

Data Standards Update

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Why Data Standards

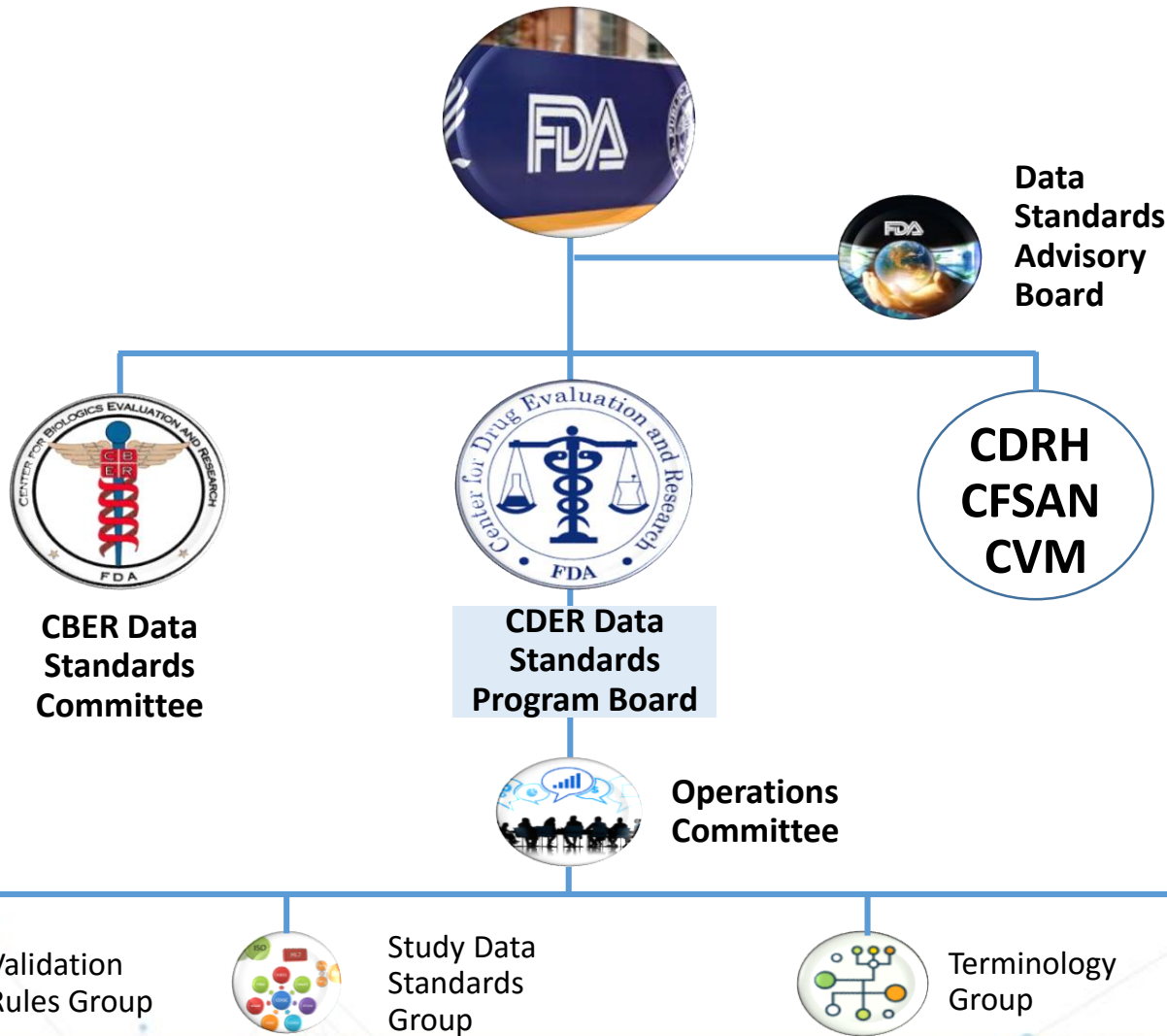


Predictability **+** Traceability **+** Common Tools **+** Communication

= More efficient & transparent review process

Data Standards Governance in CDER

FDA



Data Standards Strategy and Action Plan

FDA



Data Standards Strategy 2015-2017

**Center for Drug Evaluation and
Research (CDER)
Food and Drug Administration**



Data Standards Program Action Plan

Version: 2.5

Document Date: March 15, 2017

Data Standards Program Portfolio*



Drug Development and Pre-Market Review



Drug Safety Performance and Promotion



Drug Manufacturing and Quality



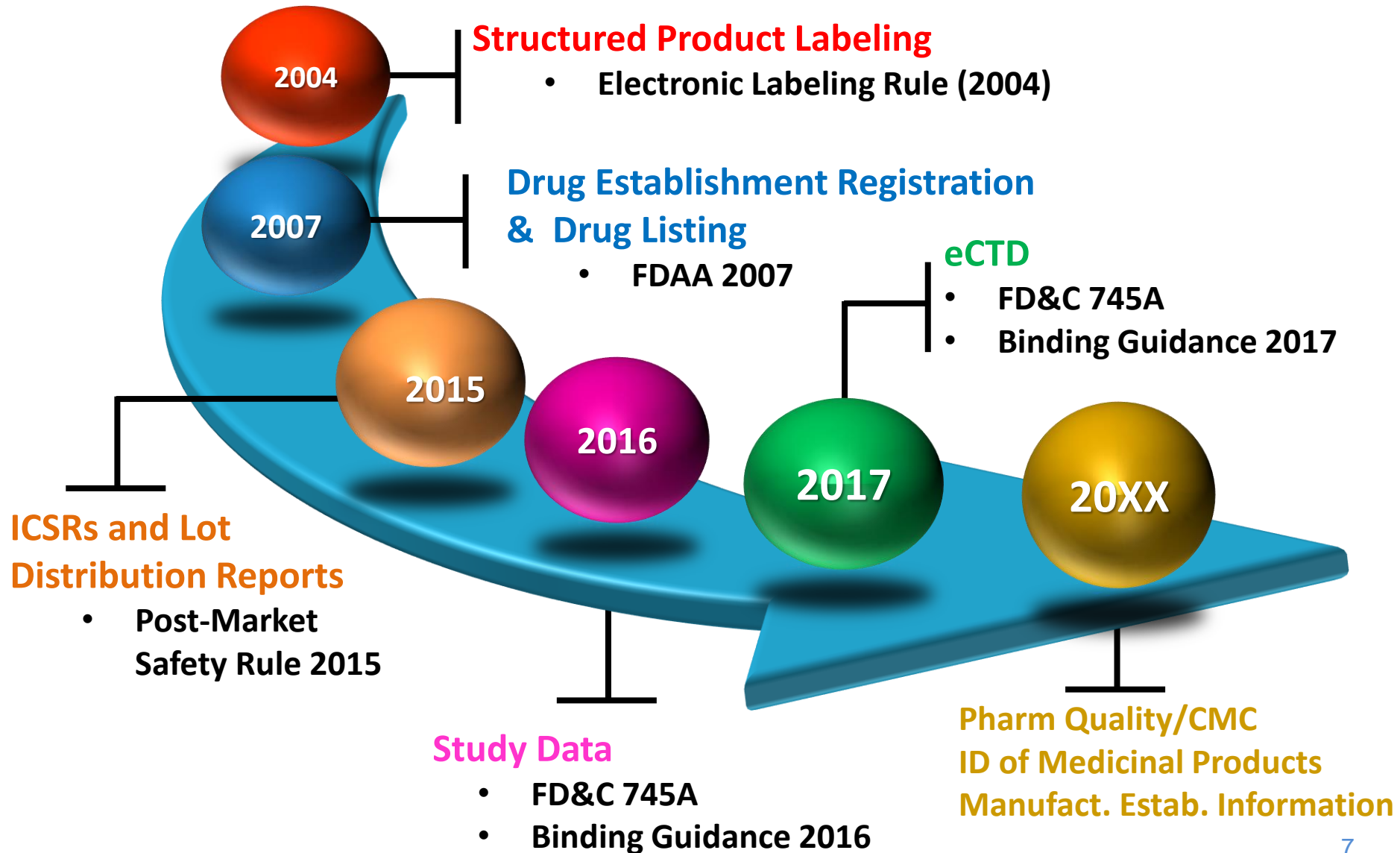
Policy

- Full list:

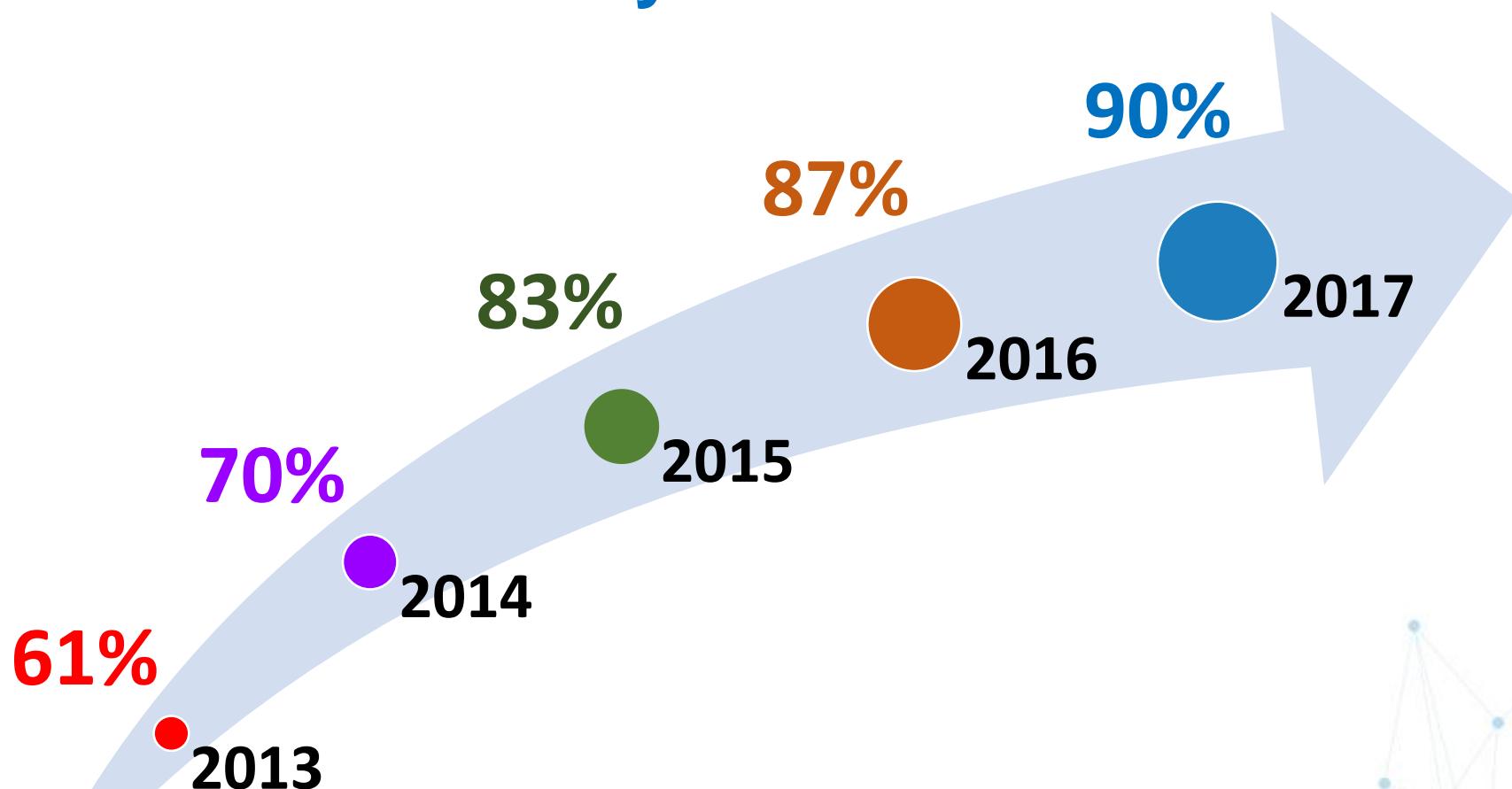
<https://www.fda.gov/drugs/developmentapprovalprocess/formssubmissionrequirements/electronic submissions/ucm249979.htm>

www.fda.gov

Road to Required Electronic Submission Standards



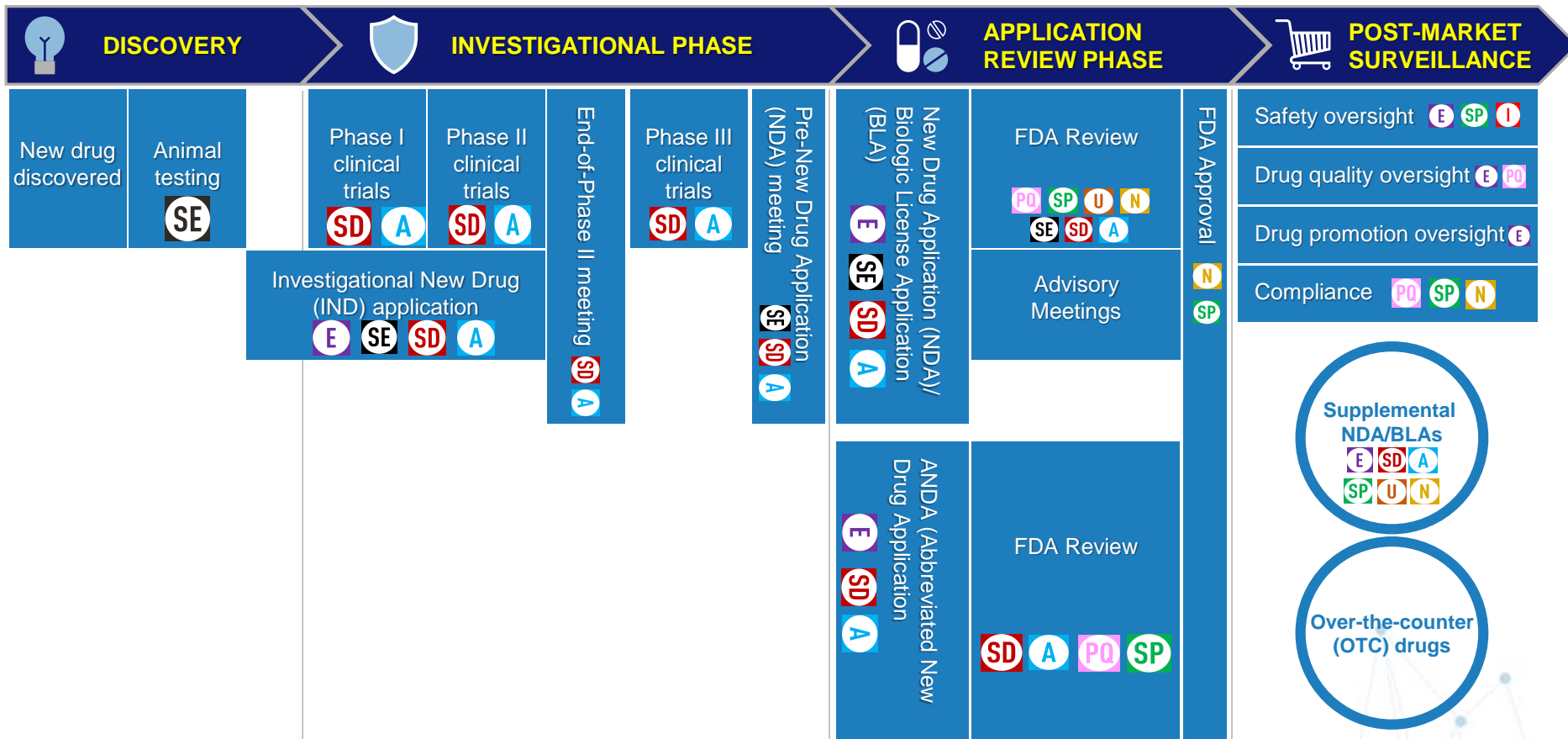
Percent of New NDA Submissions with Standardized Study Data - FY13- FY17*



* One or more explicitly stated **SDTM** studies (or study data structure that resembled SDTM) in NEW NDAs. FY2013-F2017(Q1-Q2), Source: Office of Business Informatics, CDER

Project Updates for Standards in the Drug Development Lifecycle

FDA



FDA COMPLIANCE INSPECTIONS THROUGHOUT THE PROCESS (SE, SD, A, PQ)

DATA STANDARDS

E eCTD Electronic Common Technical Document	SE SEND Standard for Exchange of Nonclinical Data	SD SDTM Study Data Tabulation Model	A ADaM Analysis Data Model	N NDC/MPID National Drug Code/Medicinal Product Identifier
PQ PQ/CMC Pharmaceutical Quality/Chemistry, Manufacturing, and Controls	SP SPL Structured Product Labeling	I ICSR Individual Case Safety Report	U UNII Unique Ingredient Identifiers	

Project Updates for Standards in the Drug Development Lifecycle

FDA



New
disco



APPLICATION



POST-MARKET
CE

- Project identified standard data elements, terminologies, and data structures to enable automation of important analyses of PQ/CMC data.
- Proposed use of SPL standards for data exchange.
- Planned 2017 FR Notice for public comment on draft data elements and terminologies.
- Initiative will align, where possible, with substance and product identifiers described by ISO for IDMP standards.

DATA STANDARDS

E eCTD
Electronic Common
Technical Document

PQ PQ/CMC
Pharmaceutical
Quality/Chemistry,
Manufacturing, and Controls

SE SEND
Standard for Exchange
of Nonclinical Data

SP SPL
Structured
Product Labeling

SD SDTM
Study Data
Tabulation Model

I ICSR
Individual Case
Safety Report

A ADaM
Analysis Data
Model

U UNII
Unique Ingredient
Identifiers

N NDC/MPID
National
Drug Code/
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Project Updates for Standards in the Drug Development Lifecycle



- Updated the SEND section of Study Data Technical Conformance Guide
- Finalizing FDA validator rules for SEND and will update the FDA webpage.
- Finalizing Testing & Acceptance to support SENDIG v 3.1.

FDA COMPLIANCE INSPECTIONS THROUGHOUT THE PROCESS

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Project Updates for Standards in the Drug Development Lifecycle



- Posted Business and Validator Rules to FDA webpage
- Developed and posted SDTM technical rejection criteria
- Testing & acceptance of TA extensions of SDTM
- LOINC codes in LBLOINC: studies starting after 3-15-2018
 - External and Internal workgroups formed
 - Planned guidance on submission of LOINC codes

FDA COMPLIANCE INSPECTIONS THROUGHOUT THE PROCESS

SE SD A PU

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Project Updates for Standards in the Drug Development Lifecycle



New drug
discovery

MARKET
PLACE



PD

ht E

- Integrating Risk, Evaluation and Mitigation Strategies into SPL
 - Completed the pilot and now able to receive REMS in SPL format.
 - Guidance is in development.
- Draft Guidance on Submission of Manufacturing Establishment Information published December 2016
 - Requires: Establishment Name and Address, Unique Facility Identifier, PoC, Operations being conducted

FDA COMPLIANCE INSPECTIONS THROUGHOUT THE PROCESS

SE SD A PQ

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FDA'S THERAPEUTIC AREA (TA) STANDARDS PROJECT

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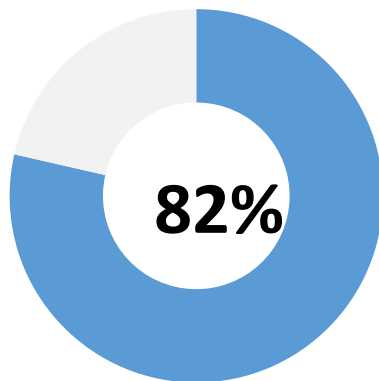
Overview

In 2012, as part of a PDUFA V commitment, CDER compiled a prioritized list of disease and therapeutic areas (TAs) for which standardization was needed.

Approach

Focus is on regulatory review needs

Current Status



Of the 55 TAs* prioritized, 45 have been initiated as of April 2017

CFAST Key Players

CDISC, C-Path, NIH, FDA, TransCelerate, Duke, HL7 and many other stakeholders

FDA'S THERAPEUTIC AREA STANDARDS PROJECT

FDA

TA's Supported by FDA*

QT Studies

Chronic Hepatitis C

Diabetes

Dyslipidemia

Tuberculosis

Diabetic Kidney Disease

Ebola

Kidney Transplant

Malaria

TA Standards in FDA Review - 2017

Asthma

Breast Cancer

Colorectal Cancer

CV Study

CV Imaging

Duchenne's MD

Prostate Cancer

Schizophrenia

Virology

*May, 2017- listed in Technical Conformance Guide



eCTD Technical Rejection of Submissions

FDA can Refuse to File (RTF) or Refuse to Receive (RTR) an Application for Non-Conformance to Standardized Study Data



**Please no
RTF/RTR**

eStudy Guidance
requires the electronic
submission of NDAs, BLAs,
ANDAs, INDs in the formats
in the Data Standards Catalog

**...so we will start with eCTD technical rejection of
submissions**

eCTD Technical Rejection of Submissions



- CDER has been validating incoming submissions for conformance to *eCTD format* for **~8** yrs.
 - If a submission fails eCTD format validation a technical rejection notice will be sent to the submitter.
 - eCTD validation occurs upon receipt of the submission, prior to being written to the EDR and review division notification.
- The same process will be used for validating submissions for conformance to study data standards.
- It is NOT the same as RTF or RTR.

eCTD Technical Rejection of Submissions

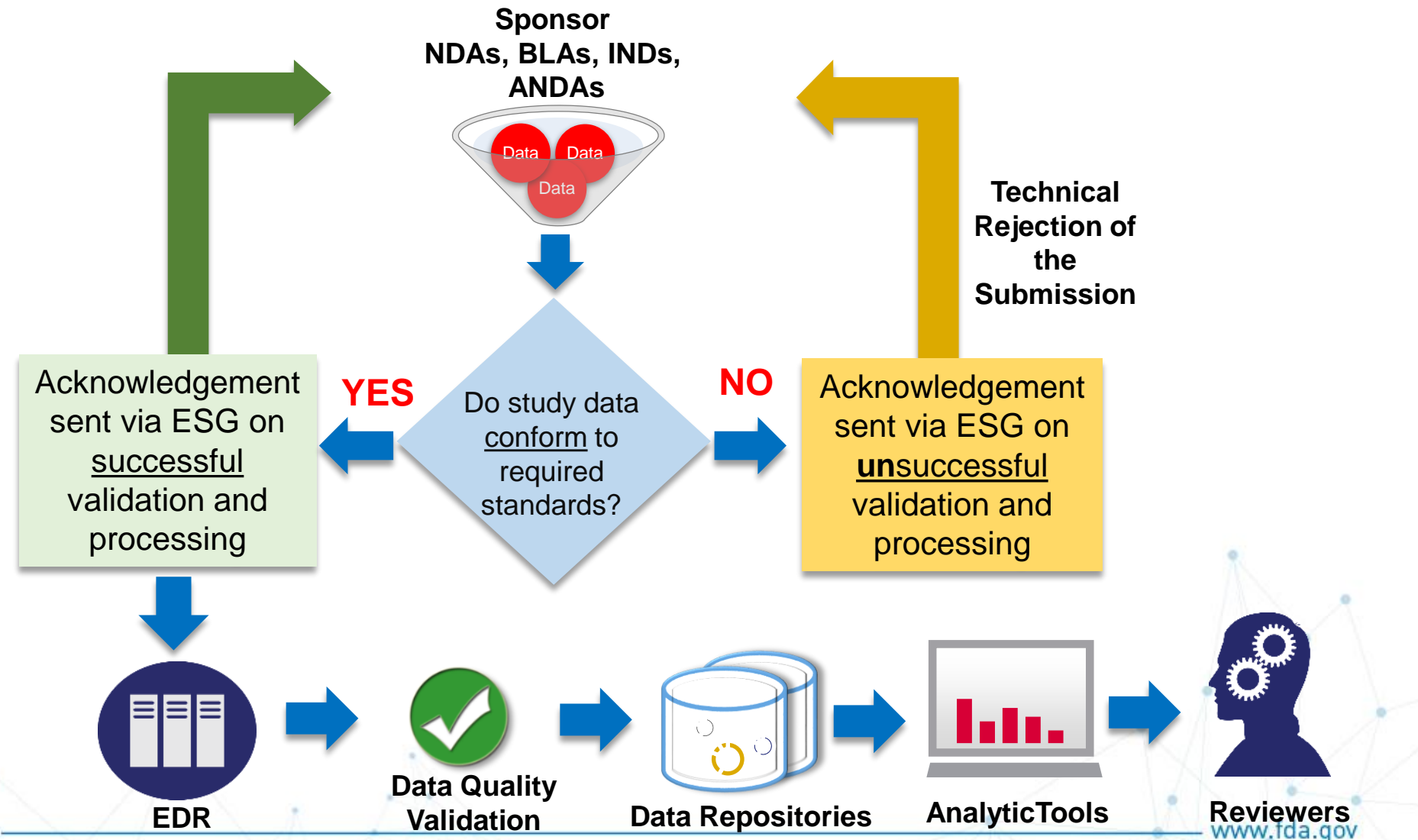


- Sponsors will be able to correct the technical errors and re-submit
- For study data standards validation, FDA will notify submitters, at least 30 days, prior to ‘going live’ with the technical rejection of submissions.

eCTD Technical Rejection...



How will it work?



eCTD Technical Rejection Criteria for Study Data Standards

FDA

The screenshot shows the FDA's website for Electronic Common Technical Document (eCTD) submissions. The header includes the FDA logo, 'U.S. FOOD & DRUG ADMINISTRATION', and navigation links like 'A to Z Index', 'Follow FDA', and 'En Español'. A search bar is also present. The main navigation bar lists various product categories: Home, Food, Drugs, Medical Devices, Radiation-Emitting Products, Vaccines, Blood & Biologics, Animal & Veterinary, Cosmetics, and Tobacco Products. The 'Drugs' section is selected, leading to a breadcrumb trail: Home > Drugs > Development & Approval Process (Drugs) > Forms & Submission Requirements > Electronic Submissions to CDER. The page title is 'Electronic Common Technical Document (eCTD)'. On the left, a sidebar lists links: 'Electronic Submissions to CDER', 'CDER Data Standards Program', 'Data Standards in the Drug Lifecycle', 'Electronic Common Technical Document (eCTD)' (highlighted), 'Electronic Regulatory Submissions and Review Helpful Links', 'Electronic Submissions Presentations', and 'Study Data for Submission to CDER and CBER'. The main content area describes the eCTD as the standard format for submitting applications, amendments, supplements, and reports to FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER). It includes 'Important Dates' stating that after May 5, 2017, new drug applications (NDAs), abbreviated NDAs (ANDAs), and biologics licenses will require eCTD. A 'Quick Links' section lists several PDFs, with 'Technical Rejection Criteria for Study Data (PDF - 921 KB) NEW' circled in red. A 'Notices' section is also visible.

U.S. FOOD & DRUG ADMINISTRATION

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Drugs

Home > Drugs > Development & Approval Process (Drugs) > Forms & Submission Requirements > Electronic Submissions to CDER

Electronic Submissions to CDER

CDER Data Standards Program

Data Standards in the Drug Lifecycle

Electronic Common Technical Document (eCTD)

Electronic Regulatory Submissions and Review Helpful Links

Electronic Submissions Presentations

Study Data for Submission to CDER and CBER

Electronic Common Technical Document (eCTD)

The eCTD is the standard format for submitting applications, amendments, supplements, and reports to FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER).

Important Dates

After the dates listed below, eCTD requirements for submissions to CDER and CBER will go into effect and submissions that do not use eCTD will not be filed or received.

- May 5, 2017: New Drug Applications (NDAs), Abbreviated NDAs (ANDAs), and Biologics License

Quick Links

- eCTD Guidance (PDF - 11 KB)
- eCTD Submission Standards (PDF - 91 KB)
- FDA Data Standards Catalog
- eCTD Technical Conformance Guide (PDF - 303 KB)
- Drug Master Files (DMFs)
- Technical Rejection Criteria for Study Data (PDF - 921 KB) **NEW**

Notices

Technical Rejection Criteria for Study Data

Study Data Standards are required in clinical and nonclinical studies that start after December 17, 2016.¹ Technical rejection criteria is being added to the existing eCTD validation criteria to enforce the deadlines (see below). FDA will give the industry 30 days' notice on the eCTD website prior to the criteria becoming effective.

The FDA may **refuse to file (RTF) for NDAs and BLAs, or refuse to receive (RTR) for ANDAs**, an electronic submission that does not have study data in conformance to the required standards specified in the FDA Data Standards Catalog.

The standards apply to the following types of submissions to CDER and CBER:

- NDAs, ANDAs, BLAs, and all subsequent submissions to these types of applications, including amendments, supplements, and reports, even if the original submission was filed before the requirements went into effect.
- Commercial INDs (for products that are intended to be distributed commercially).

Deadlines: Sponsors whose studies started after December 17, 2016 must use the data standards listed in the FDA Data Standards Catalog for NDAs, BLAs and ANDAs. For Commercial INDs, the requirement starts after December 17, 2017.

Although CDER and CBER can RTF or RTR submissions that do not conform to the required standards, we will implement a process to assess high-level study data standards conformance at the time the submission is submitted and validated. The criteria to be used to assess conformance are listed in the tables on page 2. If the submission fails these criteria, it will be rejected and the sponsor will be notified.

¹ Guidance to Industry: "Providing Regulatory Submissions In Electronic Format — Standardized Study Data"

eCTD Module Sections Included and Excluded



IMPORTANT

A Trial Summary dataset (ts.xpt) must be presented for each study in sections identified below even if the study started prior to December 17, 2016. Nonclinical legacy data submitted in PDF format should be submitted with a TS dataset.

Study data validation **WILL APPLY** to the following eCTD sections:

- 4.2 Study Reports
- 5.3 Clinical Study Reports and Related Information

Study data validation **WILL NOT APPLY** to the following eCTD sections:

- 4.2.1 Pharmacology
- 4.2.2 Pharmacokinetics
- 4.2.3.3 Genotoxicity
- 4.2.3.5 Reproductive and Developmental Toxicity
- 4.2.3.6 Local Tolerance
- 4.2.3.7 Other Toxicity Studies
- 5.3.1.3 In Vitro – in Vivo correlation Study reports and related information
- 5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies
- 5.3.2 Reports of studies pertinent to pharmacokinetics using human biomaterials
- 5.3.3.5 Population PK study reports and related information
- 5.3.5.3 Reports of Analyses of Data from More than One Study
- 5.3.5.4 Other Study Reports and Related Information
- 5.3.6 Reports of Postmarketing Experience

eCTD Data Validation Criteria and Severity

High

Demographic dataset (DM) and the define.xml must be submitted in Module 4 for nonclinical data; DM dataset, the subject-level analysis dataset (ADSL) and define.xml must be submitted in Module 5 for clinical data

High

Trial Summary (TS) dataset must be present for each study in eCTD section 4.2 and 5.3

Medium

Correct STF file-tags must be used for all standardized datasets in section 4.2 and 5.3

- Data-tabulations-dataset-sdtm
- Data-tabulations-dataset-send
- Analysis-dataset-adam

Medium

For each study in eCTD section 4.2 and section 5.3, no more than one dataset of the same name should be submitted as new.



Thank You

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