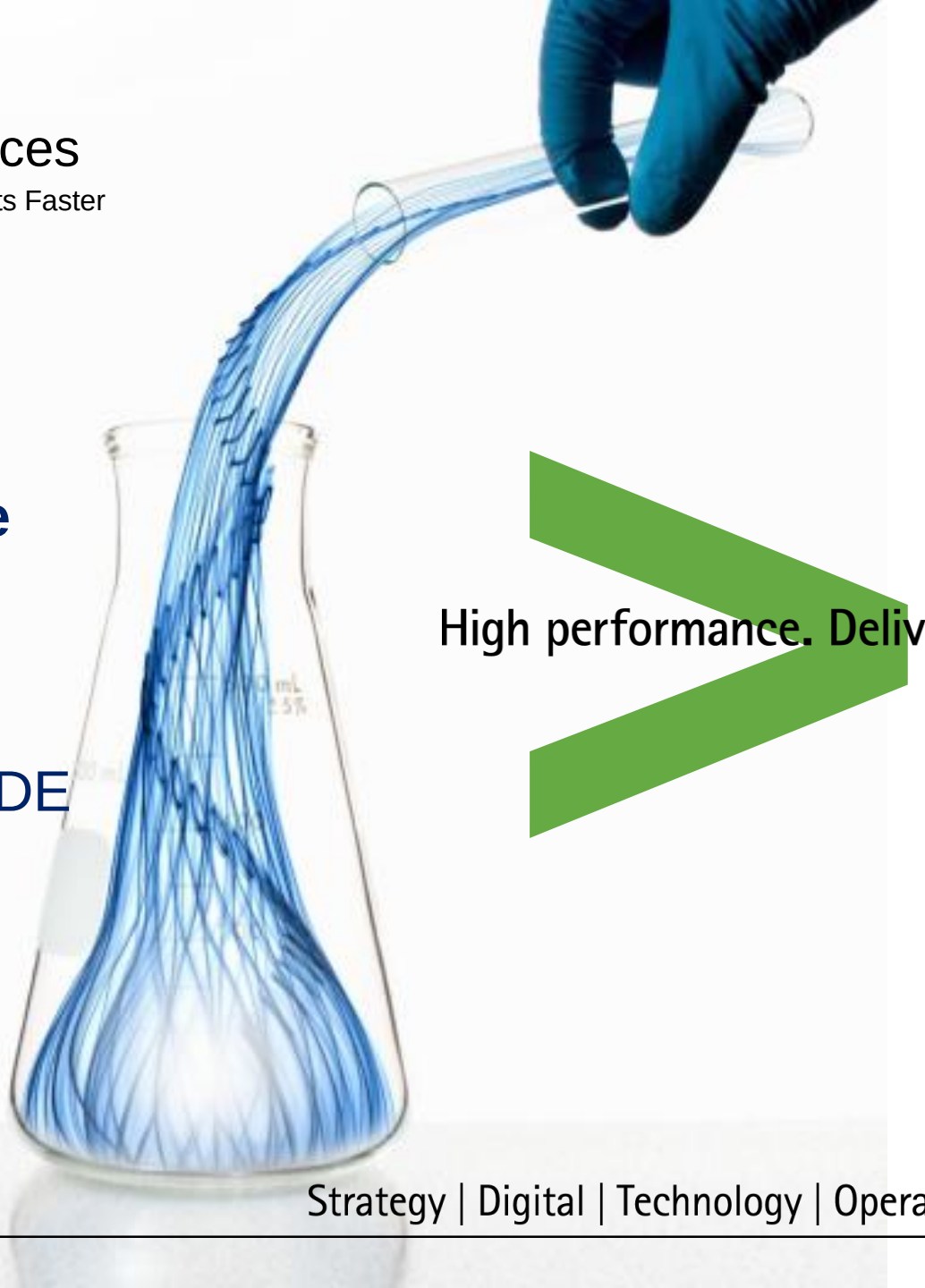
Life Sciences

Accelerated R&D Services

The Science of Getting Products to Patients Faster



New & Enhanced Expectations for the Use of Controlled Terminology

PharmaSUG Philly SDE
22 October 2015

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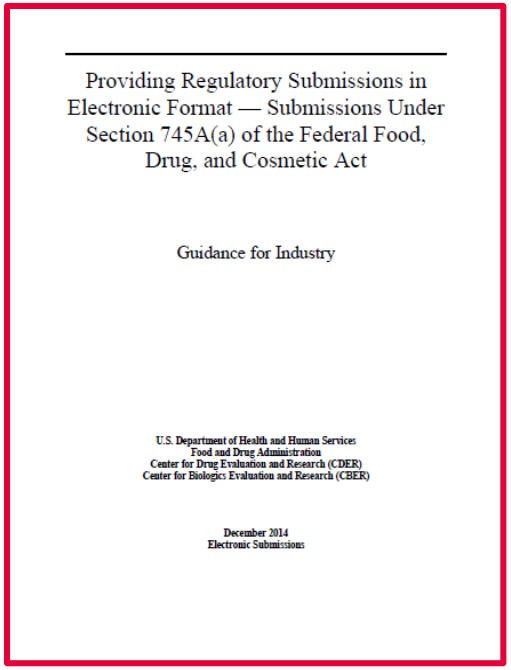
Goals for This Presentation

The FDA mandate for standards

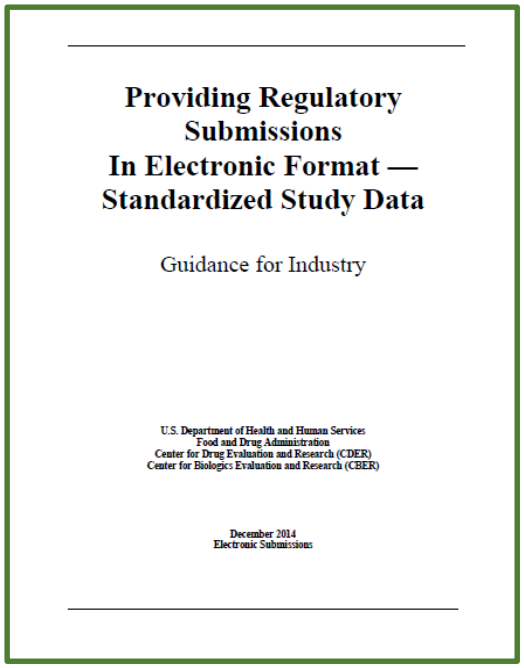
- Impact on controlled terminology deployment
- Expectations for controlled terminology maintenance
- Considerations when preparing for regulatory submission

Specific controlled terminology articulated today

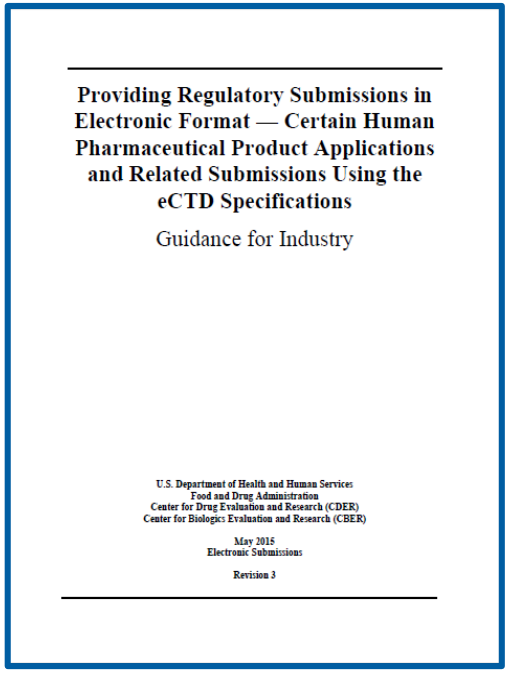
Binding Guidance Documents



Guidance for Industry:
Providing Regulatory Submissions in Electronic Format – Submissions Under Section 745A (a) of the Federal Food Drug, and Cosmetic Act

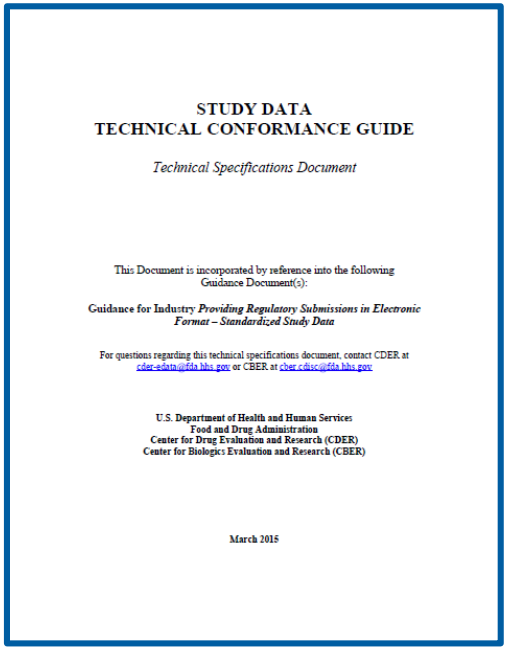


Guidance for Industry:
Providing Regulatory Submissions in Electronic Format – Standardized Study Data



Guidance for Industry:
Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

Companion Documents



STUDY DATA
TECHNICAL CONFORMANCE GUIDE

Technical Specifications Document

This Document is incorporated by reference into the following Guidance Document(s):

Guidance for Industry *Providing Regulatory Submissions in Electronic Format – Standardized Study Data*

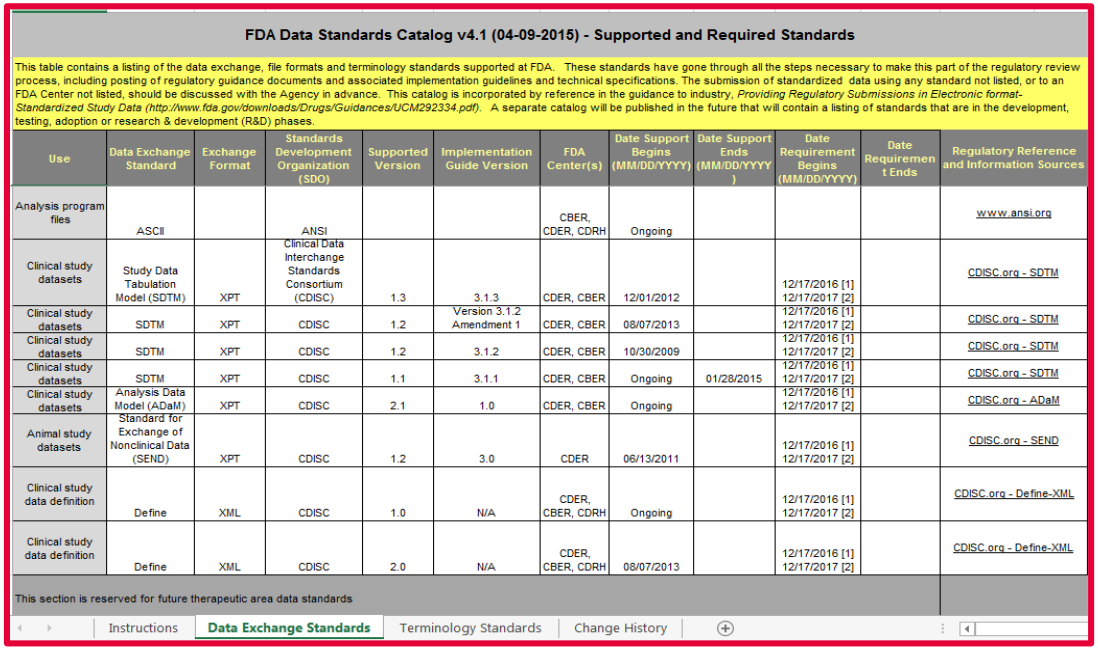
For questions regarding this technical specifications document, contact CDER at cder-edata@fda.hhs.gov or CBER at cber.cdisc@fda.hhs.gov

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

March 2015

Study Data Technical Conformance Guide

Technical Specifications Document



FDA Data Standards Catalog v4.1 (04-09-2015) - Supported and Required Standards

This table contains a listing of the data exchange, file formats and terminology standards supported at FDA. These standards have gone through all the steps necessary to make this part of the regulatory review process, including posting of regulatory guidance documents and associated implementation guidelines and technical specifications. The submission of standardized data using any standard not listed, or to an FDA Center not listed, should be discussed with the Agency in advance. This catalog is incorporated by reference in the guidance to industry, *Providing Regulatory Submissions in Electronic format-Standardized Study Data (http://www.fda.gov/downloads/Drugs/Guidances/UCM292334.pdf)*. A separate catalog will be published in the future that will contain a listing of standards that are in the development, testing, adoption or research & development (R&D) phases.

Use	Data Exchange Standard	Exchange Format	Standards Development Organization (SDO)	Supported Version	Implementation Guide Version	FDA Center(s)	Date Support Begins (MM/DD/YYYY)	Date Support Ends (MM/DD/YYYY)	Date Requirement Begins (MM/DD/YYYY)	Date Requirement Ends	Regulatory Reference and Information Sources
Analysis program files	ASCII		ANSI			CBER, CDER, CDRH	Ongoing				www.ansi.org
Clinical study datasets	Study Data Tabulation Model (SDTM)	XPT	Clinical Data Interchange Standards Consortium (CDISC)	1.3	3.1.3	CDER, CBER	12/01/2012		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.2	Version 3.1.2 Amendment 1	CDER, CBER	08/07/2013		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.2	3.1.2	CDER, CBER	10/30/2009		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	SDTM	XPT	CDISC	1.1	3.1.1	CDER, CBER	Ongoing	01/28/2015	12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SDTM
Clinical study datasets	Analysis Data Model (ADaM)	XPT	CDISC	2.1	1.0	CDER, CBER	Ongoing		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - ADaM
Animal study datasets	Standard for Exchange of Nonclinical Data (SEND)	XPT	CDISC	1.2	3.0	CDER	06/13/2011		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - SEND
Clinical study data definition	Define	XML	CDISC	1.0	N/A	CDER, CBER, CDRH	Ongoing		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - Define-XML
Clinical study data definition	Define	XML	CDISC	2.0	N/A	CDER, CBER, CDRH	08/07/2013		12/17/2016 [1] 12/17/2017 [2]		CDISC.org - Define-XML
This section is reserved for future therapeutic area data standards											

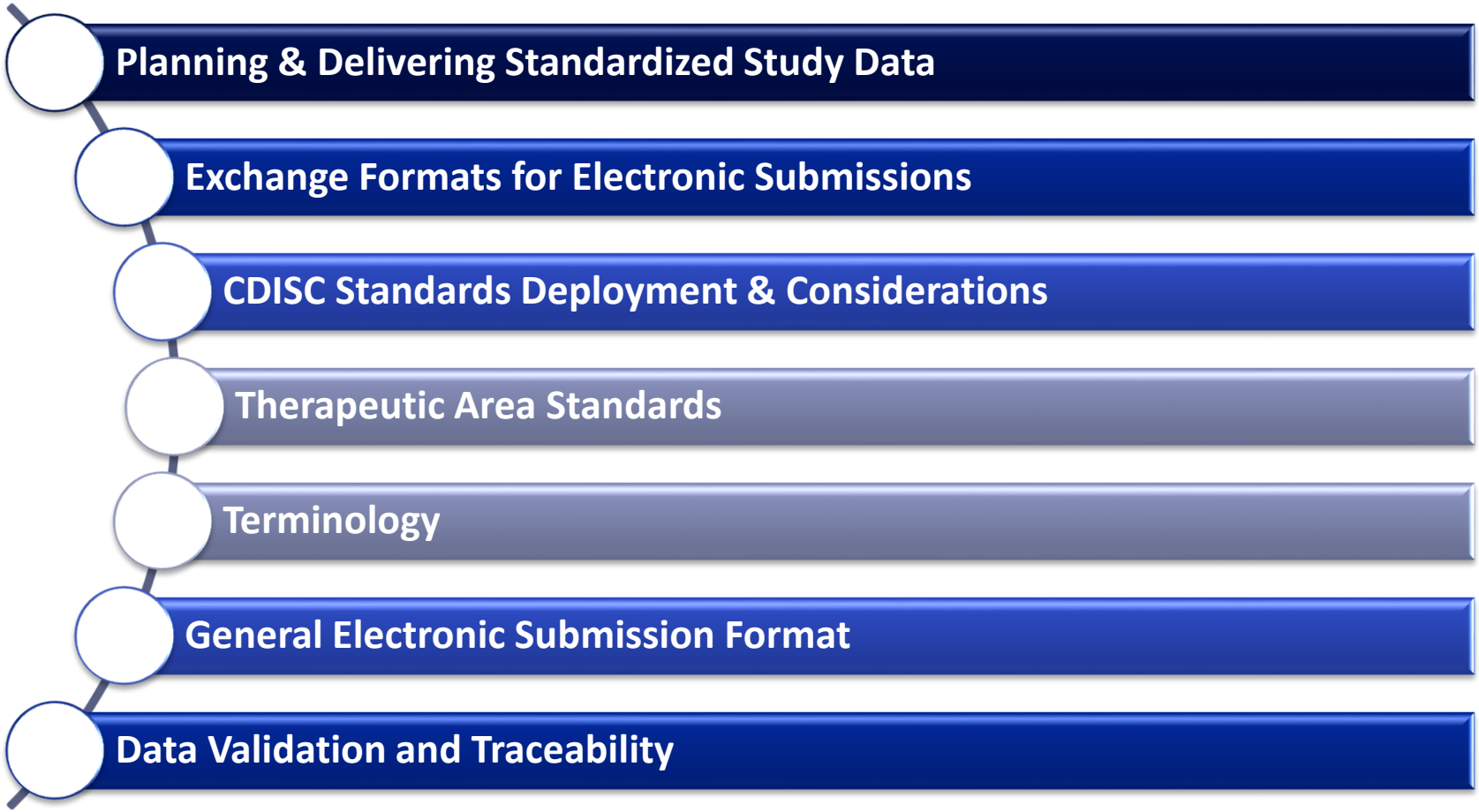
Instructions | Data Exchange Standards | Terminology Standards | Change History

Data Standards Catalog

Guidance for Industry
Standardized Study Data

- Clarifies…
  - When you will be required to initiate studies based on FDA recognized data standards
    - 24 months – NDAs, ANDAs, BLAs (clinical studies)
    - 36 months – INDs (non-clinical studies)
  - VERY high level summary of
    - Study data exchange formats
    - Study data exchange standards
    - Terminology

Study Data Technical Conformance Guide Organization



Data Standards Catalog
Controlled Terminology Standards

FDA Data Standards Catalog v4.4 (08-17-2015)

This table contains a listing of the standard terminology code sets. When the Catalog expresses support for more than one terminology for a given type of regulatory information, the submitter may choose which one to use. Submissions using any terminology not listed should be discussed with the Agency in advance.

The listing of the data exchange standards developed at FDA are listed in a separate tab. Please look at the "Data Exchange Standards" tab to find data exchange standards information supported by FDA. The data exchange standards listed have established processes and technology infrastructure to support the process, review, and archive of the data. The submission of standardized data using any standard not listed, or to an FDA component not listed, should be discussed with the Agency in advance.

Terminology Standard	Terminology Type	Terminology Standards Development and/or Maintenance Organization	Version(s)	FDA Centers That Use This Terminology	Date Support Begins (MM/DD/YYYY)	Date Support Ends	Date Requirement Begins (MM/DD/YYYY)	Date Requirement Ends	Examples of Use	Regulatory References and Information Sources
Clinical Data Interchange Standards Consortium (CDISC) Terminology	General Clinical Data	CDISC	2011-06-10 or later	CBER, CDER	06/13/2011		12/17/2016 [1] 12/17/2017 [2]		Use CDISC Submission values	Index of CDISC SDTM Terminology
Clinical Data Interchange Standards Consortium (CDISC) Terminology	General Clinical Data	CDISC	All Previous Version	CBER, CDER	Ongoing				Use CDISC Submission Values. Do not use for studies initiated after 2011-06-13.	Index of CDISC SDTM Terminology
Medical Dictionary for Regulatory Activities (MedDRA)	Adverse Events	Maintenance and Support Services Organization (MSSO)	8 or later	CBER, CDER	Ongoing		12/17/2016 [1] 12/17/2017 [2]		CDISC AE Domain	MedDRA.org
Event Problem Codes	Adverse Events	CDRH	Latest Version	CDRH	Ongoing				CDISC AE Domain	Medical Devices Event Problem Codes
WHO Drug		World Health					03/15/2018 [1]		Use in SDTM CMDECOD and	

Location: http://www.fda.gov/downloads/ForIndustry/DataStandards/StudyDataStandards/UCM340684.xlsx

Study Data Technical Conformance Guide, Section 6 Controlled Terminology

Concept	Controlled Terminology for Concept	Location in SDTM
Adverse Events	MedDRA	AE domain
Concomitant Medications	WHODrug	CM domain
Study Medication	FDA Unique Ingredient Identifier (UNII)	TS trial design domain • Investigational product (TSPARM=TRT or TRTUNII) • Active comparator (TSPARM=COMPTRT) • Background Treatments (TSPARM=CURTRT)

Study Data Technical Conformance Guide, Section 6 Controlled Terminology

Concept	Controlled Terminology for Concept	Location in SDTM
Laboratory Tests	LOINC	SDTM LB.LBLOINC
Pharmacologic Class	Veterans' Administration's National Drug File – Reference Terminology (NDF-RT)	TS trial design domain • Pharmacologic class (TSPARM=PCLAS)
Indication	SNOMED Clinical Terms	TS trial design domain • Indication (TSPARM=INDIC) • Diagnosis Group (TSPARM=TDIGRP)
Just about everything else	**CDISC Controlled Terminology**	**Just about anything with a codelist**

Controlled Terminology – Some Observations
What is the scope of terminology use?

Protocol & Subject

- CDISC CT
- MedDRA
- WHODrug
- Medical Devices Event Problem Codes
- LOINC

Protocol Only

- FDA UNII Codes
- National Drug File – Reference Terminology
- SNOMED

Controlled Terminology – Some Observations
Who determines CT values?

Skilled Coders

- MedDRA
- WHODrug
- Medical Devices Event Problem Codes
- LOINC

Data Professionals

- CDISC CT

Clinical Professionals

- FDA UNII Codes
- National Drug File – Reference Terminology
- SNOMED

Controlled Terminology – Some Observations
What domains does the CT end up in?

Subject Level Data

- CDISC CT
- MedDRA
- WHODrug
- Medical Devices Event Problem Codes
- LOINC

Trial Design Domains

- CDISC CT
- FDA UNII Codes
- National Drug File – Reference Terminology
- SNOMED

Controlled Terminology Resources
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Controlled Terminology Resources
LOINC

https://loinc.org

Downloads
- LOINC
- RELMA
- Accessory Files
- Go Premium

Documentation
- Quick Start Guide
- Document Library
- About LOINC
- LOINC Users' Guide
- Recommended Readings
- Presentations/Tutorials
- FAQ

Community
- International
- User's Forum
- Meetings
- News
- Mailing Lists
- Directory of Adopters
- Collaboration with other SDOs
- Wisdom of the Crowd

Content
- Top Result and Order Code Lists
- Newborn Screening
- Document Ontology
- HIPAA Attachments
- What's Coming in the Next Release
- Request New LOINC Terms
- FHIR Vocab Service (pilot)
- NLM/RI LForms Widget

Controlled Terminology
FDA Expectations

- The FDA acknowledges that clinical trials are run over time and that terminology versions will likely differ from one study to the next as a result (Study Data TCG, Section 6.1.2, 1st paragraph)
- The FDA expects sponsors to use the most current version of an FDA-supported terminology available at the time of coding (Study Data TCG, Section 6.1.2, 1st paragraph)
- Regardless of the specific versions used for individual studies, the FDA expects sponsors to utilize a single version of a controlled terminology when pooling data in support of an integrated analysis (Study Data TCG, Section 6.1.2, 2nd paragraph)

Controlled Terminology
FDA Expectations

- The FDA expects sponsors to utilize controlled terminology wherever available and, if the controlled terminology does not contain the information needed by the sponsor for submission, it is incumbent upon the sponsor to work with the controlled terminology maintenance organization with enough lead time to ensure that necessary controlled terminology is available at the time of regulatory filing (Study Data TCG, Section 6.1.3)

Controlled Terminology
Additional Reading & Resources

- The Data Standards Catalog
- The Structured Product Labeling resources on the FDA web site
  - http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
- Introductory presentation on maintaining controlled terminology in your environment
  - http://www.pharmasug.org/download/sde/boston2014/PharmaSUG_Boston2014SDE_02_Hinkson_Simion.pdf

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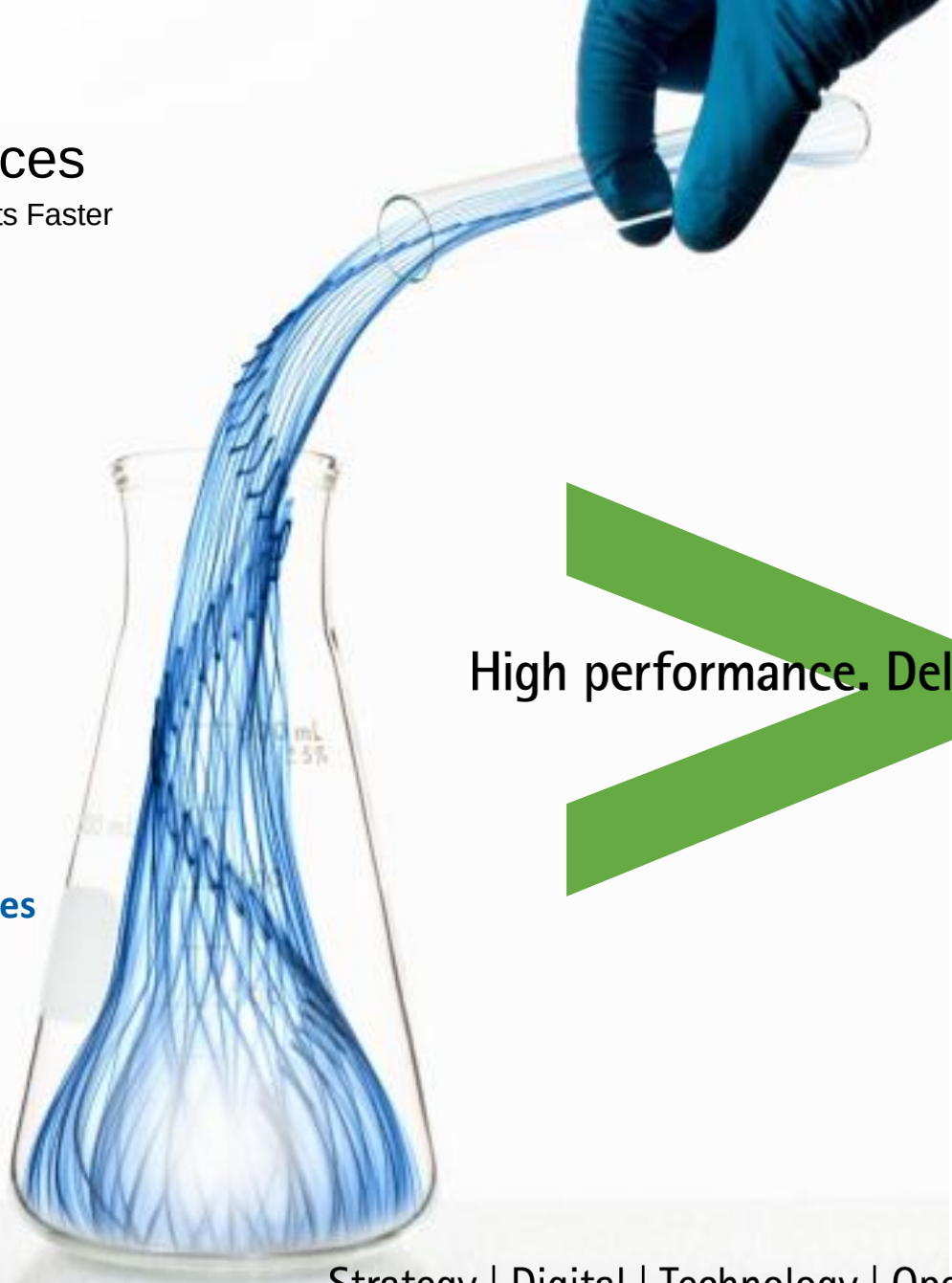
The Science of Getting Products to Patients Faster



Thank you!

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