

PP15 Bili's Journey

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eCTD Submission!

Please visit the FDA web page ucm535180.htm for more information on the following eCTD resources:

FDA Guidances
eCTD Submission Standards Catalog
Data Standards Catalog
Technical Conformance Guide
Validation Specifications
Fact Sheets
Additional Resources

This poster will trace the path of a single piece of data and identify all the regulatory and standards compliance considerations that dot the landscape from initial data collection all the way through submission through the eCTD. We'll follow the journey of the lab parameter Total Bilirubin, NCI Thesaurus Code C38037, and affectionately known in this poster as "Bili", while demonstrating every influencing factor in the standards and regulatory environment as Bili's data values and metadata are transformed along the way from start to finish. Standards concepts of CDASH, SDTM and ADaM will be considered along with all the regulations defined in the FDA Data Standards Catalog. Other items will be demonstrated such as data anonymization and Define-XMLv2.0 which have an effect of transforming data or metadata for data sharing and submission. From start to finish, Bili's journey is truly remarkable.

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NCI Thesaurus
Version: 18.034 (Release date: 2018-03-20)

Total Bilirubin Measurement (Code C38037)

Synonym Details

Term	Source	Type	Code	Subsource Name
Bilirubin	CDISC	PT	SDTM.LBTEST	
Bilirubin	CDISC	SY		
BLI	CDISC	PT	SDTM.LBTESTCD	
Total Bilirubin Measurement	NCI	PT		
Total Bilirubin Measurement	NCI	SY		
Total Bilirubin	CDISC	SY		

FDA Data Standards Catalog v5.0 (04-20-2018)

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.

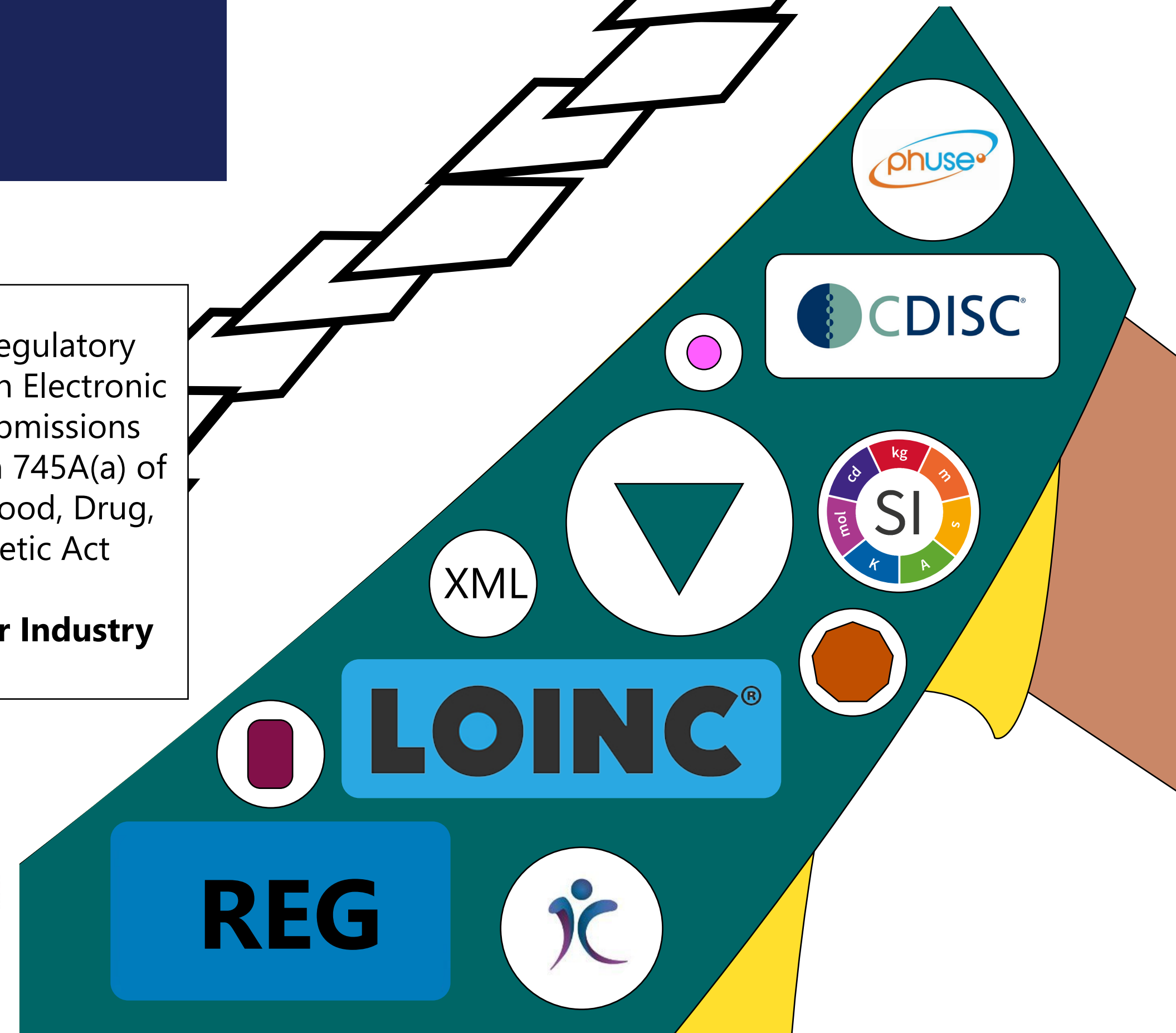
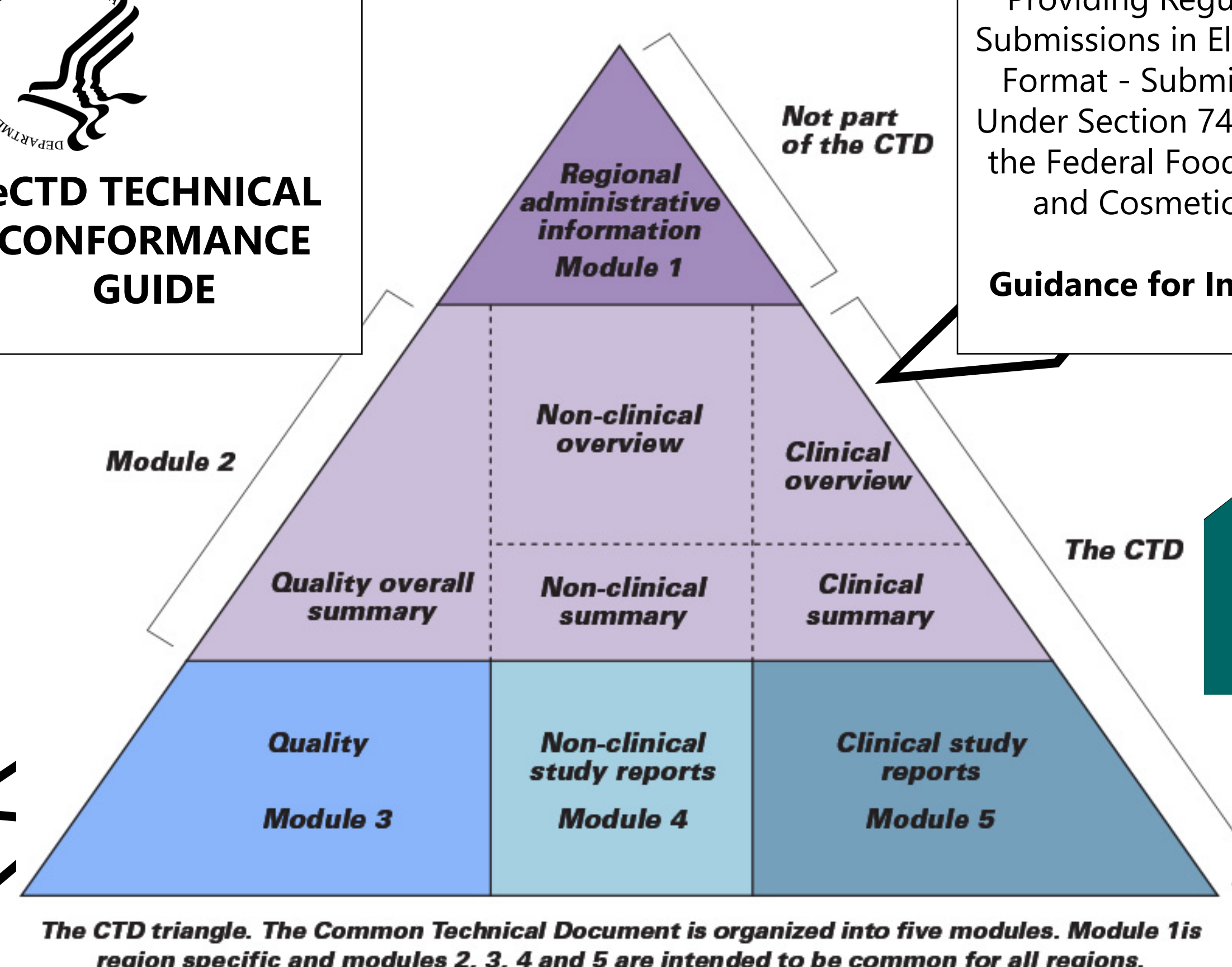
This listing of the data exchange standards developed by FDA are listed in a separate tab. Please look at the "Data Exchange Standards" tab to find data exchange standards information supported by the FDA. The data exchange standards listed have established processes and technology infrastructure to 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 Standards Development and/or Maintenance Organization	Version(s)	FDA Center(s)	Date Support Begins (MM/DD/YYYY)	Date Support Ends	Date Requirement Begins (MM/DD/YYYY)	Date Requirement Ends	Examples of Use	Statutory, Regulatory, or Guidance Authority	Information Sources
Logical Observation Identifiers Names and Codes (LOINC)	Regenstrief Institute	Latest Version	CDER, CDOR	10/20/2017		03/19/2020 [1] 03/19/2021 [2]		Use in SDTM.LB.LOINC	Standardized Study Data	LOINC Study Data Technical Conformance Guide

With each new standard, regulation or guidance, Bili earns a merit badge as he moves along the continuum from collection to submission.

eCTD TECHNICAL CONFORMANCE GUIDE

CTD Triangle

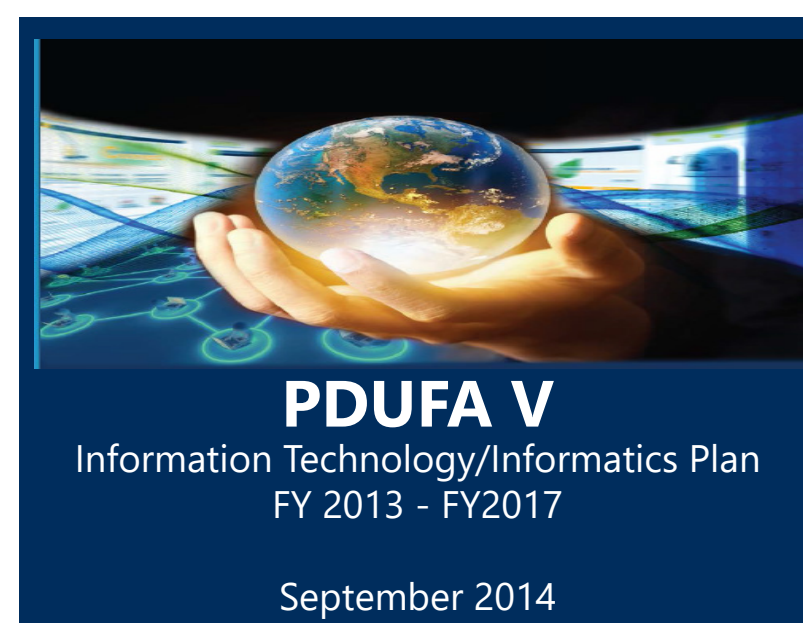


Bilirubin is produced within the reticuloendothelial system through a process called hemolysis and is a by-product resulting from the breakdown of hemoglobin in red blood cells. The liver filters bilirubin from the body into the bile, which gives its color, and a small amount is normally found in serum. An excess of red blood cell destruction, or a reduced capacity of the liver to excrete the normal amounts of bilirubin, will result in elevated levels and is important in evaluating hemolytic anemias, hyperbilirubinemia and liver function.



Total Bilirubin
0.2-1.0 mg/dL for those under 18 years old

A Manual of Laboratory Diagnostic Tests by Frances Fischbach 3rd Ed. Pages 280-281



Food and Drug Administration, HHS
PART 50—PROTECTION OF HUMAN SUBJECTS
Subpart A—General Provisions
Sec. 50.1 Scope.
50.3 Definitions.
Subpart B—Informed Consent of Human Subjects
50.20 General requirements for informed consent.

VIEWTABLE: Adam.Adlb

STUDYID	DOMAIN	USUBID	SUBID	SITEID	AGE	AGEU	SEX	RACE	ARMCD	ARM	RANFL	ADT	VISIT	LBST	ADY	TIMPOINT
133	PRM001	ADLB	PRM001-01-111	01-111	01	57	YEARS	WHITE	FLB	FLB	Y	11APR0802	SCREENING WEEK 2	25APR12 08:00:00	-14	PRE-DIALYSIS
134	PRM001	ADLB	PRM001-01-111	01-111	01	57	YEARS	WHITE	FLB	FLB	Y	23MAY12	WEEK 1 VISIT 2	23MAY12 09:00:00	1	PRE-DIALYSIS
135	PRM001	ADLB	PRM001-01-111	01-111	01	57	YEARS	WHITE	FLB	FLB	Y	23MAY12	WEEK 5 VISIT 2	23MAY12 10:40:00	29	PRE-DIALYSIS

Bilirubin values are not likely to change but direct and quasi-identifiers may change to protect personally identifiable information for data sharing.

VIEWTABLE: Adam.Adlb

AVISIT	PARAM	PARAMCD	PARCAT	LABFL	AVAL	AVALC	BASE	CHG	PREBASE	PRECHG	ANRLO	ANRHI	ANRIND	BNRIND	SHIFT
133	WEEK 2	Bilirubin (uMol/L)	BLI	CHEMISTRY	8.55	8.55	6.84	1.71	6.84	-	1.71	20.52	NORMAL	NORMAL	NORMAL-NORMAL
134	BASELINE	Bilirubin (uMol/L)	BLI	CHEMISTRY	6.84	6.84	6.84	-	6.84	-	1.71	20.52	NORMAL	NORMAL	NORMAL-NORMAL
135	WEEK 5	Bilirubin (uMol/L)	BLI	CHEMISTRY	6.84	6.84	6.84	0.00	6.84	-	1.71	20.52	NORMAL	NORMAL	NORMAL-NORMAL

SDTM-IG 3.1.2 Value Level Metadata - LB [LBORRES]

Variable	Where	Type	Length / Display Format	Controlled Terms or Format	Origin	Derivation/Comment
LBORRES	LBTESTCD EQ BLI (Bilirubin) AND LBST EQ CHEMISTRY AND LBSTEQ EQ BLOOD	float	3		eDT	

Position on Use of SI Units for Lab Tests

CDER and CDOR are evaluating an approach to transition to general acceptance of laboratory data in clinical trials that are measured and reported in Systeme International (SI) units instead of U.S. Conventional units. The objective is to establish an agency-wide policy on the acceptance of SI units in product submissions.

Conversion factor to derive SI values from conventional for LBSTRESN, LBSTNRLO & LBSTNRHI within SDTM LB

CDISTEST	CDISTSCD	FROMUNIT	TOUNIT	CONFACTOR
Bilirubin	BLI	mg/dL	umol/L	17.1

List of Standards, Guidance, Regulation, etc.

Food and Drug Administration HHS Part 50—Protection of Human Subjects
21 CFR Part 312 Investigational New Drug Application
45 CFR Part 46 Protection of Human Subjects
Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2)
ICH E9 Statistical Principles for Clinical Trials
FDA Electronic Source Data in Clinical Investigations
21 CFR Part 11 Electronic Records; Electronic Signatures
FDA PDUFA V Information Technology/Informatics Plan FY 2013 – FY 2017
FDA Providing Regulatory Submissions in Electronic Format Standardized Study Data
FDA Providing Regulatory Submissions in Electronic Format — Submissions Under Section 745A(a) of the Federal Food, Drug, and Cosmetic Act
"FDA Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

FDA eCTD Technical Conformance Guide
FDA Statistical Software Clarifying Statement
FDA Study Data Standards for Regulatory Submissions Position Statement
FDA Data Standards Catalog
SDTM Model Documents
SDTM and ADaM Implementation Guides
FDA Validator Rules Final Dec 2017 v1.2
FDA Technical Rejection Criteria for Study Data
FDA Position Statement - Use of SI Units for Lab Tests
NCI Controlled Terminology
CDASH Clinical Data Acquisition Standards Harmonization (CDASH)
PhUSE Reviewer's Guides for SDTM and ADaM
PhUSE Study Data Standardization Plan
FDA Study Data Technical Conformance Guide