
# Data Standards Strategy
# 2015-2017

## Center for Drug Evaluation and Research (CDER)

## Food and Drug Administration

## REVISION HISTORY

| Version Number | Implemented By | Revision Date | Description of Change |
|---|---|---|---|
| 1.0 | CDER DSPB | December 5, 2012 | Initial Document |
| 2.0 | OSP | July 15, 2015 | Editorial Updates |

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# 1.0 Introduction

## 1.1 Purpose

The mission of FDA Center for Drug Evaluation and Research (CDER) is to protect and promote public health by helping to ensure human drugs are safe and effective for their intended use, meet established quality standards, and are available to patients.[1] The CDER Data Standards Program promotes the development of data standards for the effective and efficient review of regulatory submissions through stakeholder collaboration, policy development, and project implementation.

CDER follows an open, consensus-based process to develop and maintain data standards for adoption. Open, consensus-based data standards are necessary to integrate, analyze, report, and share regulatory information. CDER's data standards development and maintenance program aligns with three principles[2]:

1. Ensure the use of high quality data standards, through the use of voluntary and consensus-based standards development processes in accredited standards development organizations (SDO), in place of government-unique standards; unless such standards are inconsistent with law or otherwise impractical.
2. Reduce the burden of regulation through alignment with existing health IT initiatives, laws, regulations, and mandates such as executive orders.
3. Ensure the efficiency of data standards through the adoption or adaptation of other standards currently in use, when feasible.

The purpose of this Strategy is to reinforce CDER's ongoing commitment to the development, implementation, and maintenance of a comprehensive data standards program that will facilitate the regulatory review process so that safe and effective products are available to the market sooner.

## 1.2 Background

This Strategy considers assumptions, available resources, and statutory requirements of the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA). FDASIA added 745A(a) to the FD&C Act which requires electronic submission of certain information and data in standardized formats in Investigational New Drug Applications (INDs), New Drug Applications (NDAs), Biologics License Applications (BLAs), and Abbreviated New Drug Applications (ANDAs).[3] Currently, CDER encourages the

[1] http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM376545.pdf

[2] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM416602.pdf

[3] http://www.fda.gov/downloads/Drugs/Guidances/UCM292334.pdf

submission of study data in conformance to the data standards listed in the FDA Data Standards Catalog (DSC). Standardized study data will be required in submissions for clinical and non-clinical studies that start on or after December 17, 2016 (December 17, 2017 for INDs).

Under Section XII of the Prescription Drug User Fee Act (PDUFA) V performance goals, FDA agreed to develop and implement electronic data standards using a public process that allows for stakeholder input. A focus area of PDUFA V Section XII is the development of clinical terminology standards to support efficacy analyses for distinct therapeutic areas (TAs) using Clinical Data Interchange Standards Consortium (CDISC) standards. Standardization of data elements, terminologies, and data structures will enable automation of important analyses of clinical study data to support more efficient and effective regulatory decision making.

CDER will continue to foster collaboration with regulated industry, SDOs, and other stakeholders (e.g., International Conference on Harmonisation (ICH)) to develop or refine data standards to support new use cases, such as studies for specific therapeutic areas (TAs), other study types, as well as additional data that may be required in electronic regulatory submissions under Section 505(b), (i) and (j) of the FD&C Act. The benefit of using data standards must both be recognized and deliver value through sustainable data resources (or sustainable systems with which to store and access data). CDER reviewers must have the opportunity to review the standards and related implementation guides in order to ensure that they meet rigorous scientific and regulatory requirements.

Data standards developed through the use of collaborating consortia, such as Coalition for Accelerating Standards and Therapies (CFAST), academic centers, and other federal agencies such as the National Institute of Health (NIH) and the Office of the National Coordinator for Health IT (ONC) in the Department of Health and Human Services (DHHS), should allow for quick and accurate transfer of data-specific details for research and assessment purposes. CFAST, a partnership by CDISC and Critical Path Institute (C-Path), should help further data standards in these areas.

### 1.3 Audience

We recognize that there are stakeholders who play a critical role in CDER's efforts to achieve its goals to promote the use of open, consensus-based data standards. Stakeholders include: regulated industry, health care professionals, consumers, other government agencies, and the public. These groups inform, participate, and collaborate to help shape, and in some cases, help to implement, data standards programs. FDA collaborates with stakeholders to develop new and refine existing data standards. As specified in the PDUFA V Reauthorization Goals, FDA fosters collaboration with industry, SDOs, and other stakeholders to develop or refine data standards.

### 1.4 Scope

This Strategy encompasses the identification of need, development, testing, adoption, implementation, and maintenance of data standards required for the efficient and effective review of regulatory submissions. The Strategy is aligned with performance goals of the PDUFA V Reauthorization, the PDUFA V IT/ Informatics Plan, as well as,

CDER's Strategic Plan[4]. This Strategy is mapped to the five major areas of regulatory business activity of the CDER Strategic Plan. These areas include:

1. Drug Development and Pre-Market Review
2. Drug Safety Performance and Promotion
3. Pharmaceutical Quality
4. Policy
5. Planning and Governance

## 2.0 Drug Development and Pre-Market Review

Establishing common data standards will provide new opportunities to transform the massive amount of data generated from clinical and nonclinical studies into useful information to potentially speed the delivery of new therapies to patients. Standardized data elements and relationships that are important to a particular disease or therapeutic area are essential so that data from multiple trials can be more easily grouped for analysis and reporting, as well as for meta-analyses within and across drug classes. Standards will also make it possible to develop and utilize predefined analysis panels for common analyses, thus freeing reviewers to spend their limited time on more complex questions during a review.

The Drug Development and Pre-Market Review area encompasses: review of INDs, development-phase consultations with sponsors, corresponding with industry sponsors, development of regulations and guidance to industry, development of drug bioequivalence standards, oversight of the conduct of clinical trials, improvement of labeling, review of submissions, including NDAs, BLAs, ANDAs and their supplements.

[4] http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM376545.pdf

| | | | Data Standards Strategy |
|---|---|---|---|
| Drug Development and Pre-Market Review | Standards Focus | | Conduct rigorous science-based pre-market review to help ensure that drugs marketed to the public are safe and effective by leveraging standardized Clinical and Non-clinical Study Data submitted in INDs, NDAs, BLAs and ANDAs. |
| | Standards Initiatives | | • CDISC Dataset XML for study data exchange<br>• Système International (SI) Units vs. U.S. Conventional Units<br>• SDTM, SEND, ADaM, Define.xml for Clinical and Non-Clinical Study Data<br>• Development of Therapeutic Area Endpoint Standard<br>• LOINC Codes for Laboratory Values<br>• Bioanalytical Methods Validation Standards |

## 3.0 Drug Safety Performance & Promotion

An objective of Drug Safety Performance & Promotion is to provide oversight of post-market risk management strategies, as well as drug marketing and promotion. CDER will continue its efforts on systems and standards to support how CDER obtains and analyzes post-market drug safety data and manages emerging drug safety information.

Efforts encompassed by this area include the review of Adverse Event Reports (AERs) and other drug safety information for marketed drugs and taking appropriate regulatory action such as requiring safety-related labeling changes. Other review activities include the review of sponsor reports from Post-Marketing Requirements (PMRs) and Post-Marketing Commitments (PMC)s, review of proprietary drug names to reduce the risk of name confusion and related medical errors, review of drug marketing and advertising, including promotional materials and Direct-to-Consumer advertisements, and the review of sponsor-proposed Risk Evaluation and Mitigation Strategy (REMS) and related assessment plans. Examples of data standards in Drug Safety Performance and Promotion areas are listed below.

| | | | Data Standards Strategy |
|---|---|---|---|
| Drug Safety Performance and Promotion | Standards Focus | | Oversight of post-market risk management strategies as well as drug marketing and promotion which includes pharmacovigilance and surveillance. |
| | Standards Initiatives | | • Risk Evaluation and Mitigation Strategy (REMS)<br>• Unique Ingredient Identifier (UNII) for substances<br>• Identification of Medicinal Products (IDMP)<br>• Integrity Product Dictionary (IPD)<br>• Individual Case Safety Reports R3 (E2B R3) |

## 4.0 Pharmaceutical Quality

Our objective is to improve the efficiency of regulatory review, compliance, inspection policies and practices (e.g., risk-based inspection scheduling of drug manufacturers), in order to improve the Agency's ability to predict, and possibly mitigate, future drug shortages, and to encourage the pharmaceutical industry to implement state-of-the-art, robust quality management systems for pharmaceutical manufacturing.

Pharmaceutical Quality (PQ) focuses on the review of Chemistry, Manufacturing, and Controls (CMC) of a new drug application and/or supplement. In addition, PQ facilitates the establishment of manufacturing quality and testing standards, oversight of product Quality-by-Design (QbD) standards, and development of regulations and guidance to industry. Moreover, PQ is key to the conduct of pre-approval manufacturing facility inspections, facility inspections for compliance with current Good Manufacturing Practices (cGMPs), surveillance to detect counterfeit drugs or other product issues, and monitoring and enforcement to help ensure the authenticity and integrity of drug products, the availability of drugs of acceptable quality, and the safety of the global drug supply chain.[5]

PQ data and information submitted in a new application and/or supplement are focused on ensuring continued product quality (i.e., the identity, strength, purity, and potency). The information submitted includes: 1) description and composition of the drug product / substance, (2) manufacturer, (3) control of excipients, (4) control of drug products / substance, (5) reference standards or materials, (6) container closure systems, and (7)

[5] http://www.fda.gov/Drugs/DevelopmentApprovalProcess/Manufacturing/QuestionsandAnswersonCurrentGoodManufacturingPracticescGMPforDrugs/ucm071836.htm

stability.[6] Examples of data standards in the area of Pharmaceutical Quality are listed below.

| | | Data Standards Strategy |
|---|---|---|
| Pharmaceutical Quality | Standards Focus | Regulatory Review of INDs, NDAs, BLAs, ANDAs; pre-approval manufacturing facility inspections; product availability. |
| | Standards Initiatives | • Pharmaceutical Quality/CMC Data Standardization<br>• Quality Metric Terminology<br>• Drug Supply Chain Security Act (DSCSA)<br>• Annual Report Project |

## 5.0 Policy

CDER publishes policies, guidance to industry and technical specifications documents to improve understanding in the use of data standards in electronic submissions for internal and external stakeholders. FDA intends to publish additional guidance relevant to specific submissions types or when FDA implements new data standards. FDA has published the FDA Data Standards Catalog (DSC) containing essential information on what standards FDA supports, requires, or retires for different types of information. The FDA DSC is an information source on data standards used for submitting data to FDA.

There will be periodic development and issuance of guidance documents on electronic submissions and the standardization of electronic drug application data. It is important for both FDA and regulated industry that guidance documents be developed, internally reviewed / cleared, issued for public comment and finalized in a timely manner. In addition, FDA will develop, as needed, technical specifications documents that will provide recommendations on how to submit electronic regulatory submissions and data. Examples of providing policy and guidance to industry are listed below.

[6] http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073293.pdf

| | | | Data Standards Strategy |
|---|---|---|---|
| Policy | Standards Focus | | Oversight of the development of CDER regulations and guidance related to data standards. |
| | Policy / Guidance Related to Data Standards Initiatives | | • Providing Regulatory Submission in Electronic Format – Under 745A(a) of the Food, Drug & Cosmetic Act<br>• Providing Regulatory Submission in Electronic Format – Standardized Study Data<br>• Study Data Technical Conformance Guide<br>• FDA Data Standards Catalog |

## 6.0 Planning and Governance

Our objective of this area is to establish a governance framework for the development of the data standards program. This framework encompasses the implementation of program initiatives and performance metrics. FDA's new Data Standards Advisory Board (DSAB) will provide the overarching Agency framework for the management of data standards throughout their lifecycle, including policies, procedures, accountabilities, and decision-making. At the Center level, CDER's Data Standards Program Board (DSPB) provides well-defined data standards governance structures that ensure cross-Center collaboration, communication, and alignment with respect to data standards development, implementation, and policy.

The CDER DSPB coordinates data standards activities within CDER and with other Centers and stakeholders. The Board oversees the CDER Data Standards Strategy and Program Action Plan execution and the ongoing planning, coordination and progress-tracking of data standards projects.

FDA collaborates with stakeholders (e.g., regulated industry, SDOs, academia, and medical-clinical societies, as well as other government agencies and FDA's review divisions) to develop new and refine existing data standards. For example, in the area of Therapeutic Area data standards, CFAST, an initiative sponsored by CDISC and C-Path and supported by FDA and TransCelerate BioPharma, has been involved with the TA development work streams leading to the delivery of standard data elements, concepts and terminologies for prioritized therapeutic areas. Examples of planning and governance framework in the area of data standards are provided below.

| | | | Data Standards Strategy |
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| Planning and Governance | Standards Focus | | Establishment of governance framework for the development of a data standards program. Implementation of program initiatives and performance metrics. |
| | Governance Framework Related to Data Standards Initiatives | | Internal to FDA<br>• FDA Data Standards Advisory Board<br>• CDER Data Standards Program Board<br>o Operations Sub-Committee<br>▪ Working Groups (e.g., CDISC)<br>o Terminology Sub-Committee<br>External to FDA<br>• Coalition for Accelerating Therapies & Standards (CFAST)<br>• International Conference on Harmonization (ICH) |

## 7.0 Summary

Data standards are a critical factor in improving the overall effectiveness and efficiency of the regulatory review process. CDER encourages on-going research in and development of data standards and innovative technologies to enhance the review process and improve the analytical and visualization tools available to reviewers. This Strategy expresses the Center's commitment to the development and use of study data and submission standards, as well as the proactive collaboration with SDOs, industry and other stakeholders to ensure that the standards are optimized to support analysis and decision-making. To leverage data and submission exchange standards, research and implementation requires collaboration with all stakeholders, including government, industry, SDOs, and technology providers. CDER is committed to proactive communication and collaboration. For further information on projects, review the CDER Data Standards Strategy Action Plan.

## Appendix A. Glossary of Terms

| | |
|---|---|
| ADaM | Analysis Dataset Model |
| API | Active Pharmaceutical Ingredient |
| CBER | Center for Biologics Evaluation and Research |
| CDA | Clinical Document Architecture |
| CDASH | Clinical Data Acquisition Standards Harmonization |
| CDER | Center for Drug Evaluation and Research |
| CDISC | Clinical Data Interchange Standards Consortium |
| CDRH | Center for Devices and Radiological Health |
| CRO | Contract Research Organization |
| CSC | Computational Science Center |
| DMF | Drug Master File |
| DSC | Data Standards Catalog |
| DSCSA | Track and Trace |
| DSPB | Data Standards Program Board |
| eCTD | Electronic Common Technical Document |
| EHR | Electronic Health Record |
| FDASIA | FDA Safety and Innovation Act |
| FDF | Finished Dosage Form |
| FAERS | FDA Adverse Event Reporting System |
| FARs | Field Alert Reports |
| GDUFA | Generic Drug User Fee Act |
| HL7 | Health Level 7 |
| ICH | International Conference on Harmonization |
| IDMP | Identification of Medicinal Product |
| LOINC | Logical Observation Identifiers Names and Codes |
| NIMS | Nonclinical Information Management System |
| OpSC | CDER Operations Subcommittee |
| Quality by Design (QbD) | Quality by Design |
| OSI | Office of Scientific Investigations |
| PDUFA | Prescription Drug User Fee Act |
| REMS | Risk Evaluation & Mitigation Strategy |
| RPS | Regulated Product Submission |

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|---|---|
| SDO | Standards Development Organization |
| SDTM | Standard Data Tabulation Model |
| SDSP FRN | Study Data Standardization Process? |
| SEND | Standard for Exchange of Non-clinical Data |
| Système International (SI) Units | Système International (SI) units |
| Sponsors | Regulated Industry |
| SPL | Structured Product Labeling |
| WHO | World Health Organization |

## Appendix B. Annotated Glossary

**Table 1. Drug Development and Pre-Market Review**

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|---|---|
| CDISC Dataset XML for study data exchange | Supports the interchange of tabular data for clinical research applications using ODM-based XML technologies. |
| Système International (SI) Units vs. U.S. Conventional Units | The CDER and CBER are evaluating common and therapeutic area-specific lab tests to determine which pose significant interpretation risks during the review of new drug applications. |
| SDTM, SEND, ADaM, Define.xml for Clinical and Non-Clinical Study Data | The process, review, and archival of electronic submissions that provide study data using the standards, formats, and terminologies as specified in the Data Standards Catalog. |
| Development of Therapeutic Area Endpoint Standard | Develop FDA data recommendations for the review of clinical efficacy and analysis; Collaborate with external stakeholders (e.g., CFAST) and develop the standard; Develop methodology for testing and implementation of TA standards. |
| LOINC Codes for Laboratory Values | Logical Observation Identifiers Names and Codes (LOINC): a database and universal standard for identifying medical laboratory observations. It was developed and is maintained by the Regenstrief Institute, a US non-profit medical research organization, in 1994. |
| Bioanalytical Methods Validation Standards | Transform Office of Generic Drug (OGD) technical specifications into a terminology that can be used by sponsors for the submission of these data. |

**Table 2. Drug Safety Performance & Promotion**

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| Risk Evaluation and Mitigation Strategy (REMS) | The capture and submission of structured information about REMS from manufacturers to ensure that the benefits of a drug or biological product outweigh its risks. |
| Unique Ingredient Identifier (UNII) for substances | The UNII is a non- proprietary, free, unique, unambiguous, non-semantic, alphanumeric identifier based on a substance's molecular structure and/or descriptive information. |
| Identification of Medicinal Products (IDMP) | Provides an internationally-accepted framework for consistent documentation, coding and exchange of product information between global regulators, manufacturers, suppliers and distributors. |
| Integrity Product Dictionary (IPD) | The focus is to publish the next version of the internal product dictionary that will leverage an ongoing CDER Master Data Management effort to create an ISO IDMP compliant Product Dictionary. |
| Individual Case Safety Reports (ICSR) R3 (E2B R3) | Assesses ICSR implementation requirements and considerations to develop implementation plan based on findings. |

**Table 3. Pharmaceutical Quality**

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| Pharmaceutical Quality (PQ)/Chemistry, Manufacturing and Controls (CMC) Data Standardization | Overall objective is to identify and standardize data elements, terminologies, and data structure to enable automation of PQ/CMC data. |
| Quality Metric Terminology | An objective measure of effectiveness of systems associated with the manufacture of pharmaceutical products, including the pharmaceutical quality system. |
| Drug Supply Chain Security Act (DSCSA) | Objective is to develop an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the US; Facilitate the exchange of information in the drug supply chain by providing information about a drug and who handled it each time. |
| Annual Report Project | Seeks to develop and implement new regulatory requirements to obtain site level distribution data by facility, capture an up-to-date view of PQ/CMC process along with submission of summary of all changes, and require electronic submission for |

| | |
|---|---|
| | Field Alert Reports (FAR) and Biological Product Deviation Reports (BPDR). |

**Table 4. Policy**

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|---|---|
| Providing Regulatory Submission in Electronic Format – Under 745A(a) of the Food, Drug & Cosmetic Act | This guidance describes how FDA interprets and plans to implement the requirements of section 745A(a) of the FD&C Act. Specifically, this guidance discusses (1) the submission types that must be submitted electronically, (2) exemptions from and waivers of the electronic submission requirements, and (3) the timetable and process for implementing the requirements. |
| Providing Regulatory Submission in Electronic Format – Standardized Study Data | This guidance and the technical specifications documents it incorporates by reference describe the requirements for an electronic submission of standardized clinical and nonclinical study data under section 745A(a) of the FD&C Act. In accordance with section 745A(a), following the issuance of a final guidance on this topic, study data contained in the submission types identified in this guidance must be submitted electronically in a format that FDA can process, review, and archive. |
| Study Data Technical Conformance Guide | The Guide provides technical recommendations to sponsors for the submission of animal and human study data and related information in a standardized electronic format in INDs, NDAs, ANDAs, and BLAs. |
| FDA Data Standards Catalog | The Catalog provides a listing of currently 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 (or will end), the date the requirement to use a particular standard will begin (or has begun), the date such requirement ends (or will end), and other pertinent information. |

**Table 5. Planning and Governance**

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| FDA Data Standards Advisory Board (DSAB) | This council is responsible to coordinate the evaluation, development, maintenance, and adoption of health and regulatory data standards to ensure that common data standards are used throughout the agency and the standards are consistent with those used outside the FDA. |

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| CDER Data Standards Program Board (DSPB) | Responsible for the overall governance of the Center's data standards activities. The board is comprised of senior level data standards representatives from the CDER Offices that are involved with conducting regulatory review. For more information. |
| Coalition for Accelerating Therapies & Standards (CFAST) | A joint initiative of the Critical Path Institute (C-Path) and the Clinical Data Interchange Standards Consortium (CDISC) to accelerate clinical research and medical product development by facilitating the establishment and maintenance of data standards, tools and methods for conducting research in therapeutic areas important to public health. |
| International Conference on Harmonisation (ICH) | Objective is to increase international harmonisation of technical requirements to ensure that safe, effective, and high quality medicines are developed and registered in the most efficient and cost-effective manner. |

## Appendix C. Further Information

For more information regarding the CDER Data Standards Program and initiatives, please see the following links:

1. CDER Study Data Standards Resources—Data Standards Catalog
2. CDER Data Standards Program—Action Plan
3. CDER Study Data Standards Resources—Technical Conformance Guide
4. CDER Data Standards Program—Data Standards Program Board Charter
5. CDISC Dataset XML for study data exchange
6. Système International (SI) Units vs. U.S. Conventional Units
7. Development of Therapeutic Area Endpoint Standards
8. Risk Evaluation and Mitigation Strategy (REMS)
9. Unique Ingredient Identifier (UNII) for substances
10. Identification of Medicinal Products (IDMP)
11. Individual Case Safety Reports R3 (E2B R3)
12. Drug Supply Chain Security Act (DSCSA)
13. Providing Regulatory Submission in Electronic Format – Under 745A(a) of the Food, Drug & Cosmetic Act
14. Providing Regulatory Submission in Electronic Format – Standardized Study Data
15. International Conference on Harmonisation