Data Standards Program Action Plan

Version: 5.2

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REVISION HISTORY

Version Number	Revision Date	Description of Change
1.0	February 21, 2013	Initial Document
1.1	July 29, 2013	Quarterly Update
1.2	October 23, 2013	Quarterly Update
1.3	February 5, 2014	Quarterly Update
1.4	May 30, 2014	Quarterly Update
1.5	October 2, 2014	Quarterly Update
1.6	January 21, 2015	Quarterly Update
1.7	April 8, 2015	Quarterly Update
1.8	July 8, 2015	Quarterly Update
2.0	October 14, 2015	Update to reflect Data Standards Strategy v2.0 and quarterly project update
2.1	February 3, 2016	Quarterly Update
2.2	May 25, 2016	Quarterly Update
2.3	August 31, 2016	Quarterly Update
2.4	November 18, 2016	Quarterly Update
2.5	March 15, 2017	Quarterly Update
2.6	June 29, 2017	Quarterly Update
2.7	December 26, 2017	Quarterly Update
3.0	February 28, 2018	Update to reflect Data Standards Strategy FY2018-2022 and quarterly project update
3.1	April 30, 2018	Quarterly Update Identification of Medicinal Product (IDMP) Project description was updated to reflect the use cases for the adoption of the IDMP standards (e.g., quality and safety of medicinal products).
3.2	July 18, 2018	Quarterly Update
3.3	October 25, 2018	Quarterly Update
3.4	January 18, 2019	Quarterly Update
3.5	April 17, 2019	Quarterly Update
3.6	July 31, 2019	Quarterly Update
3.7	November 6, 2019	Quarterly Update
4.0	February 12, 2020	Project stages updated as applicable to each project Appendix A: Updated to reflect internal project stages Quarterly Update
4.1	April 22, 2020	Quarterly Update
4.2	July 29, 2020	Quarterly Update
4.3	October 21, 2020	Quarterly Update
5.0	January 29, 2021	Quarterly Update

5.1	May 25, 2021	Quarterly Update
5.2	August 27, 2021	Quarterly Update

Table of Contents

Tables

Figures

1 Introduction

The purpose of the CBER-CDER Data Standards Strategy is to reinforce the ongoing commitment to the development, implementation, and maintenance of a comprehensive data standards program that will facilitate the pre- and post-market regulatory review process so that safe and effective medical products are available to patients.

This action plan aligns to the CBER-CDER Data Standards Strategy and reflects progress in CBER and CDER towards the defined goals and objectives. Projects selected for this action plan have started, and are resourced and funded, and have a scope that is primarily standards related.

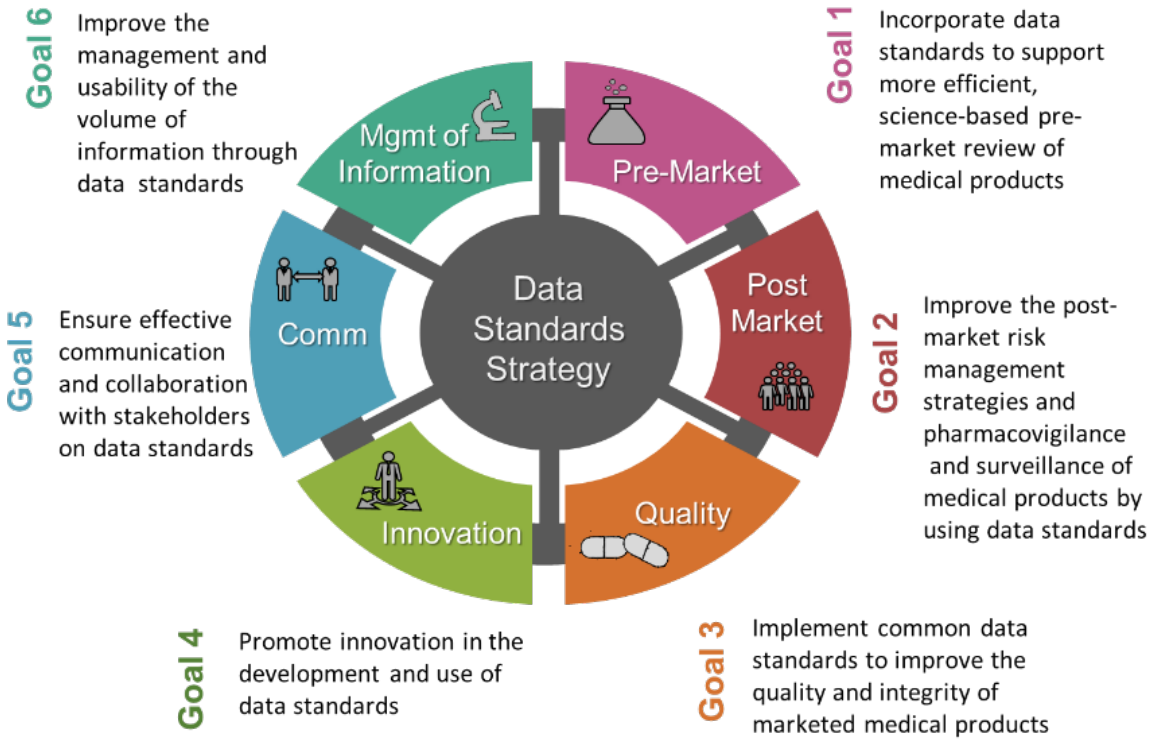
2 Purpose

This action plan provides a quarterly update to internal and external stakeholders, with an overview and progress update of current data standards initiatives. The plan will continue to be updated quarterly to reflect progress of current projects, as well as initiation of new projects.

3 Program Goals and Initiatives

The program goals are derived from the major areas of regulatory business activities. A detailed description of these major areas can be found in the CBER-CDER Data Standards Strategy. Projects in this section are organized by the goals outlined in the CBER-CDER Data Standards Strategy and shown below in **Figure 1.**

Figure 1. Data Standards Strategy Goals



For each project in this section, a project title, description, update, and project stage are provided. The project update reflects work done in the previous quarter (i.e., the February 2018 report highlights work from October to December 2017). The project stage lists the typical stages a project might address during work for the project and are generally conducted in sequence from left to right. Completed or planned stages are shown in gray, stage(s) in progress are in green and have an asterisk, and stage(s) that do not apply to a project are marked with diagonal stripes. The definitions of the project stage are defined in **Appendix A**.

Goal 1: Incorporate Data Standards to Support More Efficient, Science-Based Pre-Market Review of Medical Products

Projects under Goal 1 generally address pre-market and submission standards. These include collaboration with stakeholders and Standards Development Organizations (SDO), and testing standards to be used for submission, content, and storage. Projects that highlight participation in initiatives focused on the harmonization of healthcare and clinical research data standards are highlighted here and further addressed in Goal 4.

Table 1. Pre-Market Projects

Project Title and Description	Project Status	Project Stage
Study Data Standards Testing This CBER-CDER project tests new and updated study data standards and standards adjacent properties to establish FDA support.	Q1: • Closed out the old contract • Onboarded the new Contractors • Evaluated CDISC MSG v2.0 • Evaluating SDTMIG v3.4 Q2: • Evaluated SDTMIG v3.4 (Phase 2), ADaM Structure for Occurrence Data (OCCDS) v1.1, and TAUG-COVID-19 v1.0 and submitted comments to CDISC • Submitted comments to CDISC for FHIR-to-CDISC Mapping v1.0 and SDTM Metadata Submission Guidelines v1.0 • Evaluated the ADaM Guidance for Ongoing Studies Disrupted by the COVID-19 Pandemic Q3: • Evaluated FHIR to CDISC mapping • Evaluated TAUG-Pancreatic Cancer v1.0 • Evaluated TAUG-SSM for T1D v1.0	**Not Applicable**

Project Title and Description	Project Status	Project Stage						
		Req Definition	Alt Analysis	Development	Testing	Adoption*	Implementation	Policy
eCTD v4.0 Project This CBER-CDER project focus is the development, testing, adoption, and implementation of the next major version of the electronic Common Technical Document. (eCTD) version 4 which includes two-way communication. FDA currently uses eCTD version 3.2.2.	Q1: FDA has completed review of the public comments received on the draft eCTD v4.0 Technical Conformance Guide and FDA eCTD v4.0 Module 1 Implementation Package v1.2. The updated documents will be posted on the FDA eCTD v4.0 webpage by the end of January. Q2: FDA posted the eCTD v4.0 Technical Conformance Guide and FDA eCTD v4.0 Module 1 Implementation Package v1.2. The documents are posted on the FDA eCTD v4.0 webpage. (https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd-v40). Q3: FDA posted the Specifications for eCTD v4.0 Validation Criteria and eCTD v4.0 Comprehensive Table of Contents Headings and Hierarchy on the FDA eCTD v4.0 webpage. (https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd-v40).							
E2B IND Safety Report This CDER and CBER pilot project is testing the receipt and processing of Investigational New Drug (IND) safety reports submission using E2B standards.	Q1: Posted the updated ICH E2B(R2) Technical Specifications Document on the FAERS Electronic Submissions website. The revision includes regional requirements for IND Safety Report and Bioavailability/ Bioequivalence (BA/BE) Studies Not Conducted Under an IND. Q2: Posted clarification on requirement for A.1.FDA.16 (FDA Safety Report Type) new regional data element Q3: Working on technical specifications and regional data elements							

Project Title and Description	Project Status	Project Stage
Source Data Capture from EHRs: Using Standardized Clinical Research Data This CDER project is working to demonstrate an approach to collecting data for clinical trials that populates an electronic data capture (EDC) system directly from an electronic health record (EHR) system and document improvements to efficiency and accuracy compared to traditional methodologies.	Q1: Development continues, establishing mechanisms to facilitate additional data transfer from EHR to EDCs. Q2: Development continues, establishing mechanisms to facilitate additional data transfer from EHR to EDCs. Q3: Development continues.	**Not Applicable**
Clinical Outcomes Assessment This CDER project is focused on the development and evaluation of clinical outcome assessments (COA) submitted in support of regulatory submissions.	Q1: FDA is developing an overview document to link the development across CDISC properties (TAUGs, QRS SDTM, QRS ADaM, and FDA COA). Q2: Completed overview document and created a QRS tracking mechanism to manage intake of CDISC review requests for proposed properties. Q3: Assessments of various instruments are ongoing.	**Not Applicable**

Goal 2: Improve the postmarket risk management strategies and pharmacovigilance & surveillance of medical products by using data standards

Projects for Goal 2 address standards identification and use in FDA's mission to protect public health through medical product safety and postmarketing surveillance. Projects that highlight the communication of essential risk evaluation and mitigation strategies and standards for electronic transmission of individual case safety reports with external stakeholders are highlighted here.

Table 2. Postmarket Projects

Project Title and Description	Project Update	Project Stage						
		Req Definition	Alt Analysis	Development*	Testing	Adoption	Implementation	Policy
Grant Project: Investigating Support for 21 CFR 11 Compliance Using HL7 FHIR: As a use case for enabling implementation of audit trailing and provenance capabilities in Real World Data research, this grant is evaluating approaches to build out elements of the HL7 FHIR standard to support these capabilities. An initial use case is to add audit trail support to FHIR Resources used for recording Patient Reported Outcomes (PROs).	Q1: Conducted internal planning and early development of internal proofs-of-concept. Q2: Developing potential approaches to using HL7 FHIR resources for this project Q3: No update			■				
Biologics Effectiveness and Safety (BEST) Innovative Methods (IM) Leverages AI, ML, FHIR standards and SMART-on-FHIR to develop a semi-automated adverse event reporting system from EHRs. The system uses such innovative methods to detect exposures/outcomes of biologics and facilitates validation and reporting of flagged cases to the FDA. Project goals include development of tools, methods and techniques needed to reduce the burden on providers to report adverse events (AEs) accurately and efficiently, which is critical to strengthen the postmarket active surveillance program of CBER-regulated products.	Q3: Finalized the BEST FHIR Implementation Guide (IG) to make it ready for Balloting; Promoting the needed data elements for inclusion in USCDI; Explored developing collaborations with internal and external parties to advance AE resources.				■			

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

Projects for Goal 3 address medical product quality and identification of contamination and other production failures with common data standards. Projects that highlight the development and implementation of data standards that describe manufacturing and testing of medical products, International Standards Organization (ISO) standards implementation, and complete essential facility and manufacturing information through submission requirements are highlighted here.

Table 3. Quality Projects

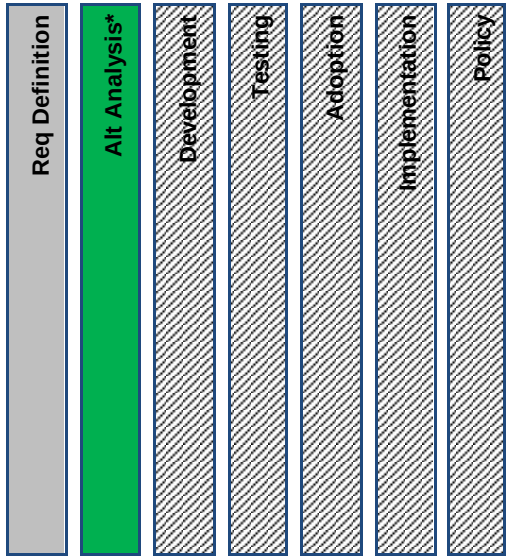
Project Title and Description	Project Update	Project Stage						
		Req Definition	Alt Analysis	Development*	Testing*	Adoption	Implementation	Policy
Pharmaceutical Quality/ Chemistry, Manufacturing, and Controls Data Standardization This CDER project with participation from CBER and CVM will identify and standardize data elements, terminologies, and data structures to enable automation of key analyses of Pharmaceutical Quality (PQ)/ Chemistry, Manufacturing, and Controls (CMC) data to support more efficient and effective regulatory decision-making.	Q1: Continued mapping PQ/CMC requirements to FHIR resources and development of FHIR exchange standards. Q2: Continued working on FHIR mapping. Q3: Continued working on FHIR mapping.			■	■			
IDMP Project This project has multiple use cases focused on the adoption of ISO Identification of Medicinal Product (IDMP) standards: 1. Medicinal Product ID (MPID) , 2. Substance ID (SubID), 3. Pharmaceutical Product ID (PhPID), 4. Route of Administration, Dosage Form, and 5. Units of Measure. These ISO standards define medicinal product information for regional and global data sharing. Generally, the use cases focus on safety (e.g., ICSRs) and can support quality (e.g., PQ / CMC).	Q1: Continued pursuing global harmonization in IDMP implementation via EU/FDA collaboration, ISO, and EU UNICOM project. • ISO 11239 and TS 20440 revision underway. • In-depth analysis on UNICOM Work Package 1 Gaps Analysis Report. Q2: Conducting a WHO UMC-FDA pilot to evaluate the feasibility of using Dose Form Characteristics for the generation of Global PhPIDs. Q3: Presented UMC-FDA Global PhPID Pilot results and findings at ISO TC215 WG6 meetings. Finishing final report and recommendations for the September ISO meetings.			■	■			

Project Title and Description	Project Update	Project Stage
Post Approval Changes Rulemaking & Submission Standards This CBER-CDER project is focused on improving the usability of post approval submissions data.	Q1: The project is in the proposed rule stage and is undergoing internal agency review. Q2: No updates at this time. Q3: No updates at this time.	Req Definition* / Alt Analysis / Development / Testing / Adoption / Implementation / Policy

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

Projects for Goal 4 address research and development in pursuit of innovation to keep pace with advances in medical science and regulatory review. Projects that highlight implementation of new data standards, encourage the use of electronic health records to support clinical trials, and evaluation of the feasibility of representing real world data in an electronic standardized format are highlighted here.

Table 4. Innovation Projects

Project Title and Description	Project Update	Project Stage
Common Data Model Harmonization Project: Phase II This CDER project is focused on leveraging nearly all aspects of the previous phase of work to expand the utility of a real-world evidence research tool which, in addition to support queries across four distinct Common Data Models (FDA's Sentinel Program, the Observational Health Data Sciences and Informatics program, the National Patient-Centered Clinical Research Network, and the Accrual of Patients to Clinical Trials network), will support querying HL7 FHIR-compliant data sets, making it useable in a wide variety of research settings. For the phase of work, FDA is coordinating with its partner the National Institutes of Health National Center for Advancing Translational Sciences.	Q1: Continued development of FHIR-supporting infrastructure. Q2: Continued development of FHIR-supporting infrastructure. Finalizing test data partnerships. Q3: Continued development of FHIR-supporting infrastructure. Finalizing test data partnerships.	

Project Title and Description	Project Update	Project Stage
Assessing Applicable Data Standards for Use in Submission of Real World Data to FDA FDA is examining the gaps between the Real World Data (RWD) needs of FDA and capability of various data standards to support submission of RWD to FDA. This assessment will help determine a roadmap for applying data standards for RWD submission to FDA.	Q1: Internally assessed FDA information systems that would be potentially impacted by any modifications to data standards, continued gap analysis of RWD needs and existing data standards. FDA recognizes the importance of developing data standards to maximize the utility of RWD and is working on identifying relevant standards and methodologies for collection and analysis of RWD. Q2: Continued data domain analysis. Q3: Continued data domain analysis.	Req Definition | **Alt Analysis*** | Development | Testing | Adoption | Implementation | Policy

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

Program operations for Goal 5 execute CBER and CDER's communication and collaboration with internal and external stakeholders for the successful development, implementation, and use of data standards to support regulatory review of medical products. Document updates that report progress towards meeting FDA goals are highlighted here.

Table 5. Communication Efforts

Program Operations	Updates
Webpage Updates	The following webpages were updated with documents referenced below: • CDER Data Standards Program • Electronic Common Technical Document (eCTD) • Study Data Standards Resources • Study Data for Submission to CDER and CBER • eCTD v4 • Electronic Submission Presentations
Federal Register Notices (FRNs)	The below FRNs were published: • March 5, 2021: Data Standards; Requirements begin for the Clinical Data Interchange Standards Consortium Version 1.1 of the Standard for Exchange of Nonclinical Data Developmental and Reproductive Toxicology Implementation Guide and Version 1.6 of the Study Data Tabulation Model. Clarification to the FDA Data Standards Catalog • June 10, 2021: Electronic Study Data Submission; Data Standards; Support and Requirement Begin for Study Data Tabulation Model Version 1.8 With Standard for Exchange of Nonclinical Data Implementation Guide-Animal Rule Version 1.0 • July 29, 2021: Electronic Study Data Submission; Data Standards; Technical Rejection Criteria for Study Data Effective Date
eCTD Submission Standards	May 2021: • Videos to demonstrate use of TRC Self Check Worksheet • Video to demonstrate Creation of Simplified TS.XPT June 2021: • Specifications for eCTD v3.22 Validation Criteria, v4.0 • Specifications for eCTD v3.22 Validation Criteria, v4.1 • File Format Specifications, v6 • eCTD v4 Validation Criteria, eCTD v4 Comprehensive Table of Contents Headings and Hierarchy, eCTD v4 Regional Implementation Guide • Transmitting Electronic Submissions Using eCTD Specifications v1.9 July 2021 Updates to eCTD documents in preparation for TRC full implementation

Program Operations	Updates
Technical Specifications and Conformance Guide Updates	• The Study Data Technical Conformance Guide (sdTCG) v4.7 was published in April 2021, v4.7.1 was published in June 2021, and v.4.7.2 was published in August 2021 • Submitting Nonclinical Datasets for Evaluation of Rodent Carcinogenicity Studies of Pharmaceuticals, Guidance for Industry, Technical Specifications Document v. 1.0 (May 2021) • FDA Data Standards Catalog updated to reflect content in sdTCG, July 2021
Action Plan	The Data Standards Action Plan v5.1 was published May 25, 2021.
Outreach Opportunities, Public Meetings & Educational Activities	FDA Webinars are planned to focus on various data standards topics. FDA PDUFA VI Public Meeting on Data Standards and Electronic Submissions was held April 7, 2021. May 2021: SBIA Webinar: FDA Technical Rejection Criteria for Study Data: What you need to know PharmaSUG 2021: FDA Technical Rejection Criteria for Study Data June 2021: PhUSE US Connect 2021: Data-driven CDER Regulatory Review: Now and Future PhUSE US Connect 2021: FDA Conformance Analysis and Upcoming Implementation of Technical Rejection Criteria for Study Data

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

As outlined in the Data Standards Strategy document, technology is critically important and serves as an enabler for reviewers to access and use large amounts of data and information that is received and generated. Several data standards development projects are already underway, as highlighted earlier in this document, to promote access to high-quality, standardized data including the PQ/CMC Standardization and IDMP projects. CDER also continues to define and enhance ways to better capture information created

internally to support continued knowledge management activities. Progress towards the Goal 6 objectives will be highlighted annually in the Data Standards Program Annual Assessment and not tracked quarterly.

Appendix A. Project Stage and Description

Table 6. Standard Development Project Stages

Stage Name	Stage Description
Define Scope and Requirement (Req Definition)	A plan is developed that can include a description of the data standard need, impact on tools, processes, and information technology infrastructure, high-level concept of operations, future state benefits, and high level requirements. For study data-related projects, FDA subject matter experts and document resources (e.g., case report forms, guidance documents) are used to develop requirements for study data standards development.
Analyze Alternatives (Alt Analysis)	If needed, FDA can conduct alternative analyses to assess options and recommendations for addressing the data standards need defined in the business case. Stakeholder input is a critical part of this effort and could include a request for public comment or input in addition to planned communications.
Development	The FDA subject matter experts conduct an iterative process of data element identification (e.g., elements need to describe the study primary endpoint), definition, validation, and conduct a review with defined expert groups.
Test Standards (Testing)	A project may be required to test that all identified factors are assessed (e.g., scale, impact, suitability for FDA regulatory review needs, compatibility with FDA infrastructure) and that all policy, regulatory, guidance, and technical specification needs are identified.
Determine Data Standard Adoption (Adoption)	If needed, policy, regulatory, guidance, and technical specification needs that were identified for a given data standards change are addressed to support implementation.
Implement Standard (Implementation)	The data standard change is being implemented into the FDA environment. This phase includes all the steps to make this part of the regulatory review process. Implementation is considered complete when data can be successfully processed, reviewed, and archived utilizing the new standard.
Policy	FDA may publish an FRN or guidance, as well as post relevant technical specifications or technical conformance guides, as needed.

Appendix B: Project to Goals/Objectives Mapping

The following table maps the projects listed in the tables above to the objectives outlined for each goal in the CBER-CDER Data Standards Strategy. Some projects may align to more than one goal and objective.

Table 7. Project Mapping

Projects	Goal 1				Goal 2		Goal 3			Goal 4			
	1.1	1.2	1.3	1.4	2.1	2.2	3.1	3.2	3.3	4.1	4.2	4.3	4.4
Evaluation and Testing of the SEND standard for CBER	x												
Study Data Standards Testing	x												
eCTD v4.0 Project	x												
Source Data Capture from EHRs: Using Standardized Clinical Research Data				x								x	
E2B IND Safety Report	x												
Clinical Outcomes Assessment	x	x									x		
Integrating REMS Information into SPL					x								
Grant Project: Investigating Support for 21 CFR 11 Compliance Using HL7 FHIR	x												
Pharmaceutical Quality (PQ)/, Chemistry, Manufacturing, and Controls (CMC) Data Standardization							x						
IDMP Project						x		x					
Post Approval Changes Rulemaking & Submission Standards									x				
Common Data Model Harmonization Project: Phase II													x
Assessing Applicable Data Standards for Use in Submission of Real World Data to FDA													x

Appendix C: Glossary of Acronyms

ADaM	Analysis Data Model
AI	Artificial Intelligence
API	Applied Program Interfaces
BR&R	HL7 Biomedical Research and Regulation Group
BRIDG	Biomedical Research Integrated Domain Group
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDISC	Clinical Data Interchange Standards Consortium
COA	Clinical Outcomes Assessment
DF	Dosage Form
eCTD	Electronic Common Technical Document
EDC	Electronic Data Capture
EDQM	European Directorate for Quality Medicines
EHR	Electronic Health Record
FHIR	Fast Healthcare Interoperability Resources
FRN	Federal Register Notices
FY	Fiscal Year
GSRS	Global Substance Registration System
HCT/P	Human Cells, Tissues and Cellular and Tissue-Based Products
HL7	Health Level Seven
ICH	International Council for Harmonisation
ICSR	Individual Case Safety Report
IDMP	Identification of Medicinal Product
IND	Investigational New Drug
ISO	International Organization for Standardization
ML	Machine Learning
MPID	Medicinal Product Identifier
MSG	Metadata Submission Guideline
NDC	National Drug Codes
PCORTF	Patient-Centered Outcomes Research Trust Fund
PDUFA	Prescription Drug User Fee Act
PhPID	Pharmaceutical Product Identifier
PQ/CMC	Pharmaceutical Quality/ Chemistry, Manufacturing, and Controls
REMS	Risk Evaluation and Mitigation Strategies
RoA	Route of Administration
SDO	Standards Development Organization
SDTMIG	Study Data Tabulation Model Implementation Guide
SEND	Standard for Exchange of Nonclinical Data
SENDIG	Standard for Exchange of Nonclinical Data Implementation Guide
SENDIG-AR	Standard for Exchange of Nonclinical Data Implementation Guide: Animal Rule
SME	Subject Matter Expert
SPL	Structured Product Labeling
TA	Therapeutic Area
TAUG	CDISC Therapeutic Area User Guide
TCG	Study Data Technical Conformance Guide
UMC	Uppsala Monitoring Centre

UNICOM	Up-scaling the global univocal identification of medicines
UNII	Unique Ingredient Identifier
UoM	Units of Measure
USCDI	United States Core Data for Interoperability
WHO	World Health Organization