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Everything you want to know about CTUG, CT Relationships and other Controlled Terminology topics

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Meet the Speakers

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Organization: SolCur/argenx

Standards manager with a focus on eCRF/SDTM development, lab controlled terminology expert

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Title: Clinical/Biomedical Information Specialist; CDISC Terminology Lead

Organization: US NCI-EVS [c] & MSC, a Guidehouse company

CDISC Controlled Terminology Program Lead for CDISC and EVS

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Agenda

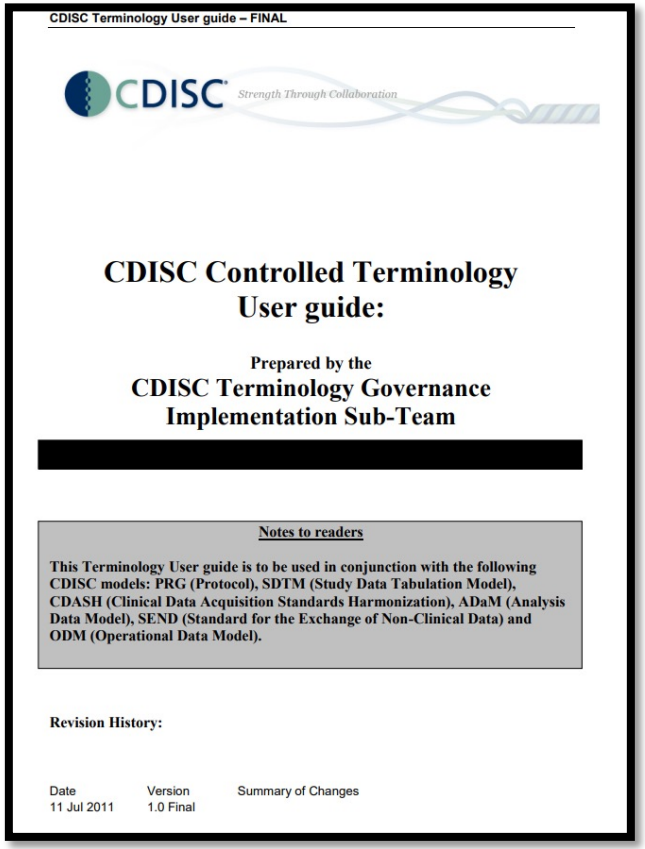
1. Controlled Terminology User Guide
2. CT Relationships
3. LB/MB/IS domain scope changes
4. MRCT Plain Language Glossary
5. Honorable Mentions

Controlled Terminology User Guide

A document to help users find their way in the world of CDISC Controlled Terminology

Controlled Terminology User Guide Team

- Team was formed in 2019 to evaluate and update the published Controlled Terminology User Guide drafted in 2011.
- Co-lead by Anna Pron-Zwick, Erin Muhlbradt, and Ward Puttemans
- Sections were outlined/refined and started recruiting volunteers from industry, regulatory, and CDISC to write the new version.


CDISC Terminology User guide – FINAL

CDISC Strength Through Collaboration

CDISC Controlled Terminology User guide:

Prepared by the
CDISC Terminology Governance Implementation Sub-Team

Notes to readers

This Terminology User guide is to be used in conjunction with the following CDISC models: PRG (Protocol), SDTM (Study Data Tabulation Model), CDASH (Clinical Data Acquisition Standards Harmonization), ADaM (Analysis Data Model), SEND (Standard for the Exchange of Non-Clinical Data) and ODM (Operational Data Model).

Revision History:

Date	Version	Summary of Changes
11 Jul 2011	1.0 Final	

Document structure

CTUG Sections – A Walkthrough

1. Introduction

- Purpose and scope
  - Intend to guide users on processes and considerations when adopting standards or optimizing processes surrounding controlled terminology adoption
- CT stakeholders
- Description of CT
- Why do we have CT

2. CDISC CT Development Process

- Change request system
- Development teams
- Public review process
- Publication
- Process timelines

CTUG Sections – A Walkthrough

3. CDISC CT Implementation and Formats

- Terminology file storage and types
- Terminology metadata
  - Section describes the structure of the controlled terminology file that is published by NCI each quarter

4. CDISC CT Related files

- CDISC CT change files
- Codetable mapping files
- Team rules for CDISC CT development
- CDISC CT requests denied
- CDISC change request tracking file
- External terminology standards mapping to CDISC
- Paired codelists
- Controlled terminology relationships

CTUG Sections – A Walkthrough

5. Considerations for terminology management

- Version management
  - Consideration for foundation standards and TAUG/CT versions
  - What to do when terms or codelists are deprecated
- Submission to different regulators
- Codelist extensibility
- NCIt C-Code management
- CDISC IG conventions for sponsor-controlled terminology
  - --ALL convention for TEST codes
  - The multiple convention

Next Steps

- Team is hard at work to finalize section 5
- Will go out for internal review later this year and public review thereafter.
- We are looking forward to your feedback during these two review cycles!

Thanks to the Team!

(Active): Anna Pron-Zwick, Erin Muhlbradt, Ward Puttemans, Barbara Lentz, Craig Zwickl, Mihaela Simion, Hon-Sum Ko, Trish Gleason, Aileen St. Marie, Debbie O'Neill, Elaine Hazzard, Venkat Lajapathirajan, Noemie Charpentier, Dinnelle Palmer, Dhananjay Thakur

(Past): Dana Booth, Staffan Palerius, Richard Phillips, Vivek Kumar, Assia Bouhadouza

LB/MB/IS domain scope changes

A special thank you to Dr. Jordan Li and the SDS MB/IS team for the following slides…

LB/MB/IS Domain Scope Changes Across SDTMIG v3.2 through SDTMIG v3.4

IGv3.2

- **IS** domain scoped for study therapy-induced subject immune response.
- **LB** domain scoped to include non-host microorg tests and other subject immune response assessments.
- **MB** domain scoped to include some non-host microorg tests used for microbial identification purposes only.

IGv3.3

- **IS** domain scoped for study therapy-induced subject immune response.
- **LB** domain scoped to include other subject immune response assessments, it no longer contains non-host microorg tests.
- **MB** domain scope broadened to include all detection, identification, quantification, and other characteristics assessments of non-host microorg, via direct detection methods and indirect, induced-host/subject immune response.

IGv3.4

- **IS** domain scoped for any antigen-induced subject immune response, not restricted to study therapy.
- **LB** domain no longer contains subject immune response assessments, or any non-host microorg tests.
- **MB** domain contains “direct” detection, identification, quantification, and other characteristics assessments of non-host microorg at the time of specimen testing. It no longer contains microorg induced-subject/host immune assessments.

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Domain and variable level structure limitation for LB/MB/IS

- Domain Scope SDTMIGv3.2/v3.3:
  - Certain kinds of immune response testing data were jammed into MB and LB domains as they were out of scope for IS.
  - Suppquals were heavily used to map key information in both LB and MB for the above data.
  - Heavy pre-coordination and overloading of info in –TEST/TESTCD variables.
- Domain Scope SDTMIGv3.4:
  - New variables were created in IS to support all antigen-induced immune response data.
- Pros -> Creation of specific variables that support IS data and no overloading of Topic Variables.

Multiple domains used to represent specimen-based immune response testing data

- Domain Scope SDTMIGv3.2/v3.3:
  - IS domain scope limited its use to study therapy-induced immune response testing data.
  - LB domain was used to contain Baseline immune response testing data *prior to study treatment exposure*
- Domain Scope SDTMIGv3.4:
  - All immune response testing data modeled in IS domain.
- Pros -> Consolidating like data into a single domain – easier to find and review.

LB/MB/IS Domain Scope Changes Affect CDISC Controlled Terminology

Deprecation of approximately 400 antibody TEST and TESTCD values from both the Lab and Microbiology domains.

- Remodeled in the IS domain, using IS domain standard variables including but not limited to: ISTEST-CD, ISBDAGNT (Binding Agent), and ISTSTDTL (Test Detail)
- CDISC will no longer publish humoral immune response antibody tests, as well as other antigen-stimulated cellular immune response tests, in LB and MB.
- Actual terminology changes (deprecation) will happen in Dec 2023.

Increase in use of Extensible Terminology for a time.

- Users submitting under the IGv3.2/v3.3 should use extensible terms in LB and MB for antigen-stimulated immune response testing data.

Change in modeling strategies (Pre- vs Post-Coordination of Test CT values).

- IGv3.2/v3.3, Pre-Coordination: --TEST = Neut. Respirat. Syncytial Virus IgG NT50
- IGv3.4, Post-Coordination:
  1. --TEST = Neutralizing Microbial-induced IgG Antibody
  2. --BDAGNT = Respiratory Syncytial Virus
  3. --TSTDTL = 50% NEUTRALIZATION TITER

Additional Resource published on CDISC.org

- IS_Codetable_Mapping file: https://www.cdisc.org/standards/terminology/controlled-terminology#standard__Codetable_Mapping_Files
- Knowledge Base Article: https://www.cdisc.org/kb/articles/domain-scope-update-sdtmig-v3-4-development-history-and-difficulties-standardizing
- Public Communications:
  - Interchange Presentation
  - CDISC Education courses
  - Webinar Archives: Controlled Terminology Updates for Q3 2022
- Email Dr. Jordan Li directly: jordan.li@nih.gov

CT Relationships

"Relationships between published terminology codelists and variable metadata are not explicit enough or are incomplete in published IGs and TAUGs."

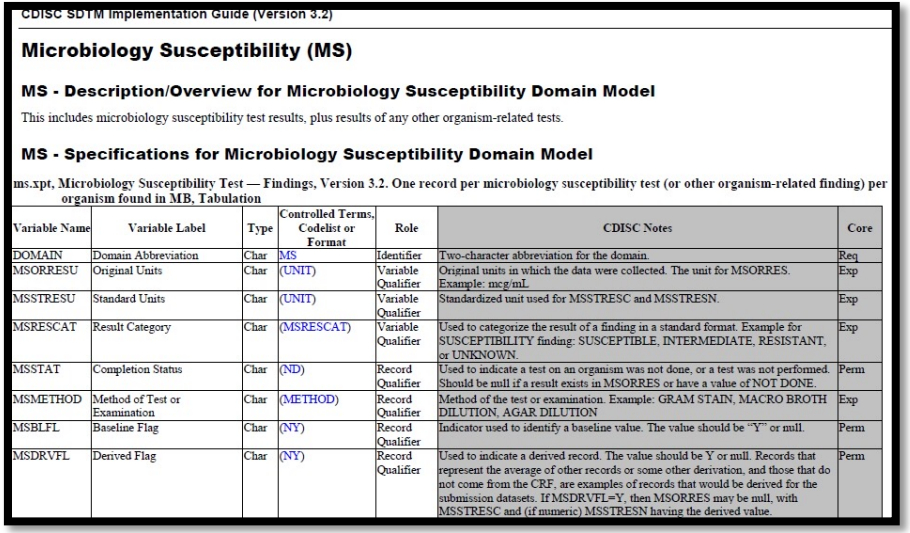
Supporting Problem Statements

- The use case of Controlled Terminology has matured from simple “one variable, one codelist.”
  - Conditional codelists, value subsets, and other new scenarios are becoming prevalent in various CDISC products. We need to provide implementers information how to apply these scenarios when they implement the standards.
- Industry feedback tells us codetables posted on https://www.cdisc.org/standards/semantics/terminology are very useful to jumpstart implementation.
  - But to improve consistency and increase production, we need some kind of formalism such as value-level metadata.
- Publication frequency of Controlled Terminology outpaces Implementation Guides and User Guides.
  - This creates a late binding effect where new codelists are created (or, codelists renamed and deprecated) post-publication. It is time to re-evaluate our current process and tackle this historical problem.
- Lastly, new information cited above cannot be effectively managed and maintained in [two-dimensional] spreadsheets.

But don’t take my word for it!

SDTMIG v3.2/SDTM v1.4 (An example)

- In SDTMIG v3.2: 8 variables with associated CT codelists for the MS domain.
- In SDTM v3.2: 3 additional variables with associated CT codelists for the MS domain that were **not** acknowledged in the IG.
  - MSTEST/CD, LOINC



CDISC SDTM Implementation Guide (Version 3.2)

Microbiology Susceptibility (MS)

MS - Description/Overview for Microbiology Susceptibility Domain Model

This includes microbiology susceptibility test results, plus results of any other organism-related tests.

MS - Specifications for Microbiology Susceptibility Domain Model

ms.xpt, Microbiology Susceptibility Test — Findings, Version 3.2. One record per microbiology susceptibility test (or other organism-related finding) per organism found in MB, Tabulation

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
DOMAIN	Domain Abbreviation	Char	MS	Identifier	Two-character abbreviation for the domain.	Req
MSORRESU	Original Units	Char	(UNIT)	Variable Qualifier	Original units in which the data were collected. The unit for MSORRES. Example: mcg/mL	Exp
MSSTRESU	Standard Units	Char	(UNIT)	Variable Qualifier	Standardized unit used for MSSTRESC and MSSTRESN.	Exp
MSRESCAT	Result Category	Char	(MSRESCAT)	Variable Qualifier	Used to categorize the result of a finding in a standard format. Example for SUSCEPTIBILITY finding: SUSCEPTIBLE, INTERMEDIATE, RESISTANT, or UNKNOWN.	Exp
MSSTAT	Completion Status	Char	(ND)	Record Qualifier	Used to indicate a test on an organism was not done, or a test was not performed. Should be null if a result exists in MSORRES or have a value of NOT DONE.	Perm
MSMETHOD	Method of Test or Examination	Char	(METHOD)	Record Qualifier	Method of the test or examination. Example: GRAM STAIN, MACRO BROTH DILUTION, AGAR DILUTION	Exp
MSBLFL	Baseline Flag	Char	(NY)	Record Qualifier	Indicator used to identify a baseline value. The value should be "Y" or null.	Perm
MSDRVFL	Derived Flag	Char	(NY)	Record Qualifier	Used to indicate a derived record. The value should be Y or null. Records that represent the average of other records or some other derivation, and those that do not come from the CRF, are examples of records that would be derived for the submission datasets. If MSDRVFL=Y, then MSORRES may be null, with MSSTRESC and (if numeric) MSSTRESN having the derived value.	Perm

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
MSTESTCD	Microbiology Organism Finding Short Name	Char	*	Topic	Short name of the measurement, test, or finding described in MSTEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in MSTESTCD cannot be longer than 8 characters, nor can it start with a number (e.g."1TEST). MSTESTCD cannot contain characters other than letters, numbers, or underscores. Examples for GROWTH findings: EXTGROW, COLCOUNT. For SUSCEPTIBILITY findings, the test is the drug the organism was tested with, i.e. PENICLLN, AMOXCLLN.	Req
MSTEST	Organism Test or Finding Name	Char	*	Synonym Qualifier	Verbatim name of the test or examination used to obtain the measurement or finding. Examples for GROWTH findings: Extent of Growth, Colony Count. Examples for SUSCEPTIBILITY findings: Amoxicillin Susceptibility, Penicillin Susceptibility	Req
MSLOINC	LOINC Code	Char	*	Synonym Qualifier	1. Dictionary-derived LOINC Code for MSTEST. 2. The sponsor is expected to provide the dictionary name and version used to map the terms utilizing the define.xml external codelist attributes	Perm

- In SDTM v1.4 Findings table: 9 additional variables with associated CT codelists for the MS domain.

Variable Name	Variable Label	Type	Role	Description
--SPEC	Specimen Material Type	Char	Record Qualifier	Defines the type of specimen used for a measurement. Examples: SERUM, PLASMA, URINE, DNA, RNA.
--SPCUFL	Specimen Usability for the Test	Char	Record Qualifier	Describes the usability of the specimen for the test. The value will be N if the specimen is not usable, and null if the specimen is usable.
--LOC	Location Used for the Measurement	Char	Record Qualifier	Anatomical location of the subject relevant to the collection of the measurement. Examples: RECTAL for temperature, ARM for blood pressure.
--LAT	Laterality	Char	Variable Qualifier of --LOC	Qualifier for anatomical location or specimen further detailing laterality. Examples: RIGHT, LEFT, BILATERAL
--DIR	Directionality	Char	Variable Qualifier of --LOC	Qualifier for anatomical location or specimen further detailing directionality. Examples: ANTERIOR, LOWER, PROXIMAL
--PORTOT	Portion or Totality	Char	Variable Qualifier of --LOC	Qualifier for anatomical location or specimen further detailing the distribution, which means arrangement of, apportioning of. . Examples: ENTIRE, SINGLE, SEGMENT, MANY.
--EVAL	Evaluator	Char	Record Qualifier	Role of the person who provided the evaluation. Used only for results that are subjective (e.g., assigned by a person or a group). Examples: ADJUDICATION COMMITTEE, INDEPENDENT ASSESSOR, RADIOLOGIST.
--ACPTFL	Accepted Record Flag	Char	Record Qualifier	In cases where more than one assessor provides an evaluation of a result or response, this flag identifies the record that is considered, by an independent assessor, to be the accepted evaluation. Expected to be Y or null.
--NRIND	Normal/Reference Range Indicator	Char	Variable Qualifier of --ORRES	Used to indicate the value is outside the normal range or reference range. May be defined by --ORNRLO and --ORNRHI or other objective criteria. Examples: Y, N; HIGH, LOW; NORMAL; ABNORMAL.

- In SDTM v1.4 Timing variables table: 1 additional variable with CT.

EPOCH	Epoch	Char	Epoch associated with the start date/time of the observation, or the date/time of collection if start date/time is not collected. (See Section 3.2.2).

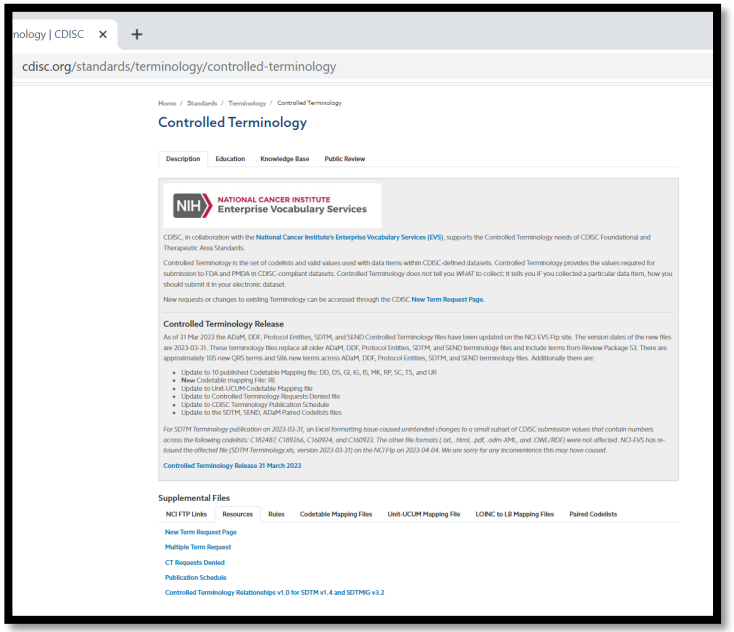
Suppquals/NSVs Associated with MS Domain

QNAM	QLABEL	QVAL	Published Document
MSSPCIES	Species	Values from codelist: C116111/SPCIES	**TAUG-Virology**
COLMETH or CLMTH	Specimen Collection Method	Values from codelist: C132314/CLMETH	**SDTMIG v3.2 (though not in appendix C and only associated with MB); TAUG-Asthma; TAUG-DMD, TAUG-TB**
MEDTYPE	Culture Medium Type	Values from codelist: C127264/CLTMDTYP	**TAUG-TB**

Instead of just 8 variables, we've now identified 24 variables with CT associations, scattered across multiple documents. We need a 'One-Stop' Shop!

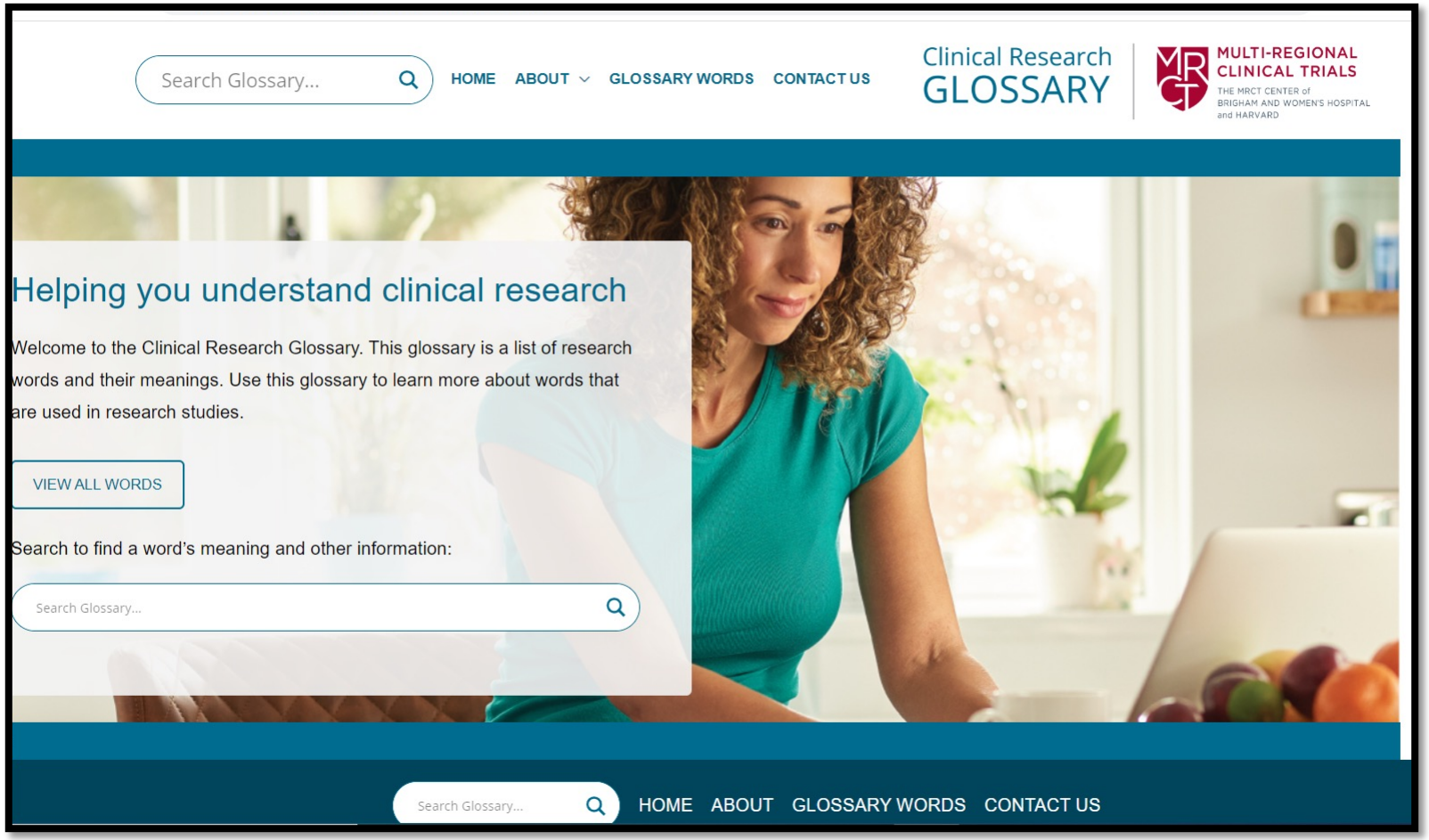
The Solution

- Explicitly identify and document all relationships between CDISC variables, NSVs, TEST/PARMs and their terminology codelists/valid value sets or subsets with **metadata tables**.
- Published on CDISC website in Excel and YAML
  - Version SDTM1.4/SDTMIGv3.2 is published and version SDTM1.7/SDTMIGv3.3 is nearing public review.
- Use Cases:
  - Improve process automation to create Trial Design datasets for regulatory submissions.
  - Streamlines input to data validation software for additional terminologies requirements for regulatory submissions.
  - Enables data to comply to Controlled Terminology requirements upfront, providing inherit high-quality data at SDTM dataset generation.
  - Enables software integration with CDISC Library.



MRCT Plain Language Glossary

Terminology for patients, participants, their caregivers, and families!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- An online, browsable, and searchable resource that contains multiple aspects:
  - Plain Language Definition
  - Pronunciation
  - Image
  - Use in a sentence
  - Additional information/Notes
  - Related/Opposite words
  - Links to other resources
- Plain Language definitions can be used for patient/participant-facing documents
  - Consent Forms
  - Participant Information Sheet
  - Results Summary
  - Protocol Synopsis
  - Patient Labeling Summary
  - Certificates of Confidentiality

CDISC and MRCT Collaboration

- **MRCT** will continue to develop plain language terms and manage their glossary website content.
- **CDISC** will be part of the content development teams, shepherd terms through CDISC CT public review and host links to the e-glossary on their website.
- **CDISC Glossary team** is part of the content development team and will ensure all terms in the plain language glossary will have technical definitions in CDISC CT.
- **NCI-EVS** will code, publish, and maintain the plain language definitions in NCIt to preserve the linkage between the plain language definition and CDISC technical definition.

Schedule of Reviews and Publication

- Batch 1 – 53 terms went out for CDISC CT public review with P54 on April 24, 2023
- Batch 2 – ~150 terms will go out for CDISC CT public review with P55 on June 23, 2023
- First official publication of MRCT Plain Language Glossary will take place on December 15, 2023
- Considering twice yearly releases going forward into 2024 and beyond.

Honorable Mentions

-LAB Model Updates

-NSV Registry

LAB Model Updates

"LAB provides a standard model for the acquisition and exchange of laboratory data, primarily between labs and sponsors or CROs. The LAB standard was specifically designed for the interchange of lab data acquired in clinical trials."

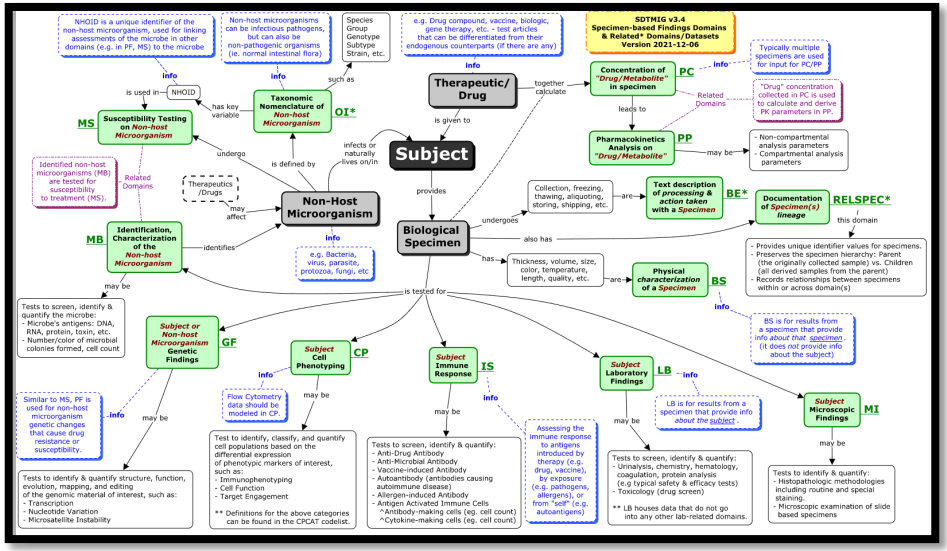
- Published in Sept 2003 and updated in April 2004.
  - Contains a list of standard Variable Names, some of which are incorporated in SDTM (red boxes) and some of which are specific to the LAB model (purple boxes).

FIELD NAME	REQD	SAS VARIABLE NAME	DEFAULT REPRE-SENTATION	MAX LEN	DATA TYPE	EXPLANATION	SUGGESTED CODELIST
Base Test Level							
Performing Laboratory ID	Yes	PLBNUM	(none)	20	Text	The ID of the laboratory that performed the test.	(none)
Performing Laboratory Name	No	PLBNAM	(none)	40	Text	The name of the laboratory that performed the test.	(none)
Lab Test ID	Yes	LBTESTCD	(none)	20	Text	The ID of the test performed as defined by the data provider.	(none)
Lab Test Name	No	LBTEST	(none)	100	Text	The name of the test performed as defined by the data provider.	(none)
Test ID	Cond.	TSTCD	(none)	20	Text	The ID of the test performed as defined by the data recipient.	(none)
Test Name ID	No	TSTNAM	(none)	100	Text	The name of the test performed as defined by the data recipient.	(none)
LOINC Code	No	LBLOINC	(none)	10	Code	The LOINC code ID for the test performed.	LOINC
LOINC Code List ID	No	LOINCCD	(none)	40	Text	If utilized, the code list identifier and version number for the LOINC code.	

Specimen Based Lab Data is Heterogenous and Complex!

The Topic of Interest Determines To Which Domain the Data Belongs:

- Microorganism – MB, MS, OI, GF
- Drug or Substance – PC, PP
- Biospecimen – BS, BE, RELSPEC
- Subject Assessment – LB, MI, CP, IS, GF



***The LAB Model may need to be expanded to better serve the needs of ALL specimen-based lab data.

CDISC development teams have continued to expand the models to support more different and complex kinds of 'Lab' data.

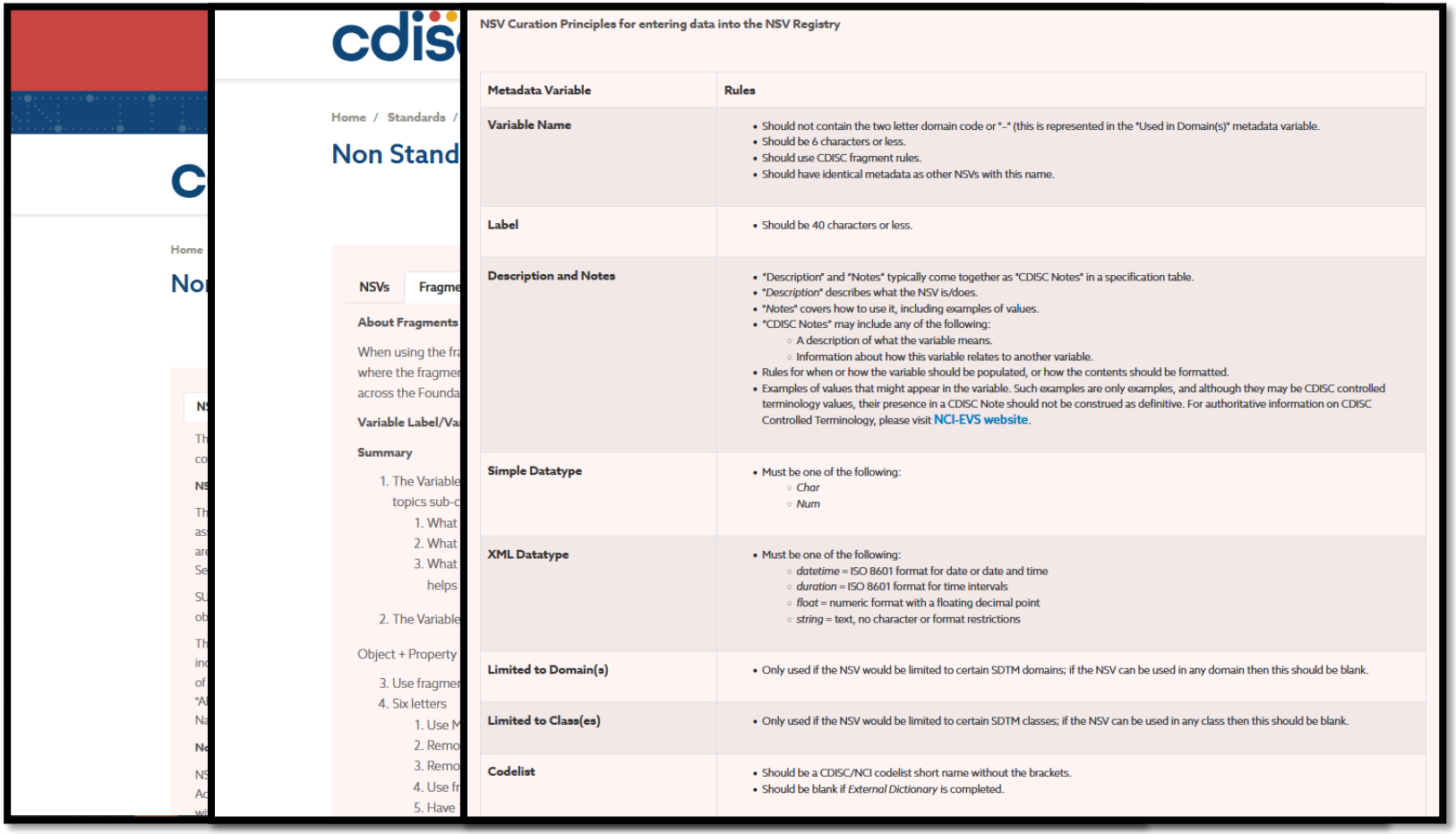
NSV Registry on the CDISC Website

www.cdisc.org/standards/terminology/non-standard-variables

Functionality to Find, Use, and Request Non-Standard Variables:

- NSVs are used to populate Supplemental Qualifiers special-purpose datasets to capture data concepts that don't fit into standard model variables.
- While they are considered 'non-standard' (not published in a version of a CDISC data model), promoting re-use of NSVs will support data standardization.
- NSVs are curated by the NSV Registry Team, lead by Rebecca Baker, and work closely with CDISC project teams to support CDISC standards development (IGs, TAUGs, QRS supplements, other specialty projects).
- Files containing approved NSVs and Variable Naming Fragments will be published in Excel and updated semi-annually.

NSV Registry on the CDISC Website



NSV Curation Principles for entering data into the NSV Registry

Metadata Variable	Rules
Variable Name	• Should not contain the two letter domain code or "--" (this is represented in the "Used in Domain(s)" metadata variable. • Should be 6 characters or less. • Should use CDISC fragment rules. • Should have identical metadata as other NSVs with this name.
Label	• Should be 40 characters or less.
Description and Notes	• "Description" and "Notes" typically come together as "CDISC Notes" in a specification table. • "*Description*" describes what the NSV is/does. • "*Notes*" covers how to use it, including examples of values. • "CDISC Notes" may include any of the following: ◦ A description of what the variable means. ◦ Information about how this variable relates to another variable. • Rules for when or how the variable should be populated, or how the contents should be formatted. • Examples of values that might appear in the variable. Such examples are only examples, and although they may be CDISC controlled terminology values, their presence in a CDISC Note should not be construed as definitive. For authoritative information on CDISC Controlled Terminology, please visit NCI-EVS website.
Simple Datatype	• Must be one of the following: ◦ *Char* ◦ *Num*
XML Datatype	• Must be one of the following: ◦ *datetime* = ISO 8601 format for date or date and time ◦ *duration* = ISO 8601 format for time intervals ◦ *float* = numeric format with a floating decimal point ◦ *string* = text, no character or format restrictions
Limited to Domain(s)	• Only used if the NSV would be limited to certain SDTM domains; if the NSV can be used in any domain then this should be blank.
Limited to Class(es)	• Only used if the NSV would be limited to certain SDTM classes; if the NSV can be used in any class then this should be blank.
Codelist	• Should be a CDISC/NCI codelist short name without the brackets. • Should be blank if *External Dictionary* is completed.

Gratitude and Acknowledgements

- Anna Pron-Zwick
- CDISC CT User Guide Team
- Anthony Chow, Smitha Karra and the CT Relationships Team
- Dr. Jordan Li and the SDS MB/IS Domains Sub-Team
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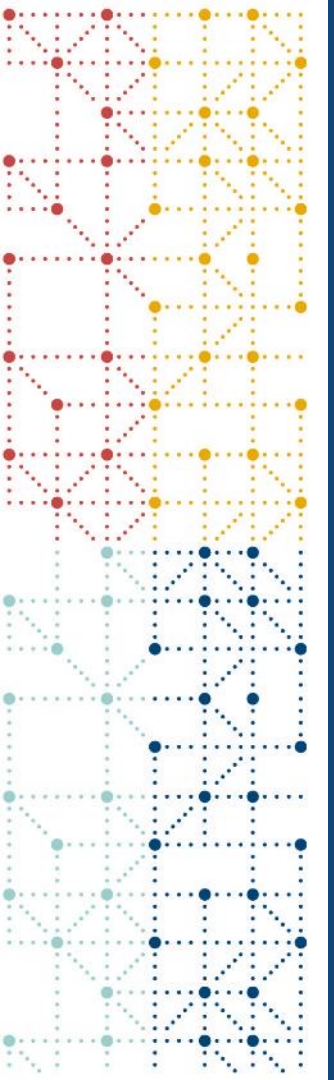
- Anna Pron-Zwick, Phil Pochon, Nik Pemble and the CDISC Lab Team
- Rebecca Baker and the NSV Registry Team



THANK YOU FOR LISTENING TODAY!

Any questions or input?

Thank You!