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Raising Awareness for Additional FDA Data Standards Submission Recommendations

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Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

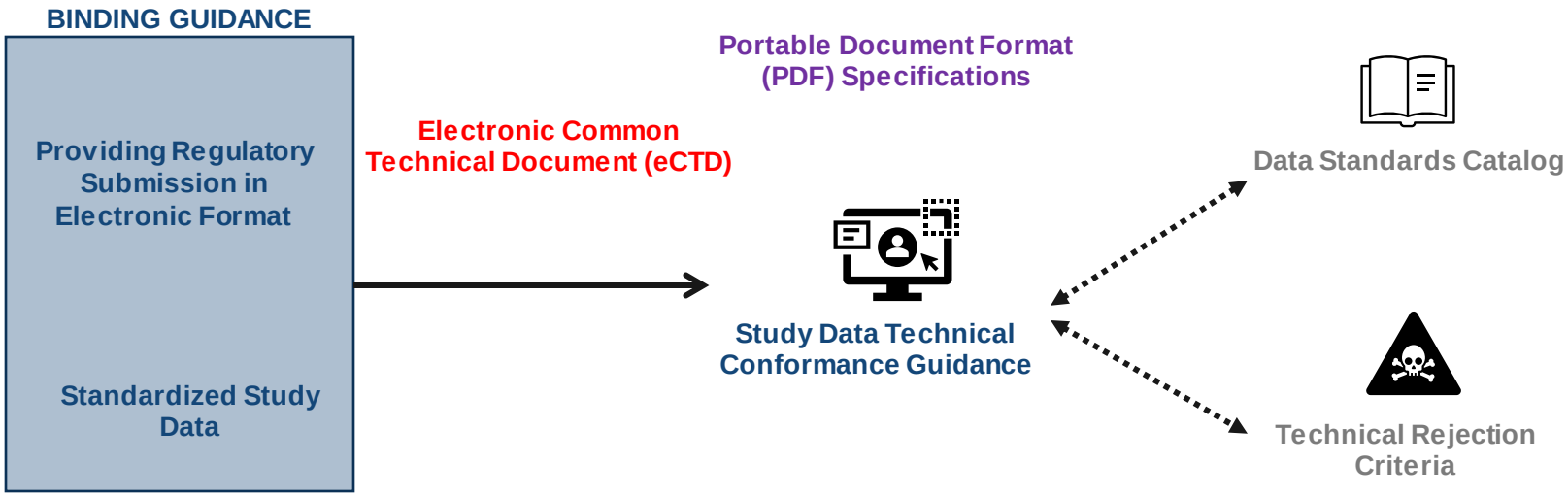
- *I have no real or apparent conflicts of interest to report.*

Agenda

1. FDA Data Submission Technical Guidance
2. Overview of the “Additional” FDA Data Technical Guidance
3. Conclusions

FDA Data Submission Technical Guidance

FDA Data Technical Specifications Guidance



FDA Data Technical Specifications Guidance Other Guidance / Document

- Referenced **CDISC TAUGs** in the FDA SDTCG
- Providing Regulatory Submissions in Electronic Format - General **Considerations, 1999 (Legacy Submission)**
- **Bioresearch Monitoring** Technical Conformance Guide Technical Specifications
- Creating **Simplified TS.XPT** Files
- Submit an eCTD or Standardized Data **Sample** to the FDA (https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/submit-ectd-or-standardized-data-sample-fda)
- Model Data Format for submitting **pharmacometric data and models** (https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/model-data-format)

FDA Data Technical Specifications Guidance

Can you cite any other FDA guidance?

√ Endpoint **Bioequivalence** Study Analysis Datasets for Abbreviated NDA

X Technical Specifications for Submitting Clinical Trial Datasets for **Treatment of Advanced Breast Cancer**

√ Technical Specifications for Submitting Clinical Trial Data Sets for **Treatment of NASH**

X **Diabetes** Technical Specification Guidance

√ **Vaccines** Technical Specification Guidance

√ Submitting Select Clinical Trial Data Sets for **Human Immunodeficiency Virus-1 Infection**

X **ISS and ISE** Datasets Integration for NDA

√ **QT Studies** Technical Specification Document

Can you cite any other FDA guidance?

All these guidance are referenced in the **FDA SDTCG in the section 5 "List of FDA Technical Specification Documents"** and at the **Study Data Standards Resources FDA webpage** in the section **"3. Technical Guidance"** and listed in the table **FDA Study Data Standards Resources**

https://www.fda.gov/industry/fda-data-standards-advisory-board/study-data-standards-resources

Overview of the “Additional” FDA Data Technical Guidance

Overview of Additional FDA Data Technical Guidance

#	FDA Additional Data Standards Guidance References	SDTM	ADaM	Other
1	**Vaccines** Technical Specification Guidance v2.1 (Apr 2018 / Dec 2019) 10 Pages	√		CRF design recommendations
2	**QT Studies** Technical Specification Document v1.0 (Jun 2019) 24 Pages		√	Good examples
3	Submitting Select Clinical Trial Data Sets for Drugs Intended to Treat **Human Immunodeficiency Virus-1 Infection** v1.0 29 Pages (Mar 2018)		√	Big Summary SL dataset
4	Technical Specifications—**Comparative Clinical Endpoint Bioequivalence Study** Analysis Datasets for Abbreviated New Drug Applications v.1.0 (Sep 2018) 46 Pages		√	
5	Technical Specifications for Submitting Clinical Trial Data Sets for Treatment of **Noncirrhotic Nonalcoholic Steatohepatitis (NASH)** v1.1 44 Pages (Aug 2021 / Jan 2022)	√	√	Controlled Terminology NSV Good examples

Overview of Additional FDA Data Technical Guidance
Vaccines Technical Specification Guidance

- **CBER OVRR** Unit
- **SDTM** Only
- **CRF design** and mapping recommendations for **Reactogenicity data** (flat vs nested model)
- Ref. Vaccines CDISC TAUG

Adapting and Evolving with OVRR Requirements
Sarah McLaughlin and Jenn Mastri, MSD

Overview of Additional FDA Data Technical Guidance
QT Studies Technical Specification Document

- **CDER** Division
- **ADaM** only e.g., ADEG, ADPC
- Examples provided for ADPC and ADEG e.g., use of BASETYPE
- Recommend use of **consistent CT** e.g., for AVISIT
- Ref. QT CDISC TAUG

Overview of Additional FDA Data Technical Guidance
Submitting Select Clinical Trial Data Sets for Drugs Intended to Treat Human Immunodeficiency Virus-1 Infection

- **CDER** Division
- **ADaM Only**
  - ADAE (non-OCCDS)
  - ADLB (list of main laboratory parameters of interest, including Viral Load)
  - ADEFFOUT (ADSL-like focusing on efficacy endpoints plus many other “summary” variables)
- Ref. HIV CDISC TAUG

Overview of Additional FDA Data Technical Guidance

Technical Specifications—Comparative Clinical Endpoint Bioequivalence Study Analysis Datasets for Abbreviated NDAs

- **CDER** Division
- **ADaM Only**
  - ADSL (cross-over study) and other ADaM specific for each type of study Bioequivalence study
  - Definition of mITT population
  - Suggested PARAMCD/PARAM

Overview of Additional FDA Data Technical Guidance

Technical Specifications for Submitting Clinical Trial Data Sets for Treatment of Noncirrhotic Nonalcoholic Steatohepatitis (NASH)

- **CDER** Division, 44 pages
- **SDTM** (14 domains)
  - Events adjudication recommendations (ZA)
  - Correct mapping into MB for Hepatitis A Virus Antibody
  - Recommend RELREC e.g., to link AE and CM
- **ADaM** (7 domains)
  - "Dual" standard unit reporting SI and US Conv Unit
  - Key time to event e.g., Time to Liver Transplant
  - Several baseline characteristics / "value" (ADSL)
  - Good Traceability

Cytel Experience with the FDA Reviewers and these Additional Requirements / Guidance

- Mainly **CBER** for Vaccine Submission
- Very **detailed assessment of our SDSP** and **sample CRF**
- **Adherence** to Vaccine TAUGs and Vaccines Technical Specification Guidance
- Some requests couldn't be satisfied e.g., impacting CRF design (documented discussion / agreement in the SDSP)

Conclusions

Conclusions

- Be **aware** of these additional guidance and Avoid the **unexpected**
- **CDISC Teams Review** is Needed (Peer Review)
- Still a bit of **variability** across divisions and reviewers
- **Lack of examples** (except NASH and QT)
- **Opportunity** for further standardization

Thank You!

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4	"FDA Study Data Technical Conformance Guidance » (FDA, March 2023) https://www.fda.gov/media/153632/download
5	"Pilot OCE/OOD Safety Team Standard Data Requests" (FDA, February 2021) https://www.fda.gov/media/133252/download
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7	"Challenges with Implementation of New Standards and Guidance – A Sponsor's Experience with the April 2018 CBER Vaccine Guidance", S. VanPelt Nguyen and L. Zhang, PHUSE US Connect 2020 https://www.lexjansen.com/phuse-us/2020/ds/DS05.pdf
8	"Vaccines Technical Specification Guidance" v2.1 (FDA, December 2019) https://www.fda.gov/media/112581/download
9	"Providing Regulatory Submission in Electronic Format" (FDA, December 2014) https://www.fda.gov/media/88120/download
10	"Providing Regulatory Submission in Electronic Format - Standardized Study Data" (FDA, Revision 2 June 2021) https://www.fda.gov/media/82716/download

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11	"Data Standards Catalog" (FDA, August 2022) https://www.fda.gov/regulatory-information/search-fda-guidance-documents/data-standards-catalog-v90
12	"Technical Rejection Criteria for Study Data" (FDA, May 2018) https://www.fda.gov/files/drugs/published/Technical-Rejection-Criteria-for-Study-Data.pdf
13	"Portable Document Format (PDF) Specifications" (FDA, September 2016) https://www.fda.gov/media/76797/download
14	"Electronic Common Technical Document (eCTD)" (FDA, March 2023) https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd
15	"Bioresearch Monitoring Technical Conformance Guide Technical Specifications" (FDA, August 2022) https://www.fda.gov/media/85061/download
16	"Submit an eCTD or Standardized Data Sample to the FDA" (FDA, January 2022) https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/submit-ectd-or-standardized-data-sample-fda
17	"Providing Regulatory Submissions in Electronic Format - General Considerations" (FDA, January 1999) https://www.fda.gov/media/71200/download
18	"Creating Simplified TS.XPT Files" (FDA, November 2019) https://www.fda.gov/media/132457/download
19	"Model Data Format for submitting pharmacometric data and models" (FDA, August 2021) https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/model-data-format
20	"Impact of FDA Technical Specifications on CDISC Implementation for NASH Trials", Cécile Cornou; Henning Pontoppidan, Novo Nordisk A/S CDISC EU Interchange 2022
21	PHUSE "Best Practices for Submission of Event Adjudication Data" (October 2019) https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Optimizing+the+Use+of+Data+Standards/Best+Practices+for+Submission+of+Event+Adjudication+Data.pdf

Abstract

For years, CDISC implementers have struggled to find good examples and use cases beyond those provided in the CDISC Implementation Guidance (IG). However, in recent years several CDISC Therapeutic Area User Guidance (TAUG) have become available, and their use is recommended by the FDA in its Study Data Technical Conformance Guidance (SDTCG). Additionally, the FDA has released other guidance to reduce variability in the interpretation of CDISC IG.

The purpose of this presentation is to increase awareness of these often-overlooked additional FDA guidance, by providing details on key topics covered by each of them and sharing our experience with FDA agencies commenting on our data packages by referencing these guidance.