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A Little Bit of This and That: Use cases, implementation, and documentation when using multiple IG standards, CTs, and regulatory guidances in an SDTM study

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ABSTRACT

In the past, organizations typically selected and adhered to a single version of the SDTM Implementation Guide and CDISC CT when creating tabulation data for a study. However, the landscape of clinical data standards has evolved significantly with the introduction of Therapeutic Area User Guides (TAUGs), QRS supplements, and regulatory recommendations like "Submitting Patient-Reported Outcome Data in Cancer Clinical Trials". Additionally, frequent updates to the FDA "Study Data Technical Conformance Guide" may contain agency recommendations that have not found their way into CDISC standards that are updated less frequently. This evolution has led to the increasingly common and encouraged practice of implementing multiple CDISC standards and regulatory guidances within a single study.

The adoption of Define-xml 2.1 has provided a robust framework for documenting the use of multiple Implementation Guides and standards in the submission required define.xml file. However, mixing standards, versions, supplements, and regulatory documentation on a trial presents unique challenges for ensuring regulatory compliance, data quality, and proper documentation.

This paper explores practical use cases and provides solutions for studies using a combination of Implementation Guides, supplements, and regulatory guidance to create the SDTM data and submission documentation. We'll discuss best practices for creating high-quality data packages that clearly document which standards and guidances were implemented while maintaining data integrity, ensuring traceability, and preventing inconsistencies where information and metadata exist in multiple locations.

INTRODUCTION

CDISC released the first SDTM model and Implementation Guide (IG) in 2004. Initially, many organizations were slow to adopt CDISC SDTM standards, approaching them cautiously or with a “wait and see” perspective. In those early days, transforming collected source data to SDTM format required referencing only a few CDISC documents so the main challenge was managing the internal disruption caused by introducing a new standard to existing systems and personnel.

Today’s standards landscape has evolved from a straightforward implementation challenge into a complex navigation through multiple overlapping standards and guidance documents. We now recognize that relying on a single CDISC Implementation Guide for study tabulation guidance is no longer sufficient (Kelly and Beers, 2024). Organizations must invest in continuing education for staff performing CDISC conversions to successfully balance these rules with regulatory guidelines, controlled terminology updates, specialized TAUGs, and supplemental materials—all of which update at different frequencies.

Regulatory reviewers now expect significantly higher SDTM data quality and thorough documentation than ever before. Fortunately, Define-xml 2.1 (required for FDA submissions after March 15, 2023) provides enhanced capabilities for documenting the multiple standards used in creating SDTM datasets, supplemented by documentation in the SDTM TS domain and study reviewer's guide.

Author’s note – Since submission standards and documentation practices vary based on review agencies, the focus of this paper will be based on SDTM data and submissions intended for FDA review.

SCENARIO #1 – USE OF MORE THAN ONE SDTM IG IN SDTM TABULATION

Organizations may prefer using an established SDTM IG version while selectively implementing newer IG versions for specific domains that better represent collected data. This hybrid approach offers practical benefits but requires clear documentation of which standards apply to each domain.

A common example occurred when organizations using SDTM IG 3.3 began mapping the Subject Visits (SV) domain according to IG 3.4 specifications in response to FDA pandemic-related guidance. In the sdTCG the FDA requested additional variables to be added directly to SV to capture additional visit information outside the standard supplemental qualifier approach.

To address this need, CDISC released SDTM IG 3.4 with formal changes to the SV domain structure to include the additional variables. However, in the year or two between the FDA request and the release and finalization of SDTM IG 3.4, many organizations simply added those additional variables as requested into their IG 3.3 SV domain. Selectively implementing the forthcoming IG 3.4 for just the SV domain satisfied regulatory expectations and data conformance issues resulting in the addition of the variables not standard to IG 3.3 were explained in the reviewer's guide

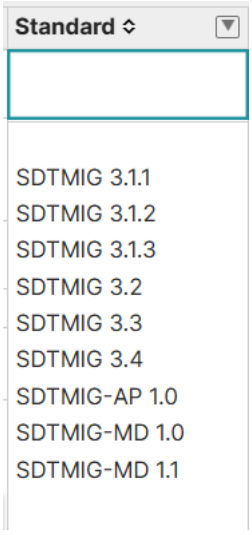
While this hybrid approach offers practical benefits, it introduces documentation challenges that must be addressed to ensure regulatory reviewers understand which standards apply to each domain. Proper documentation becomes essential for transparency during the review process.

DEFINE-XML 2.1

The Define-xml 2.1 specification provides an elegant solution to this documentation challenge by allowing users to explicitly indicate which standard has been applied to each individual dataset. In the example described above, all domains would be documented as using SDTM IG 3.3 except for the SV domain, which would be specifically identified as implementing SDTM IG 3.4.

Define-xml 2.1 allows explicit documentation of which standard applies to each dataset. Using Pinnacle 21 Enterprise, users can select the specific standard for each dataset in the "Standards" column of the "Datasets" tab.

For organizations using Pinnacle 21 Enterprise (now known as Pinnacle 21 by Certara) to generate their define.xml files, this differentiation can be easily accomplished in the "Datasets" tab within the define creation interface. Users can select the specific standard for each dataset in the "Standards" column as shown below.



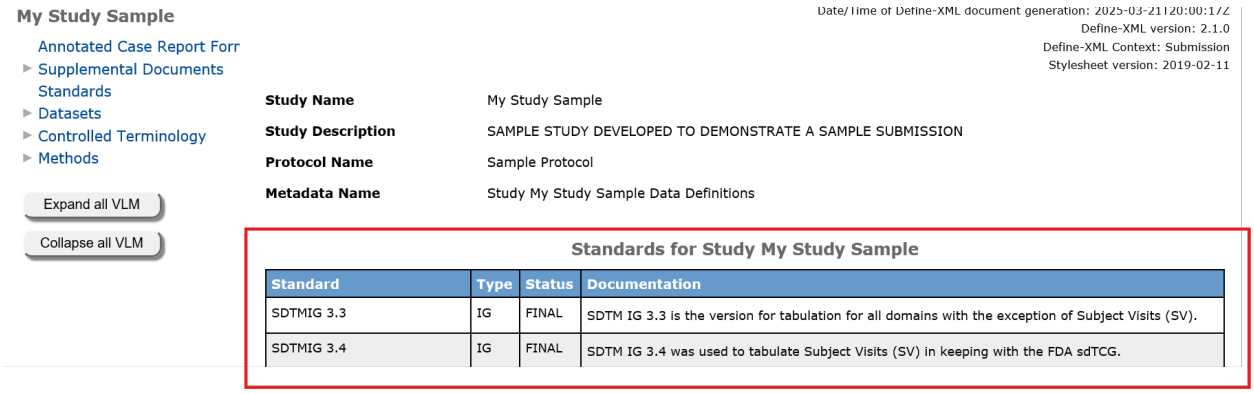
Display 1. Standard option drop down selection as it appears for Pinnacle 21 Enterprise users

The resulting define.xml (pictured below) should clearly display which IG version governs each domain, showing SV under IG 3.4 while other domains follow IG 3.3.

SE [SDTMIG 3.3]	Subject Elements	SPECIAL PURPOSE
SV [SDTMIG 3.4]	Subject Visits	SPECIAL PURPOSE
CM [SDTMIG 3.3]	Concomitant Medications	INTERVENTIONS

Display 2. Selection of domains from Define-xml 2.1

Additionally, the Standards table at the beginning of the define.xml will include all implemented IG versions



Display 3. Standards Table in define.xml

CONFORMANCE REPORTING

When running conformance checks on study data, most tools will only allow the user to select a single SDTM Implementation Guide version to use for those data conformance checks. This presents a challenge when running data conformance on mixed standards.

In this scenario, implementing conformance using SDTM IG 3.3 rules, the additional variables in your SV domain will trigger findings that require explanation. In such cases, it's appropriate to explain these findings by referencing the FDA guidance from the sdTCG that recommends following the SDTM IG 3.4 structure for the SV domain.

Using this scenario as an example, you may still want to verify that your SV domain properly meets SDTM IG 3.4 standards. Consider this practical approach: temporarily change your conformance tool settings to SDTM IG 3.4, run data conformance, review the SV results only, and then switch back to SDTM IG 3.3 for your final comprehensive data conformance run. However, once your define.xml has been created, your final data and define.xml combined conformance run should consider the standard used for each domain as it is in the metadata.

THE TRIAL SUMMARY (TS) DOMAIN

The TS domain must contain a row with TSPARM = “SDTIGVER”. The TSVAL for this row describes the SDTM IG version used in the study. If a study uses more than one SDTM IG version, it should be possible to create a row for each IG version used by utilizing the TSSEQ variable to differentiate the rows for the TSPARM SDTIGVER.

REVIEWER'S GUIDE

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	•SDTM v1.7 •SDTMIG v3.3 •SDTMIG v3.4
Controlled Terminology	•CDISC SDTM Controlled Terminology, 2019-12-20
Data Definitions	Define-XML v2.1
Medications Dictionary	WHODD GLOBALB3Sep19
Medical Events Dictionary	MedDRA v22.1
Other standards (optional)	LOINC 2.69, UNII 2019-07-12, MED-RT 2019-09-03

Display 4. Study Data Standards Table in csdrg.pdf

Document all standards used in Section 1.3 "Study Data Standards and Dictionary Inventory" of your csdrg.pdf (shown above). For domains using different standards, add specific explanations in their respective domain sections (sample wording shown below).

3.4.17 SV - Subject Visits

The SV domain was tabulated using SDTM IG 3.4 based on guidance in the FDA sdTCG. Variables SVPRESP, SVOCCUR, SVREASOC, SVCNTMOD, and SVEPCHGI were added to the domain to provide additional subject visit information as outlined in SDTM IG 3.4. Data conformance for the study was checked using SDTM IG 3.3 which resulted in conformance findings for these additional non-standard variables. See conformance summary for additional details.

Display 5. Sample wording in csdrg.pdf SV domain section

SCENARIO #2 – USE OF A TAUG THAT INCLUDES A CUSTOM DOMAIN

Implementing an applicable CDISC Therapeutic Area User Guide (TAUG) can significantly enhance your data package by providing reviewers with specialized structure and information relevant to your study's therapeutic area. TAUGs frequently recommend custom domains that improve data representation for specific therapeutic areas. These recommendations typically include:

- Detailed specifications for implementation
- Structures that follow established SDTM conventions
- Content that often becomes standardized in future SDTM IGs

The QT Studies TAUG exemplifies this evolution. Drafted in 2014 and based on SDTM IG 3.2, this TAUG recommends adding a custom QT domain for studies where QTc serves as a primary or secondary endpoint. Though not yet incorporated into the CDISC SDTM model, the TAUG provides comprehensive draft QT specifications following SDTM Findings domain conventions.

In this scenario, we'll explore how to properly document both the use of a TAUG in your study and a custom domain recommended by the TAUG.

ECG QT Correction Model Data (QT)

QT – Description/Overview for ECG QT Correction Model Data Domain Model

Data describing the description, correction formula and the coefficients of the correction formula used in correction of QT values. CDISC controlled terminology handles standard correction factors such as Bazett's and Fredericia's; however, due to the large and growing number of correction methods used, will not develop controlled terminology for those alternative correction factors. Therefore, this new findings domain was proposed to store the correction formula information.

The ECG QT Correction Model Data domain is a draft domain at the time of this publication, but it fully conforms to the SDTM findings structure for versions 1.0 through 1.4, and could be used be used by sponsors under this name as a custom domain.

No CDISC controlled terminology definition yet exists for this domain.

QT – Specification for ECG QT Correction Model Data Domain Model

qt.xpt, ECG QT Correction Model Data — Findings, Version x.x. One record per QT correction observation per subject, Tabulation.

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	QT	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
QTSEQ	Sequence Number	Num		Identifier	Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
QTGRPID	Group ID	Char		Identifier	Used to tie together a block of related records in a single domain for a subject. Example: use EGTESTCD as value for QTGRPID for easier relating of QT dataset to the EG dataset.	Perm
QTREFID	QTc Reference ID	Char		Identifier	Internal or external QT identifier. Generally not used for QT dataset.	Perm

Display 6. Proposed QT domain in the QT Studies TAUG

DEFINE-XML 2.1

The QT domain is not a part of any SDTM IG at this time, but it's also not technically "Non Standard" since a custom Findings domain is allowed as part of the CDISC model. In this instance, for the purposes of data conformance, define metadata, and documentation the custom QT domain could be given a standard of SDTM IG 3.4 and evaluated and documented that way. The image below shows the custom QT domain represented in the Datasets section of the study define.xml.

QSPS [SDTMIG 3.4]	Questionnaires-QSPS (QS)	FINDINGS	One record per questionnaire per question per time point per visit per subject
QT [SDTMIG 3.4]	ECG QT Correction Model Data	FINDINGS	One record per QT correction observation per subject
SC [SDTMIG 3.4]	Subject Characteristics	FINDINGS	One record per characteristic per subject

Display 7. Selection of domains from Define-xml 2.1

SDTM TRIAL SUMMARY (TS) DOMAIN

When implementing TAUG guidance, add a specific row to the TS domain with:

- TSPARMCD = "CTAUG"
- TSPARM = "CDISC Therapeutic Area User Guide"
- TSVAL = exact TAUG name as listed in sdTCG (e.g., "QT Studies Therapeutic Area User Guide v1")

Include this TS row regardless of whether the TAUG implementation resulted in non-standard datasets or variables.

REVIEWER'S GUIDE

The Clinical Study Data Reviewer's Guide (csdrg.pdf) should document all TAUG implementation details. At minimum:

1. Identify TAUG-impacted domains in their respective sections
2. Explain any conformance issues resulting from TAUG implementation
3. Consider adding a row to the "Study Data Standards and Dictionary Inventory" table to highlight TAUG usage

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	•SDTM v1.7 •SDTMIG v3.3 •SDTMIG v3.4
Controlled Terminology	•CDISC SDTM Controlled Terminology, 2019-12-20
Data Definitions	Define-XML v2.1
Medications Dictionary	WHODD GLOBALB3Sep19
Medical Events Dictionary	MedDRA v22.1
CDISC Therapeutic Area User Guide	QT Studies Therapeutic Area User Guide v1
Other standards (optional)	LOINC 2.69, UNII 2019-07-12, MED-RT 2019-09-03

Display 8. Study Data Standards Table in csdrg.pdf

Author note - Always consult the FDA sdTCG TAUG section before implementation, as it may contain additional recommendations or exceptions.

SCENARIO #3 – CREATION OF CUSTOM OR NON-STANDARD DOMAINS FROM OTHER INDUSTRY GUIDANCE

In Scenario #2, the TAUG provided complete specifications consistent with an SDTM Findings domain, enabling confident implementation of the QT domain. But what happens when guidance suggests a custom domain without detailed specifications?

Unlike TAUGs, regulatory guidance may request custom domains without providing comprehensive implementation details. The FDA sdTCG identifies two such examples:

1. A laboratory custom domain (LC) containing conventional units—allowing the standard LB domain to contain only SI units
2. A domain similar to DM (Demographics) for subjects with multiple enrollments. The FDA sdTCG did not give a name to this dataset but the tentative name being used in industry groups at this time is "DC".

The LC domain implementation is relatively straightforward since it mirrors the existing LB domain structure, differing primarily in that result and unit variables reflect conventional units rather than SI units.

In contrast, the multiple-enrollment domain (DC) presents greater complexity due to:

- Limited implementation guidance

- Potential impacts on other domains (particularly TE, SE, and study findings domains)
- The DM domain that DC is to be based on is a Special Purpose domain. The CDISC model doesn't currently allow custom Special Purpose domains.
- Ambiguity about which variables to include and how to populate them

Without finalized guidance in the CDISC SDTM framework, implementing these sdTCG-requested domains requires extensive documentation to explain your approach and any resulting conformance issues.

DEFINE-XML 2.1

In this scenario, the LC domain would be handled like the QT custom domain in Scenario 2. LC is an allowable custom Findings domain per CDISC standards so the standards field should contain the SDTM IG version you wish to use for LC.

The DC domain is a custom Special Purpose domain which isn't part of the CDISC model so the guidance is less clear, and the sponsor has some flexibility. Until the DC domain has been included in an agency accepted SDTM IG, sponsors have 2 options:

1. Treat the DC domain as "Non Standard" in the final define.xml as pictured below.
2. Include an allowed SDTM IG standard for DC like the custom QT and LC examples assigned to SDTM IG 3.4.

Either of these options for DC should be acceptable to regulatory authorities given the sdTCG request to include the domain and their understanding that DC isn't currently a part of the CDISC model.

As described above, neither the LC nor DC domains include the specifications or implementation guidance typically found in a TAUG custom domain. However, since the FDA has requested these domains, both are likely to be prioritized for standardization by CDISC, and there has been significant industry discussion about both. Until CDISC formally standardizes these domains, users will need to make assumptions about the final name, label, and content of these datasets. Below is the author's best estimate to date:

LB [SDTMIG 3.4]	Laboratory Test Results	FINDINGS	One record per lab test per time point per visit per subject	Tabulation	STUDYID, USUBJID, LBTESTCD, LBSPEC, VISITNUM
LC [SDTMIG 3.4]	Laboratory Findings in Conventional Units	FINDINGS	One record per lab test per time point per visit per subject	Tabulation	STUDYID, USUBJID, LCTESTCD, LCSPEC, VISITNUM

DC [Non Standard]	Demographics as Collected	SPECIAL PURPOSE	One record per subject participation	Tabulation	STUDYID, USUBJID, SUBJID
DM [SDTMIG 3.4]	Demographics	SPECIAL PURPOSE	One record per subject	Tabulation	STUDYID, USUBJID
SE [SDTMIG 3.3]	Subject Elements	SPECIAL PURPOSE	One record per actual Element per subject	Tabulation	STUDYID, USUBJID, ETCD, SESTDTC

Display 9. Selection of domains from Define-xml 2.1

The content above is a good starting place for these domains but if official guidance from CDISC is released before your study is finalized, adjustments should be made to update your domains to comply with that guidance if possible.

When creating a DC domain, the Define-xml 2.1 structure offers an excellent opportunity to handle some of the heavy lifting needed to describe how variables were populated. These same variables exist in the DM domain, but depending on how your organization creates DC, the variables may have identical values across all DC rows, different values for some or all rows, or even missing values on some rows. Because the DC domain lacks implementation details, it's crucial to use the define.xml to clearly describe your implementation strategy.

REVIEWER'S GUIDE

In this scenario where custom domains are created in response to a regulatory request with minimal implementation details, thorough documentation in the csdrg.pdf becomes extremely important.

For the LC domain, since its structure will closely mirror the standard LB domain, documentation will be relatively straightforward. The LC domain section in the reviewer's guide could simply state that the custom LC domain was created to provide lab results in conventional units consistent with the sdTCG.

For the sdTCG proposed multiple participation domain (DC), csdrg.pdf documentation will need to be much more comprehensive until CDISC releases formal guidance. The author suggests including at least the following details in the DC section of the csdrg.pdf:

1. How SUBJID was managed for each enrollment at the sites and/or programmatically
2. Whether DC contains all enrollments or only those not included in DM
3. Population methodology for reference date variables and demographic variables common to both domains
4. A table linking each SUBJID to their corresponding USUBJID as requested in the sdTCG

SCENARIO #4 – USE OF AN FDA TECHNICAL SPECIFICATION

The FDA has released numerous technical specifications that are typically therapeutic area specific but may include implementation details requiring additional documentation in your study submission materials. While the FDA publishes these specifications expecting industry implementation, it's crucial to discuss their implementation with your review division early in your study planning or implementation process.

Although documentation requirements may vary depending on the technical specification implemented, let's examine one example - the "Submitting Patient-Reported Outcome Data in Cancer Clinical Trials" (PROCCT) FDA technical specification, with particular focus on its application to SDTM data and documentation. The PROCCT guidance provides specific instructions for tabulating missing responses and non-standard values (NSVs). While these instructions build upon CDISC standards, they may necessitate programmatic derivations of additional records when your source PRO data doesn't include records for missing responses. Since adding records isn't typical SDTM practice, you should thoroughly document your PROCCT implementation in the define.xml, the csdrg.pdf, and TS domain documentation.

DEFINE-XML 2.1

When implementing the PROCCT SDTM guidance that requests sponsors to add records for missing responses (if they weren't collected along with completed responses), you may need to get creative in differentiating between collected records and derived records. Using QSDRVFL = 'Y' can help indicate which records were derived by utilizing value level metadata. Alternatively, you could include a flag in SUPPQS to identify derived records. The key is to proactively plan how you will document manually added missing response records in the define.xml.

QSCAT		Category of Question	text	Grouping Qualifier	50	Category of Questionnaire • "CLINICAL GLOBAL IMPRESSIONS (CGI-I)"	Assigned
QSORRES VLM		Finding in Original Units	text	Result Qualifier	20		
	QSDRVFL = "Y"	Sponsor Derived QS record	text		1		Derived (Source: Sponsor) When QSDRVFL = 'Y', the record is sponsor generated as a missing response record. When QSDRVFL = 'Y', QSORRES and other result values will be missing.
	QSDRVFL ≠ "Y"	Vendor Collected QS record	text		20		Collected (Source: Vendor)

Display 10. Utilizing QSDRVFL to describe derived records in define.xml value level metadata

TS DOMAIN

When incorporating implementation advice from an FDA Technical Specification, your TS domain should include a row describing the Technical Specification used. See the study data standards resources link in the references for a full list of available FDA Technical Specifications.

- TSPARMCD = 'FDATCHSP'
- TSPARM = 'FDA Technical Specification'
- TSVAL = 'Submitting Patient-Reported Outcome Data in Cancer Clinical Trials'

Note that the current FDA sdTCG contains a few typos relating to the TSPARM/TSPARMCD that the user should be aware of. First, the variables are incorrectly named TSPARAM and TSPARAMCD. Second, the correct TSPARM in the latest CDISC CT is "FDA Technical Specification" but the sdTCG states to use the value "FDA Tech Spec". To avoid conformance issues in your TS domain, use the TSPARM and TSPARMCD that matches the CDISC CT version codelist in your study.

REVIEWER'S GUIDE

When implementing advice from a Technical Specification, thoroughly document in the relevant domain sections of the csdrg.pdf:

1. Which portions of the specification you implemented
2. How you implemented these specifications
3. Any deviations or special considerations

Additionally, add the Technical Specification to the "Study Data Standards and Dictionary Inventory" in Section 1.3 to improve visibility for reviewers.

SECNARIO #5 – USING MULTIPLE CONTROLLED TERMINOLOGY VERSIONS

One of the most significant enhancements in Define-xml 2.1 is the ability to use multiple CDISC Controlled Terminology (CT) versions within a single study. Consider this scenario: a sponsor using CDISC CT version 2023-12-15 discovers that the PROMIS-29 Profile 2.1 Questionnaire in their study appears only in the newer 2024-09-27 codelist. In the newer CT version, TEST and TESTCD codelists have been added for the instrument and the instrument was also added to the QSCAT codelist.

Prior to Define-xml 2.1, sponsors had only two options:

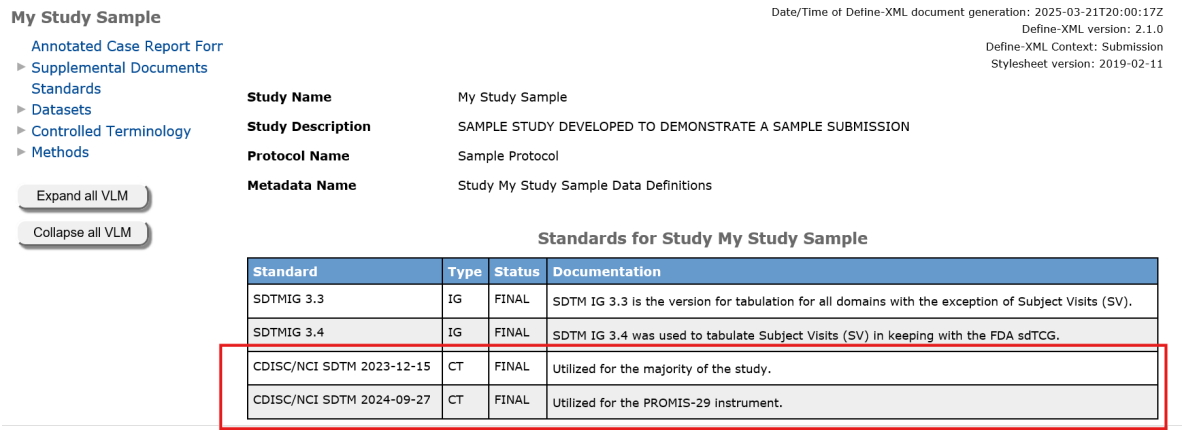
1. Up version their entire study to the 2024-09-27 codelist, potentially introducing unpredictable conformance results leading to re-work
2. Use the older codelist for the entire study and treat the PROMIS-29 Profile 2.1 codelist items as non-standard

While both approaches were acceptable, the ability to use multiple CT versions offers substantial advantages, particularly given the frequent CT updates that occur each year—especially for QRS items and newly introduced domains. Define-xml 2.1 now provides the flexibility to leverage different CT versions when necessary, as this scenario demonstrates.

DEFINE-XML 2.1

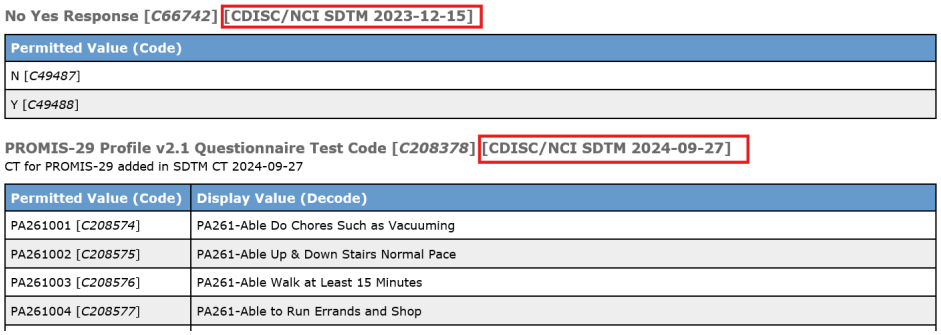
The use of multiple codelists for a study will be documented in your define.xml in a few places:

First, in the Standards table at the top of your define.xml. As shown below, both versions of CDISC CT used in the study are documented in this table. The rightmost column labeled “Documentation” can be used to add information or details about each codelist being used.



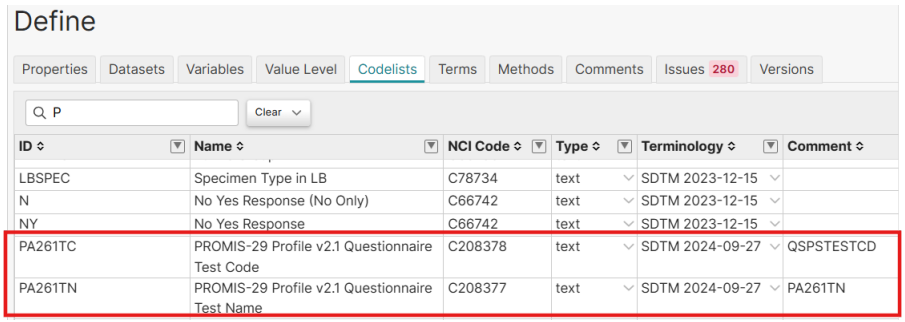
Display 11. Standards Table in define.xml

Second, in the Controlled Terminology section for each individual codelist used in your study. Below you can see a snapshot of two codelists: one from version 2023-12-15 and the PROMIS-29 Profile v2.1 codelist from version 2024-09-27. Define-xml 2.1 also includes a feature allowing sponsors to add optional additional information about the codelist under the codelist title and version, as shown below.



Display 12. Selection of codelists in define.xml

For Pinnacle 21 Enterprise users, selection of terminology version for each codelist is done on the Codelist tab in the define designer. The optional comment for each codelist is added to the Comment tab in the define design and attached via the comment name for each Codelist.



Display 13. Pinnacle 21 Enterprise Terminology selection and Comment columns

REVIEWER'S GUIDE

If your study uses more than one codelist, this should be documented in the "Study Data Standards and Dictionary Inventory" section of your reviewer's guide. Depending on the tools you use to create your submission materials, this section may be populated for you from the define.xml metadata. An example of multiple codelists shown below:

1.3 Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	•SDTM v1.7 •SDTMIG v3.3 •SDTMIG v3.4
Controlled Terminology	•CDISC SDTM Controlled Terminology, 2023-12-15 •CDISC SDTM Controlled Terminology, 2024-09-27
Data Definitions	Define-XML v2.1
Medications Dictionary	WHODD GLOBALB3Sep19
Medical Events Dictionary	MedDRA v22.1
Other standards (optional)	LOINC 2.69, UNII 2019-07-12, MED-RT 2019-09-03

Display 14. Study Data Standards Table in csdrg.pdf

DOCUMENTATION CONSISTENCY ACROSS SUBMISSION MATERIALS

When implementing multiple standards in a single study, maintaining consistency across all submission documentation is critical. Discrepancies between your define.xml, reviewer's guide, and TS domain can raise questions about data quality and potentially delay regulatory review.

Key consistency considerations include:

- **Standards versions**: Ensure all references to implementation guides, controlled terminology versions, and technical specifications match exactly across all documentation
- **Standard naming conventions**: Use identical terminology and formatting when referring to the same standard in different locations
- **Scope of implementation**: Clearly document which domains use which standards consistently across all materials
- **Version control**: Implement quality checks to verify that updates to one document are reflected in all related documentation

Beyond CDISC based standards, ensure consistency in other referenced terminologies. For example, MedDRA versions are frequently updated during a study's lifecycle and should be consistently documented across SDTM data, ADaM data, CSR displays, define.xml, and the reviewer's guide.

Best Practice: Implement a specific quality check before finalizing your submission package to verify consistency across all documentation components. Don't rely solely on automated tools to populate this information, as manual verification can catch discrepancies that automated processes might miss.

CONCLUSION

CDISC standards have evolved from voluntary frameworks to regulatory requirements, with proper implementation now extending beyond basic compliance. When implementing multiple standards within a single study, comprehensive documentation becomes essential for regulatory success.

Thorough documentation throughout your implementation process ensures alignment between your data and its documentation. This approach:

- Facilitates efficient regulatory review
- Demonstrates commitment to data integrity and compliance
- Reduces the likelihood of queries during submission review
- Minimizes potential delays in the approval process

CDISC SDTM IG guidance alone is no longer sufficient for regulatory acceptance. To maximize submission success, ensure your metadata and documentation accurately reflect all industry guidances and conventions used in your SDTM implementation.

REFERENCES

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Kelly, K. and Beers, B. 2024. “Guidance Beyond the SDTM Implementation Guide.” *Proceedings of the PharmaSUG 2024 Conference*.

RECOMMENDED READING

- CDISC. (2022). *Study Data Tabulation Model Implementation Guide for Human Clinical Trials, version 3.4.* https://www.cdisc.org/system/files/members/standard/foundational/SDTMIG%20v3.4-FINAL_2022-07-21.pdf
- Food and Drug Administration. (2024). *Study Data Technical Conformance Guide, version Oct 2024*. https://www.fda.gov/media/153632/download
- CDISC. Questionnaires, Ratings, and Scales. https://www.cdisc.org/standards/foundational/qrs
- CDISC. Therapeutic Area Guides. https://www.cdisc.org/standards/therapeutic-areas
- CDISC. SDTM Metadata Submission Guidelines 2.0. https://www.cdisc.org/standards/foundational/sdtm/sdtm-metadata-submission-guidelines-v2-0
- PhUSE. (2019). Best Practices for Documenting Dataset Metadata: Define-xml Versus Reviewer’s Guide. https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Optimizing+the+Use+of+Data+Standards/Best+Practices+for+Docu

menting+Dataset+Metadata-Define-xml+Versus+Reviewers+Guide.pdf

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