Data Standards Update

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Baltimore, MD
May 17, 2017
The views and opinions presented here represent those of the speaker and should not be considered to represent advice or guidance on behalf of the U.S. Food and Drug Administration.
Why Data Standards

Predictability + Traceability + Common Tools + Communication

= More efficient & transparent review process
Data Standards Governance in CDER
Data Standards Program Portfolio*

Drug Development and Pre-Market Review

Drug Safety Performance and Promotion

Drug Manufacturing and Quality

Policy

• Full list: https://www.fda.gov/drugs/developmentapprovalprocess/formssubmissionrequirements/electronicsubmissions/ucm249979.htm
Road to Required Electronic Submission Standards

**Structured Product Labeling**

**Drug Establishment Registration & Drug Listing**
- FDAA 2007

**ICSRs and Lot Distribution Reports**
- Post-Market Safety Rule 2015

**Study Data**
- FD&C 745A
- Binding Guidance 2016

**eCTD**
- FD&C 745A
- Binding Guidance 2017

**Pharm Quality/CMC**
- ID of Medicinal Products
- Manufact. Estab. Information

2004

2007

2015

2016

2017

20XX
Percent of New NDA Submissions with Standardized Study Data - FY13- FY17*

*One or more explicitly stated SDTM studies (or study data structure that resembled SDTM) in NEW NDAs.
FY2013-F2017(Q1-Q2), Source: Office of Business Informatics, CDER
# Project Updates for Standards in the Drug Development Lifecycle

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<th>DISCOVERY</th>
<th>INVESTIGATIONAL PHASE</th>
<th>APPLICATION REVIEW PHASE</th>
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<td>Investigational New Drug (IND) application</td>
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<td>ANDA (Abbreviated New Drug Application)</td>
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## DATA STANDARDS

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<th>ADaM</th>
<th>NDC/MPID</th>
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<td>Electronic Common Technical Document</td>
<td>Standard for Exchange of Nonclinical Data</td>
<td>Study Data Tabulation Model</td>
<td>Analysis Data Model</td>
<td>National Drug Code/Medicinal Product Identifier</td>
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<td>PQ/CMC</td>
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<td>ICSR</td>
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<td>Pharmaceutical Quality/Chemistry, Manufacturing, and Controls</td>
<td>Structured Product Labeling</td>
<td>Individual Case Safety Report</td>
<td>Unique Ingredient Identifiers</td>
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**FDA COMPLIANCE INSPECTIONS THROUGHOUT THE PROCESS**

- eCTD
- SEND
- SDTM
- ADaM
- NDC/MPID
Project Updates for Standards in the Drug Development Lifecycle

• Project identified standard data elements, terminologies, and data structures to enable automation of important analyses of PQ/CMC data.

• Proposed use of SPL standards for data exchange.

• Planned 2017 FR Notice for public comment on draft data elements and terminologies.

• Initiative will align, where possible, with substance and product identifiers described by ISO for IDMP standards.

DATA STANDARDS

- eCTD: Electronic Common Technical Document
- PQ/CMC: Pharmaceutical Quality/Chemistry, Manufacturing, and Controls
- SEND: Standard for Exchange of Nonclinical Data
- SPL: Structured Product Labeling
- SDTM: Study Data Tabulation Model
- ADaM: Analysis Data Model
- UNII: Unique Ingredient Identifiers
- NDC/MPID: National Drug Code/Medicinal Product Identifier
Project Updates for Standards in the Drug Development Lifecycle

- Updated the SEND section of Study Data Technical Conformance Guide
- Finalizing FDA validator rules for SEND and will update the FDA webpage.
- Finalizing Testing & Acceptance to support SENDIG v 3.1.
Project Updates for Standards in the Drug Development Lifecycle

- Posted Business and Validator Rules to FDA webpage
- Developed and posted SDTM technical rejection criteria
- Testing & acceptance of TA extensions of SDTM
- LOINC codes in LBLOINC: studies starting after 3-15-2018
  - External and Internal workgroups formed
  - Planned guidance on submission of LOINC codes
New drug discovered

Animal testing

Phase I clinical trials

Phase II clinical trials

Investigational New Drug (IND) application

Investigational New Drug APPLICATION

End of Phase II meeting

Phase III clinical trials

New Drug Application (NDA)/Biologic License Application

FDA Approval

Drug promotion oversight

Compliance

Pre-New Drug Application (NDA) meeting

FDA COMPLIANCE INSPECTIONS THROUGHOUT THE PROCESS

Project Updates for Standards in the Drug Development Lifecycle

• Integrating Risk, Evaluation and Mitigation Strategies into SPL
  • Completed the pilot and now able to receive REMS in SPL format.
  • Guidance is in development.

• Draft Guidance on Submission of Manufacturing Establishment Information published December 2016
  • Requires: Establishment Name and Address, Unique Facility Identifier, PoC, Operations being conducted

FDA COMPLIANCE INSPECTIONS THROUGHOUT THE PROCESS

DATA STANDARDS

eCTD Electronic Common Technical Document

SEND Standard for Exchange of Nonclinical Data

SDTM Study Data Tabulation Model

ADaM Analysis Data Model

PD PQ/CMC Pharmaceutical Quality/Chemistry, Manufacturing, and Controls

SPL Structured Product Labeling

UNII Unique Ingredient Identifiers

UN NDC/MPID National Drug Code/Medicinal Product Identifier

SDM ABaM Individual Case Safety Report

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FDA’S THERAPEUTIC AREA (TA) STANDARDS PROJECT
In 2012, as part of a PDUFA V commitment, CDER compiled a prioritized list of disease and therapeutic areas (TAs) for which standardization was needed.

Focus is on regulatory review needs

Of the 55 TAs* prioritized, 45 have been initiated as of April 2017.

### TA’s Supported by FDA*

- QT Studies
- Chronic Hepatitis C
- Diabetes
- Dyslipidemia
- Tuberculosis
- Diabetic Kidney Disease
- Ebola
- Kidney Transplant
- Malaria

### TA Standards in FDA Review - 2017

- Asthma
- Breast Cancer
- Colorectal Cancer
- CV Study
- CV Imaging
- Duchenne’s MD
- Prostate Cancer
- Schizophrenia
- Virology

*May, 2017- listed in Technical Conformance Guide
eCTD Technical Rejection of Submissions
FDA can Refuse to File (RTF) or Refuse to Receive (RTR) an Application for Non-Conformance to Standardized Study Data

Please no RTF/RTR

eStudy Guidance requires the electronic submission of NDAs, BLAs, ANDAs, INDs in the formats in the Data Standards Catalog

...so we will start with eCTD technical rejection of submissions
eCTD Technical Rejection of Submissions

• CDER has been validating incoming submissions for conformance to eCTD format for ~8 yrs.
  • If a submission fails eCTD format validation a technical rejection notice will be sent to the submitter.
  • eCTD validation occurs upon receipt of the submission, prior to being written to the EDR and review division notification.

• The same process will be used for validating submissions for conformance to study data standards.

• It is NOT the same as RTF or RTR.
eCTD Technical Rejection of Submissions

• Sponsors will be able to correct the technical errors and re-submit

• For study data standards validation, FDA will notify submitters, at least 30 days, prior to ‘going live” with the technical rejection of submissions.
Technical Rejection of the Submission

Sponsor NDAs, BLAs, INDs, ANDAs

Data

Data

Data

Do study data conform to required standards?

NO

Acknowledgement sent via ESG on unsuccessful validation and processing

Technical Rejection of the Submission

YES

Acknowledgement sent via ESG on successful validation and processing

EDR

Data Quality Validation

Data Repositories

Analytic Tools

Reviewers

How will it work?

eCTD Technical Rejection…
I M P O R T A N T

A Trial Summary dataset (ts.xpt) must be presented for each study in sections identified below even if the study started prior to December 17, 2016. Nonclinical legacy data submitted in PDF format should be submitted with a TS dataset.

Study data validation WILL APPLY to the following eCTD sections:
- 4.2 Study Reports
- 5.3 Clinical Study Reports and Related Information

Study data validation WILL NOT APPLY to the following eCTD sections:
- 4.2.1 Pharmacology
- 4.2.2 Pharmacokinetics
- 4.2.3.3 Genotoxicity
- 4.2.3.5 Reproductive and Developmental Toxicity
- 4.2.3.6 Local Tolerance
- 4.2.3.7 Other Toxicity Studies
- 5.3.1.3 In Vitro – in Vivo correlation Study reports and related information
- 5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies
- 5.3.2 Reports of studies pertinent to pharmacokinetics using human biomaterials
- 5.3.3.5 Population PK study reports and related information
- 5.3.5.3 Reports of Analyses of Data from More than One Study
- 5.3.5.4 Other Study Reports and Related Information
- 5.3.6 Reports of Postmarketing Experience
Demographic dataset (DM) and the define.xml must be submitted in Module 4 for nonclinical data; DM dataset, the subject-level analysis dataset (ADSL) and define.xml must be submitted in Module 5 for clinical data.

Trial Summary (TS) dataset must be present for each study in eCTD section 4.2 and 5.3.

Correct STF file-tags must be used for all standardized datasets in section 4.2 and 5.3:
- Data-tabulations-dataset-sdtm
- Data-tabulations-dataset-send
- Analysis-dataset-adam

For each study in eCTD section 4.2 and section 5.3, no more than one dataset of the same name should be submitted as new.
Thank You

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