



U.S. FOOD & DRUG
ADMINISTRATION

**CDER Data Standards Program
2018 Annual Assessment**

February 2019

Table of Contents

1	Introduction	1
2	CDER Data Standards Program at a Glance	1
3	Impact of Requiring Standards	2
4	2018 Electronic Submission Metrics	3
5	2018 Data Standards Program Year in Review	3
	5.1 Goal 1: Incorporate data standards to support more efficient, science-based pre-market review of medical products	4
	5.2 Goal 2: Improve the post-market risk management strategies and pharmacovigilance and surveillance of medical products by using data standards.	6
	5.3 Goal 3: Implement common data standards to improve the quality and integrity of marketed medical products.....	6
	5.4 Goal 4: Promote innovation in the development and use of data standards.	7
	5.5 Goal 5: Ensure effective communication and collaboration with stakeholders on data standards	9
	5.6 Goal 6: Improve management and usability of the volume of information through data standards.....	10
6	Moving Forward - 2019 CDER Data Standards Program Direction	11
	Appendix A: Glossary of Acronyms	12

List of Figures

Figure 1. Comparison: Overall Submissions vs. eCTD Submissions	3
Figure 2. eCTD Submissions by Application Type	3
Figure 3. Study Data Standards Tested in 2018.....	5
Figure 4. CDMH Concept	8
Figure 5. Implementation Dates – Update	9
Figure 6. Updates to Data Standards Catalog, TCG, and Technical Rejection Criteria	10
Figure 7. 2019 Direction Highlights	11

1 Introduction

The Center for Drug Evaluation and Research (CDER) publishes an Annual Assessment for CDER's Data Standards Program (DSP) to provide a progress update to stakeholders reflecting the last calendar year. The previous year's assessment is available on the CDER DSP website. Further information for most projects referenced throughout this Annual Assessment is available in the [Action Plan](#).

2 CDER Data Standards Program at a Glance

This assessment highlights the projects and ongoing efforts that cover the identification of need, development, testing, adoption, implementation, and maintenance of data standards required for the efficient and effective review of regulatory submissions. The Annual Assessment is organized to align with the [Data Standards Strategy](#) and is mapped to the six major areas of regulatory business activity of the CBER-CDER Strategic Plan. The following sections below highlight program accomplishments.

2018 Summary of Accomplishments

Goal 1



Goal 1: Incorporate data standards to support more efficient, science-based pre-market review of medical products.

- Completed assessments for nine Therapeutic Area Standards
- Supported further evaluation of SENDIG v3.1
- Updated Study Data Business Rules
- Clinical Outcome Assessment (COA) – Completed eight Questionnaire, Rating, & Scales (QRS) assessments

Goal 2



Goal 2: Improve the post-market risk management strategies and pharmacovigilance and surveillance of medical products by using data standards.

- Initiated the FDA's Adverse Event Reporting System (FAERS) 2 / ICSR Implementation effort, established project framework and associated processes
- Launched FAERS Public Dashboard to expand access of FAERS data to the general public to search for information related to human adverse events

Goal 3



Goal 3: Implement common data standards to improve the quality and integrity of marketed medical products.

- Pharmaceutical Quality/ Chemistry, Manufacturing, and Controls (PQ/CMC) continued review of comments on draft data elements and terminologies and conducted a public meeting on Standardized Data
- Continued progress on improving usability of Annual Reports submissions
- Continued assessment of Identification of Medicinal Product (IDMP) standards to ensure conformance with FDA regulatory requirements

Goal 4



Goal 4: Promote innovation in the development and use of data standards.

- Completed mapping of Biomedical Research Integrated Domain Group (BRIDG) classes to the Fast Healthcare Interoperability Resources (FHIR) resources
- Collaborated with HL7 Biomedical Research and Regulation (BR&R) workgroup to develop FHIR resource use cases/scenario in clinical research
- Assessed proof-of-concept implementation for eSource initiatives to identify best practices to support future development
- Completed most of the foundational design and implementation milestones for the Common Data Model Harmonization (CDMH) project

Goal 5



Goal 5: Ensure effective communication and collaboration with stakeholders on data standards

- The Technical Conformance Guide (TCG) was updated in March and October of 2018
- Continued updates to the FDA Data Standards Catalog

Goal 6



Goal 6: Improve the management and usability of the volume of information through data standards

- Initiated the Data Governance effort to develop an operating model and support the implementation of a data governance framework across CDER

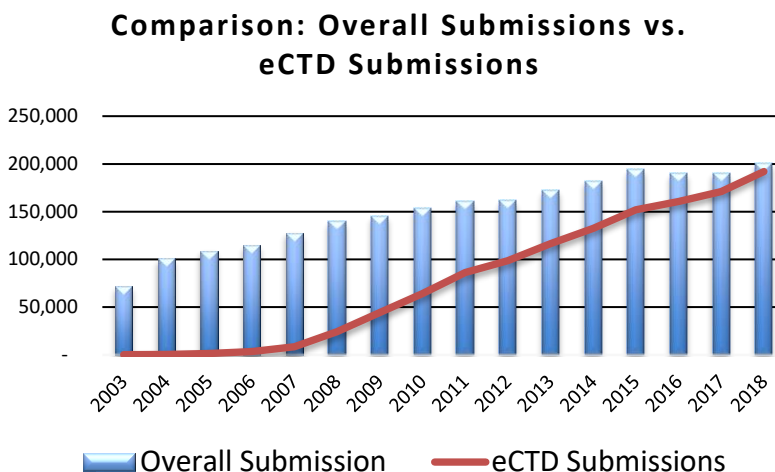
3 Impact of Requiring Standards

FDA continues to implement data standards for study data and submissions and requires applications use these standards as defined in the FDA data standards catalog. In 2017, FDA published the [Assessment of the Impact of Electronic Submissions and Data Standards on the Efficiency and Other Performance Attributes of the Human Drug Review Process](#), which assessed the degree of implementation of electronic submissions and data standards, the readiness of data standards, effectiveness of electronic review tools and training, and impact of standards and electronic submission on the review environment. The assessment identified potential actions to consider for improving the FDA electronic submission and review environment.

4 2018 Electronic Submission Metrics

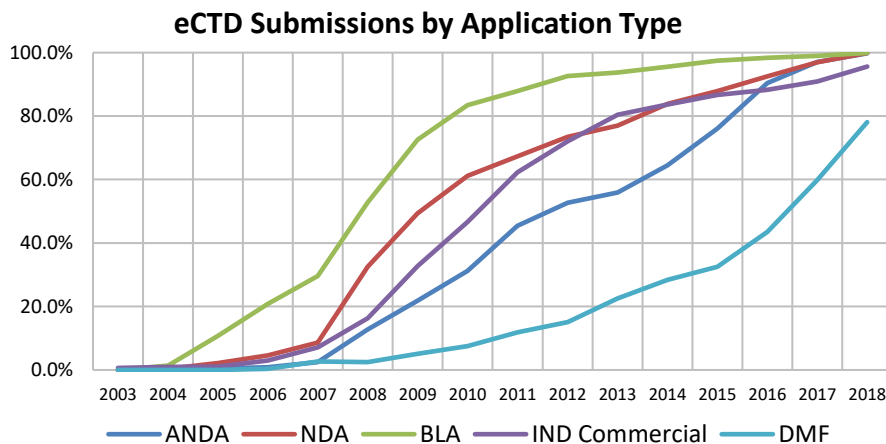
Analyses of FDA’s submissions showed a clear trend of improvement in compliance to eCTD format requirements. CDER receives approximately 200,000 electronic submissions via Electronic Submission Gateway annually. In FY2018, about 96% of all submissions were in eCTD.

Figure 1.



Further analyzing the FY2018 submission metrics by application type, nearly 100% of the regulatory submissions for NDA, BLA, and ANDA were in eCTD. For Commercial IND and DMF, 96% and 78% (Type II, IV, V).

Figure 2.



5 2018 Data Standards Program Year in Review

The CDER DSP continued to make significant progress in 2018 which is highlighted in the sections below. The published Guidance and Technical Specifications updates along with

standard operating procedures and templates, supported the program as it continued to focus on participating in the development and testing of standards and evaluating standards which has led to several updates of the FDA Data Standards Catalog.

5.1 Goal 1: Incorporate data standards to support more efficient, science-based pre-market review of medical products

The Prescription Drug User Fee Act (PDUFA) VI Performance Goals indicate FDA will develop and update therapeutic area user guides (TAUGs) to include the appropriate content for the analysis data standards used in submission and review. Significant progress continued in 2018 in the planning, development and testing of TA data standards which focus primarily on efficacy review and evaluation of new medical products.

The [list of the prioritized TAs](#) and their development status was updated to reflect progress made and changes in CDER priorities. Of the fifty-five TAs on this list, forty-eight have commenced either within FDA to capture business needs or in collaboration with external parties to develop standards. The relevant recommendations documents are provided to serve as input to the project scope in SDO projects, ensuring Review Division input early in each project.

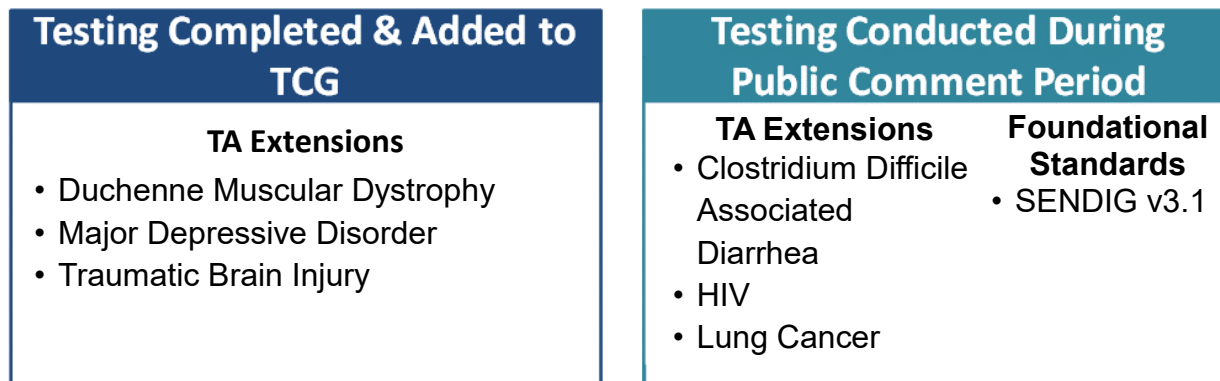
The Center continued to implement and refine its comprehensive testing approach to ensure that



data standards meet FDA's needs as well as to assess impact to the current review environment and tools. The Clinical Data Interchange Standards Consortium (CDISC) foundational standards and TA extensions were prioritized for testing by

the Study Data Standards Working Group, when possible, testing activities were conducted while the standard was available for public review. In 2018, the Study Data Standards Working Group assessed nine study data standards leading to updates in the Technical Conformance Guide for six TAs supported by FDA.

Figure 3. Study Data Standards Tested in 2018



Following CDER’s announcement to support SENDIG v3.1 in August of 2017, FDA has continued to improve the Technical Conformance Guide and further support evaluations of the SENDIG v3.1. In 2018, CDER Office of Computational Science (OCS) conducted a comparison of the SENDIG v3.0 and SENDIG v3.1 to analyze the differences and the potential impacts on the DataFit tool. Furthermore, SENDIG v3.1 was assessed for impacts that the new version will have on Janus. Findings from the assessment helps to better prepare OCS and the Janus team when the new version is available for use by sponsors.

In addition to testing the SEND foundational standard, CDER is collaborating with Critical Path Institute and CDISC to develop improved data standards for Animal Efficacy Studies and Natural History Studies for Animal Rule studies. This project is in the development stage and is planning to publish a Standard for Exchange of Nonclinical Data Implementation Guide: Animal Rule.

The FDA Business Rules (BR) Change Control Board (CCB) maintains and updates the list of business rules on the Study Data Standards Resources website which are used to communicate in a human-readable format the Agency’s business needs and practices around regulatory review. The goals of the BR CCB are to help industry understand how best to submit study data that are compliant, useful, and will support meaningful review and analysis and mature existing data standards along these same lines. Regulatory review is a complex and multi-faceted task, the BR CCB focuses on one piece of the process at a time and works with subject matter experts in that area to distill any business rules that are appropriate across the Agency. The list of business rules has been updated twice in 2018. In January 2018, version 1.3 was published to include novel rules that describe how to submit data elements describing subject race and ethnicity to align with the guidance document published in October 2016. Version 1.4 was later published in October 2018 and focused primarily on developing novel rules to more fully characterize traceability between SEND datasets and tumor.xpt.

CDER’s Clinical Outcome Assessment project is focused on the development and evaluation of COAs submitted in support of regulatory submissions. COAs capture patient experience data in Phase I-III of clinical trials in drug development programs. The purpose of COAs is to assess

treatment efficacy, treatment safety and tolerability, and used to formulate labelling claim language. During 2018, eight QRS supplements were completed.

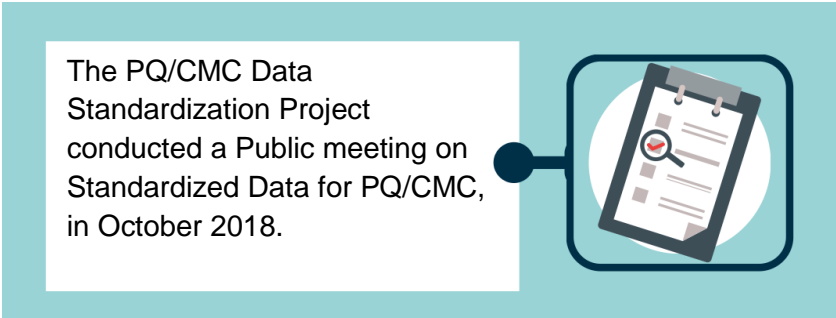
5.2 Goal 2: Improve the post-market risk management strategies and pharmacovigilance and surveillance of medical products by using data standards.

FAERS is a mission critical system for FDA, it supports the CDER/CBER's post-marketing safety surveillance program for all marketed drug and therapeutic biologic products. The FAERS II program is initiated in summer 2018 to provide a modernized system for safety surveillance including pre-market and post-market safety reports along with product quality defect reports. The goal for the system is to become a one-stop shop solution for intake, triage, and case processing. It will also allow for enhanced and unified data analytics and signal management lifecycle solution utilizing ICH E2B R3 standard.

Meanwhile, a highly interactive and user friendly [FAERS Public Dashboard](#) was launched in 2018 to provide the general public access to information related to human adverse events reported to the FDA by the pharmaceutical industry, healthcare providers and consumers.

5.3 Goal 3: Implement common data standards to improve the quality and integrity of marketed medical products.

The PQ/CMC Data Elements and Terminologies Data Standardization Project continued work related to characterizing data elements and terminologies for information used in support of Module 3 of eCTD based drug applications. An overall goal of this initiative is the development of standardized, structured and computable data standards for PQ/CMC submissions, ensuring consistent representation of concepts. In 2018 the project



The PQ/CMC Data Standardization Project conducted a Public meeting on Standardized Data for PQ/CMC, in October 2018.

finished the review of public comments submitted to the draft data elements and terminologies docket, and completed an evaluation of IDMP standards for alignment with PQ/CMC¹.

As FDA focuses on the challenges of the global supply chain and foreign sourcing of medicinal products, FDA continues to participate and promote the conformance to international harmonized IDMP to ensure the safety of medications throughout the world. In 2018, FDA continued assessment of IDMP standards to ensure conformance with FDA regulatory requirements.

¹ Draft Standardization of Pharmaceutical Quality/Chemistry Manufacturing and Control Data Elements and Terminologies; Request for Comments ([FDA-2017-N-2166](#))

The Annual Report project seeks to improve the usability of Annual Report submissions pertaining to Distribution data, Field Alert Reports, and PQ/CMC information. The project will ensure that essential facility location and production information, and an up-to-date view of the CMC process are captured completely and in a format conducive to electronic receipt, storage and usage. This project continues to assess and refine the proposed changes that are undergoing internal agency reviews.

5.4 Goal 4: Promote innovation in the development and use of data standards.

CDER co-leads the HL7 BR&R workgroup. The BR&R areas of interest encompass clinical and translational research, both regulated and non-regulated, and the subsequent regulatory submissions and information exchanges to bring new products to market and to ensure safe use throughout the product lifecycle. BR&R creates and promotes standards to facilitate biomedical research and any subsequent regulatory evaluation of the safety, efficacy and quality of medical products that may arise from research. BR&R maintains the BRIDG information model representing a shared view of the concepts of basic, pre-clinical, clinical, and translational research. This structured information model is being used to support development of data exchange standards and technology solutions that will enable semantic interoperability within the biomedical/clinical research arena and between research and the healthcare arena.

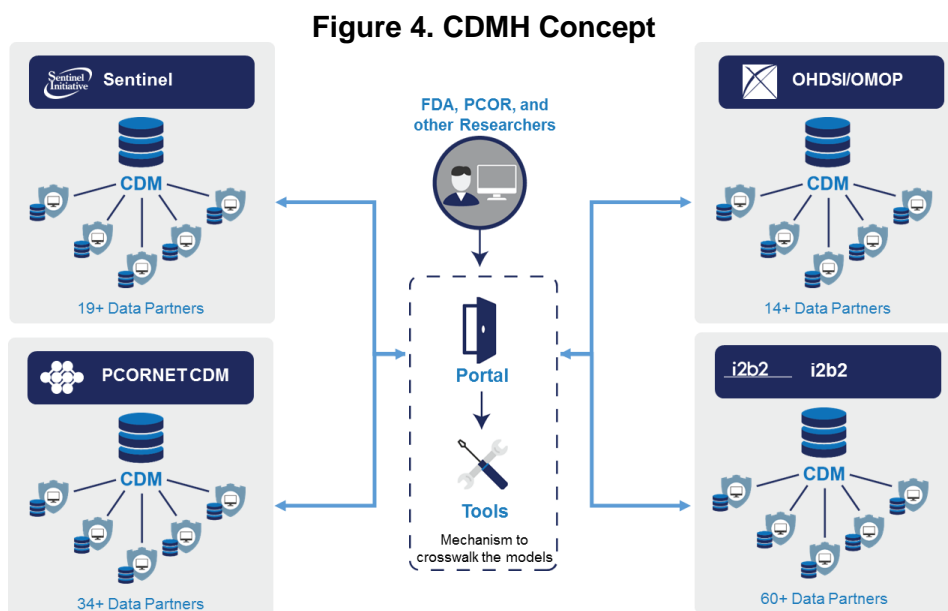
In collaboration with the BR&R workgroup, CDER currently has a project to support the architecture review of BRIDG to make it more sustainable, accessible and usable. The project identified an initial list of BRIDG model re-architecture changes and developed approaches to expanding use of BRIDG in biomedical research by linking to pre-existing standards (termed “modelling by reference”). The project objectives also include harmonizing BRIDG with FHIR, a modern HL7 standard for exchanging healthcare information electronically. By the end of 2018, the project mapped all BRIDG classes to FHIR resources and worked with the HL7 BR&R workgroup to develop use cases/scenarios in clinical research where FHIR resources could be leveraged (such as the semantics of research studies and research subjects), and subsequently balloted them at HL7.

eSource data (electronic source data) refers to the use of electronically recorded information as a source of data directly transferred to data systems used for clinical trials. The device or system that records the original data can include many items such as wearable devices, mobile apps. One of the larger potential sources of eSource data is Electronic Health Records (EHR) systems. A large amount of clinical trials participant data, which needs to be entered in research electronic case report forms (eCRFs), already exists in healthcare provider’s Electronic Health Records systems. However, EHR and eCRF data are generally collected in separate, non-compatible formats and exist in separate systems. This results in patient information being manually re-entered into the eCRF system, dramatically slowing down workflow and increasing the risk of inaccuracies due to duplicate entry. This is a major barrier to research on real-world use of drugs and biologics.

CDER is supporting two projects that aim to demonstrate approaches for collecting eCRF data, stored on research Electronic Data Collection (EDC) systems, directly from an EHR system in an FDA-compliant way. These projects will also demonstrate relevant improvements in efficiencies and potential returns on investment from using an automated approach versus the current manual methodology. One of these projects, Transforming Research Through eSource and Standards, plans to collaborate with clinical research sites and organizations to develop and evaluate EHR-to-EDC solutions in conjunction with ongoing research. The project objective is to use identified metrics to measure the relative benefits of using an EHR-to-EDC solution compared to traditional manual entry methods. The second project, Source Data Capture from EHRs: Using Standardized Clinical Research Data, has similar overall goals and is being performed as part of an existing phase 3 trial. In 2018, the project made significant strides in system development, specifying the data elements to be incorporated in an EHR-to-EDC system for pilot testing, and working through the complexities of their EHR system Applied Program Interfaces to allow bi-directional communication between systems. Proof-of-concept implementation was assessed for the best practices to build upon in continued development.

Real World Data (RWD) is data gathered in everyday settings, not generated by research protocol-driven methods, such as entries into patient EHRs during routine visits. CDER is working to outline the conceptual and logistical groundwork around efforts that began in 2018, culminating in the first output, the [Framework for FDA's Real-World Evidence Program](#) released December 2018.

The Common Data Model (CDM) Harmonization project started in 2017 to build a data infrastructure for conducting research using RWD derived from the delivery of health care in routine clinical settings. Shown in Figure 4, the objective of this project is to create a proof of concept solution that enables a researcher to make a single query usable across data from four distinct CDM research formats - FDA's Sentinel CDM, the Observational Health Data Sciences and Informatics CDM, PCORnet CDM, and the Accrual of Patients to Clinical Trials i2b2 CDM.



This Patient-Centered Outcomes Research Trust Fund (PCORTF) project is a collaborative effort involving five organizations: FDA, NCATS, National Cancer Institute, National Library of Medicine, and the Office of the National Coordinator and is led by FDA. The project has worked to define requirements, determine the architectural approach, conduct a tools evaluation, and continues core data mapping activities. In 2018 a large portion of the foundational design work and implementation was completed with work continuing into 2019.

5.5 Goal 5: Ensure effective communication and collaboration with stakeholders on data standards

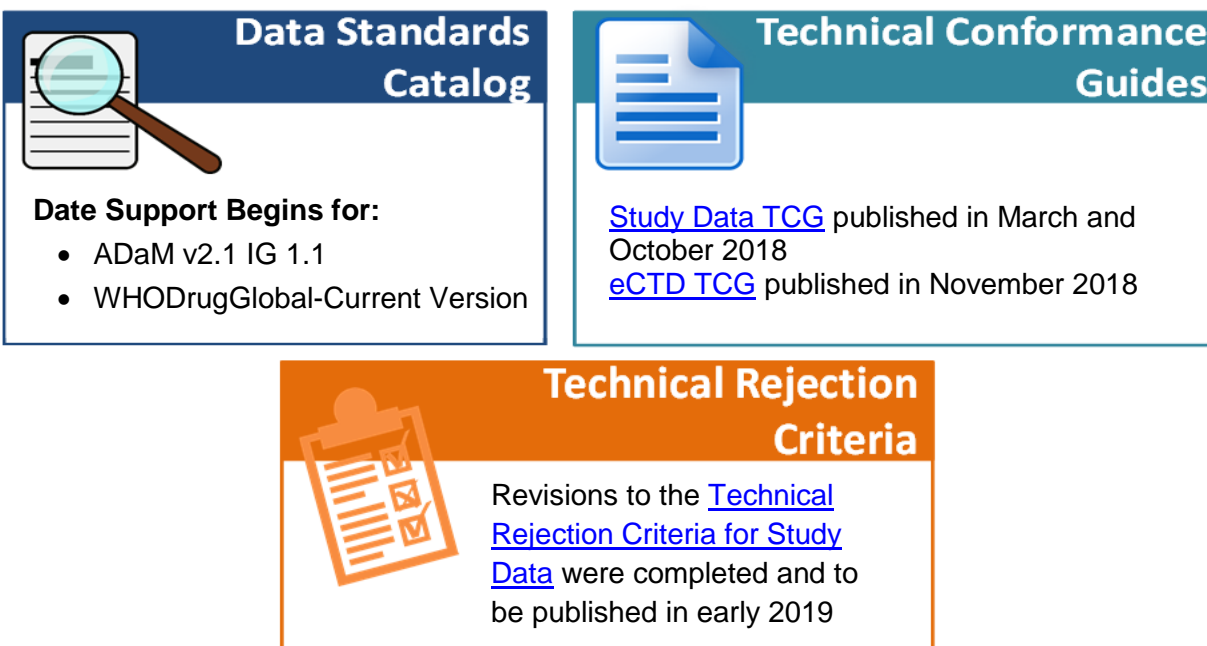
On December 17, 2016, the first requirement implemented under the provisions of FDASIA that authorized the electronic submission of information for NDAs, BLAs, and ANDAs went into effect requiring clinical and nonclinical trials that started on or after that date to use the standards in the FDA Data Standards Catalog. Requirements for submissions to use the electronic eCTD format began on May 5, 2017. Figure 5 highlights these implementation dates.

Figure 5. Implementation Dates – Update



To ensure that submissions meet expected requirements, CDER and Center for Biologics Evaluation and Research (CBER) will validate submissions upon receipt and will assess conformance to required study data standards. The [Technical Rejection Criteria for Study Data](#) was published in November 2016 and outlines the approach and validations planned for study data. During 2017 CDER and CBER initiated the development of the electronic technical rejection validation criteria and started testing.

To ensure that current information continues to be available, new versions of the technical specifications associated with Providing Regulatory Submissions in Electronic Format — Standardized Study Data guidance (eStudy Guidance), specifically the *Data Standards Catalog* and *Study Data TCG*, were updated in 2018. The Data Standards Catalog lists the data standards and terminologies that FDA supports for use in regulatory submissions to better enable the evaluation of safety, effectiveness, and quality of FDA-regulated products. The Study Data TCG provides specifications, recommendations and general considerations on how to submit standardized study data using standards listed in the data standards catalog. These documents provide a detailed revision history but in general reflect feedback from industry and FDA staff as well as results of testing and acceptance activities discussed above. Figure 6 highlights the new versions published in 2018.

Figure 6. Updates to Data Standards Catalog, TCG, and Technical Rejection Criteria

As part of its role in defining and governing CDER’s Data Standards program, the Data Standards Program Board (DSPB) updated the Data Standards Strategy document in 2017 to create a joint CBER-CDER Data Standards Strategy. The Action Plan, updated quarterly, continued to highlight progress across the program as progress has been made to the Center’s strategy. The Action Plan was updated in 2018 to align with the CBER-CDER Data Standards Strategy. The Data Standards Operations Subcommittee continued to conduct primary operations on behalf of the DSPB. The Study Data Standards and TCG workgroups remained very active all year supporting testing and updates to the guide that were published. All progress and decisions are briefed to the DSPB bi-monthly or on an as needed basis.

The DSP conducted an annual review of the Data Standards Program Manual of Policies and Procedures and supporting standard operating procedures (SOPs) to assess the need for updates or refinements. Minor updates and process step clarifications were incorporated into the SOPs.

The DSP continued its communication efforts by refining the study data standards resource webpage. The program is developing a series of fact sheets related to study data, eCTD, MFs, electronic gateway, creating a new data standards video and refining the interactive Drug Lifecycle webpage.

5.6 Goal 6: Improve management and usability of the volume of information through data standards.

The CDER Data Governance project was initiated in 2018 with the objective of developing and implementing a data governance framework across CDER data domains such as Regulatory

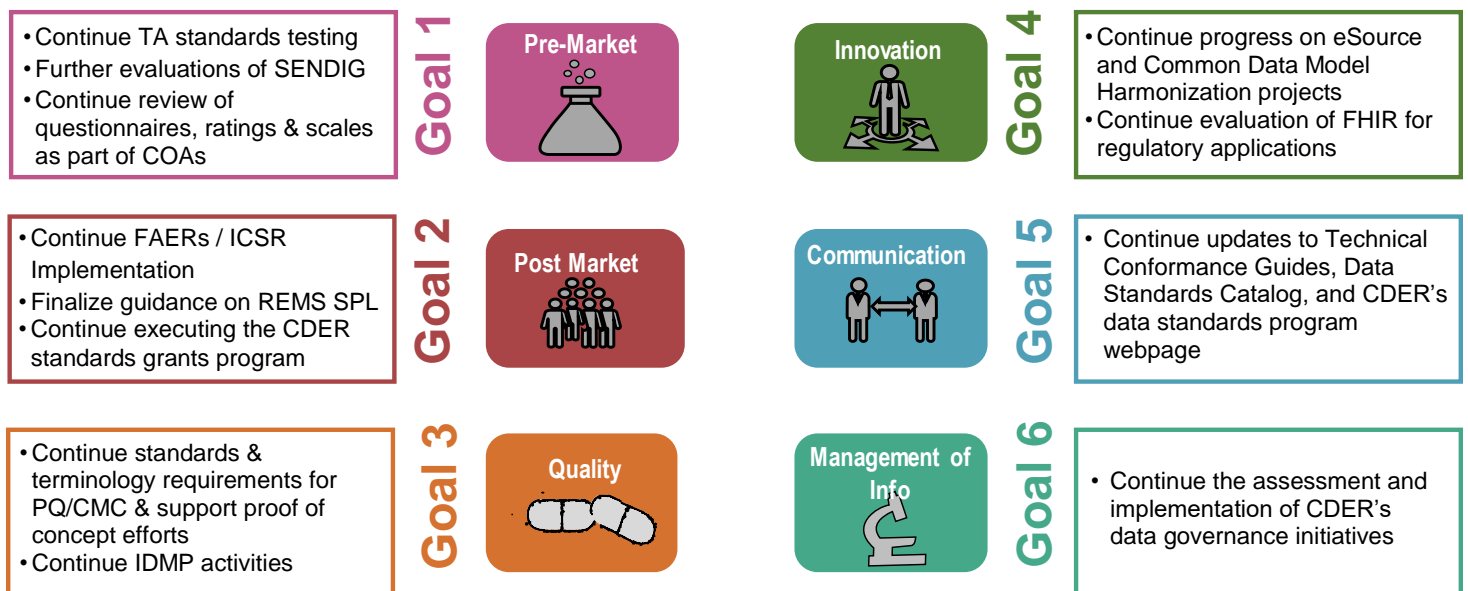
Sciences, Facilities Data and Products, etc. The preliminary assessment of the current state has been completed in 2018, going forward in 2019, the project will continue the development of an operating model that supports the management of an effective Data Governance program within CDER.

6 Moving Forward - 2019 CDER Data Standards Program Direction

With required electronic study data standards and electronic submissions in effect or coming into effect, respectively, CDER continues to focus on ensuring that the review environment is capable to support receipt, processing and review of all electronic data. Continued collaboration with SDOs and stakeholders to ensure long-term sustainability of supported data standards, as well as the testing of new standards and terminologies will be a key focus of the DSP.

To support communication of new technical specifications and conformance guides, as well as relevant standards information, TCG will be updated in March and October of 2019, new FDA webpage updates (e.g., PDUFA VI Informatics webpage) are planned for deployment throughout 2019. These updates will ensure a consistent external web presence, revised materials, and interactive tools for both internal and external stakeholders. Figure 7 highlights focus areas in 2019.

Figure 7. 2019 Direction Highlights



In addition to these project areas, the Center is committed to continuing support for demonstration efforts that highlight standards-based technology solutions for collection of related healthcare and clinical research information. For updates on this, and other ongoing projects ongoing in 2018, see the DSP Action Plan published quarterly on the [CDER Data Standards Program](#) webpage.

Appendix A: Glossary of Acronyms

ANDA	Abbreviated New Drug Applications
BLA	Biologics License Applications
BR	Business Rules
BR&R	HL7 Biomedical Research and Regulation Group
BRIDG	Biomedical Research Integrated Domain Group
CBER	Center for Biologics Evaluation and Research
CCB	Change Control Board
CDER	Center for Drug Evaluation and Research
CDISC	Clinical Data Interchange Standards Consortium
CDM	Common Data Model
COA	Clinical Outcomes Assessment
DSP	Data Standards Program
DSPB	Data Standards Program Board
eCRF	Electronic Case Report Forms
eCTD	Electronic Common Technical Document
EDC	Electronic Data Collection
EHR	Electronic Health Record
FAERS	FDA's Adverse Event Reporting System
FDASIA	Food and Drug Administration Safety and Innovation Act
FD&C Act	Federal Food, Drug, and Cosmetic Act
FHIR	Fast Healthcare Interoperability Resources
FRN	Federal Register Notices
FY	Fiscal Year
GSRs	Global Substance Registration System
IDMP	Identification of Medicinal Product
IND	Investigational New Drug
ISO	International Organization for Standardization
MF	Master File
NCATS	National Center for Advancing Translational Sciences
NDA	New Drug Applications
NIH	National Institutes of Health
PCORTF	Patient-Centered Outcomes Research Trust Fund
PDUFA	Prescription Drug User Fee Act
PhUSE	Pharmaceutical Users Software Exchange
PQ/CMC	Pharmaceutical Quality/ Chemistry, Manufacturing, and Controls
REMS	Risk Evaluation and Mitigation Strategies
RWD	Real World Data
RWE	Real World Evidence
SDO	Standards Development Organization
SEND	Standard for Exchange of Nonclinical Data
SENDIG	Standard for Exchange of Nonclinical Data Implementation Guide
SOP	Standard Operating Procedures
SPL	Structured Product Labeling
TA	Therapeutic Area
TCG	Technical Conformance Guide