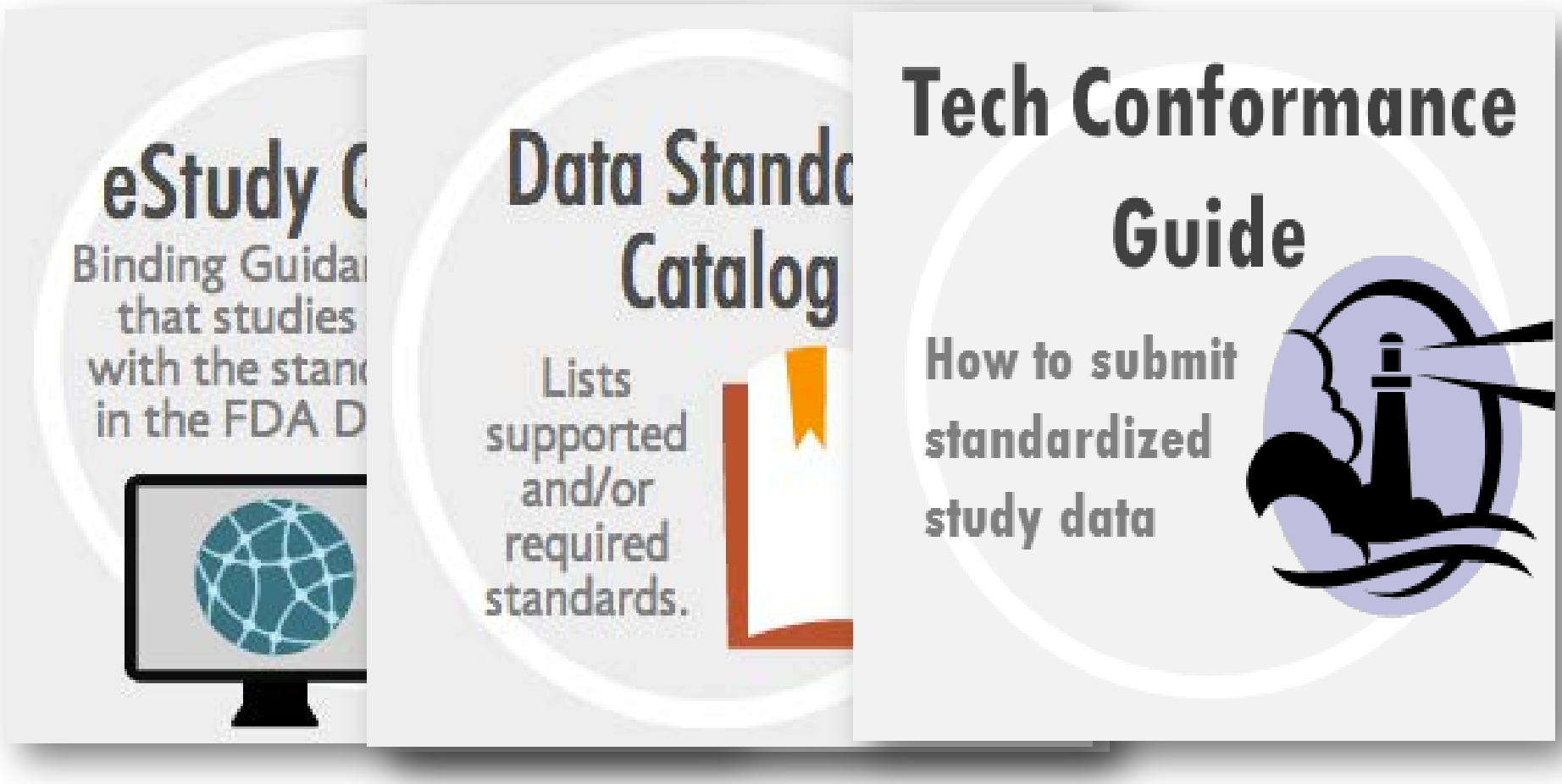
Improve Efficiency & Decision-making

FY2013, FY2014, FY2015(Q1)
Number (%) of NDAs with Study Data Submissions in CDISC SDTM*

Fiscal Year	# of Submissions	% with CDISC SDTM
2013	223	**55 %**
2014	233	**64 %**
2015 (Q1)	66	**69 %**

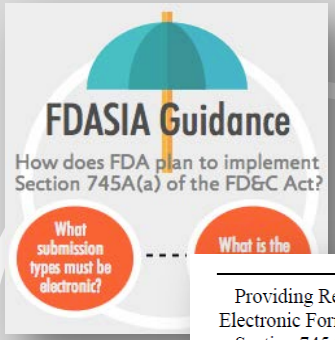
*Source: Office of Business Informatics, CDER - **One or more** explicitly stated SDTM studies (or study data structure that resembled SDTM).

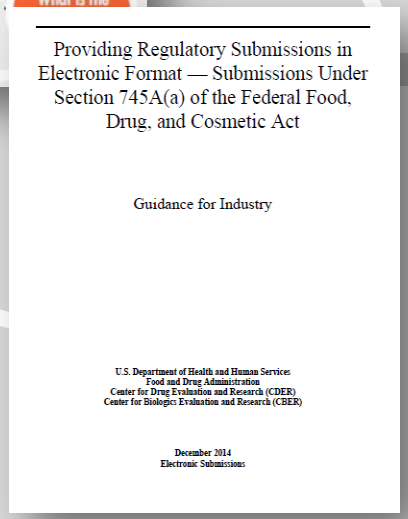
Binding Guidances
Standards Catalog & Tech Guide



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

How will eSubmissions be Implemented?




Providing Regulatory Submissions in Electronic Format — Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

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)

December 2014
Electronic Submissions

Final Published December, 2014

No earlier than 24 Months

Framework for Submissions in Electronic Format

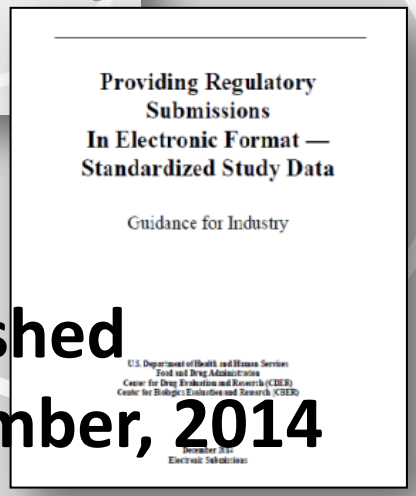
Individual Guidances

NDAs, ANDAs, BLAs, INDs

- Timetable
- Content
- Format

When will Study Data Standards be Required?

eStudy Guidance
Binding Guidance– Requires that studies are compliant with the standards outlined in the FDA Data Standards Catalog



Final Published December, 2014

December 2014

24 Months*

December 2016

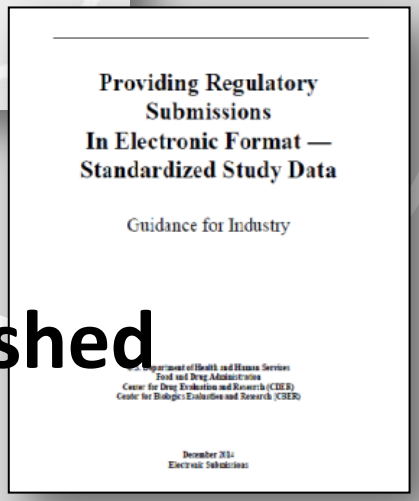
Compliance

Studies starting after MUST use the standards in the Data Catalog (NDAs, ANDAs, BLAs)**

*36 months for INDs **Study Start Date in the SDTM Trial Summary Domain (TSPARMCD = SSTDTC).

What Study Data Standards will be Required?

eStudy Guidance
Binding Guidance– Requires that studies are compliant with the standards outlined in the FDA Data Standards Catalog


Providing Regulatory Submissions In Electronic Format — Standardized Study Data

Guidance for Industry

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

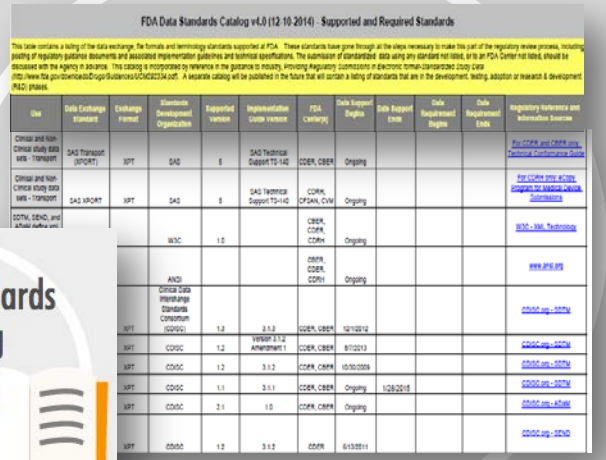
December 2014
Electronic Submissions

Final Published

December 2016

Data Standards Catalog

Study Data….SDTM, ADaM, SEND, Define.XML


FDA Data Standards Catalog v4.0 (12-10-2014) - 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 in 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	Supported Version	Implementation Guide Version	FDA Center(s)	Date Support Begins	Date Support Ends	Date Requirement Begins	Date Requirement Ends	Regulatory Reference and Information Sources
Clinical and Non-Clinical study data sets - transport	SAS Transport (XPORT)	XPT	SAS	5	SAS Technical Support TS-140	CDER, CBER	Ongoing				For CDER and CBER see "Technical Conformance Guide"
Clinical and Non-Clinical study data sets - transport	SAS XPORT	XPT	SAS	5	SAS Technical Support TS-140	CDRH, CFSAN, CVM	Ongoing				For CDRH only: eCOA program for standard device submissions
SDTM, SEND, and ADaM define.xml			W3C	1.0		CBER, CDER, CDRH	Ongoing				W3C - XML Technology
			ANSI			CBER, CDER, CDRH	Ongoing				www.ansi.org
	XPT	Clinical Data Interchange Standards Consortium (CDISC)		1.2	3.1.3	CDER, CBER	12/17/2012				CDISC.org - SDTM
	XPT	CDISC		1.2	Version 3.1.2 Amendment 1	CDER, CBER	8/7/2013				CDISC.org - SDTM
	XPT	CDISC		1.2	3.1.2	CDER, CBER	10/30/2009				CDISC.org - SDTM
	XPT	CDISC		1.1	3.1.1	CDER, CBER	Ongoing	11/28/2015			CDISC.org - SDTM
	XPT	CDISC		2.1	1.0	CDER, CBER	Ongoing				CDISC.org - ADaM
	XPT	CDISC		1.2	3.1.3	CDER	6/15/2011				CDISC.org - SEND

Data Standards Catalog
Lists supported and/or required standards.

What Study Data Standards will be Required?

Data Standards Catalog

FDA Data Standards Catalog v4.0 (12-10-2014) - Supported and Required Standards

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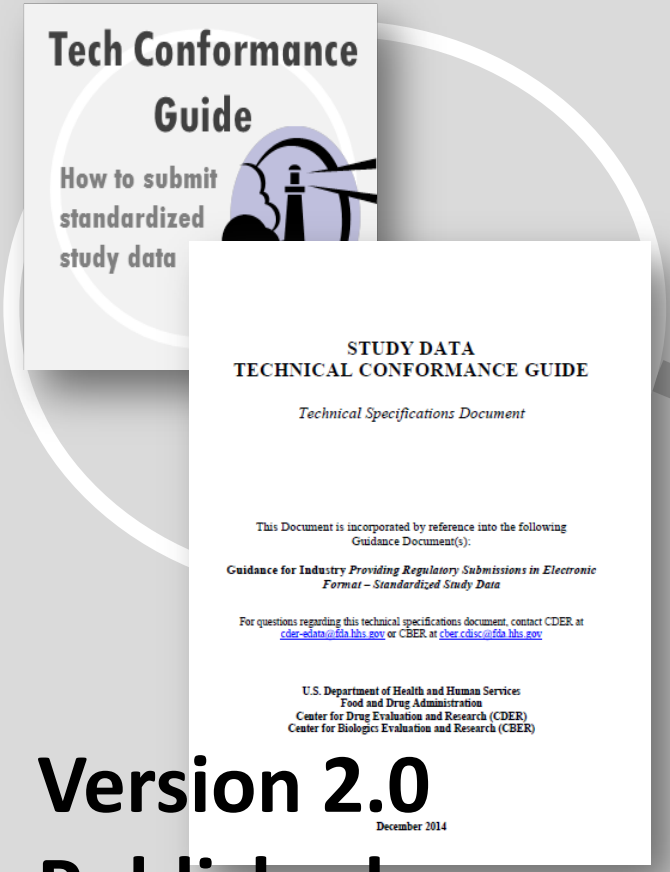
Clinical and Non-Clinical study data sets - Transport	SAS XPORT	XPT	SAS	5	SAS Technical Support TS-140	CDRH, CFSAN, CVM	Ongoing				For CDRH only: eCopy Program for Medical Device Submissions
SDTM, SEND, and ADaM define.xml file	XML		W3C	1.0		CBER, CDER, CDRH	Ongoing				W3C - XML Technology
Analysis program 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	12/1/2012				CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.2	Version 3.1.2 Amendment 1	CDER, CBER	8/7/2013				CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.2	3.1.2	CDER, CBER	10/30/2009				CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.1	3.1.1	CDER, CBER	Ongoing	1/28/2015			CDISC.org - SDTM
Clinical study datasets	Analysis Data Model (ADaM)	XPT	CDISC	2.1	1.0	CDER, CBER	Ongoing				CDISC.org - ADaM
Animal study datasets	Standard for Exchange of Nonclinical Data (SEND)	XPT	CDISC	1.2	3.1.2	CDER	6/13/2011				CDISC.org - SEND

How Study Data Standards will Be Required?



Version 2.0 Published

Use it NOW

Technical Conformance Guide (non-binding)

- Study Data Standardization Plan
- Analysis Data Reviewer's Guide
- Study Data Reviewer's Guide
- SDTM Domain Specs
- Exchange Formats
- File Transport
- SDTM General Considerations
- Efficacy, Safety, Timing Variables
- SEND Domain Specs
- ADaM Domain Specs
- Controlled Terminologies
- Therapeutic Area Standards
- Data Validation & Traceability
- Elect Sub Format

Timetable for New Study Data Standards

Transition Date

Beginning Date of Implementation Period
(Not the Requirement Date)

March 15th

Transition Date is the next March 15th… *always*… following FRN

So…an Example

Sept 5, 2018

FRN - New standard

Transition Date is March 15, 2019

Requirement Date

In Submissions* for studies that start** 24 Months after transition date or
March 15, 2021

*NDAs, BLAs, ANDAs, **Earliest date of informed consent among any subject that enrolled in the study. Study Start Date in the SDTM Trial Summary Domain (TSPARMCD SSTDTC).

Timetable for Version Updates to Study Data Standards

Example

SDO Releases Version Update	Date Released by SDO (yyyy-mm-dd)	FR Notice of FDA Support (yyyy-mm-dd)	Update Data Standards Catalog (yyyy-mm-dd)	Transition Date (yyyy-mm-dd)	Date Requirement Begins (yyyy-mm-dd)
SDTM 4.1	2016-02-15	2016-05-06	2016-05-06	2017-03-15	2018-03-15
SEND 2.1.1	2016-09-18	2016-10-03	2016-10-03	2017-03-15	2018-03-15
PDF 2.0	2018-01-15	2018-06-28	2018-06-28	2019-03-15	2020-03-15

In Submissions for studies that start 12 Months after transition date or March 15, 2018

eStudy Guidance
Binding Guidance– Requires that studies are compliant with the standards outlined in the FDA Data Standards Catalog

Waivers and Exemptions

Are there Waivers from the Requirement?

No.

Are there Exemptions from the Requirement?

Yes.

eStudy Guidance

Binding Guidance– Requires that studies are compliant with the standards outlined in the FDA Data Standards Catalog

Can FDA Refuse to File / Receive?

Yes.

But,


FAQS

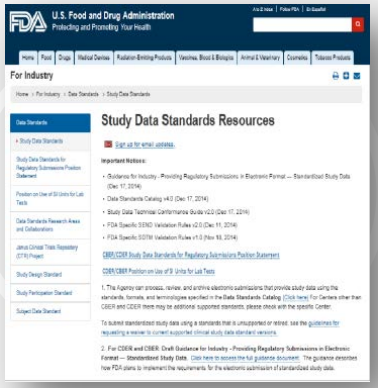
- **When does all this start?**
  - *The Clock has started. Clinical and nonclinical studies that start after December 17, 2016 must use the standards in the Data Catalog.*
- **Can sponsors use the standards in the Data Catalog now?**
  - *Yes, we strongly encourage you to do so.*
- **How often will FDA update the Data Catalog?**
  - *New versions or new standards will be posted to the Data Catalog. A Federal Register Notice will accompany all updates. Identified errata will be corrected, as needed.*

- **What is a Transition Date?**
  - *Always March 15th and Always the March 15th following the Federal Register Notice. It is used to determine the requirement date.*
- **What is a Requirement Date?**
  - *24 months after the Transition Date for a new standard.*
  - *12 months after the Transition Date for a version update.*
- **How does the FDA determine that a version update or new standard can be supported?**
  - *We have a process that is executed to evaluate if we can process, review and archive a new update or standard.*

- **Is there a limit to what can be required under FDASIA 745A(a)?**
  - *Any the data / information that is determined to be part of a submission under subsection (b), (i), or (j) of section 505 of the FD&C Act may be within scope.*
- **Are the recommendations in the Conformance Guide required?**
  - *No. But we encourage sponsors to submit using the recommendations in the Guide.*
- **How often will there be updates to the Conformance Guide?**
  - *Generally, we will provide updates on an annual basis (or more frequently for hot topics)*.

- **Does FDASIA 745A(a) only apply to study data ?**
  - *No. There will be additional binding guidance issued, for example, the eCTD guidance will be issued as a binding guidance.*
- **Are there validation rules for SDTM and SEND datasets?**
  - *Yes. The FDA Study Data Standards Web page provides access to the rules.*

FDA Webpage



eDataTeam

eData@fda.hhs.gov

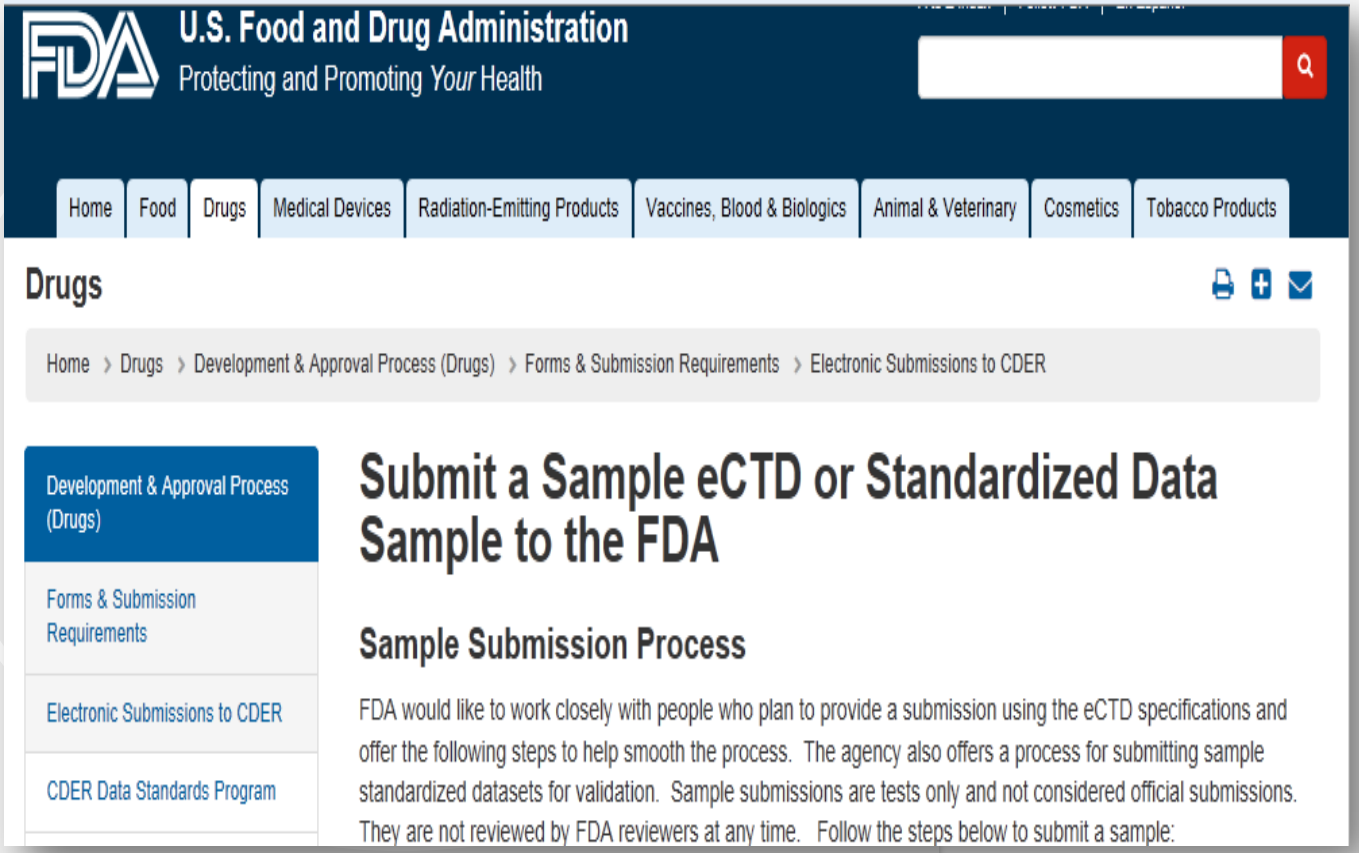
eSub Team

eSubs@fda.hhs.gov

CDER OCS
Center for Drug Evaluation and Research
CSC Computational Science Center

CDER OSP
Data Standards Program

CDER OBI
eData Team



http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm174459.htm

Key References

- Guidance for Industry - Providing Regulatory Submissions in Electronic Format — Standardized Study Data
- Guidance for Industry – Providing Regulatory Submissions in Electronic Format – Submissions Under 745A(a) of the FD&C Act
- Data Standards Catalog v. 4.0
- Study Data Technical Conformance Guide v. 2.0

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