Overview of Trial Design Domains

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Agenda

01 Overview of Trial Design Model

02 Trial Summary

03 Trial Inclusion

04 Trial Visit

05 Trial Element

06 Trial Arm

Overview of Trial Design Domains

- Trial Design domains :
  - ✓ Define the standard structure of representing the planned sequence of events and treatment plan for the trial
  - ✓ Provide a standard way to define treatment groups and planned visits
  - ✓ Also support in comparison of designs of different trials
  - ✓ Used to compare planned and actual treatments and visits.

- Things to remember :
  - ✓ Accurate representation of the treatment paths and rules defined in the protocol
  - ✓ These domains serve as the basis for deriving the actual treatment path for a given subject
  - ✓ Subject Elements (SE) and Subject Visits (SV) represent a subject's actual path
  - ✓ SE and SV are created using rules defined in the trial design domains TE, TV

Trial Design Domains

- There are 5 Trial design datasets
  - **Trial Arms (TA)**
  - **Trial Visits (TV)**
  - **Trial Element(TE)**
  - **Trial Inclusion/Exclusion(TI)**
  - **Trial Summary(TS)**
- These datasets provide a complete summary of the clinical trial protocol
- These datasets do not contain any subject level information
- These datasets are created first and then remaining SDTM domains

Example clinical trial

- This is a 14 weeks randomized, double-blind, placebo-controlled trial phase II clinical trial for patients with Type -2 Diabetes Miletus
- Comparing the dosage of active drug versus placebo in 1:1 ratio in capsule form for patients suffering with Type -2 Diabetes Miletus.
- Patients with >=18 years of age who have been diagnosed with Type -2 Diabetes Miletus and have been on Metformin for more than 6 months.
- Type-2 Diabetes patients were with the HbA1c levels >6.5%.
- Dosage will be administered BID before lunch and dinner
- Safety of the drug will be periodically assessed.
- Effectiveness of the active drug will be ascertained if the reduction of HbA1c values from the baseline is > 3%
- 200 patients both male and female will be enrolled in the trial. Pregnant or lactating women will be excluded from the study.

Trial Summary (TS) Domain

- TS describes basic information item of the protocol in a structured format – At a glance summary
- TS contains one record for each trial summary parameter
- TS records information about the trial phase, protocol title, and design objectives

Variable Name	Variable Label	Type	Description
STUDYID	Study Identifier	Char	Unique identifier for a study.
DOMAIN	Domain Abbreviation	Char	Two-character abbreviation for the domain, which must be TS.
TSSEQ	Sequence Number	Num	Sequence number to ensure uniqueness within the dataset.
TSGRPID	Group ID	Char	Used to tie together a group of related records.
TSPARMCD	Trial Summary Parameter Short Name	Char	TSPARMCD (the companion to TSPARM) is limited to 8 characters and does not have special character restrictions. These values should be short for ease of use in programming, but it is not expected that TSPARMCD will need to serve as variable names. Examples: AGEMIN, AGEMAX
TSPARM	Trial Summary Parameter	Char	Term for the Trial Summary Parameter. The value in TSPARM cannot be longer than 40 characters. Examples Planned Minimum Age of Subjects, Planned Maximum Age of Subjects
TSVAL	Parameter Value	Char	Value of TSPARM. Example: “ASTHMA” when TSPARM value is “Trial Indications”. If TSVAL is null; a value is required for TSVALNF. Text over 200 characters can be added to additional columns TSVAL1-TSVALn.
TSVALNF	Parameter Null Flavor	Char	Null flavor for the value of TSVAL describing the reason the value is null, to be populated if and only if TSVAL is null.
TSVALCD	Parameter Value Code	Char	Code of the ter REF.
TSVCDREF	Name of the Reference Terminology	Char	The name of th For example; CDISC, SNOMED, ISO 8601.
TSVCDVER	Version of the Reference Terminology	Char	The version number of the Reference Terminology cited in TSVCDREF, if applicable.

Would be filled only when TSVAL is null

Trial Summary (TS) Domain - Metadata

#	Variable Name	Variable Label	Type	Role	Description
1	STUDYID	Study Identifier	Char	Identifier	Unique identifier for a study.
2	DOMAIN	Domain Abbreviation	Char	Identifier	Two-character abbreviation for the domain, which must be TS.
3	TSSEQ	Sequence Number	Num	Identifier	Sequence number to ensure uniqueness within the dataset.
4	TSGRPID	Group ID	Char	Identifier	Used to tie together a group of related records.
5	TSPARMCD	Trial Summary Parameter Short Name	Char	Topic	TSPARMCD (the companion to TSPARM) is limited to 8 characters and does not have special character restrictions. These values should be short for ease of use in programming, but it is not expected that TSPARMCD will need to serve as variable names. Examples: AGEMIN, AGEMAX.
6	TSPARM	Trial Summary Parameter	Char	Synonym Qualifier of TSPARMCD	Term for the Trial Summary Parameter. The value in TSPARM cannot be longer than 40 characters. Examples Planned Minimum Age of Subjects, Planned Maximum Age of Subjects.
7	TSVAL	Parameter Value	Char	Result Qualifier	Value of TSPARM. Example: "ASTHMA" when TSPARM value is "Trial Indications". If TSVAL is null; a value is required for TSVALNF. Text over 200 characters can be added to additional columns TSVAL1-TSVALn.

Trial Summary (TS) Domain - Implementation

STUDYID	DOMAIN	TSSEQ	TSGRPID	TSPARMCD	TSPARM	TSVAL	TSVAL 1
CDISCtraining	TS	1	1	ADDON	Added on to Existing Treatments	Yes	
CDISCtraining	TS	1	1	AGEMAX	Planned Maximum Age of Subjects	NA	
CDISCtraining	TS	1	1	AGEMIN	Planned Minimum Age of Subjects	18	
CDISCtraining	TS	1	1	LENGTH	Planned Trial Length	14 weeks	
CDISCtraining	TS	1	1	PLANSUB	Planned Number of Subjects	200	
CDISCtraining	TS	1	1	RANDOM	Trial is Randomized	Yes	
CDISCtraining	TS	1	1	SEXPOP	Sex of Participants	Both	
CDISCtraining	TS	1	1	STOPRULE	Study Stop Rules	None	
CDISCtraining	TS	1	1	TBLIND	Trial Blinding Schema	Double blind	
CDISCtraining	TS	1	1	TCNTRL	Control Type	Placebo	
CDISCtraining	TS	1	1	TDIGRP	Diagnosis Group	Type -2 Diabetes Miletus	
CDISCtraining	TS	1	1	TINDTP	Trial Indication Type	Treatment	
CDISCtraining	TS	1	1	TITLE	Trial Title	14 weeks randomized, double-blind, placebo-controlled trial phase II clinical trial for patients with Type -2 Diabetes Miletus	comparing the dosage of active drug versus placebo in 1:1 ratio in capsule form
CDISCtraining	TS	1	1	TPHASE	Trial Phase Classification	Phase II Trial	
CDISCtraining	TS	1	1	TTYPE	Trial Type	Efficacy	
CDISCtraining	TS	2	1	TTYPE	Trial Type	Safety	

Trial Inclusion/Exclusion (TI) Domain

- Not subject-oriented
- Contains one record for each of the inclusion and exclusion criteria for the trial
- Populate this domain with the data from IE domain if already present; else create from protocol

Variable Name	Variable Label	Type	Description
STUDYID	Study Identifier	Char	Unique identifier for a study.
DOMAIN	Domain Abbreviation	Char	Two-character abbreviation for the domain, which must be TI.
IETESTCD	Inclusion/Exclusion Criterion Short Name	Char	Short name IETEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in IETESTCD cannot be longer than 8 characters, nor can it start with a number (e.g., "1TEST"). IETESTCD cannot contain characters other than letters, numbers, or underscores. The name "IE" prefix is used to ensure consistency with the IE domain
IETEST	Inclusion/Exclusion Criterion	Char	Full text of the inclusion or exclusion criterion. The prefix "IE" is used to ensure consistency with the IE domain.
IECAT	Inclusion/Exclusion Category	Char	Used for categorization of the Inclusion/Exclusion Criterion: INCLUSION, EXCLUSION.
IESCAT	Inclusion/Exclusion Subcategory	Char	A further categorization of the exception criterion. Can be used to distinguish criteria for a sub-study or for to categorize as a major or minor exceptions. Examples: MAJOR, MINOR.
TIRL	Inclusion/Exclusion Criterion Rule	Char	Rule that expresses the criterion in computer-executable form.
TIVERS	Protocol Criteria Versions	Char	The number of this version of the Inclusion/Exclusion criteria. May be omitted if there is only one version.

Trial Inclusion/Exclusion (TI) Domain - Metadata

#	Variable Name	Variable Label	Type	Role	Description
1	STUDYID	Study Identifier	Char	Identifier	Unique identifier for a study.
2	DOMAIN	Domain Abbreviation	Char	Identifier	Two-character abbreviation for the domain, which must be TI.
3	IETESTCD	Inclusion/Exclusion Criterion Short Name	Char	Topic	Short name IETEST. It can be used as a column name when converting a dataset from a vertical to a horizontal format. The value in IETESTCD cannot be longer than 8 characters, nor can it start with a number (e.g., "1TEST"). IETESTCD cannot contain characters other than letters, numbers, or underscores. The prefix "IE" is used to ensure consistency with the IE domain.
4	IETEST	Inclusion/Exclusion Criterion	Char	Synonym Qualifier of IETESTCD	Full text of the inclusion or exclusion criterion. The prefix "IE" is used to ensure consistency with the IE domain.
5	IECAT	Inclusion/Exclusion Category	Char	Grouping Qualifier	Used for categorization of the Inclusion/Exclusion Criterion: INCLUSION, EXCLUSION.
6	IESCAT	Inclusion/Exclusion Subcategory	Char	Grouping Qualifier	A further categorization of the exception criterion. Can be used to distinguish criteria for a sub-study or for to categorize as a major or minor exceptions. Examples: MAJOR, MINOR.
7	TIRL	Inclusion/Exclusion Criterion Rule	Char	Rule	Rule that expresses the criterion in computer-executable form.
8	TIVERS	Protocol Criteria Versions	Char	Record Qualifier	The number of this version of the Inclusion/Exclusion criteria. May be omitted if there is only one version.

Trial Inclusion/Exclusion (TI) Domain - Implementation

STUDYID	DOMAIN	IETESTCD	IETEST	IECAT	IESCAT	TIVERS	TIRL (Programming conditions to be defined only if programmable
CDISCtraining	TI	INCL01	Has Type -2 diabetes	INCLUSION	Major	1	HbA1c> 6.5%
CDISCtraining	TI	INCL02	Age 18 years or greater	INCLUSION	Major	1	AgeN >=18
CDISCtraining	TI	EXCL01	Pregnant or lactating	EXCLUSION	Major	1	
CDISCtraining	TI	INCL03	Greater than 6 months use of Metformin	INCLUSION	Major	1	
CDISCtraining	TI	INCL01	Has Type -2 diabetes	INCLUSION	Major	2	
CDISCtraining	TI	INCL02A	Age 18 years or greater and Less than 65 years	INCLUSION	Major	2	
CDISCtraining	TI	EXCL01	Pregnant or lactating	EXCLUSION	Major	2	
CDISCtraining	TI	INCL03	Greater than 6 months use of Metformin	INCLUSION	Major	2	

Trial Visit (TV) Domain

- Describes the planned visits in a trial
- Timing variables VISIT, VISITNUM and VISITDY describe these visits
- VISIT and VISITDY permissible, VISITNUM is Required
- VISITNUM is numeric version of Visit, used for sorting
- 1 record per planned visit per arm
  - ✓ A visit may span over several days (eg screening visit)
- Planned Treatment arm (ARMCD) is Expected variable
  - ✓ ARMCD is blank if schedule of visits is same for all arms

Variable Name	Variable Label	Type	Description
STUDYID	Study Identifier	Char	Unique identifier for a study.
DOMAIN	Domain Abbreviation	Char	Two-character abbreviation for the domain, which must be TV.
VISITNUM	Visit Number	Num	Clinical encounter number. Numeric version of VISIT can be used for sorting.
VISIT	Visit Name	Char	Protocol-defined description of the clinical encounter. May be used in addition to VISITNUM and/or VISITDY as a text description of the clinical encounter.
VISITDY	Planned Study Day of Visit	Num	Planned study day of VISIT. Due to its sequential nature, can be used for sorting.
ARMCD	Planned Arm Code	Char	ARMCD is limited to 20 characters and does not have special character restrictions. If the timing of visits for a trial does not depend on which ARM a subject is in, then ARMCD should be null.
ARM	Description of Planned Arm	Char	Name given to Arm or treatment group.
TVSTRL	Visit Start Rule	Char	Rule describing when the visit starts, in relation to the sequence of Elements.
TVENRL	Visit End Rule	Char	Rule describing when the visit ends, in relation to the sequence of Elements.

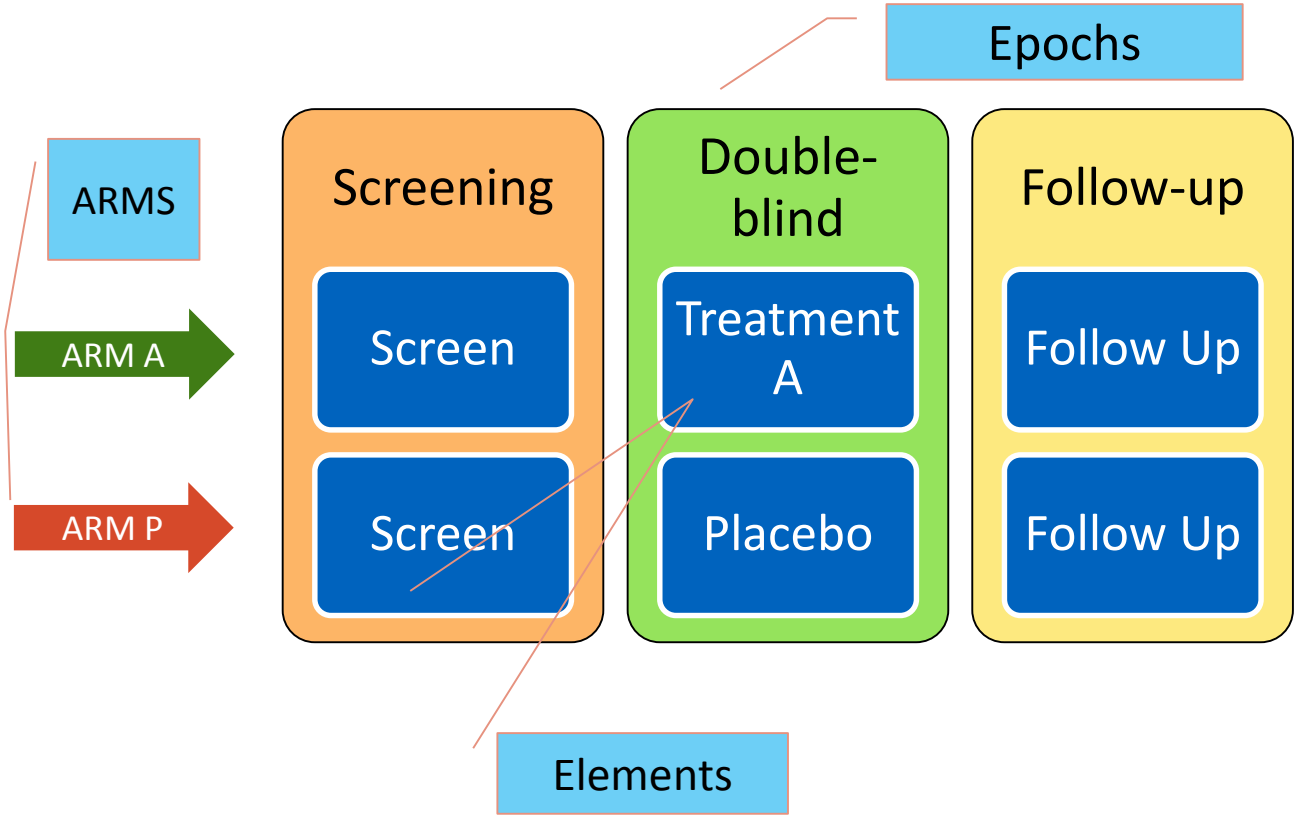
Trial Visit (TV) Domain - Metadata

#	Variable Name	Variable Label	Type	Role	Description
1	STUDYID	Study Identifier	Char	Identifier	Unique identifier for a study.
2	DOMAIN	Domain Abbreviation	Char	Identifier	Two-character abbreviation for the domain, which must be TV.
3	VISITNUM	Visit Number	Num	Topic	Clinical encounter number. Numeric version of VISIT can be used for sorting.
4	VISIT	Visit Name	Char	Synonym Qualifier of VISITNUM	Protocol-defined description of the clinical encounter. May be used in addition to VISITNUM and/or VISITDY as a text description of the clinical encounter.
5	VISITDY	Planned Study Day of Visit	Num	Timing	Planned study day of VISIT. Due to its sequential nature, can be used for sorting.
6	ARMCD	Planned Arm Code	Char	Record Qualifier	ARMCD is limited to 20 characters and does not have special character restrictions. If the timing of visits for a trial does not depend on which ARM a subject is in, then ARMCD should be null.
7	ARM	Description of Planned Arm	Char	Synonym Qualifier of ARMCD	Name given to Arm or treatment group.
8	TVSTRL	Visit Start Rule	Char	Rule	Rule describing when the visit starts, in relation to the sequence of Elements.
9	TVENRL	Visit End Rule	Char	Rule	Rule describing when the visit ends, in relation to the sequence of Elements.

Trial Visit (TV) Domain - Implementation

STUDYID	DOMAIN	VISITNUM	VISIT	VISITDY	TVSTRL	TVENRL
CDISCtraining	TV	100	Screening		Start of screening period 28 days prior to day 1	1 day prior to Day 1
CDISCtraining	TV	200	Day 1	1	First day of intake of study drug	
CDISCtraining	TV	300	Week 1	7	1 week after start of study drug	
CDISCtraining	TV	400	Week 2	14	2 weeks after start of study drug	
CDISCtraining	TV	500	Week 3	21	3 weeks after start of study drug	
CDISCtraining	TV	600	Week 4	28	4 weeks after start of study drug	
CDISCtraining	TV	700	Week 5	35	5 weeks after start of study drug	
CDISCtraining	TV	800	Week 6	42	6 weeks after start of study drug	
CDISCtraining	TV	900	Week 7	49	7 weeks after start of study drug	
CDISCtraining	TV	1000	Week 8	56	8 weeks after start of study drug	
CDISCtraining	TV	1100	Week 9	63	9 weeks after start of study drug	
CDISCtraining	TV	1200	Week 10	70	10 weeks after start of study drug	
CDISCtraining	TV	1300	Week 11	77	11 weeks after start of study drug	
CDISCtraining	TV	1400	Week 12	84	12 weeks after start of study drug	
CDISCtraining	TV	1500	Week 13	91	13 weeks after start of study drug	
CDISCtraining	TV	1600	End of Treatment	98	14 weeks after start of study drug	
CDISCtraining	TV	1700	Post Treatment Follow-up		28 days post End of treatment	

Our example study design – Arms, Elements and Epoch



- Columns shown with large rectangles are epochs. 3 epochs
- We have 2 Arms; Arm A and Arm P; An Arm is a planned sequence of Elements within Epochs, and is often referred to as a treatment group.
- We have 4 Elements; Screening, Treatment A, Placebo and Follow-up

Trial Elements (TE) Domain

- Describes the Element code unique for each element
- Provides the element description and the rules for starting and ending an Element
- An Element is the basic building block that is used to describe the administration of planned interventions
- Periods of time when there are no planned interventions (such as screening or washout) are also considered Elements

Variable Name	Variable Label	Type	Description
STUDYID	Study Identifier	Char	Unique identifier for a study.
DOMAIN	Domain Abbreviation	Char	Two-character abbreviation for the domain, which must be TV.
ETCD	Element Code	Char	ETCD (the companion to ELEMENT) is limited to 8 characters and does not have special character restrictions. These values should be short for ease of use in programming, but it is not expected that ETCD will need to serve as a variable name.
ELEMENT	Description of Element	Char	The name of the Element.
TESTRL	Rule for Start of Element	Char	Expresses the rule for beginning the Element.
TEENRL	Rule for End of Element	Char	Expresses the rule for ending the Element. Either TEENRL or TEDUR must be present for each Element.
TEDUR	Planned Duration of Element	Char	Planned Duration of Element in ISO 8601 format. Used when the rule for ending the Element is applied after a fixed duration.

Trial Elements (TE) Domain - Metadata

#	Variable Name	Variable Label	Type	Format	Role	Description
1	STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.
2	DOMAIN	Domain Abbreviation	Char		Identifier	Two-character abbreviation for the domain, which must be TE.
3	ETCD	Element Code	Char		Topic	ETCD (the companion to ELEMENT) is limited to 8 characters and does not have special character restrictions. These values should be short for ease of use in programming, but it is not expected that ETCD will need to serve as a variable name.
4	ELEMENT	Description of Element	Char		Synonym Qualifier of ETCD	The name of the Element.
5	TESTRL	Rule for Start of Element	Char		Rule	Expresses the rule for beginning the Element.
6	TEENRL	Rule for End of Element	Char		Rule	Expresses the rule for ending the Element. Either TEENRL or TEDUR must be present for each Element.
7	TEDUR	Planned Duration of Element	Char	ISO 8601	Timing	Planned Duration of Element. Used when the rule for ending the Element is applied after a fixed duration.

Trial Elements (TE) Domain - Implementation

STUDYID	DOMAIN	ETCD	ELEMENT	TESTRL	TEENRL
CDISCtraining	TE	SCREEN	Screening	Informed consent	1 Day prior to Day 1 of study drug
CDISCtraining	TE	TRTA	Treatment A BID	First dose of study treatment where drug is Treatment A	Study treatment End
CDISCtraining	TE	PBO	Placebo BID	First dose of study treatment where drug is Placebo	Study treatment End
CDISCtraining	TE	FU	Follow-up	Last Dose of study medication + 1	28 days after the start of the element

Trial Arms (TA) Domain

- High level treatment plan
- Based on the concepts of Elements, Arms and Epochs
- Composed of Elements from Trial Elements
- Planned ARM values in DM correspond to ARM values in Trial Arms
- Describes the sequence of Elements within each Arm, as well as rules for moving through these Elements, referred to as Branches (TABRANCH) and Transitions (TATRANS)
- Names of ARM should reflect the protocol

Variable Name	Variable Label	Type	Description
STUDYID	Study Identifier	Char	Unique identifier for a study.
DOMAIN	Domain Abbreviation	Char	Two-character abbreviation for the domain, which must be TA.
ARMCD	Planned Arm Code	Char	ARMCD is limited to 20 characters and does not have special character restrictions. If the timing of visits for a trial does not depend on which ARM a subject is in, then ARMCD should be null.
ARM	Description of Planned Arm	Char	Name given to Arm or treatment group.
TAETORD	Planned Order of Element within Arm	Num	Number that gives the order of the Element within the Arm.
ETCD	Element Code	Char	ETCD (the companion to ELEMENT) is limited to 8 characters and does not have special character restrictions. These values should be short for ease of use in programming, but it is not expected that ETCD will need to serve as a variable name.
ELEMENT	Description of Element	Char	The name of the Element.
TABRANCH	Branch	Char	Condition subjects meet, at a "branch" in the Trial Design at the end of this Element, to be included in this Arm. Example: Randomization to DRUG X.
TATRANS	Transition Rule	Char	If the trial design allows a subject to transition to an Element other than the next Element in sequence, then the conditions for transitioning to those other Elements, and the alternative Element sequences, are specified in this rule (e.g., Responders go to washout).
EPOCH	Epoch	Char	Name of the Trial Epoch with which this Element of the Arm is associated.

Trial Arms (TA) Domain - Metadata

#	Variable Name	Variable Label	Type	Role	Description
1	STUDYID	Study Identifier	Char	Identifier	Unique identifier for a study.
2	DOMAIN	Domain Abbreviation	Char	Identifier	Two-character abbreviation for the domain, which must be TA.
3	ARMCD	Planned Arm Code	Char	Topic	ARMCD is limited to 20 characters and does not have special character restrictions.
4	ARM	Description of Planned Arm	Char	Synonym Qualifier of ARMCD	Name given to Arm or treatment group.
5	TAETORD	Planned Order of Element within Arm	Num	Timing	Number that gives the order of the Element within the Arm.
6	ETCD	Element Code	Char	Record Qualifier	ETCD (the companion to ELEMENT) is limited to 8 characters and does not have special character restrictions. These values should be short for ease of use in programming, but it is not expected that ETCD will need to serve as a variable name.
7	ELEMENT	Description of Element	Char	Synonym Qualifier of ETCD	The name of the Element.
8	TABRANCH	Branch	Char	Rule	Condition subjects meet, at a "branch" in the Trial Design at the end of this Element, to be included in this Arm. Example: Randomization to DRUG X.
9	TATRANS	Transition Rule	Char	Rule	If the trial design allows a subject to transition to an Element other than the next Element in sequence, then the conditions for transitioning to those other Elements, and the alternative Element sequences, are specified in this rule (e.g., Responders go to washout).
10	EPOCH	Epoch	Char	Timing	Name of the Trial Epoch with which this Element of the Arm is associated.

Note: The same Element may occur more than once within an Arm, but each occurrence would have a different value for TAETORD and EPOCH, and may have different values for TABRANCH and TATRANS.

Trial Arms (TA) Domain - Implementation

STUDYID	DOMAIN	ARMCD	ARM	EPOCH	TAETORD	ETCD	ELEMENT	TABRANCH	TATRANS
CDISCtraining	TA	A	ARM A	Screen Epoch	1	SCREEN	Screening	Randomized to Treatment A	
CDISCtraining	TA	A	ARM A	Treatment Epoch	2	TRTA	Treatment A BID		
CDISCtraining	TA	A	ARM A	Follow-up Epoch	3	FU	Follow-up		
CDISCtraining	TA	P	ARM P	Screen Epoch	1	SCREEN	Screening	Randomized to Placebo	
CDISCtraining	TA	P	ARM P	Treatment Epoch	2	PBO	Placebo BID		
CDISCtraining	TA	P	ARM P	Follow-up Epoch	3	FU	Follow-up		

Trial Design Domain - Summary

Challenges

- Finding the information needed for an accurate representation of the study.
- Creating TDM tables can be as much of an art as it is a science
- Keep consistency across domains

Effects of these Domains:

- TI:
  - ✓ IE (IETESTCD, IETEST, IECAT – all required)
- TE:
  - ✓ TA, SE (ETCD (req.), ELEMENT)
- TV:
  - ✓ SV (VISITNUM (req.), VISIT, VISITDY)
- TA:
  - ✓ DM (ARMCD, ARM – all required)
  - ✓ CO (TAETORD)
  - ✓ SE, SV, CM, EX, SU, AE, DS, MH, DV, CE, EG, IE, LB, PE,
  - ✓ QS, SC, VS, DA, MB, MS, PC, PP, FA (EPOCH, TAETORD)

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