



CBER STUDY DATA STANDARDS UPDATE

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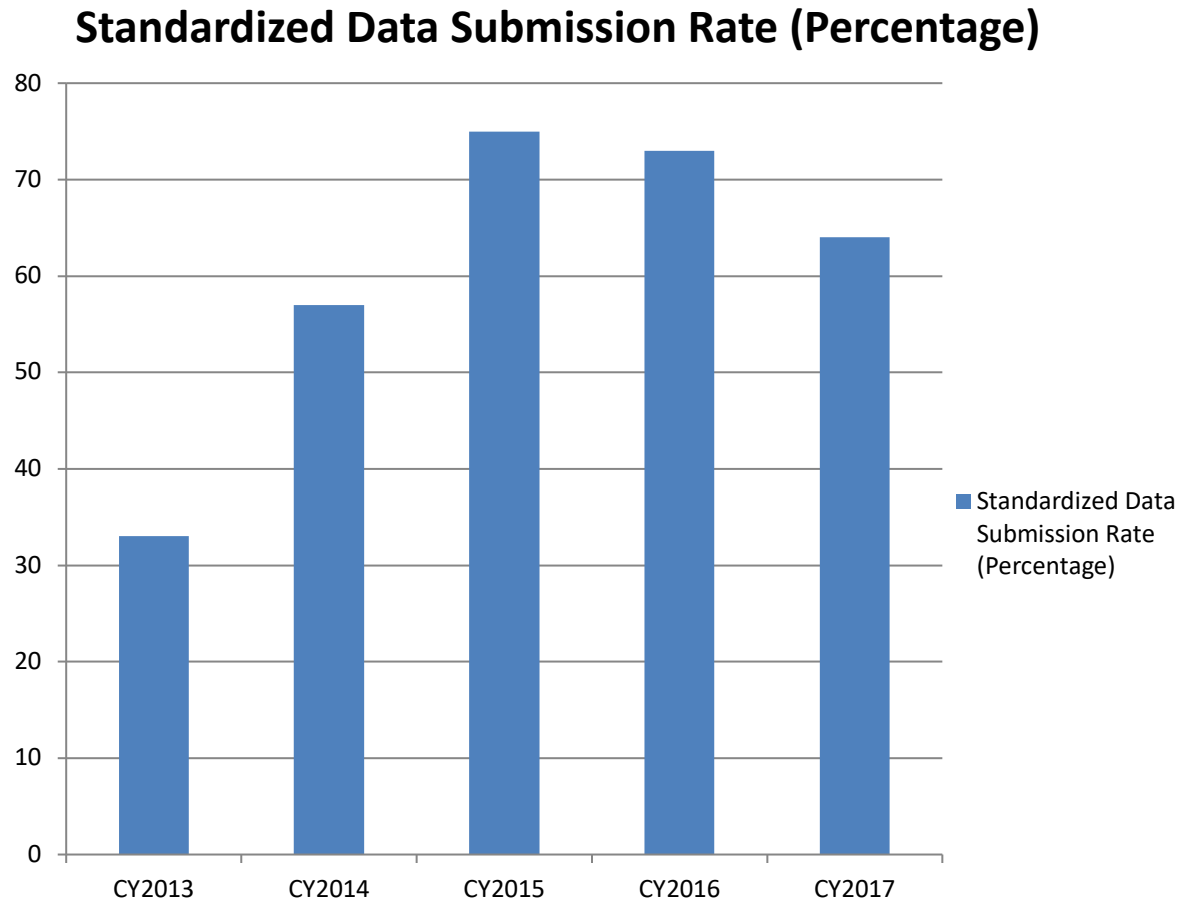
CBER Updates for Standardized Study Data

- Standardized Data Submission Metrics
- New Data Standards Staff has been established
- Standardized Study Data Validation
 - SDTM datasets
 - ADaM datasets
 - Define.xml
 - ISS and ISE datasets

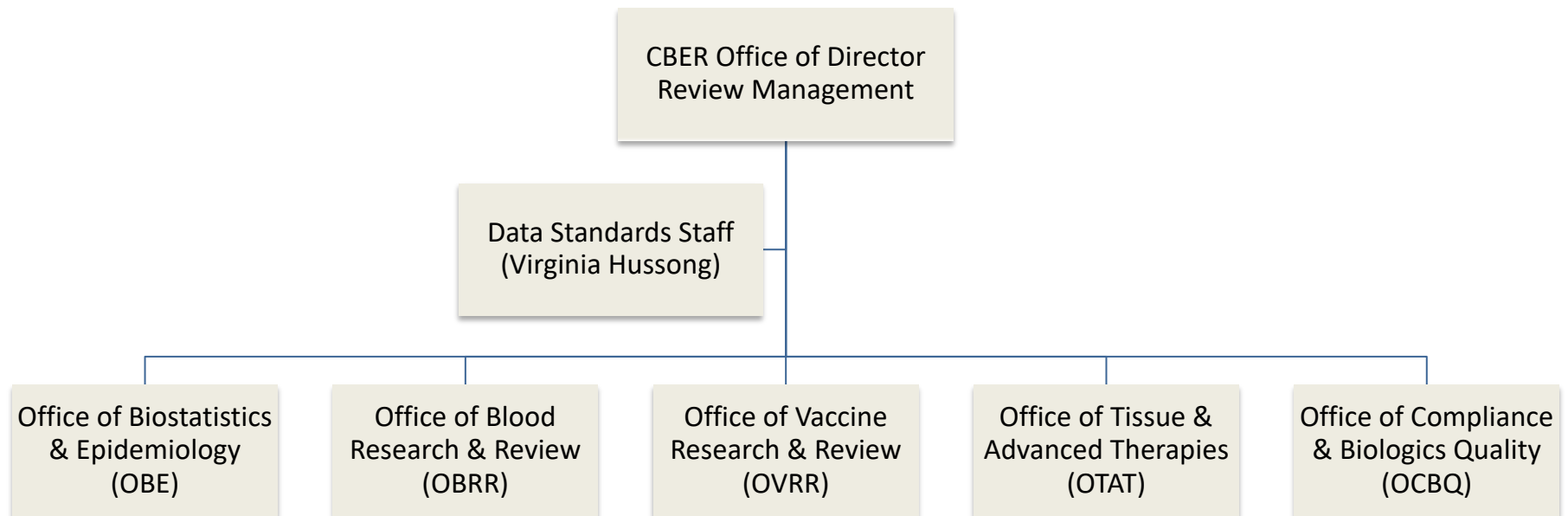
CBER Updates for Standardized Study Data

- Implementation of Study Data Standardization Plan (SDSP CBER appendix)
- Vaccine TAUG & Vaccine Technical Specifications Document
- Training programs & Consultation Service to CBER reviewers
- SEND (Standard for Exchange of Nonclinical Data) project, evaluation and testing of the SEND standard for CBER

CBER Standardized Data Submission Metrics



CBER Data Standards Staff



Standardized Study Data Validation

- New validation process in place starting the end of 2017
- DataFit validation for all incoming BLAs, Supplements
- Ensure study data meets the standards, in good quality for review
- Help review division issue Information Request (IR) or Refuse to File (RTF) if needed

Standardized Study Data Validation



Information Request Examples

Issue 1

The xxxx and xxxx studies are **missing** the AE, CE and CM domains, even though the SUPPAE, SUPPCE and SUPPCM domains have been provided. The reviewer's guides do not explain why these domains are missing. The reviewer's guides and define.xml document the AE, CE and CM domains, explain validation rules, etc.

Issue 2

File names: most supporting documents (e.g. reviewer's guides, protocols, etc.) hyperlinked within the define.xml files have the **incorrect** filename listed in the **hyperlink**. All the documents appear to be present, however, they can only be opened manually rather than using the hyperlinks in the define.xml). Please correct the file names so that the hyperlinks are functional.

Study Data Validation

Information Request Examples

Issue 3

In study xxx, 126 (3.6%) events are **missing** start date/time. Please insert the missing information.

Issue 4

Some of the values in EXSTDTC is not **ISO8601 format**, “-----T19:00”, so EXSTDY has missing value. This needs to be fixed.

Study Data Standardization Plan (SDSP)



- [Study Data Technical Conformance Guide](#) recommends sponsors to include a plan (eg. in the IND) describing the submission of standardized study data to FDA for clinical and nonclinical studies
- SDSP assists FDA in identifying potential data standardization issues early in the development program
- CBER recommends sponsor to submit SDSP no later than the end-of-phase 2 meeting
- PhUSE (Pharmaceutical Users Software Exchange) has developed a SDSP template for sponsors to follow <https://www.phuse.eu/css-deliverables>

Study Data Standardization Plan (SDSP)



- CBER SDSP appendix should include tables of proposed SDTM domain/variable usage, supplemental domain usage and proposed analysis
- SDSP is a working document, the cover letter accompanying a study data submission should describe the latest version of SDSP

CBER Appendix

1. Introduction

1.1 Purpose

The purpose of this appendix is to document additional study data information. This document should be submitted well in advance of any licensing application (ie, no later than the end of phase 2 meeting) to CBER. Receipt of this document in a timely manner will help to ensure an efficient review process.

1.2 Scope

The scope of this document is to facilitate study data review by CBER reviewers.

2. SDTM Datasets

List all SDTM datasets used/planned for each clinical study in the submission.

SDTM Version:			
STUDY ID:		TITLE:	
DOMAIN	Select Domains to be Submitted X	Variables to be utilized (besides required)	Additional Comments
Trial Design			
TA (Trial Arms)	<X>		
TE (Trial Elements)	<X>		
TI (Trial Inclusion/Exclusion Criteria)	<X>		

Vaccine TAUG and Vaccine Technical Specifications



- Vaccine TAUG has been republished by CDISC 04/10/18
<https://www.cdisc.org/standards/therapeutic-areas/vaccines>
- Vaccine Technical Specifications Document has been published by CBER FDA 04/19/18, webinar was held 05/08/18
<https://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/General/UCM605147.pdf>
- These will be added to Study Data Technical Conformance Guide future release

Vaccine Technical Specifications

Submitting Study Datasets for Vaccines to the Office of Vaccines Research and Review

Guidance for Industry

Technical Specifications Document

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(4)(i). Submit one set of either electronic or written comments on this guidance at any time. Submit electronic comments to <https://www.regulations.gov>. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. You should identify all comments with docket number FDA-2018-D-1358.

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at <https://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
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Training Program & Consultation Service to CBER Reviewers



- Joint effort with CDER to leverage existing training resources
 - Study Data Standards
 - JMP
 - JMP Clinical
 - MAED
- Develop CBER specific Study Data Standards Training which will be held in October
- Provide consultation service to CBER reviewers on study data review and analysis

SEND Project



SEND (Standard for Exchange of Nonclinical Data)

Background:

- CDER requires SEND for Single Dose Toxicity, Repeat Dose Toxicity and Carcinogenicity studies in NDAs and BLAs for studies initiated after 12/17/16; INDs for studies initiated after 12/17/17
- SEND is not required by CBER at this time

Next Steps:

- “Evaluation and Testing of the SEND standard for CBER” is one of the CBER & CDER Joint Data Standards Program Action Plan projects to improve efficiency in the review process for nonclinical toxicology studies

Next Steps: (Cont.)

- Collect requirements from dedicated CBER nonclinical Pharmacologist Reviewers
- CDISC sub-team is formed to discuss CBER specific data points and data models to be added in SENDIG, regular telecon is scheduled to decide on the scope and charter of the project, and to create CDISC project request
- Once the project is chartered, a call for participation will be made to SEND (and possibly SDTM) team members
- Evaluate tools for analyzing SEND Data
- Pilot to have sponsor to submit SEND data to CBER

Conclusion

CBER works closely with CDER to 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 submissions of safety and efficacy data.

References

- Send your questions to CBER:
cber_cdisc@fda.hhs.gov
- FDA Data Standards Catalog:
<https://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm>
- Study Data for Submission to CDER and CBER:
<https://www.fda.gov/ForIndustry/DataStandards/StudyDataStandards/ucm587508.htm>
- Study Data Technical Conformance Guide:
<https://www.fda.gov/downloads/forindustry/datastandards/studydatastandards/ucm384744.pdf>

Any Questions ?



THANK YOU!

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