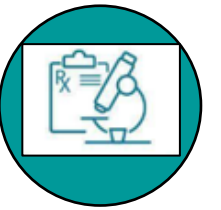


# DS22: Optimizing Trial Design Dataset/s Creation to Minimize P21 Compliance Issues

3-26-2026

Rama Kudaravalli

(Merck & Co., Inc., Rahway, NJ, USA)



# Agenda

---

- Which trial domains (TDs) are needed for a study?
- When to create trial domains?
- Core causes of P21 issues
- Controlled terminology
- Summary



# Which trial domains are needed for a study?

| SDTMIG v3.2                    | SDTMIG v3.3                   | SDTMIG v3.4 |
|--------------------------------|-------------------------------|-------------|
| TA – Trial Arms                | TA                            | TA          |
| TE – Trial Elements            | TE                            | TE          |
| TI – Trial Inclusion/Exclusion | TI                            | TI          |
| TS – Trial Summary             | TS                            | TS          |
| TV – Trial Visits              | TV                            | TV          |
| TD – Trial Disease Assessments | TM                            | TD          |
|                                | TM – Trial Disease Milestones | TM          |

**Trial domains introduced with SDTMIG Versions**



# Which trial domains are needed for a study?

| Domain Name                    | Purpose                                                                                                                   |
|--------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| <b>TA</b> – Trial Arms         | Planned arms and their sequences of elements                                                                              |
| <b>TE</b> – Trial Elements     | The building blocks of the study – unique ETCD/ELEMENT, rules for starting and ending an element                          |
| TI – Trial Inclusion/Exclusion | Planned eligibility criteria                                                                                              |
| <b>TS</b> – Trial Summary      | Summary of a trial in a structure. High-level study attributes (phase, indication, objectives, randomization, blinding)   |
| TV – Trial Visits              | Planned visit schedule (names, days, windows)                                                                             |
| TD – Trial Disease Assessments | The planned schedule of efficacy assessments related to the disease under study                                           |
| TM – Trial Disease Milestones  | Observations or activities anticipated to occur in the course of the disease under study, triggers the collection of data |

**TA, TE and TS are required for Submission**



# When to create trial domains?

| STUDY START | PROS                                                                      | CONS                                                            |
|-------------|---------------------------------------------------------------------------|-----------------------------------------------------------------|
| BEFORE      | Trial domains (TDs) can be generated as soon as the protocol is finalized | Additional amendments may lead to update of trial domains       |
|             | TDs may be used as inputs in creation of other SDTM domains (DM, SE, SV)  | Trial summary domain may need to be updated for some parameters |
| AFTER       | Trial domains are more stable                                             | TDs cannot be used as inputs for other SDTM domains             |
|             | No more updates are required for TDs                                      | Challenging to keep track of all study documents                |

**Creation of trial domains prior to study start is recommended**



# Core causes of P21 issues

- ❖ P21 rules vary with the SDTMIG version used in creating trial domains
- ❖ Missing TDs in Submission?
  - Missing TA, TE and TS domains - **SD1112, SD1113** and **SD1115**
- ❖ TA and TE are interrelated
  - Provide the building blocks for the development of subject-level TRT information in DM, SE
  - Inconsistent ETCD/ELEMENT
- ❖ Relationship between TA and TV
  - Inconsistent ARMCD/ARM
  - Inconsistent ARMCD/TAETORD
- ❖ TE domain
  - ELEMENT, TEDUR, TESTRL, TEENRL combination should be unique

**Missing TS domain is a reject issue – SDTMIG v3.1.2 and up**



# TA and TE domains

❖ ETCD and ELEMENT must be unique/match

| Rule                                 | Requirement               | Exception    | Rule ID                          | Domains  |
|--------------------------------------|---------------------------|--------------|----------------------------------|----------|
| ETCD/ELEMENT match across TA, TE, SE | Must match                | UNPLAN in SE | SD0067                           | TA       |
| ETCD length                          | ≤ 8 characters            | None         | SD1009                           | TA, TE   |
| ETCD/ELEMENT combination consistency | Must match across domains | UNPLAN in SE | SD1012                           | TA       |
| ETCD/ELEMENT uniqueness              | Must be unique            | None         | SD1050, SD1027<br>SD1064, SD1068 | TA<br>TE |

**P21 rules applicable - SDTMIG v3.1.2 and up**



# TA and TV domains

❖ ARMCD, ARM and TAETORD must be unique

| Rule                                                                           | Requirement                                         | Rule ID           | Domains |
|--------------------------------------------------------------------------------|-----------------------------------------------------|-------------------|---------|
| ARMCD length                                                                   | ≤ 20 characters                                     | SD1004            | TA, TV  |
| ARM/ARMCD uniqueness                                                           | Must be unique                                      | SD1033,<br>SD1034 | TA, TV  |
| ARMCD values ('SCRNFAIL' or 'NOTASSGN') should not be included in the TA or TV | ARMCD variable should not contain unexpected values | SD1053            | TA, TV  |
| ARMCD values from TA domain should be assigned to at least one subject in DM   | DM should have the ARMCD value from TA              | SD1354            | TA      |
| TAETORD/ARMCD uniqueness                                                       | Must be unique                                      | SD1052            | TA      |
| TAETORD value must be an integer                                               | TAETORD should have valid value                     | SD1267            | TA      |

**P21 rules - SDTMIG v3.1.2 and up**

**P21 rules - SDTMIG v3.2 and up**



# TE domain

❖ TEDUR, TESTRL and TEENRL must be unique

| Rule                                                                   | Requirement                             | Rule ID | Domains |
|------------------------------------------------------------------------|-----------------------------------------|---------|---------|
| TEDUR value must be greater than or equal to 0                         | TEDUR cannot have negative values       | SD0015  | TE      |
| TEDUR or TEENRL need to be populated                                   | TEENRL and TEDUR cannot be missing      | SD0089  | TE      |
| Combination of ELEMENT, TESTRL, TEENRL, and TEDUR unique for each ETCD | Combination of variables must be unique | SD1271  | TE      |
| ETCD value is missing in TA but present in TE                          | ETCD value must be present in TA and TE | SD1378  | TE      |

P21 rules - SDTMIG v3.1.2 and up

P21 rules - SDTMIG v3.2 and up



# TI domain

## ❖ IETESTCD, IETEST and TIVERS

| Rule                                                                                                                         | Requirement           | Rule ID        | Domains |
|------------------------------------------------------------------------------------------------------------------------------|-----------------------|----------------|---------|
| IETESTCD cannot start with a number, and cannot contain characters other than letters in upper case, numbers, or underscores | ≤ 8 characters length | SD0018         | TI      |
| IETEST/IETESTCD uniqueness                                                                                                   | Must be unique        | SD1150, SD1151 | TI      |
| IETESTCD should be unique within TIVERS                                                                                      | Must be unique        | SD1286         | TI      |

P21 rules - SDTM IG v3.1.2 and up

P21 rules - SDTMIG v3.2 and up



# TS domain – Parameters (required)

| Study Design / Trial Characteristics |                                 |         |
|--------------------------------------|---------------------------------|---------|
| TSPARMCD                             | TSPARM                          | Rule ID |
| ADDON                                | Added on to Existing Treatments | SD2201  |
| LENGTH                               | Trial Length                    | SD2204  |
| PLANSUB                              | Planned Number of Subjects      | SD2205  |
| SEXPOP                               | Sex of Participants             | SD2207  |
| STOPRULE                             | Study Stop Rules                | SD2208  |
| TBLIND                               | Trial Blinding Schema           | SD2209  |
| TCNTRL                               | Control Type                    | SD2210  |
| TITLE                                | Trial Title                     | SD2213  |
| TPHASE                               | Trial Phase Classification      | SD2214  |
| TTYPE                                | Trial Type                      | SD2215  |
| STYPE                                | Study Type                      | SD2230  |
| EXTTIND                              | Extension Trial Indicator       | SD2273  |
| ADAPT                                | Adaptive Design                 | SD2225  |

**Yellow text – Category for TS Parameters**

**P21 rules - SDTM IG v3.1.2 and up**

| Treatment / Intervention |                                                        |                |
|--------------------------|--------------------------------------------------------|----------------|
| TSPARMCD                 | TSPARM                                                 | Rule ID        |
| COMPTRT                  | Comparative Treatment Name (Invalid TSVAL and TSVALCD) | SD2253, SD2254 |
| THERAREA                 | Therapeutic Area                                       | SD2282         |
| PDPSTIND                 | Pediatric Postmarket Study Indicator                   | SD2276         |
| PDSTIND                  | Pediatric Study Indicator                              | SD2277         |
| PIPIND                   | Pediatric Investigation Plan Indicator                 | SD2278         |
| RDIND                    | Rare Disease Indicator                                 | SD2279         |

| Population / Enrollment |                                 |         |
|-------------------------|---------------------------------|---------|
| TSPARMCD                | TSPARM                          | Rule ID |
| AGEMAX                  | Planned Maximum Age of Subjects | SD2202  |
| AGEMIN                  | Planned Minimum Age of Subjects | SD2203  |
| ACTSUB                  | Actual Number of Subjects       | SD2234  |
| HLTSUBJI                | Healthy Subject Indicator       | SD2235  |
| NCOHORT                 | Number of Groups/Cohorts        | SD2274  |
| NARMS                   | Planned Number of Arms          | SD2229  |

**P21 rules - SDTMIG v3.2 and up**



# TS domain – Parameters (required)...contd

## Objectives

| TSPARMCD | TSPARM                    | Rule ID |
|----------|---------------------------|---------|
| OBJPRIM  | Trial Primary Objective   | SD2217  |
| OBJSEC   | Trial Secondary Objective | SD2275  |
| OUTMSPRI | Primary Outcome Measure   | SD2222  |

## Geography

| TSPARMCD | TSPARM                                   | Rule ID |
|----------|------------------------------------------|---------|
| FCNTRY   | Planned Country of Investigational Sites | SD2224  |

## Dates

| TSPARMCD | TSPARM                  | Rule ID |
|----------|-------------------------|---------|
| DCUTDTC  | Data Cutoff Date        | SD2226  |
| DCUTDESC | Data Cutoff Description | SD2227  |
| SSTDTC   | Study Start Date        | SD2232  |
| SENDTC   | Study End Date          | SD2233  |

## Standards Versions

| TSPARMCD | TSPARM          | Rule ID |
|----------|-----------------|---------|
| SDTIGVER | SDTM IG Version | SD2280  |
| SDTMVER  | SDTM Version    | SD2281  |

## Sponsor / Regulatory

| TSPARMCD | TSPARM                 | Rule ID |
|----------|------------------------|---------|
| SPONSOR  | Clinical Study Sponsor | SD2218  |
| REGID    | Registry Identifier    | SD2221  |

## Study Status

| TSPARMCD | TSPARM                  | Rule ID |
|----------|-------------------------|---------|
| ONGOSIND | Ongoing Study Indicator | SD2287  |

**P21 rules - SDTM IG v3.1.2 and up**

**P21 rules - SDTMIG v3.2 and up**



# TS domain – Parameters (conditional)

❖ Missing conditionally required parameters in TS domain triggers SD22xx and Other issues

| TSPARMCD | TSPARM                             | Dependency                                  | Rule ID |
|----------|------------------------------------|---------------------------------------------|---------|
| CURTRT   | Current Therapy or Treatment       | ADDON = 'Y' and CURTRT is missing           | SD2216  |
|          |                                    | TSVCDREF value must be 'UNII'               | SD2241  |
|          |                                    | Invalid TSVAL value for CURTRT              | SD2250  |
|          |                                    | Invalid TSVALCD value for CURTRT            | SD2251  |
|          |                                    | TSVAL/TSVALCD value mismatch for CURTRT     | SD2252  |
|          |                                    | ADDON = 'Y' and TSVAL is missing for CURTRT | SD1308  |
| INDIC    | Trial Disease/Condition Indication | TSVCDREF value must be 'SNOMED'             | SD2240  |
|          |                                    | Invalid TSVAL value for INDIC               | SD2257  |
|          |                                    | Invalid TSVALCD value for INDIC             | SD2258  |
|          |                                    | TSVAL/TSVALCD value mismatch for INDIC      | SD2259  |

P21 rules - SDTM IG v3.1.2 and up

P21 rules - SDTMIG v3.2 and up



# TS domain – Parameters (conditional)...contd

❖ Missing conditionally required parameters in TS domain triggers SD22xx and Other issues

| TSPARMCD | TSPARM              | Dependency                                              | Rule ID |
|----------|---------------------|---------------------------------------------------------|---------|
| PCLAS    | Pharmacologic Class | TSVCDREF value must be 'MED-RT' or 'NDF-RT'             | SD2243  |
|          |                     | Invalid TSVAL value for PCLAS                           | SD2263  |
|          |                     | Invalid TSVALCD value for PCLAS                         | SD2264  |
|          |                     | TSVAL/TSVALCD value mismatch for PCLAS                  | SD2265  |
|          |                     | STYPE = 'INTERVENTIONAL' and TSVAL is missing for PCLAS | SD1312  |
| TDIGRP   | Diagnosis Group     | TSVCDREF value must be 'SNOMED'                         | SD2266  |
|          |                     | Invalid TSVAL value for TDIGRP                          | SD2267  |
|          |                     | Invalid TSVALCD value for TDIGRP                        | SD2268  |
|          |                     | HLTSUBJI = 'Y' and TSVAL is not missing for TDIGRP      | SD1306  |
|          |                     | HLTSUBJI = 'N' and TSVAL is missing for TDIGRP          | SD1307  |

**P21 rules - SDTM IG v3.1.2 and up**

**P21 rules - SDTMIG v3.2 and up**



# TS domain – Parameters (conditional)...contd

❖ Missing conditionally required parameters in TS domain triggers SD22xx and Other issues

| TSPARMCD | TSPARM                               | Dependency                                                                                        | Rule ID |
|----------|--------------------------------------|---------------------------------------------------------------------------------------------------|---------|
| TRT      | Investigational Therapy or Treatment | TSVCDREF value must be 'UNII'                                                                     | SD2242  |
|          |                                      | Invalid TSVAL value for TRT                                                                       | SD2260  |
|          |                                      | Invalid TSVALCD value for TRT                                                                     | SD2261  |
|          |                                      | STYPE = 'INTERVENTIONAL' and TSVAL is missing for TRT                                             | SD1309  |
| INTMODEL | Intervention Model                   | STYPE = 'INTERVENTIONAL' and TSVAL is missing for INTMODEL                                        | SD1310  |
| INTTYPE  | Intervention Type                    | STYPE = 'INTERVENTIONAL' and TSVAL is missing for INTTYPE                                         | SD1311  |
| RANDQT   | Randomization Quotient               | TSVAL value must be a number between 0 and 1, with some cases where the ratio might be equal to 1 | SD1269  |

**P21 rules - SDTM IG v3.1.2 and up**



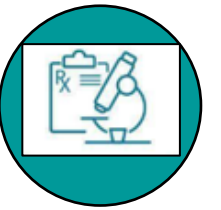
# Controlled terminology (CT)

## ❖ TYPES of CT

- CDISC CT- maintained by NCI EVS
- UNII (FDA Unique Ingredient Identifier) - to standardize active ingredients
- SNOMED (Systematized Nomenclature of Medicine) - to identify the medical condition
- NDF-RT/MED-RT - to identify the pharmacologic class
- DUNS (Data Universal Numbering System) - to identify a sponsor organization
- ISO 8601 Standard - dictates the format for dates and durations
- ISO 3166 dictionary - provides a 3-letter country code for each country

If parameter value not found in TSPARMCD/TSPARM extensible codelist - **CT2002** issue

If TSVCDREF value not found in DICTNAM extensible codelist - **CT2002** issue



# Controlled terminology.... contd

---

## ❖ Extensible CDISC CT

- DOMAIN, EPOCH

## ❖ Non-extensible CDISC CT

- IECAT

Inappropriate use of the controlled terminology triggers **CT2002** issue



# Summary

---

➤ **Trial domains and validation issues:**

- ✓TDs can be inputs for other SDTM domains in a study
- ✓TA, TE and TS domains are required for submission
- ✓Missing TS domain triggers a reject issue
- ✓P21 rules are applied based on the SDTMIG version used in mapping trial domains

➤ **Relationships:**

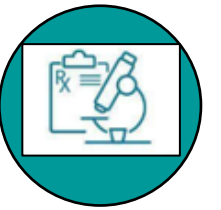
- ✓TA and TE must have unique ETCD/ELEMENT
- ✓TA and TV domains should contain unique ARMCD/ARM and ARMCD/TAETORD
- ✓Unique ELEMENT, TEDUR, TESTRL, TEENRL variables in TE

➤ **Trial Summary:**

- ✓TS is mapped with required and conditional parameters as per the FDA SD-TCG and protocol

➤ **CT Usage:**

- ✓CDISC-CT (extensible/non-extensible), UNII, SNOMED, MED-RT and other related dictionaries
- ✓Duration and dates must use ISO 8601 format, 3-letter country code - ISO 3166



# References

---

1. sdTCG-v6.1-December-2025-FINAL
2. FDA Validator Rules v1.6 December 2022\_0
3. CDISC SDTMIG v3.1.2 to v3.4



# Questions



## Contact Information:

Rama Kudaravalli

Merck & Co., Inc., Rahway, NJ, USA

[rama.kudaravalli@merck.com](mailto:rama.kudaravalli@merck.com)