U.S. FOOD & DRUG
ADMINISTRATION

Data Standards Strategy
FY2018-FY2022

Center for Biologics Evaluation and Research (CBER)
Center for Drug Evaluation and Research (CDER)

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1.0 INTRODUCTION

1.1 Purpose

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 postmarket regulatory review process so that safe and effective medical products[1] are available to patients. The mission of the Center for Biologics Evaluation and Research (CBER) is to ensure the safety, purity, potency, and effectiveness of biological products including vaccines, allergenics, blood and blood products, and cells, tissues, and gene therapies for the prevention, diagnosis, and treatment of human diseases, conditions, or injury.[2] The mission of the 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.[3] Together the two centers will leverage their combined resources, talent and expertise to maximize stakeholder collaboration, policy development, and project implementation to develop and use data standards for the effective and efficient review of pre- and postmarket submissions of safety and efficacy data.

1.2 Principles

This strategy is aligned with the FDA Strategic Policy Roadmap[4], FDA Information Technology Strategic Plan[5], CBER's Interim Strategic Plan[6], CDER's Strategic Plan[7], 21st Century Cures Act[8] and the commitments under Prescription Drug User Fee Act (PDUFA) VI[9]. FDA's data standards program is focused on three principles:

1. Ensure the use of high quality data standards, by using voluntary and consensus-based standards development processes in accredited standards development

[1]Within this document, the term "medical products" is used to represent human drugs, biological products including vaccines, allergenics, blood and blood products, and cells, tissues, and gene therapies for the prevention, diagnosis, and treatment of human diseases, conditions, or injury.
[2] https://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cber/ucm122878.htm
[3] https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm376545.pdf
[4] https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm591993.htm
[5] https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm324359.htm
[6] https://www.fda.gov/downloads/AboutFDA/CentersOffices/CBER/UCM266867.pdf
[7] https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM376545.pdf
[8] https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf
[9] https://www.fda.gov/forindustry/userfees/prescriptiondruguserfee/

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 information technology initiatives, laws, regulations, and mandates such as executive orders.
3. Ensure the effectiveness and broad utility of data standards through the adoption or adaptation of other standards currently in use, when feasible.

1.3 Stakeholders

We recognize that there are stakeholders, including regulated industry, health care professionals, patients, standards development organizations (SDOs), technology providers, as well as other government and non-government organizations (NGOs), the public who have a critical role in FDA's efforts to achieve its goals to promote the use of open, consensus-based data standards. These stakeholders, including FDA scientific and medical staff, inform, participate, and collaborate to help shape, and in some cases, help implement the data standards initiatives.

FDA collaborates with stakeholders to develop new, and to update existing data standards. Some examples of external stakeholders include, but are not limited to:

- Other Regulatory Authorities
- Other Federal Agencies
- Clinical Data Interchange Consortium (CDISC)[10]
- Critical Path Institute (C-Path)[11]
- Health Level 7 (HL7)[12]
- International Council on Harmonisation (ICH)[13]
- International Organization for Standards (ISO)[14]
- TransCelerate BioPharma (TCB)[15]
- World Health Organization (WHO)[16]

[10] https://www.cdisc.org/
[11] https://c-path.org/
[12] http://www.hl7.org/
[13] http://www.ich.org/home.html
[14] https://www.iso.org/home.html
[15] http://www.transceleratebiopharmainc.com/
[16] http://www.who.int/en/

2.0 REGULATORY FRAMEWORK

FDA's goal is to improve the predictability, consistency, transparency, and efficiency of the regulatory review process. Much of the improvement in the review process has hinged upon the submission of standardized electronic medical product application data and the implementation of electronic review tools and systems. This Strategy is supported by the regulations, statutes and guidances that promote or require the use of data standards in electronic regulatory submissions. The key areas of the regulatory framework include:

- **Requirements for Submission of Labeling for Human Prescription Drugs and Biologics in Electronic Format, 2003**
  Known as the Electronic Labeling Rule, effective in 2004, the regulation requires the submission of the content of labeling in electronic format for marketing applications. It also states that FDA will periodically issue guidance on how to provide the electronic submission.[17,18]

- **Food and Drug Administration Amendments Act (FDAAA), 2007**

  Effective in 2009, the Act amended the Federal Food, Drug, and Cosmetic (FD&C) Act to require the submission of electronic drug establishment registration and drug listing information in standardized format.[19,20]

- **Food and Drug Administration Safety and Innovation Act (FDASIA), 2012**
  - The Act amended Section 745A(a) of the FD&C (21 U.S. Code § 379k–1)[21] to require submissions to be submitted in an electronic format specified by the FDA beginning no earlier than 24 months after FDA issues a final guidance specifying an electronic submission format.
  - In 2014, FDA issued the final guidance, *Providing Regulatory Submissions in Electronic Format – Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act* which describes how FDA will implement the requirements to specify the electronic formats in individual content-specific guidances.[22]

[17] 21 CFR parts 314 and 601 (2003)
[18] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072331.pdf
[19] https://www.gpo.gov/fdsys/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf
[20] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072339.pdf
[21] https://www.gpo.gov/fdsys/pkg/USCODE-2015-title21/pdf/USCODE-2015-title21-chap9-subchapVII-partD.pdf
[22] https://www.fda.gov/downloads/drugs/guidances/ucm384686.pdf

  - Individual content-specific guidances have been published since 2014 (e.g., study data[23]), and additional guidances are planned that describe the required standard formats to be used in electronic submissions.

- **Postmarketing Safety Reports for Human Drug and Biological Products; Electronic Submission Requirements, 2014**

  Known as the Postmarketing Safety Rule**,** effective in 2015, the rule requires that persons subject to mandatory reporting requirements submit safety reports in an electronic format. It also requires the electronic submission of biological lot distribution reports.[24,25,26]

- **21st Century Cures Act, 2016**

  The Act provisions are designed to help accelerate medical product development and bring new innovations and advances to patients who need them faster and more efficiently. The Act includes FDA deliverables (Title III) related to clinical outcome assessment, biomarkers and real world evidence.[27]

3.0 DATA STANDARDS GOVERNANCE FRAMEWORK

The FDA established a data standards governance framework of policies, processes and organizational structures to manage and account for its data standards initiatives, including SDO collaboration (see Appendix A). The Data Standards Advisory Board (DSAB) serves as a review and advisory body for data, exchange, and terminology standards initiatives relevant to the FDA and to identify and sponsor cross-organizational data standardization needs of the Agency. The DSAB, with representatives from each FDA Center and Office, focuses on Agency-level data standards priorities (see Appendix B).

At the Center level, CDER's Data Standards Program Board (DSPB) and CBER's Data Standards Committee (DSS) ensure cross-center collaboration, communication, and alignment with respect to data standards strategy, development, implementation, and policy. The DSPB and DSS together are responsible for the CBER-CDER Data Standards Strategy and the associated Action Plan, as well as the ongoing planning, coordination and progress-tracking of data standards projects.

[23] https://www.fda.gov/downloads/drugs/guidances/ucm292334.pdf
[24] 21 CFR parts 310, 324 and 600 (2014)
[25] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072369.pdf
[26] https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/UCM458559.pdf
[27] https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf

4.0 STRATEGIC GOALS

The CBER-CDER data standards goals focus on key areas that will help improve the exchange, review, and management of medical product data.

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

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

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

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

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

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

These six goals are discussed below along with their related objectives. Successful accomplishment of these goals is dependent upon, but not limited to, FDA resources, budget, regulatory/ legislative factors, as well as the collaboration with external stakeholders.

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

Common data standards will provide new opportunities to transform the massive amount of data generated in regulatory submissions into useful information to potentially speed the delivery of new therapies to patients. Standardized data elements and relationships, for example, that are important to a 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 medical product classes.

Standards make it possible to develop and utilize predefined analysis panels for common analyses, thus freeing reviewers to spend their time on more complex questions and analyses during a review.

Objective 1.1: Collaborate with stakeholders and SDOs to develop, implement, and maintain standards and terminologies.[28]

Objective 1.2: Support the enhancement of analysis data standards for medical product review.[29]

[28] https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf, p.43.
[29] Ibid., p. 33.

Objective 1.3: Incorporate data standards, as needed, to support the biomarker qualification review program.[30]

Objective 1.4: Participate in initiatives focused on the harmonization of healthcare and clinical research data standards.[31]

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

Medical product safety and postmarketing surveillance throughout the product lifecycle are integral to FDA's mission to protect public health. Efforts encompassed by this area include the use of systems such as the FDA Adverse Event Reporting System (FAERS), Vaccine Adverse Event Reporting System (VAERS) and Sentinel systems to evaluate safety signals.

Other activities include the review of sponsor reports from Postmarketing Requirements (PMRs) and Postmarketing Commitments (PMCs), review of proprietary product names to reduce the risk of name confusion and related medication errors, review of product 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.

Objective 2.1: Work with external stakeholders to identify and use data standards to communicate essential risk evaluation and mitigation strategies information.[32]

Objective 2.2: Implement the E2B (R3) standard for electronic transmission of Individual Case Safety Reports and communicate with external stakeholders.[33]

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

Establishing common medical product quality data standards continues to provide new opportunities to transform submission data into useful information that may enhance FDA's drug review process. FDA is continually working to identify steps to help improve

[30] Ibid., p. 33.
[31] https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf, sections 3002, 3022.
[32] https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf, p. 34.
[33] Ibid., p. 34.

the manufacturing process to ensure consistent product quality throughout its shelf life, as well as to identify when contamination or other production failures may occur.

Objective 3.1: Participate in the development and implementation of data standards that describe manufacturing and testing of medical products, such as stability, quality specifications, manufacturing components, and batch analysis.[34]

Objective 3.2: Implement the suite of ISO standards used to uniquely identify medical products internationally and communicate with stakeholders.

Objective 3.3: Improve submission requirements to ensure that essential facility location and manufacturing information is captured completely and in a format conducive to electronic receipt, storage and usage.[35]

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

To keep pace with advances in medical science and regulatory review, FDA promotes innovation in data standards through the conduct of research and development projects with SDOs and other stakeholders. The FDA will enhance its regulatory science and expertise to facilitate the development of: 1) exposure-based, biological, and statistical models derived from preclinical and clinical data sources; and 2) clinical outcome assessment tools for the collection of meaningful patient and caregiver input for regulatory decision-making.

Although there are challenges with the harmonization of healthcare data standards with clinical research data, there is also much opportunity to improve patient safety, data accuracy, and clinical trial efficiency when data from electronic healthcare record (EHR) systems are used in clinical trials. As we harmonize disparate data sources, we will be in a better position to leverage real world evidence to support regulatory review. Successful integration and analysis of data from these disparate sources should provide knowledge and insight not possible from any one source alone.

[34] https://www.federalregister.gov/documents/2017/07/11/2017-14456/draft-standardization-of-pharmaceutical-qualitychemistry-manufacturing-and-control-data-elements-and

[35] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM534709.pdf

Objective 4.1: Evaluate and support efforts to identify, standardize, and implement standards and terminologies that support regulatory research and meta-analysis.[36]

Objective 4.2: Evaluate and support efforts to implement new standards for the submission of regulatory data (e.g., model-informed drug development, omics, and clinical outcomes assessment).[37]

Objective 4.3: Evaluate the utility of healthcare data standards for review of clinical data and encourage the use of electronic health records to support clinical trials in regulated clinical research.[38]

Objective 4.4: Evaluate the feasibility of representing real world data in an electronic standardized format that allows FDA to receive, process and analyze the data.[39,40]

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

Effective communication and collaboration with internal and external stakeholders are essential factors to the successful development, implementation and use of data standards to support regulatory review of medical products. FDA takes a collaborative approach to strengthening communications and sharing information. FDA pursues opportunities for improving stakeholder collaboration through approaches aimed at reporting progress towards meeting its goals.

FDA uses a multi-tiered approach to improve communications and distribute data standards information to industry at regular intervals.

Objective 5.1: Maintain and regularly update FDA resources webpages with current requirements and recommendations on the use of data standards in submissions (e.g., Study Data Technical Conformance Guide and FDA Data Standards Catalog).[41]

Objective 5.2: Maintain a current Data Standards Action Plan.[42]

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[36] https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf, p. 36.
[37] Ibid., pp. 28, 30.
[38] https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM501068.pdf
[39] https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf, section 3022.
[40] https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf, p. 26.
[41] https://www.fda.gov/Forindustry/DataStandards/default.htm
[42] https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf, p. 43.

Objective 5.3: Provide regular outreach opportunities (e.g., webinars) to update and provide clarification to industry on supported and required data standards.

Objective 5.4: Conduct annual public meetings for stakeholder input on electronic submissions.[43]

Objective 5.5: Provide educational activities for internal & external stakeholders to understand the impact of data standards on regulatory review activities, systems and tools.[44]

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

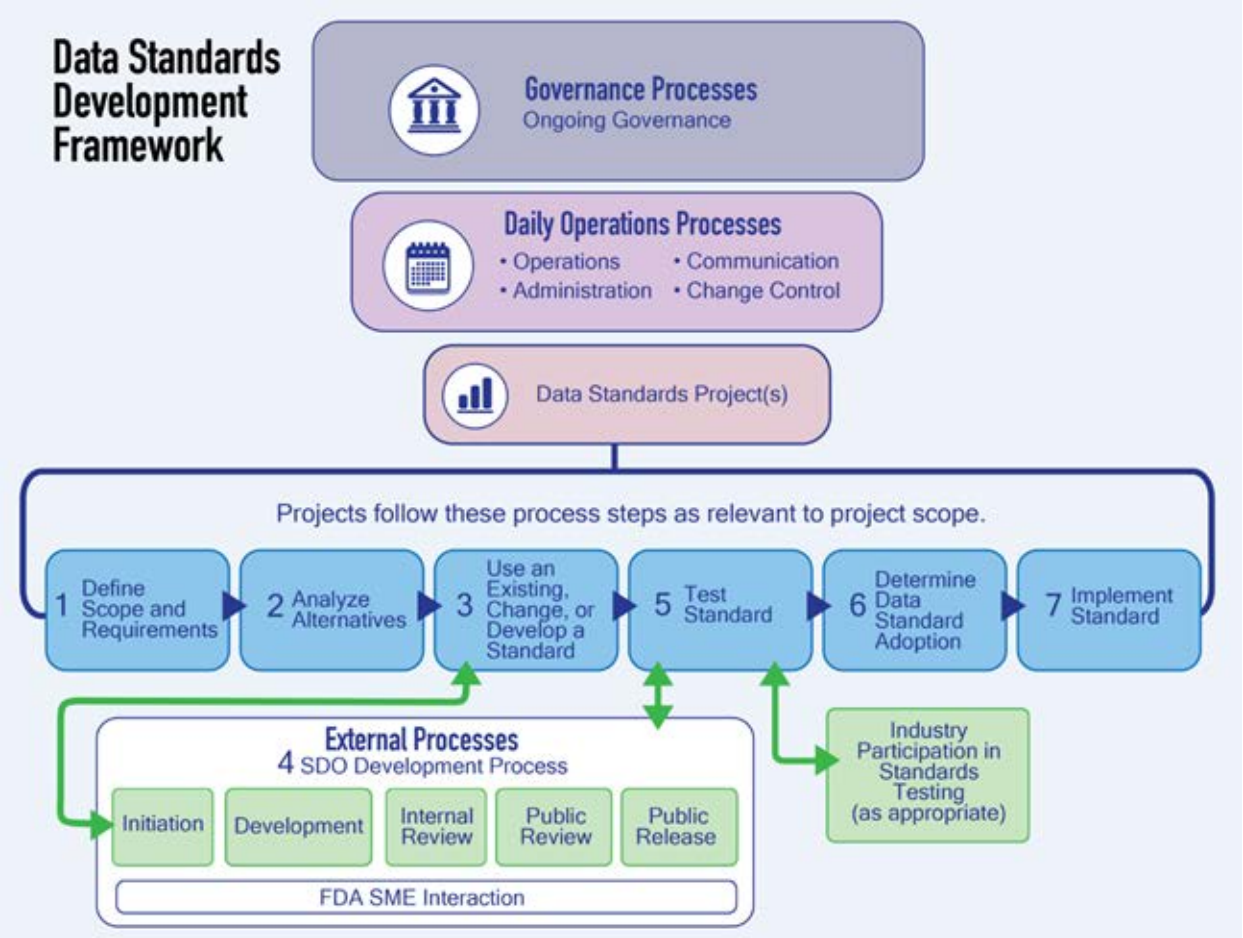
It is important to drive improved efficiency while ensuring consistent execution. This entails the potential to allow processes to evolve with science, industry, and overall public health needs. FDA will continue to identify opportunities to standardize submissions while also working to ensure that internally-generated data is systematically captured and standardized. Technology is critically important and serves as an enabler for reviewers to make use of the massive amounts of data and information that is generated and received. FDA will focus on a cohesive set of tools that work across a broad range of critical business processes to support automation and informed decision-making.

Objective 6.1: Identify consistent internal standards and practices to support business process and regulatory reviews.

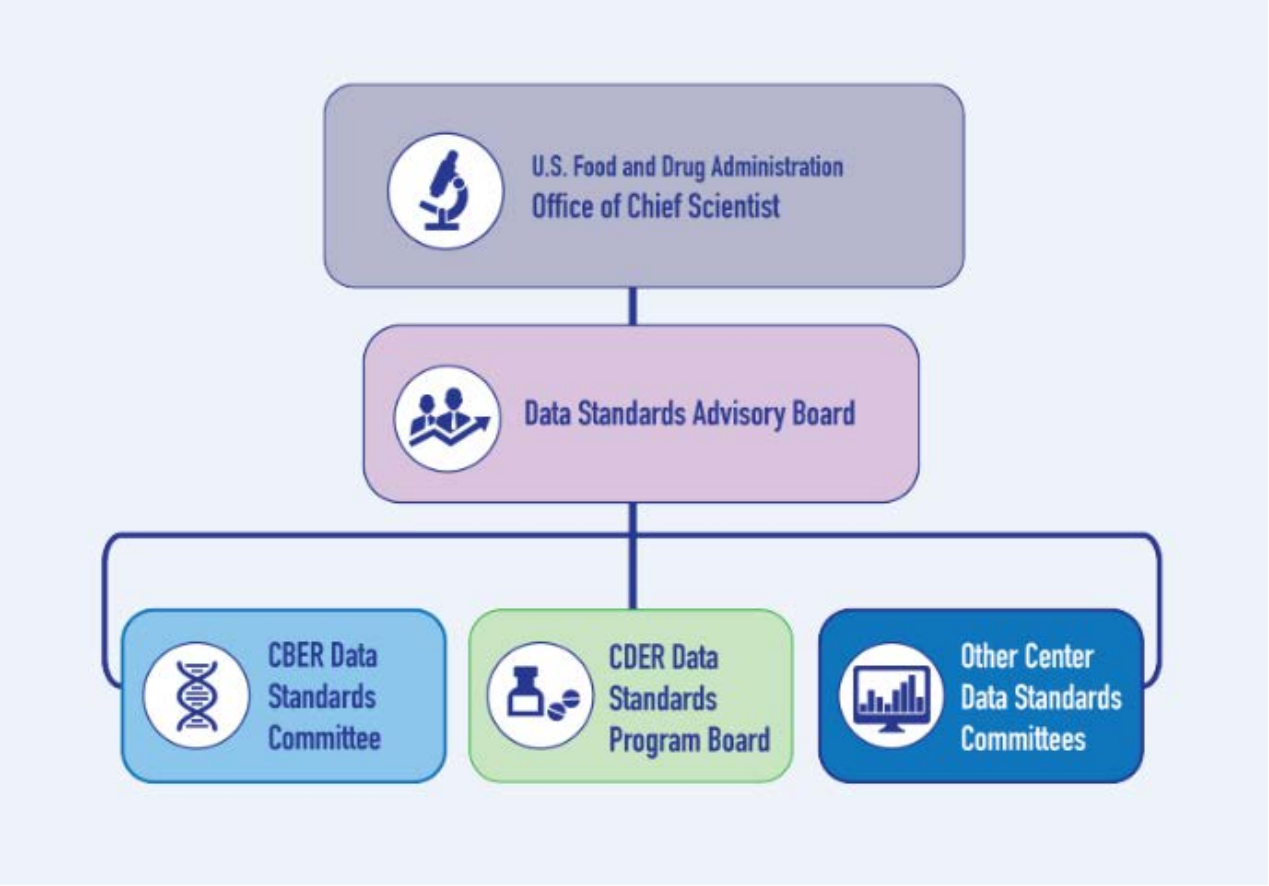
Objective 6.2: Promote access to high-quality, standardized data from both internal and external sources to make regulatory decisions.

[43] https://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM511438.pdf, p. 43.
[44] Ibid., p. 43.

APPENDIX A: DATA STANDARDS GOVERNANCE FRAMEWORK



APPENDIX B: FDA ORGANIZATIONAL STRUCTURE FOR DATA STANDARDS



APPENDIX C: GLOSSARY OF ACRONYMS

CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDISC	Clinical Data Interchange Standards Consortium
C-Path	Critical Path Institute
DSAB	FDA Data Standards Advisory Board
DSPB	CDER Data Standards Program Board
DSS	CBER Data Standards Committee
EHR	Electronic Health Record
FAERS	FDA Adverse Event Reporting System
FDAAA	Food and Drug Administration Amendments Act
FDASIA	FDA Safety and Innovation Act
FD&C	Food, Drug and Cosmetic Act
FDA	Food and Drug Administration
HL7	Health Level 7
ICH	International Council on Harmonisation
ISO	International Standards Organization
NGO	Non-Governmental Organization
PDUFA	Prescription Drug User Fee Act
PMC	Postmarketing Commitments
PMR	Postmarketing Requirements
REMS	Risk Evaluation & Mitigation Strategy
SDO	Standards Development Organization
Sponsor	Regulated Industry
TCB	TransCelerate BioPharma
VAERS	Vaccine Adverse Event Reporting System
WHO	World Health Organization