Electronic Submissions -
The Requirement for Standardized Study Data

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Food and Drug Administration

FDA Webinar

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Path to Electronic Standardized Study Data

- **1980s**
  - FDA Clinical / Statistical Sections Guideline
  - SAS Datasets or ASCII

- **1999**
  - FDA Support for SAS XPT
  - CDISC-FDA Collaboration

- **2004**
  - FDA Support for CDISC Submissions

- **2012**
  - FDASIA
  - PDUFA V

- **2014**
  - Final 745A(a) Guidance
  - Final eStudy Data Guidance
  - Tech Conformance Guide
Value Proposition for Study Data Standards

- Predictability
- Traceability
- Replication
- Aggregation
- Tools
- Interchange

Data Quality
Transparency
Interoperability

Improve Efficiency & Decision-making
<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th># of Submissions</th>
<th>% with CDISC SDTM</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>223</td>
<td>55 %</td>
</tr>
<tr>
<td>2014</td>
<td>233</td>
<td>64 %</td>
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<tr>
<td>2015 (Q1)</td>
<td>66</td>
<td>69 %</td>
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</table>

*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?

Framework for Submissions in Electronic Format

- NDAs, ANDAs, BLAs, INDs
  - Timetable
  - Content
  - Format

Individual Guidances

No earlier than 24 Months

Final Published December, 2014
When will Study Data Standards be Required?

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?

Data Standards Catalog
Study Data....SDTM, ADaM, SEND, Define.XML

December 2016

Final Published

http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm
### What Study Data Standards will be Required?

#### Data Standards Catalog

<table>
<thead>
<tr>
<th>Use</th>
<th>Data Exchange Standard</th>
<th>Exchange Format</th>
<th>Standards Development Organization</th>
<th>Supported Version</th>
<th>Implementation Guide Version</th>
<th>FDA Center(s)</th>
<th>Date Support Begins</th>
<th>Date Support Ends</th>
<th>Date Requirement Begins</th>
<th>Date Requirement Ends</th>
<th>Regulatory Reference and Information Sources</th>
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<tbody>
<tr>
<td>Clinical and Non-Clinical study datasets - Transport</td>
<td>SAS Transport (XPORT)</td>
<td>XPT</td>
<td>SAS</td>
<td>5</td>
<td>SAS Technical Support TS-140</td>
<td>CDER, CBER</td>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
<td>For CDER and CBER only: Technical Conformance Guide</td>
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<td>Clinical and Non-Clinical study datasets - Transport</td>
<td>SAS XPORT</td>
<td>XPT</td>
<td>SAS</td>
<td>5</td>
<td>SAS Technical Support TS-140</td>
<td>CDRH, CFSAN, CVM</td>
<td>Ongoing</td>
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<td></td>
<td></td>
<td>For CDRH only: eCopy Program for Medical Device Submissions</td>
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<td>SDTM, SEND, and ADaM define.xml file</td>
<td>XML</td>
<td>W3C</td>
<td>W3C</td>
<td>1.0</td>
<td></td>
<td>CBER, CDER, CDRH</td>
<td>Ongoing</td>
<td></td>
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<td>W3C - XML Technology</td>
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<td>Analysis program files</td>
<td>ASCII</td>
<td>ANS1</td>
<td>ANS1</td>
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<td>CBER, CDER, CDRH</td>
<td>Ongoing</td>
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<td><a href="http://www.ansi.org">www.ansi.org</a></td>
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<td>Clinical study datasets</td>
<td>Study Data Tabulation Model (SDTM)</td>
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<td>Clinical Data Interchange Standards Consortium (CDISC)</td>
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<td>CDISC</td>
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<td>Version 3.1.2 Amendment 1</td>
<td>CDER, CBER</td>
<td>8/7/2013</td>
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<td>CDISC.org - ADaM</td>
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<tr>
<td>Animal study datasets</td>
<td>Standard for Exchange of Nonclinical Data (SEND)</td>
<td>XPT</td>
<td>CDISC</td>
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<td>6/13/2011</td>
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<td></td>
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<td>CDISC.org - SEND</td>
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</table>

[http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm](http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm)
How Study Data Standards will Be Required?

**Tech Conformance Guide**
How to submit standardized study data

**Technical Conformance Guide (non-binding)**

Use it NOW

Version 2.0
Published

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

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*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

<table>
<thead>
<tr>
<th>SDO Releases Version Update</th>
<th>Date Released by SDO (yyyy-mm-dd)</th>
<th>FR Notice of FDA Support (yyyy-mm-dd)</th>
<th>Update Data Standards Catalog (yyyy-mm-dd)</th>
<th>Transition Date (yyyy-mm-dd)</th>
<th>Date Requirement Begins (yyyy-mm-dd)</th>
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<tbody>
<tr>
<td>SEND 2.1.1</td>
<td>2016-09-18</td>
<td>2016-10-03</td>
<td>2016-10-03</td>
<td>2017-03-15</td>
<td>2018-03-15</td>
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</tbody>
</table>

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

Are there **Waivers** from the Requirement? **No.**

Are there **Exemptions** from the Requirement? **Yes.**
Can FDA Refuse to File / Receive?

Yes.
But,
• 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 15\(^{\text{th}}\) and *Always* the March 15\(^{\text{th}}\) 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.
Submit a Sample eCTD or Standardized Data Sample to the FDA

Sample Submission Process

FDA would like to work closely with people who plan to provide a submission using the eCTD specifications and offer the following steps to help smooth the process. The agency also offers a process for submitting sample standardized datasets for validation. Sample submissions are tests only and not considered official submissions. They are not reviewed by FDA reviewers at any time. Follow the steps below to submit a sample:

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