Data Standards Program
Annual Assessment 2014

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1 Introduction

This is the fourth annual assessment of the Center for Drug Evaluation and Research's (CDER's) Data Standards program and reflects progress made since the 2013 assessment. The assessment of the previous year is available on the CDER Data Standards Program website[1]. The focus of this document is to provide stakeholders with an update on CDER's progress over the last calendar year. The Data Standards Strategy is currently under review and an update is planned for publication in early 2015. Further information on projects referenced throughout the annual assessment is available in the Action Plan.

2 Background

Beginning in late 2010, CDER focused on initiating Data Standards Program and governance, as well as conducting a data standards needs assessment in the Center. In 2012, the CDER Data Standards Program Board refined and published version 1.0 of the Data Standards Strategy along a communication plan. Several key projects were initiated in 2012, including a broad effort to define and implement terminology standards for clinical studies of distinct therapeutic areas[2].

2013 saw significant progress made in the Center's standards efforts, and expansion of the program's portfolio of standards development initiatives. Several key artifacts were published, including the Therapeutic Area (TA) Project Plan, Action Plan, CDER / CBER position statements on the use of study data standards in conformance with Clinical Data Interchange Standards Consortium (CDISC) formats and the desire to support International System of Units (SI) for lab test results in the future.

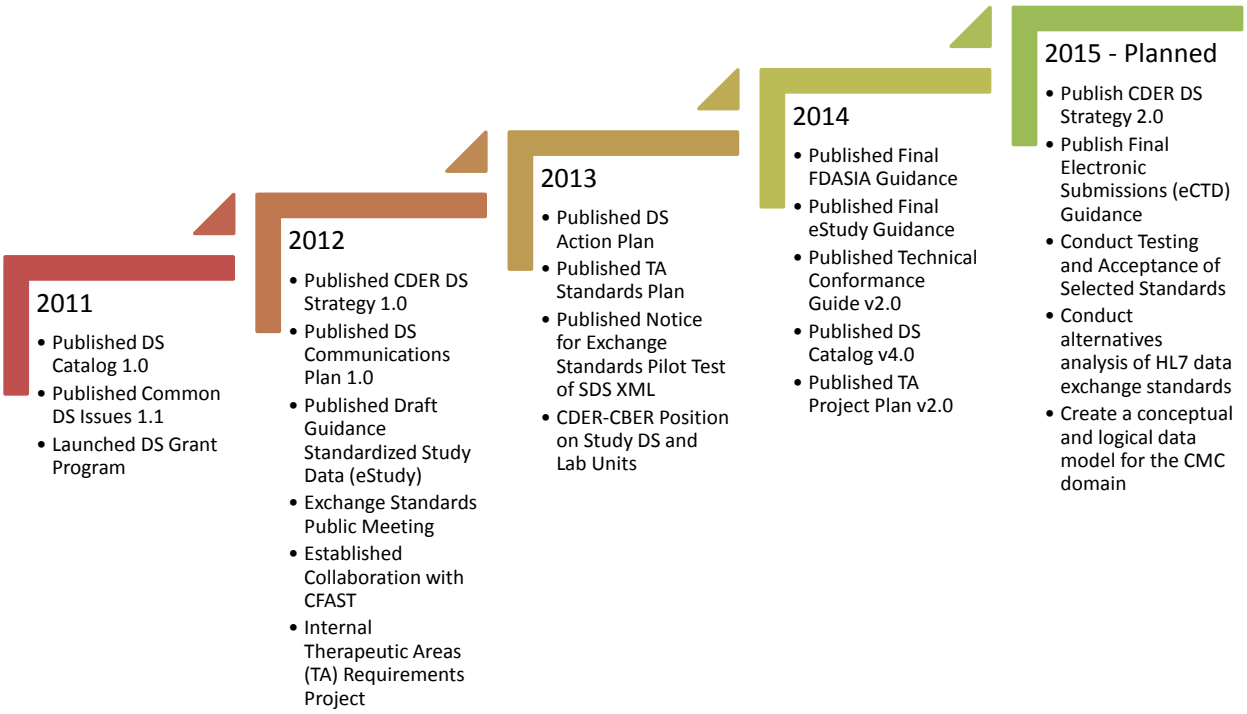
3 2014 Year in Review

Figure 1 (below) and the following sections highlight program accomplishments in policy and process, standards development, study data, and research and development.

[1] Data Standards Strategy – Action Plan is available from the CDER Data Standards Program webpage http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm249979.htm

[2] Therapeutic Area Project Plan available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm287408.htm

Figure 1 CDER's Data Standards High Level Program Accomplishments and Planned Activities



3.1 Policy and Process

The 2012 Food and Drug Administration Safety and Innovation Act (FDASIA) authorized the electronic submission of information for certain Investigational New Drugs (INDs), New Drug Applications (NDAs), Biologics License Applications (BLAs) and Abbreviated New Drug Applications (ANDAs). CDER continued the development of key guidance and governance documents related to data standards implementation. In 2013, to implement the provisions of FDASIA, CDER and the Center for Biologics Evaluation and Research (CBER) developed and in February, 2014 published, for public comment, two guidances: 1. An interpretative draft guidance on "*Providing Regulatory Submissions in Electronic Format—Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act"*; and 2. a revised draft of the guidance on "*Providing Regulatory Submissions In Electronic Format—Standardized Study Data".* These guidance documents published as final in December 2014. Additional guidances for other submission components are anticipated as the program and projects progress.

The *Data Standards Catalog* format has been revised to provide a listing of supported and/or required standards, their uses, the date FDA will begin (or has begun) to support a particular standard and the date support ends, the date the requirement to use a particular standard will begin and the date such requirement ends, as well as other pertinent information. The *Study*

Data Technical Conformance Guide (Conformance Guide) was developed in 2013 and published for public comment in February, 2014. The Conformance Guide provides specifications, recommendations, and general considerations on how to submit standardized study data using FDA-supported data standards located in the **Data Standards Catalog** (Standards Catalog). This Conformance Guide has replaced the previously available Data Standards Common Issues Document and the Study Data Specifications document.

Following good practice for standards development and governance, the CDER Data Standards Program Board (DSPB) reviewed and updated its Charter in November 2014 to refine DSPB goals and scope, update procedures, clarify voting procedures, and update the board and member responsibilities. The DSPB, which serves as CDER's executive review board, develops the Center's overall data standards strategy and is involved with monitoring progress against that strategy. The Board also ensures effective communication within and across CDER Offices and other Agency stakeholders to support attention to data standards development and implementation needs.

In 2014, the DSPB and its Operations Subcommittee (OpSC) drafted revisions to its web pages for ease-of-use and access to relevant information such as the guidance documents and Conformance Guide. The website serves as a single location for standards information. Efforts continued in 2014 to document CDER's data standard policy as part of a Manual of Policy and Procedures (MAPP). This as an important step to clarify and set governance roles and responsibilities to audiences both internal and external to FDA. The updated processes include development and implementation of a testing methodology for acceptance and readiness testing of standards, and an initiative to evaluate and develop or refine standard operating procedures (SOPs) for operational activities.

3.2 Standards Development and/or Implementation

In October 2013, CDER and CBER published a position statement on the use of SI units for lab tests. The centers recognize that SI units are the worldwide standard and plan to accept certain lab test results in SI units beginning in 2015. The CDER/CBER Position on Use of SI Units for Lab Tests is available in its entirety on the Study Data Standards webpage.

The Center recognized the need for a comprehensive and consistent testing approach to ensure that data standards meet FDA's requirements as well as its readiness to receive and utilize data in standardized form. CDER developed a *Testing and Acceptance Process for Study Data Standards* process in 2014 and embarked on a project to conduct 8 Study Data Standards tests in 2015.

With the authorization of the Generic Drug User Fee Act (GDUFA), CDER completed an internal assessment of the generic drug review process with an emphasis on data usage and submission quality. Per recommendations from the assessment, the Annual Report Project and the Chemistry, Manufacturing & Control (CMC) Data Standardization Project were initiated to improve the efficient use and review of submission data.

FDA does receive and utilize electronic healthcare data for regulatory purposes and the objective is to leverage existing standards and harmonize with healthcare standards where it

makes sense. This prompted the initiation of a Meaningful Use (MU) standards (terminologies) assessment project in 2013. The project was completed in 2014 with recommendations for several health-related standards. The project analyzed the impacts to CDER and provided strategy to adopt or harmonize with CDER existing electronic systems and data standards in several cases. In 2015 CDER will be acting on these recommendations.

3.3 Study Data Standards

The Prescription Drug User Fee Act (PDUFA) V Performance Goals indicate that FDA will develop standardized clinical data terminology for distinct therapeutic areas in collaboration with Standard Development Organizations (SDOs). Significant progress was made in 2013 in the planning and development of therapeutic area data standards which focus primarily on requirements for the efficacy review and evaluation of new medical products. The second version of the *Therapeutic Area Standards Initiative Project Plan* (Project Plan*)*, published in June 2014, serves as the annual update to the primary document for guiding all major aspects of FDA's multi-year initiative to develop and implement TA standards to support the regulatory review process for drugs and biologics. A list of the prioritized therapeutic areas and their development status may be found at:

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm287408.htm.

CDER continued to expand its TA requirements capture project in 2014. To date, 35 TAs have completed or are under way with FDA requirements being planned for 8 additional TAs by the end of FY 2015. CDER remains committed to the advancement of all data standards for clinical research and regulatory submissions by working with stakeholder groups such as Health Level Seven (HL7), CDISC, and Critical Path Institute, along with the Coalition for Accelerating Standards and Therapies (CFAST).

The Standard for the Exchange of Nonclinical Data (SEND) Cardiovascular and Respiratory Safety Pharmacology Pilot team successfully executed its proposed plan to receive sample data for review. The pilot received studies that required mapping before being made available for review. The pilot will be on hold until this mapping activity is completed.

Also in 2014 CDER published an update of the center-defined validation rules for SEND formatted files and released the initial version of the Study Data Tabulation Model (SDTM) validation rules in November 2014, both available on the Study Data Standards Resources web page.

3.4 Research and Development

Over the past few years, CDER has increased its support for standardized study data submissions using CDISC standards. Since 2007, FDA has collaborated with CDISC, HL7 and other stakeholders on potential alternatives for exchanging study data.

Building on concepts discussed at the November 2012 Solutions for Study Data Exchange Standards Meeting, CDER and CBER issued a Federal Register (FR) Notice of a Pilot Project called “Transport Format for the Submission of Regulatory Study Data” (Docket Number FDA-2013-N-1424). The pilot project was conducted during 2014. For this pilot, the FDA partnered

with six sponsors to evaluate the CDISC Data Standards (DS) Extensible Markup Language (XML) transport format[3] for the submission of regulatory study data. Its objectives were to evaluate the utility of DS-XML as a replacement transport format for SAS XPORT. A final report will be published in 2015.

CDER continues to assess Semantic Web (SW) technology as a modern approach with promising potential to address the challenges in representing and maintaining the evolving information models and standards in use by multiple stakeholders. In particular, this technology appears highly promising for enhancing the ability to automatically validate standardized data, incorporate a wide array of biomedical ontologies representing the most up-to-date medical concepts and terminologies, and support long-term interoperability with healthcare information models.

CDER completed testing and posted test results for Study Participation and Patient Narrative HL7 standards in 2014. A further pilot area is under consideration.

3 Summary and 2015 Direction

In 2014 the Data Standards Program published final FDASIA and eStudy guidance documents, which defined timelines for required study data submissions to FDA. Updates were also made to the Data Standards Catalog, documenting accepted standards and required dates, and the Conformance Guide, clarifying implementation considerations to further improve efficiency during the submissions process going forward. Quality process updates to SOPs and MAPPs allowed the program to better define and establish the operating model to support the development and implementation of data standards in CDER. The program made progress in defining FDA requirements for TAs and completed an initial testing and acceptance process in 2014.

In 2015, the program will continue to strengthen its outreach via publications and presentations at meetings, webinars, and other media (forums), both internally and externally. Additionally, the program will broaden testing activities (core SDTM and TA standards) to both refine the process and ensure CDER's readiness for acceptance. The program's portfolio will continue to develop and diversify, with projects focused on standardization needs across the drug development lifecycle.

[3] http://www.cdisc.org/studydataset-xml