

Introduction to the PhUSE CSS 2017

Crystal Allard, Special Assistant to the
Director

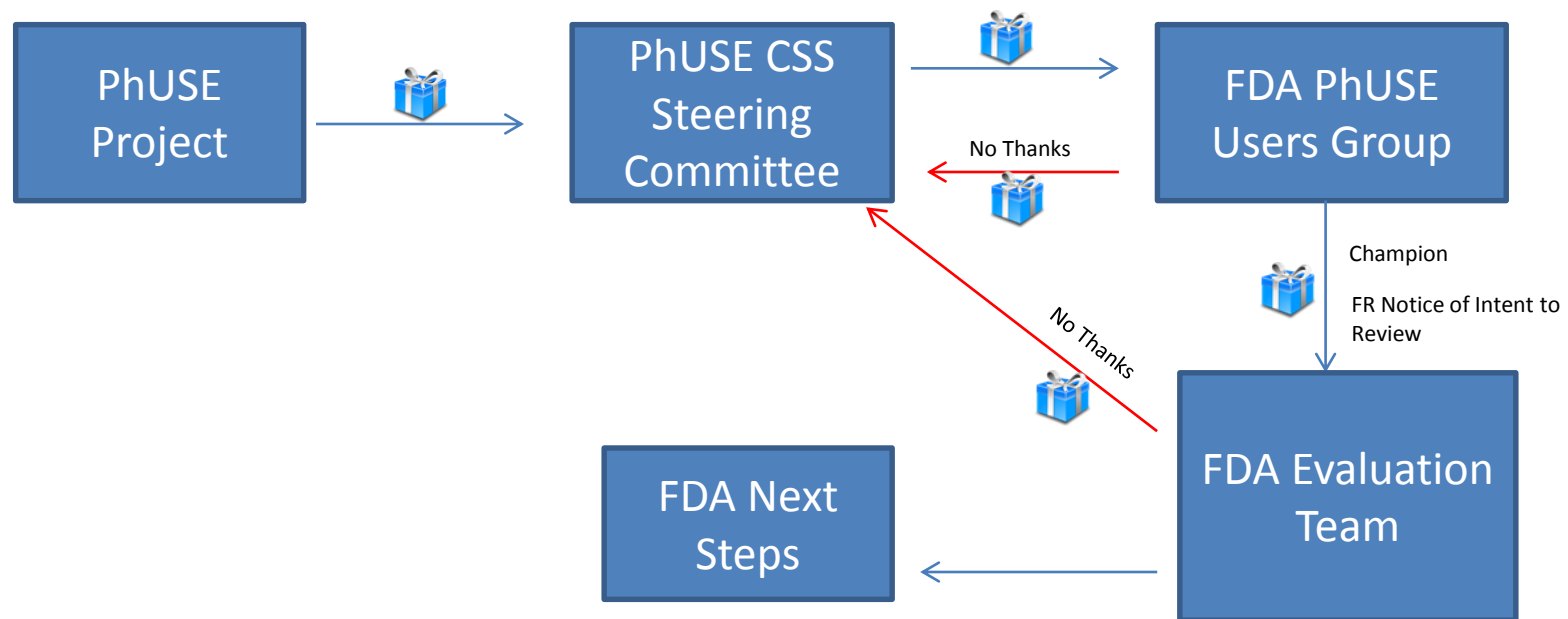
Office of Computational Science
PhUSE CSS March 2017

The Cast

- Mary Doi, M.D. – Deputy Director, OCS
- Vaishali Popat, M.D. M.P.H – Associate Director for Biomedical Informatics, OND
- Elaine Thompson, Ph.D – Senior Staff Fellow, OCS
- Steve Wilson Dr.P.H, CAPT USPHS – Director, DBIII, OB
- Jade Chen, Ph.D. – Senior Statistical Reviewer, DBV, OB

A Few Updates on FDA's Review of PhUSE Deliverables

FDA Evaluation Process – The Graphical Representation



UPDATES FROM CDER - SDRG

- SDRG = Study Data Reviewer's Guide
- The Champion: Helena Sviglin
- [FR Notice](#) published
- FDA Review Finished
- FDA Report Finalized
- Technical Conformance Guide Updated – [Nov. 2016](#)



FEDERAL REGISTER
The Daily Journal of the United States Government

Intent To Review a Study Data Reviewer's Guide Template

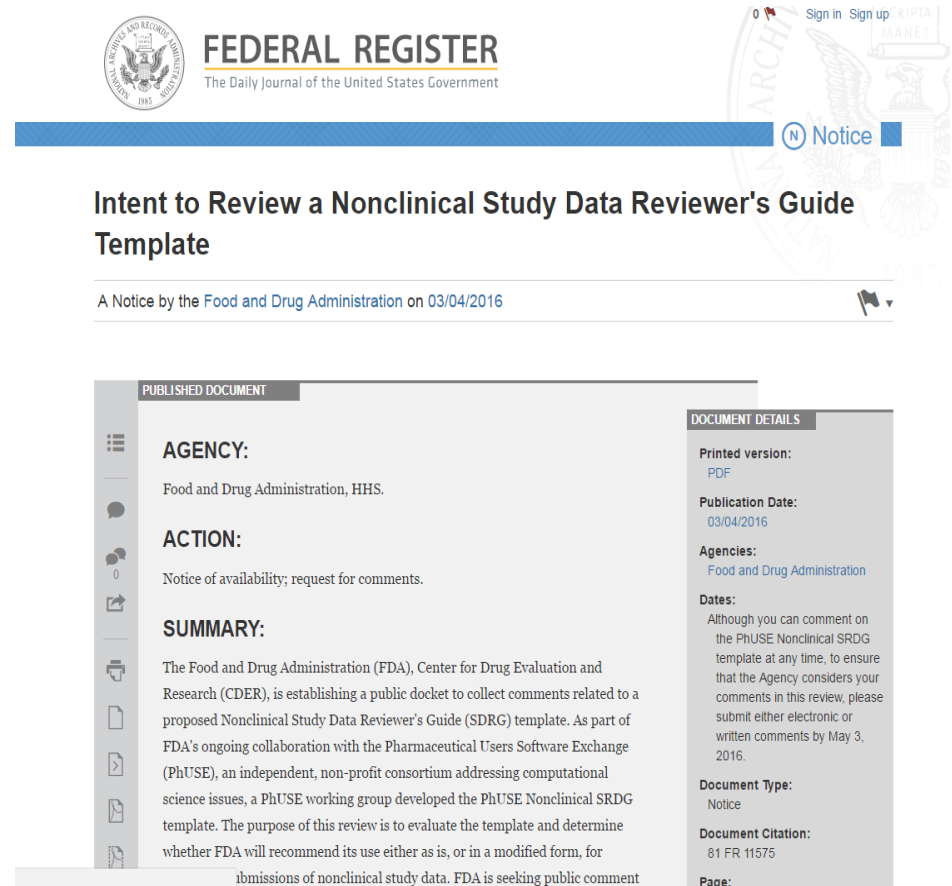
A Notice by the [Food and Drug Administration](#) on 07/23/2015

ACTION Notice Of Availability; Request For Comments.

SUMMARY □ The Food and Drug Administration (FDA), Center for Drug Evaluation and Research (CDER), is establishing a public docket to collect comments related to a proposed Study Data Reviewer's Guide (SDRG) template. As part of FDA's ongoing collaboration with the Pharmaceutical Users Software Exchange (PhUSE), an independent, non-profit consortium addressing computational science issues, a PhUSE working group developed the PhUSE SDRG template. The purpose of this review is to evaluate the template and determine whether FDA will recommend its use either as is, or in a modified form, for regulatory submissions of study data. FDA is seeking public comment on the use of the PhUSE SDRG template for regulatory submissions.

Updates From CDER - NSDRG

- NSDRG = Nonclinical Study Data Reviewer's Guide
- The Champion: Patty Brundage
- [FR Notice](#) Published
- FDA Review Finished
- FDA Report Finalized December 2016
- Technical Conformance Guide Update – March 2017



The screenshot shows the Federal Register website. At the top, the Federal Register logo and the text "The Daily Journal of the United States Government" are visible. Below the header, a blue bar contains the text "Notice". The main heading of the notice is "Intent to Review a Nonclinical Study Data Reviewer's Guide Template". Below this, it states "A Notice by the Food and Drug Administration on 03/04/2016". The notice is categorized as a "PUBLISHED DOCUMENT". The "AGENCY:" is the Food and Drug Administration, HHS. The "ACTION:" is a "Notice of availability; request for comments." The "SUMMARY:" states that the FDA, Center for Drug Evaluation and Research (CDER), is establishing a public docket to collect comments related to a proposed Nonclinical Study Data Reviewer's Guide (SDRG) template. As part of FDA's ongoing collaboration with the Pharmaceutical Users Software Exchange (PhUSE), an independent, non-profit consortium addressing computational science issues, a PhUSE working group developed the PhUSE Nonclinical SRDG template. The purpose of this review is to evaluate the template and determine whether FDA will recommend its use either as is, or in a modified form, for submissions of nonclinical study data. FDA is seeking public comment.

DOCUMENT DETAILS

- Printed version:** [PDF](#)
- Publication Date:** 03/04/2016
- Agencies:** Food and Drug Administration
- Dates:** Although you can comment on the PhUSE Nonclinical SRDG template at any time, to ensure that the Agency considers your comments in this review, please submit either electronic or written comments by May 3, 2016.
- Document Type:** Notice
- Document Citation:** 81 FR 11575
- Page:**

Updates From CDER - SDSP



- SDSP = Study Data Standardization Plan
- The Champion: Nhi Beasley
- [FR Notice](#) Published
- FDA Review Ongoing



FEDERAL REGISTER
The Daily Journal of the United States Government

Sign in Sign up

Notice

Intent To Review a Study Data Standardization Plan Template; Notice of Availability; Establishment of a Public Docket; Request for Comments

A Notice by the Food and Drug Administration on 11/08/2016

PUBLISHED DOCUMENT		DOCUMENT DETAILS
 	AGENCY: Food and Drug Administration, HHS.	Printed version: PDF
	ACTION: Notice of availability; request for comments.	Publication Date: 11/08/2016
	SUMMARY: The Food and Drug Administration (FDA), Center for Drug Evaluation and Research, is establishing a public docket to collect comments related to a proposed Study Data Standardization Plan (SDSP) template. As part of FDA's ongoing collaboration with the Pharmaceutical Users Software Exchange (PhUSE), an independent, non-profit consortium addressing computational science issues, a PhUSE working group developed the PhUSE SDSP template. The purpose of this review is to evaluate the template and determine whether FDA will recommend its use either as is, or in a modified form, for regulatory submissions of study data. FDA is seeking public comment on the use of the	Agencies: Food and Drug Administration
		Dates: Although you can comment on the PhUSE SDSP template at any time, to ensure that the Agency considers your comments in this review, please submit either electronic or written comments by January 9, 2017.
		Document Type: Notice
	Document Citation: 81 FR 78602	
	Page:	

Updates From CDER - ADRG

- ADRG = Analysis Data Reviewer's Guide
- The Chamion: Weiya Zhang
- FR Notice – expected soon
- FDA Review Ongoing

Analysis Data Reviewer's Guide

Analysis Data Reviewer's Guide Final Work Package

Version	Release Date	Downloadable Work Package	Changes from Previous Version
v1.1	26-Jan-2015	ADRG Package v1.1 2015-01-26	<ul style="list-style-type: none">• Added ADSL Header to Section 5.2• Improved ADRG Template usability• Minor revisions to instructions in ADRG Completion Guidelines• ADRG Examples updated to match revised SDRG Template
v1.01	13-May-2014	ADRG Package v1.01 2014-05-13	Initial Version

Project Overview

ADaM "provides a framework that enables analysis of the data, while at the same time allowing reviewers and other recipients of t results. Although ADaM provides a robust metadata framework, FDA Reviewers benefit from additional, human-readable, document ADaM metadata. The development of an Analysis Data Reviewer's Guide (ADRG) template will ensure this documentation is provided

Project Leads

Name	Role	Organization	E-mail
Susan Kenny	Industry Co-Lead	Independent	susankenny (at) maxlikelihodd.com 
Gail Stoner	Industry Co-Lead	Johnson & Johnson	GStoner (at) its.jnj.com 
Mina Hohlen	FDA Liaison	FDA	mina.hohlen (at) fda.hhs.gov 
John Brega	Work Package Maintenance	PharmaStat	JBrega (at) pharmastat.com 

Other PhUSE Deliverables

- Inspection Site Selection Standard Data Elements: Gap Analysis of FDA Requirements and Existing CDISC Standards
- Analysis and Displays Associated with Adverse Events: Focus on Adverse Events in Phase 2-4 Clinical Trials and Integrated Summary Documents

A Few Updates on Data Validation

eCTD Technical Validation of Study Data

High Level Rule #1	High Level Rule #2
Rule # 1734 : A Trial Summary (TS) dataset must be present for each study in module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4 and in module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2	Rule #1736: DM dataset and define.xml must be submitted in module 4, sections 4.2.3.1, 4.2.3.2, 4.2.3.4. DM dataset, ADSL dataset, define.xml must be submitted in module 5, sections 5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2

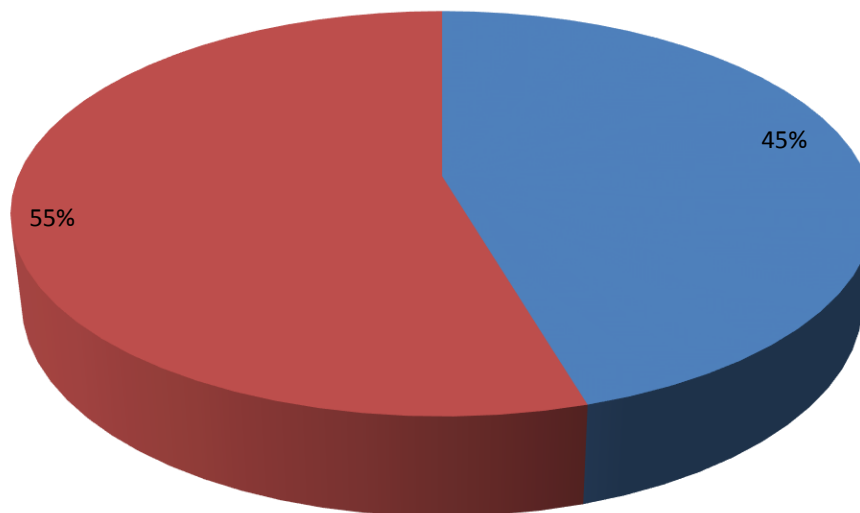
<https://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/UCM523539.pdf>

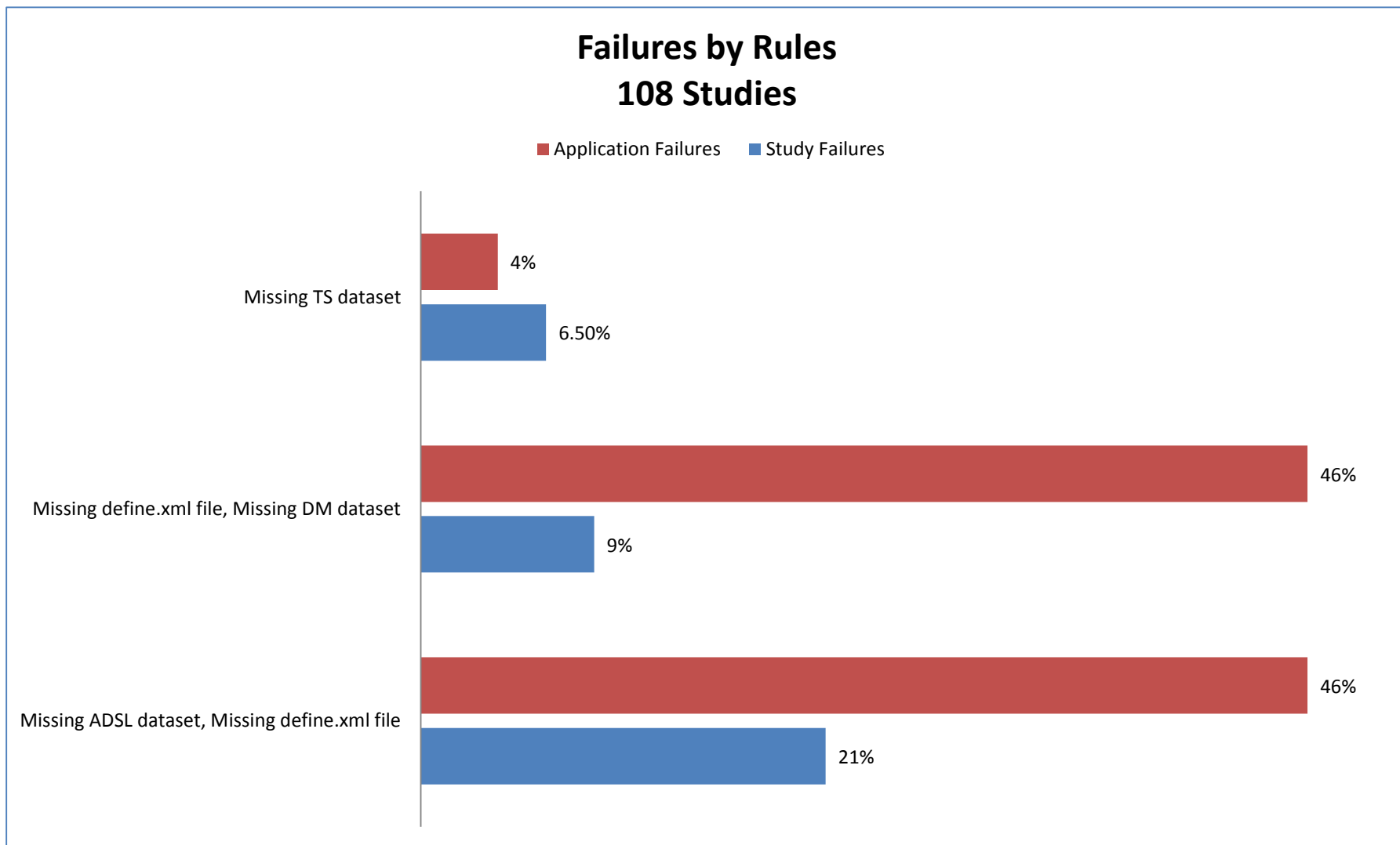
Data Validation Findings

- January 2017 – March 1, 2017

Potential Rejections/Acceptances (11 NDA Applications)

■ Potentially Rejected Applications ■ Potentially Accepted Applications





A Few Updates on New Data Standards Resources

Newly Published Conformance and Business Rules

5. Business Rules

Validation activities occur at different times during submission and review of study data, including submission receipt and at the beginning of the regulatory review. Validation of study data that occurs upon receipt of a submission follows the process for [Technical Rejection Criteria for Study Data](#).

The rules below support regulatory review and analysis of study data:

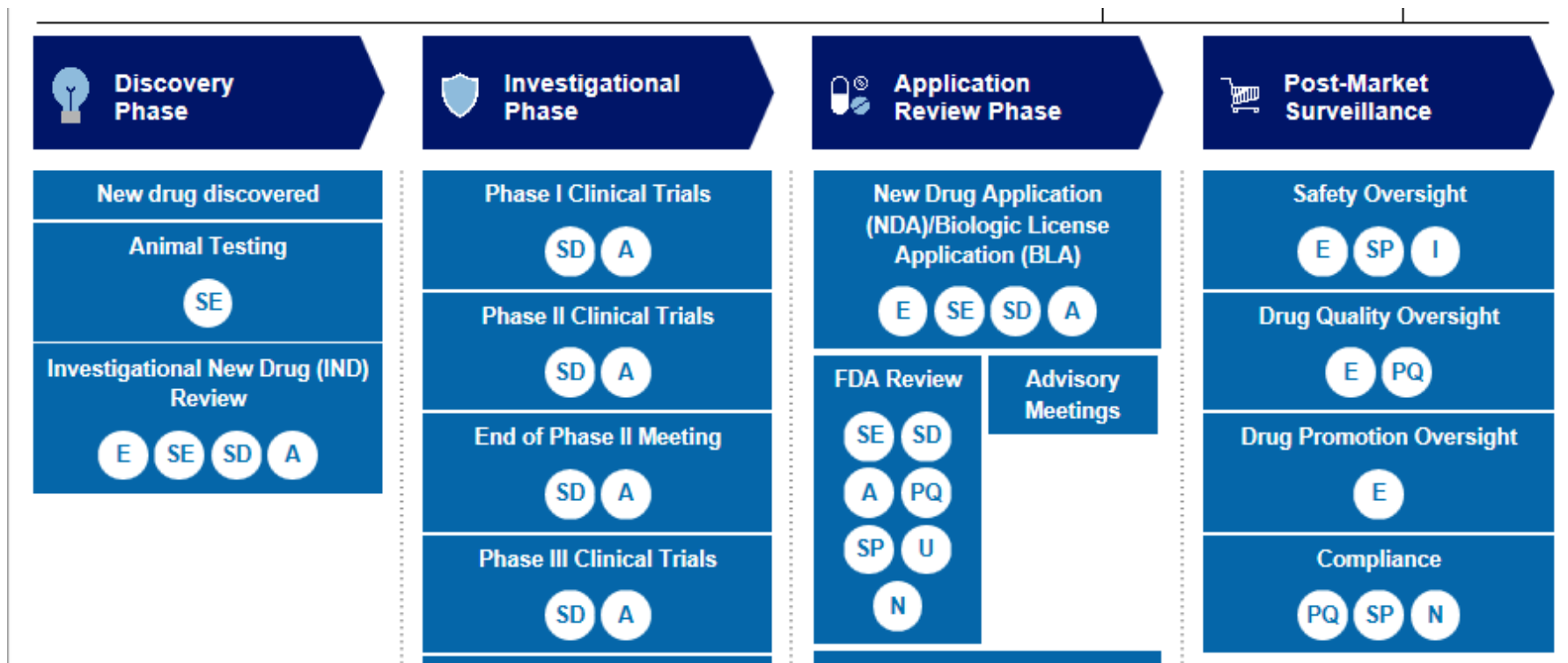
- **Business Rules**

The Business Rules help ensure that the study data are compliant, useful, and will support meaningful review and analysis. This applies to SDTM formatted clinical studies and SEND formatted non-clinical studies. For more information see Section 8 of the Technical Conformance Guide.

- **Validator Rules**

The [Validator Rules](#) are used by the FDA to ensure data are standards compliant and support meaningful review and analysis.

Data Standards in the Drug Lifecycle Infographic



VIDEO: Data Standards: Streamlining FDA Reviews and Advancing Public Health



eCTD Submission Requirements: What You Need to Know



U.S. FOOD & DRUG
ADMINISTRATION



eCTD SUBMISSION REQUIREMENTS: WHAT YOU NEED TO KNOW

eCTD

The **Electronic Common Technical Document (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).

An eCTD submission has five modules: region-specific information, summary documents, quality-related information, nonclinical study reports, and clinical study reports.

When materials are submitted electronically, it is easier for FDA to review data, approve new drugs, and monitor drugs after they go on the market. Using eCTD also simplifies the process for submitters, because it is the same format used by drug regulatory agencies in other countries.

Starting in 2017, eCTD will be required for submissions to CDER and CBER. After the dates listed below, submissions that are not in eCTD format will not be filed or received unless exempted from the requirement.

New Requirements for Electronic Submissions of DMFs



**U.S. FOOD & DRUG
ADMINISTRATION**



NEW REQUIREMENTS FOR ELECTRONIC SUBMISSIONS OF DMFs

eCTD

The Electronic Common Technical Document (eCTD) is the standard method 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). This includes Drug Master Files (DMFs), Biological Product Files (BPFs), and other master files.

Converting existing DMFs to eCTD format

If you currently hold a DMF in paper form, you are not required to resubmit it in eCTD format. However, you may convert an existing paper DMF into eCTD format if you wish. When submitting your first eCTD submission to a DMF, you will use the existing DMF number. If the existing number is four digits, you will need to add zeros on the left to convert it to a six-digit format. For example, 1234 would become 001234.

If you choose to resubmit a paper DMF in electronic format and there are changes in the content of the DMF, such as new or updated information, you must list the changes in the cover letter for the submission.

Starting May 5, 2017, new DMFs, new BPFs, and any submissions to existing DMFs and BPFs (e.g., amendments, annual reports, LOAs) must be submitted using the eCTD 3.2.2 standard. All submissions must be submitted electronically even if the remainder of the master file is on paper. DMF submissions that are not submitted in eCTD format after May 5, 2017, will not be filed or received. The eCTD standard will be updated in the future. The current requirements and supported versions can be found in the FDA Data Standards Catalog at www.fda.gov/eStudyResources.

Data Standard Resources

- [Newly Published Conformance and Business Rules](#)
- [Data Standards in the Drug Lifecycle Infographic](#)
- [VIDEO: Data Standards: Streamlining FDA Reviews and Advancing Public Health](#)
 - [YouTube link](#)
- [eCTD Submission Requirements: What You Need to Know](#)
- [New Requirements for Electronic Submissions of DMFs](#)

A Shameless Plug

Stop by our OCS Table

