

Trial Design Model

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1 Introduction

1.1 PROPOSED CHANGES TO TDM PART 1

This proposal includes changes to the existing Trial Design Model (Part 1) that provide functionality for describing trials with dissimilar arms. In the original discussion of the TDM in the SDTM Implementation guide, it was suggested that Epochs might not be defined for such trials, but the issue has been resolved by allowing the insertion of Trial Arm Segments between Trial Elements and Trial Arms.

For many trials, including blinded trials, the elements in each Arm form a similar pattern, and the trial can be described with a matrix whose rows are Arms, whose columns are Epochs, with each cell containing one Element, as in the following example.

	Screening Epoch	First Treatment Epoch	First Rest Epoch	Second Treatment Epoch	Second Rest Epoch	Third Treatment Epoch	Follow-up Epoch
P-5-10 Arm	Screen	Placebo	Rest	5 mg	Rest	10 mg	Follow-up
5-P-10 Arm	Screen	5 mg	Rest	Placebo	Rest	10 mg	Follow-up
5-10-P Arm	Screen	5 mg	Rest	10 mg	Rest	Placebo	Follow-up

A Trial Arm Segment is a sequence of Elements which fits in an Arm/Epoch cell, as in the following example, where the Treatment Epoch consists of three Elements for one Arm, but only one Element for the other Arm.

	Screening Epoch	Treatment Epoch			Follow-up Epoch
Surgery Arm	Screen	Pre-Operative	Surgery	Post-Operative	Follow-up
Drug Arm	Screen	Drug			Follow-up

The addition of Trial Arm Segments also allows for more graceful treatment of oncology trials or other trials with cycles of treatment.

1.2 PART 2: ADDITIONS TO THE TDM

Part 2 of the Trial Design Model adds functionality to describe the scheduling of Trial Activities. This information is typically represented in current protocols by means of a table called "Schedule of Activities" or "Time and Events Table" whose columns are timings (typically Visits) and whose rows are activities such as assessments, interventions, and administrative actions (obtaining informed consent, dispensing clinical trial material, reviewing diaries, etc.).

This model describes the scheduling of Trial Activities by means of a dataset with three main sections:

- A variable that names **what** activity is to be performed.
- Variables that describe **when** the activities are to be performed.
- A variable that describes **whether** an activity is to be performed.

1.2.1 ACTIVITY DEFINITION DATASETS

The "**what**" variable contains an activity name which is defined in one of two datasets:

- Planned Activities. This dataset defines activities, and also define groups of activities. Activities may include
 - Performing tests or examinations that will result in the collection of data that will be stored in SDTM Findings datasets.
 - Administering interventions planned in the protocol. Data on these interventions will be stored in SDTM Interventions datasets such as Exposure.
 - Recording data about unscheduled interventions. These data will be stored in SDTM Interventions datasets such as Con Meds.
 - Recording data about events, which will be stored in SDTM Events datasets.
 - Administrative actions that may not result in any data collection, or will result in data stored in an SDTM Events dataset such as Disposition.

Groups of activities may be defined and named. The activities within a group may have a defined order (e.g., the questions within a validated questionnaire) or not (e.g., the lab tests to be performed on a blood sample or the individual findings that result from an ECG).

- Planned Regimens defines groups of activities which must be performed according to a certain schedule, with certain times between activities, not just in a particular order. The Planned Regimens dataset is optional. The scheduling of certain related groups of activities may be defined in the Trial Activities table, without use of the Planned Regimens table. However, if a group of activities will be performed to the same schedule at multiple times during the trial, the Planned Regimens dataset provides a convenient mechanism for handling this repetition.

Trial Activities are identified with a Domain, with a Topic Variable value (TESTCD is required for findings, but not all Interventions require TRT and not all Events require TERM), and with Qualifiers as necessary. Findings are often sufficiently described with only the TESTCD (the Topic Variable value), while Interventions typically require several Qualifiers (e.g., Dose, Doseform, Route). Unscheduled Interventions and Events may need only a Domain (e.g., AE or ConMed) and a Qualifier describing the Evaluation Interval (see 1.4.3 for more detail). For Uncheduled Interventions and Events, a qualifier indicating a category (e.g., BODYSYS or CAT) may be needed (e.g, Bleeding Events, AIDS-defining Events, Migraine Medications, Arthritis Surgeries).

1.2.2 MECHANISMS FOR DESCRIBING TIMINGS

There are two basic mechanisms for describing the timing of activities.

- The activity is to be performed **during** a visit or a window (a visit-like time interval that is not a "clinical encounter").
- The activity is to be performed at a **certain time before or after** another activity.

As mentioned above, these instructions may also be modified by specifying the **order** of activities within a group (in the Planned Activities dataset) or regimen (in the Planned Regimens dataset). In addition, the order of activities within a visit or window may be specified in the Trial Activities dataset.

1.2.2.0 TRIAL ANCHORS AND OFFSETS

When the timing of an activity is described by referencing another activity, that reference activity is called a **Trial Anchor**. The germ of the Trial Anchor concept is present in the Start Rules in the Trial Elements and Trial Visits datasets. It is also present in the Reference Timepoint timing variable in the SDTM Timing Variables. The time relative to a Trial Anchor (e.g., "5 minutes before" or "2 weeks after") is called an **Offset**.

A Trial Anchor has two characteristics: something that happens (a "happening"), and the time at which it happens. Every trial has at least two Trial Anchors, Trial Entry (the happening that marks the beginning of the first element) and Trial Exit (the happening that marks the end of the last element), and there is no upper limit to the number of Trial Anchors. Any activity that serves as the reference point for describing the start of another activity is a Trial Anchor. Trial Anchors are defined in one of two datasets:

- The Trial Anchors dataset defines individual Trial Anchors.
- The Periodic Trial Anchors Group dataset defines series of Trial Anchors that are related by a common offset. The first Trial Anchor in the series, TA_1 , is defined relative to a "base" Trial Anchor, TA_o , using an Initial Offset between TA_1 and TA_o . Each Trial Anchor in the series is offset from the previous Trial Anchor by the Periodic Offset; TA_{n+1} is scheduled to take place at Periodic Offset after TA_n . The series ends when the End Condition is met, so the number of Trial Anchors in a Periodic Trial Anchors Group may be fixed, may have an upper limit, or may be indefinite.

There are several ways in which offsets may be used to schedule activities.

- A positive Offset means that the activity is scheduled after the Trial Anchor (e.g., 2 weeks after start of study drug).
- A negative Offset means that the activity is scheduled before the anticipated time of the Trial Anchor happening (e.g., 5 minutes pre-dose).
- A range of Offsets means that the activity should take place at an Offset after the lower limit of the range, but before the upper limit of the range.
- An Offset Group may be defined, and then used as often as needed. Offset Groups are created for convenience, and are optional
- A Periodic Offset Group may be defined. A Periodic Offset Group is structured much like a Periodic Trial Anchors Group, except that Activities scheduled using a Periodic Offset Group are all "tied" to the initial Trial Anchor. The 1st activity in the series is scheduled at the Initial Offset after the base Trial Anchor, while the nth activity is scheduled at (Initial Offset + (n-1)*Periodic Offset) after the base Trial Anchor.

1.2.2.1 VISITS AND WINDOWS

Visits are related to Anchors through their Start and End Rules. The instruction to perform an activity at a visit means perform the activity after the start of the visit and before the end of the visit. In fact, many protocols include only sketchy information about visit end rules. In some circumstances, this lack of precise planning can give rise to ambiguity, but for many outpatient trials this level of description is adequate. Note that for many outpatient trials, a single nominal Visit is used for screening and baseline data that may be collected at several clinical encounters. Inpatient trials typically require more careful definition of visit starts and ends.

This version of the TDM augments to concept of Visit with the following mechanisms:

- The **Trial Windows** dataset allows the definition of visit-like time intervals which are not "clinical encounters" in the usual sense. These may be used for sets of activities which take place outside the clinic.
- The **Visit Groups** dataset allows grouping of a set of visits. This is useful when the visits all have the same planned activities.

1.2.3 CONDITIONS ON ACTIVITIES

Scheduled activities may not be performed for all subjects, or in all circumstances.

- Interventions may be given only to subjects in certain arms.
- Activities may only be performed for subjects with certain characteristics (e.g., pregnancy tests are performed only for females of child bearing potential)
- Activities may be performed only under certain circumstances (e.g., creatinine clearance is obtained only if a creatinine value is above a certain threshold, or rescue medication is given only when certain criteria are met).
- Data on unscheduled interventions is collected only if they occurred within a certain time period (e.g., only adverse events that occur during the study are recorded, or only migraine medications taken in the 30 days before the start of study are recorded).

1.2.3.0 RESTRICTIONS ON PERFORMING ACTIVITIES

Restriction of activities to certain arms is indicated by populating ARM in the Trial Activities dataset. A record is required for each ARM.

Restriction of activities to certain subjects or to certain circumstances is indicated by populating IFCOND in the Trial Activities dataset. IFCOND is a text field, but it may be useful to use "pseudo-code" to make the conditions clear. For instance, restriction to females of childbearing condition might be indicated with, "If DM.SEX=F and SC.CHDPOT=Y".

1.2.3.1 TIME RESTRICTIONS ON DATA COLLECTION: EVALUATION INTERVALS AND WINDOWS

Data on unscheduled activities (e.g., Adverse Events and Concomitant Medications) is usually collected in one of the following ways.

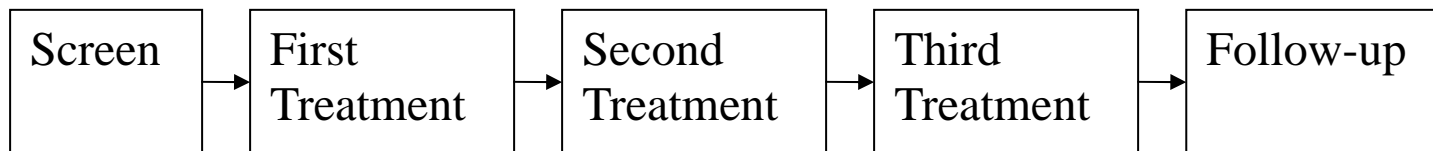
- Data is collected on the interventions or events that occurred during a time period defined by the time of data collection and a duration. Interventions or events that occurred between the time of collection and the time of collection minus the duration are to be recorded. This kind of evaluation interval was envisioned when the SDTM variable EVLINT, which contains an ISO8601 duration value, was created. This kind of data collection is described by including EVLINT and a duration in a QNAM/QVAL pair (QNAM=EVLINT, QVAL=duration).
- Data is collected about interventions or events that occurred during a time period described by a start time and an end time, rather than a duration. An example is data collected about chemotherapy toxicities collected for each cycle. Since cycles may vary in length, a duration is insufficient to describe such data collection. An Evaluation Window is defined, and used in a QNAM/QVAL pair (QNAM=EVLWIN, QVAL=name of evaluation window).
- Incremental data is collected on events or interventions that started, ended, or changed since the last data collection. In this situation, the date of data collection is of little or no interest, and may not be collected. Such "running log" data is still limited in time, for instance to the time of the subject's participation in the study. In such a case, there is a "monitoring interval" associated with the entire running log, and this monitoring interval is described with a beginning and end. Again, an Evaluation Window is defined, and used in a QNAM/QVAL pair (QNAM=EVLWIN, QVAL=name of evaluation window).
- Data is collected at the point of data collection. This is "snapshot" or point data collection, rather than collection over an interval of time, so there is no evaluation interval or evaluation window.

Evaluation intervals are included in this section on timings because it is easy to confuse the evaluation interval "timing" with the timing that occurs in the Trial Activities dataset. The evaluation interval for an activity should be included in the qualifiers when the activity is defined. The timing included in the Trial Activities dataset is the timing of data collection. This confusion does not arise for Findings or Planned Interventions, where the time of the finding or intervention is the scheduled time and (usually) the data collection time. For Unscheduled Interventions and Events, the scheduled time is the time of data collection, while the start and end time of the intervention or event are unscheduled. The evaluation interval determines whether data is collected.

2 The Trial State Machine

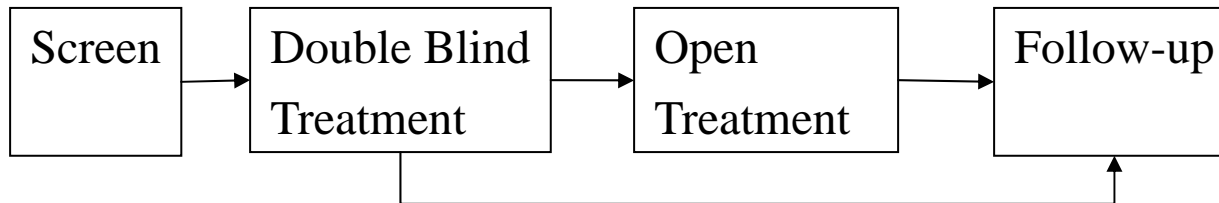
2.1 THE TRIAL STATE MACHINE

Trial Elements, Trial Arm Segments, and Trial Arms, along with Trial Epochs (which are part of the Trial Arms dataset), describe the trial "state machine." Trial Epochs describe the trial state machine. Usually, subjects transition from one Epoch to another sequentially, as in this example:

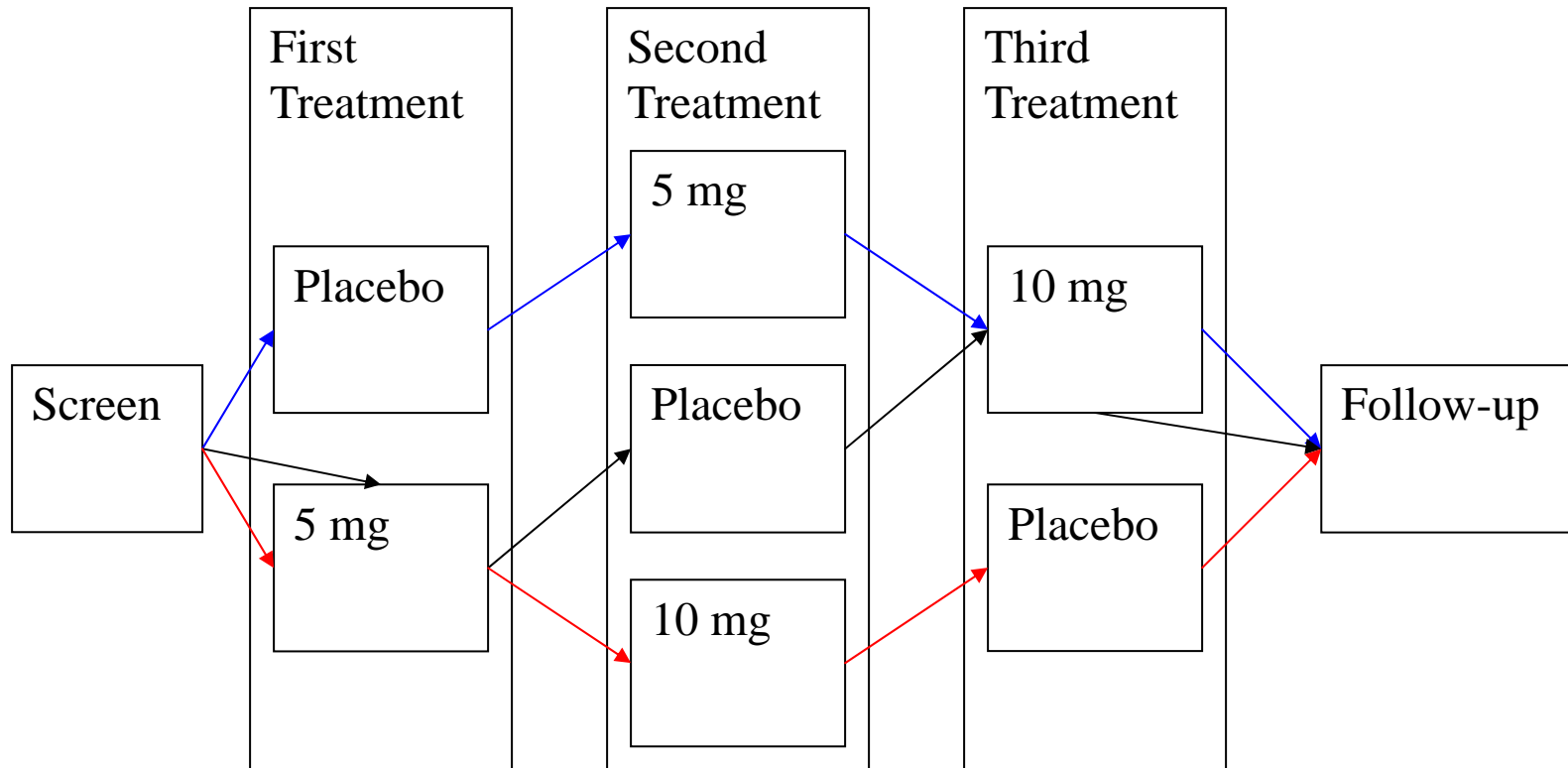


For a blinded trial, this high level view of the trial corresponds to the view of participants who are blind to treatment.

There may be alternative paths, as in the following example, where open label treatment may be skipped under certain conditions.



In the view of the trial that includes arms (i.e., the "unblended" view), the state machine is more complex. Here is the first trial again, with the arm-specific sub-states nested within the trial-level Epoch states, and the arms indicated with connecting arrows of different colors:



Thus, Trial Elements are assembled into both Arms, which represent the path of a subject through the trial, and Epochs, which are trial states that cut across arms. Commonly, the "cells" defined by the intersection of Arms and Epochs contain one element each as in this representation of the last example:

	Trial Screen Epoch	First Treatment Epoch	Second Treatment Epoch	Third Treatment Epoch	Trial Follow-up Epoch
Arm P-5-10	Screen	Placebo	Drug 5 mg	Drug 10 mg	Follow-up
Arm 5-P-10	Screen	Drug 5 mg	Placebo	Drug 10 mg	Follow-up
Arm 5-10-P	Screen	Drug 5 mg	Drug 10 mg	Placebo	Follow-up

However, sometimes cells can have more than one Element within an Epoch, as in this example:

	Screen Epoch	Treatment Epoch		Follow-up Epoch
Arm A	Screen	Investigational Treatment, Phase 1	Investigational Treatment, Phase 2	Follow-up
Arm B	Screen	Standard Care		Follow-up

The sequence of Elements within an Epoch for an Arm is the **Arm Segment**.

Another situation in which the concept of Arm Segments may be useful is a trial with repeating cycles of treatment or follow-up, as in this example:

	Screen Epoch	Treatment Epoch	Follow-up Epoch
Arm A	Screen	Treatment A, Rest 1, repeat from Treatment A until Condition X is met.	Follow-up, repeat until Condition Y is met
Arm B	Screen	Treatment B, Rest 1, repeat from Treatment B until Condition X is met.	Follow-up, repeat until Condition Y is met
Arm C	Screen	Treatment C, Rest 2, repeat from Treatment B until Condition X is met.	Follow-up, repeat until Condition Y is met

2.2 TRIAL ELEMENTS

This dataset is unchanged from the existing SDTM V1 dataset.

One record per Trial Element

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
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STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be TE.	Req
ETCD	Element Code	Char	*			Short 8-character name for ELEMENT, used for programming.	Req
ELEMENT	Description of Element	Char	*			The name of the Element	Req
TESTRL	Rule for Start of Element	Char				Expresses rule for beginning of Element.	Req
TEENRL	Rule for End of Element	Char				Expresses rule for ending the Element	Per
TEDUR	Planned Duration of Element	Char				Planned Duration of Element in ISO 8601 format. For use when the rule for ending the Element is to end after a fixed duration.	Per

Questions:

- I now think that a Trial Anchor is tied to an Epoch, rather than an Element. I.e., that an anchor should be defined in terms that can be recognized while participants are blinded (e.g., "The first dose of drug in the second treatment epoch," rather than "The first 5 mg dose"). This makes description of Element Start Rules slightly more complicated (see first assumption, below).

Assumptions/Conventions:

- TESTRL should be defined by naming a Trial Anchor or a Trial Anchor and an Offset and, where needed, information about treatment. (e.g., The first dose of a treatment epoch where dose is 5 mg).
- One of TEENRL and TEDUR must be populated.

2.3 TRIAL ARM SEGMENTS

One record per Trial Element per Arm Segment

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core	References
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req	SDTM
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be AS?	Req	SDTM
ARMSEGCD	Arm Segment Code	Char	*			Short 8-character version of ARMSEG, used for programming.	Req	
ARMSEG	Planned Arm Code	Char				The name given to the Arm Segment	Req	
ETORD	Order of Element within Arm Segment	Num				Number that gives the order for the Element within the Arm Segment	Req	
ETCD	Element Code	Char	*			Short 8-character name for ELEMENT, used for programming.	Req	SDTM
ELEMENT	Description of Element	Char	*			The name of the Element	Req	
RPTRL	Rule for Repeating Element	Char				If null, the elements within the arm segment do not repeat. If elements do repeat, this is the ETORD of the first arm segment that is repeated.	Per	
RPTENRL	Rule for Ending Repetition of Arm Segment.	Char				Expresses the rule for ending repetition of the Arm Segment. May be a fixed number of repetitions, or a condition for ending repetition.	Per	

Issues/Questions:

- What should the domain code for this dataset be? I have suggested AS.
- Is TATRANS needed in this dataset? (I think it may be. Example: under certain conditions, jump out of the Arm Segment, to the next Epoch, or skip part of the arm segment.)
- Is BRANCH needed in this dataset? (I think it may be. Example: branch to standard care or surgery. After surgery, branch to one of two post-op strategies. Second branch does not take place at an Epoch transition.)
- Allowing repetitions of Arm Segments means that there is not a unique "sequence number" (value of TAETORD) for each element for use in the Subject Elements dataset. Instead, for Epochs that repeat, you must specify the Epoch (by means of EPORD, see below), the Element (by means of ETORD) and a repeat number (CYCLE?), e.g., if a trial has three Epochs (Screen with EPORD=1, Treatment with EPORD=2, and Follow-up with EPORD=3), and two Elements within a repeating Arm Segment, then a subject might have the following elements:

EPORD	CYCLE	ETORD
1		1
2	1	1
2	1	2
2	2	1
2	2	2
2	3	1
2	3	2
3		1

I think this is an improvement, but it is a change to the Subject Elements Dataset.

Assumptions/Conventions:

- Branches can take place only at the transition from one Epoch to the next. (But see question under Trial Arm Segments.)
- If an Arm Segment consists of exactly one non-repeating element, then it is unnecessary to define it in the Arm Segments dataset. The Arm Segment can be referenced in the Trial Arms table by using the name of the Element in ARMSEG and the code for the Element in ARMSEGCD
- If there is a repeating Arm Segment, even if it consists of only one element, then there must be a Trial Arm Segments dataset.
- The names and codes of Arm Segments must be different from the names and codes for Elements.
- If all Arm Segments in the Trial consist of single, non-repeating elements, then an explicit Trial Arm Segments table is unnecessary.

2.4 TRIAL ARMS

The existing Trial Arms and Trial Elements datasets, with the addition of the new Trial Arm Segments dataset, allow the definition of Epochs. Epochs and Elements provide the basic timing skeleton of the trial.

Proposed changes from the original Trial Arms dataset:

- Arms are assembled from Arm Segments, rather than Arms
- EPOD replaces TAETORD
- EPOCH is included

One record per Arm Segment per Arm

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core	References
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req	SDTM
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be TA.	Req	SDTM
ARMCD	Arm Code	Char	*			Short 8-character name for ARM, used for programming.	Req	SDTM
ARM	Description of Arm Segment	Char	*			The name of the Element	Req	
EPOD	Order of Epoch within Arm	Num				Number that gives the order for the Epoch within the trial. This is also, by definition, the order for the Arm Segment within the Arm.	Req	
EPOCH	Trial Epoch	Char				Name of the Trial epoch with which this Arm Segment of the Arm is associated.	Req	

ARMSEGCD	Arm Segment Code	Char	*			Short 8-character version of ARMSEG, used for programming.	Req	
ARMSEG	Planned Arm Code	Char				Name given to an Arm Segment	Req	
TABRANCH	Branch	Char				Condition subjects meet, at a fork in the Trial Design, at the end of this Arm Segment (Epoch), to be included in this Arm. Example: Randomization to Drug A.		
TATRANS	Transition Rule	Char				If the Trial Design allows subjects to transition to an Arm Segment (Epoch) other than the next Arm Segment (Epoch) in sequence, then the conditions for transitioning to those Arm Segments (Epochs) are specified in this rule. Example: Responders go to washout.		

Issues/Questions:

- Change from TAETORD to EPORD okay?

Assumptions/Conventions:

- The name and code for an Element may occur in the Trial Arms table. This means that the Arm Segment consists of just the one named element.
- The order of Epochs must be the same for all Arms in the trial.
- There is one Arm Segment in each Arm for each Epoch.
- The transitions between epochs and elements occur at Trial Anchors or at an Offset after a Trial Anchors

3 Activity Definition Datasets

3.1 DEFINING ACTIVITIES

Activities fall into two general classes, each of which is defined slightly differently.

Scheduled activities are activities whose performance is scheduled. These include Findings (tests and examinations), Interventions that are planned by the trial's Protocol, and "snapshot" (point in time) evaluations of events and of interventions that are not planned by the trial's protocol.

Unscheduled activities are activities which record data about events and interventions that are not planned by the trial's protocol. They record more data over a time interval (an evaluation interval), rather than at a point in time (a "snapshot").

The information needed to define an activity varies according to whether it is Scheduled or Unscheduled, and its class (Finding, Intervention, or Event).

Scheduled Activities

- Findings require a Domain (e.g., Lab, ECG), and a TESTCD (the topic variable for a Findings domain). For some findings, the protocol may also specify qualifiers such as Position or Location.
- Scheduled Interventions require a Domain (e.g., Exposure), and a TRT (the topic variable for an Interventions domain). For most scheduled interventions, the protocol will also specify several qualifiers, such as DOSE, DOSFRM, and ROUTE.
- Activities for recording Snapshot evaluations of unscheduled interventions require a Domain (e.g., Substance Use), and a TRT or CLAS or CAT. The protocol may also specify qualifiers.
- Activities for recording Snapshot evaluations of events require a Domain (e.g., Adverse Events or Symptoms), and a TERM (the topic variable for an Events domain). [How to deal with the case where the CRF allows writing in a subject-specific TERM, which is then tracked in snapshots?]

Unscheduled Activities

- Activities to record non-snapshot data on Unscheduled Interventions require a Domain (e.g., Con Meds), and an Evaluation Interval. The protocol may also specify a CLAS or CAT.
- Activities for recording non-snapshot data on Events require a Domain (e.g., AE), and an Evaluation Interval. The protocol may also specify a BODYSYS or CAT.

3.2 GROUPING ACTIVITIES

There are two mechanisms for grouping activities. The simpler of these two mechanisms operates in the Planned Activities dataset and allows grouping, and ordered grouping, of activities. More complex groupings, that involve offsets between related activities, are specified by creating a Planned Regimen.

3.3 PLANNED ACTIVITIES

This table serves to define activities that are part of the plan of the trial.

ANAME holds the name of a planned activity. ANAME is defined by a group of records, all with the same value of TOPIC, but with different values of QNAM and QVAL. For example, if a planned intervention consists of 40 mg of Drug X, in the form of a capsule to be taken orally, there would be four records that constitute the description of that intervention, one each for DOSE, DOSEU, DOSFRM, and ROUTE. ANAME serves both to declare the name of the planned intervention and to group the records together.

AGRP holds the name of an Activities Group. If the activities in anActivities Group are to be performed in a particular order (e.g., the questions in a validated questionnaire), this may be specified in GRPORD.

One record per planned activity qualifier

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be PA?	Req
ANAME	Name of Planned Activity	Char				ANAME should be the name of an activity.	Req
ADOMAIN	Domain of Planned Activity	Char	*				Req
TOPIC	Value of Topic Variable for the Domain	Char		CRF or Randomization File or Derived	Topic	For Findings, a TESTCD, for Interventions, a TRT, for Events, a TERM.	Depends
QNAM	Qualifier of Planned Treatment	Char				Values to taken from Qualifiers in the general class (e.g., LOC, DOSE, BODYSYS) or from values used for QNAM in SUPQUAL	Per
QVAL	Value of QUALVAL	Char				Value of the variable QUAL planned for this TRT For example, QNAM= DOSE, QVAL=15	Per
AGRP	Name of Activity Group	Char					Per
GRPORD	Order of Activity with Activity Group	Num				Indicates that this activity should be performed after activities in the same AGRP with a lower value of GPORD and before activities in the same AGRP with a higher value of GPORD.	Per

* indicates variable may be subject to controlled terminology.

Development Notes:

Questions:

- What should the domain code for this dataset be? I have suggested PA.
- Is it okay to use QNAM and QVAL, which are variable names in SUPPQUAL, in this context? The values QNAM takes on could be either qualifiers from the general class or ones used in SUPPQUAL.
- TOPIC is required for some kinds of activities, not for others. So is it "Expected" over all?
- Can an Activity be part of more than one Activity Group?
- For a Finding, is TESTCD enough? When I had Planned Findings separate, I also included TEST.
- In an earlier draft, I included TEXT, the complete text of the question. I was thinking of questionnaires. Could this be treated as a Qualifier, if needed? It's something we have in TI, and is something you'd really rather have only in metadata (which is sort of what Planned Activities is), rather than subject data. If TEXT is included, then a mechanism for dealing with long text values will be needed.
- There are some things that I think of as non-data activities, like obtaining informed consent, but if these are to serve as Trial Anchors used as Element transition points, then at least a date must be collected. I think these are events, probably Disposition Events. Does that make sense?
- Is GRPID needed? I think that ANAME fulfills this purpose, though it may not work if only some of the records with an ANAME are part of the definition of that ANAME. This might happen if an ANAME can be used in more than one AGRP, or if separate records are used to define an ANAME and to put it into an AGRP.

Assumptions/Conventions:

- This dataset is required.
- "Exceptions" such as dose adjustments in response to adverse events are not modeled.
- Planned Activities is about collected data. It does not include Derived Data.
- Planned Activities does not specify what data about the activity will be collected.
- An activity may be a "singleton," not part of any Activity Group.
- If multiple records are needed to define an Activity, then all of them must have the same value of AGRP and GPORD. [Is this a problem? If so, then perhaps all grouping of activities should be moved into Planned Regimens. Or perhaps you can define an ANAME in one set of records, then use the ANAMES in other records to create an AGRP?]
- QUAL should hold aspects of the test, not aspects of the result (e.g., units, normal range, MODIFY, SEV, DTHREL) or timing variables.

- The groupings of findings described by CAT and SCAT are may or may not match the groupings in the Planned Findings dataset.
- Only supply QNAM & QVAL where needed – don't specify anything that's not needed.

3.4 PLANNED REGIMENS

This dataset groups activities that constitute a "regimen". A Planned Regimen allows for scheduling of activities within a Regimen by means of Offsets, as well as order (RGORD).

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be PR?	Req
AREG	Name of Activity Regimen	Char				The name of this group of interventions	
ANAME	Name of Planned Activity	Char				The name of this intervention. Examples: Placebo, Low Dose, Comparator	
REGORD	Sequence number	Char				Order of this intervention within the Intervention Group. Used when offsets aren't specified.	
OFFSET	Offset	ISO8601				An offset expressed as a duration using ISO8601 format	
OFFSET1	Second Offset, for use in defining ranges of offsets	ISO8601					

Issues/Questions:

- What should the domain code for this dataset be? I have suggested PR.

- An activity with a zero offset coincides with the "anchor" for the activity. Should this regimen anchor be included in the Planned Regimens dataset? If the Planned Regimen is in the Trial Activities dataset with a Visit or Window, then it has to be in the Planned Regimens dataset. If it's in the Planned Regimens dataset and also the Anchor for the regimen in the Trial Activities dataset, is that okay?
- Order & Offset may be alternative ways to provide information about the "togetherness," depending on what's needed.
- Does this dataset need any "if" mechanisms, like ARM or IFCOND?

Assumptions/Conventions:

- This dataset is optional.

The following table shows an example of a regimen for taking three blood pressures. Assume that BPSIT has been defined, in the Planned Activities dataset, as the group of two activities, SITSYS and SITDIA (systolic and diastolic blood pressure with position sitting).

AREG	ANAME	REGORD	OFFSET	OFFSET2	COMMENTS
BP	BPSIT	1	0		1 st repetition
BP	BPSIT	2	P10M		2 nd repetition, 10 minutes after first
BP	BPSIT	3	P20M		3 rd repetition, 20 minutes after first

The next table shows an example of a regimen for administering a chemotherapy drug with associated steroid treatment.

AREG	ANAME	REGORD	OFFSET	OFFSET2	COMMENTS
COMBA	STEROID		-P14H	-P10H	
COMBA	STEROID		-P2H	0	
COMBA	DRUG A		0		
COMBA	STEROID		P10H	P14H	

3.5 EVALUATION INTERVALS AND WINDOWS

Evaluation intervals are "durations." There is already a timing variable in the SDTM, EVLINT, which can be used as a Qualifier in any domain. Evaluation windows also serve as qualifiers, but as they are more complex than evaluation intervals, they must be defined for a study. They are defined in the Evaluation Windows dataset.

Assumptions/Conventions:

- If an Event activity includes an EVLINT Qualifier (i.e., QNAM=EVLINT, QVAL=duration value), then data collection is restricted to the time period that starts {value} before the time of collection, and ends at the time of collection.
- If an Event activity includes an EVLWIN Qualifier (i.e., QNAM=EVLWIN, QVAL=name of evaluation window), then data collection is restricted to the named evaluation window.
- If an Event activity includes neither an EVLINT Qualifier or an EVLWIN Qualifier, then data collection is a "snapshot," i.e., it is restricted to the status of the event at the time of data collection, where "status" may include presence or absence, severity, etc.

One record per Evaluation Window

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core	References
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req	SDTM
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be EW .	Req	SDTM
EVLWIN	Evaluation Window Name	Char	*				Req	SDTM
EWSTRL	Evaluation Window Start Rule	Char					Req	
EWENRL	Evaluation Window End Rule	Char					Req	

Issues/Questions:

- Would "monitoring window" be a better term than "evaluation window"?
- What should the domain code for this dataset be? I have suggested EW. (Or MW if this changes to Monitoring Window.)
- Is this dataset required? I think it will almost always be needed, as AEs are almost always collected, and (I think) that the Evaluation Window for AEs should be specified.

Assumptions/Conventions:

- The start and end rules should be expressed in terms of Anchors.

4 Trial Activities

4.1 VOCABULARY FOR TRIAL TIMINGS

This section describes the rationale for the timing variables in the Trial Activities dataset.

Timing of activities can be described in one of several ways:

1. Perform {activity} {offset} after {anchor point}.
2. Perform {activity} {offset} before anticipated occurrence of {anchor point}.
3. Perform {activity} after {offset 1} relative to {anchor point} and before {offset 2} relative to {anchor point}.
4. Perform {activity} at each of a {set of offsets} relative to {anchor point}.
5. Perform {activity} at each of a {periodic set of offsets} relative to {anchor point}.
6. Perform {activity} at each of a {periodic set of anchor points} until {condition} is met.
7. Perform {activity} during {visit}, after activities with a lower {order} and before activities with a higher {order}.
8. Perform {activity} during each of a {set of visits}, after activities with a lower {order} and before activities with a higher {order}.
9. Perform {activity} during {window}, after activities with a lower {order} and before activities with a higher {order}.

Where

{activity} is an activity (ANAME), an activity group (AGRP) or regimen of activities (AREG) defined in the Planned Activities dataset or the Planned Regimens dataset.

{offset} is a time interval (e.g., 2 days or 5 weeks, not a date or clock time) expressed in ISO3601. It may be zero.

{anchor point} is a "happening" defined in the Trial Anchors dataset and the time at which it happens. It must be something that participants in the trial can recognize and for which they can record the time of occurrence. Note that the "happening" may be scheduled or unscheduled and may correspond to an SDTM Event, Intervention, or Finding.

{set of offsets} is an offset group described in the Offset Groups dataset.

{periodic set of offsets} is a periodic offset group described in the Offset Groups table. It consists of offsets $y, y+1x, y+2x, y+3x$, etc., where y is the initial offset and x is the period. The value of y may be zero. The set may have a fixed number of offsets, or may end when a condition is met.

{periodic set of anchor points} is a periodic offset group described in the Anchor Groups table. In a periodic set of anchors, there is an initial {anchor point}, then the {activity} is performed at {initial offset} after the initial {anchor point}. This first occurrence of the {activity} becomes the {anchor point} for the next {activity}, which occurs at {periodic offset} after the first. The n th activity is to occur at {periodic offset} after the $n-1$ th and becomes the {anchor point} for the $n+1$ th activity in the series. The set may have a fixed number of anchors, or may end when a condition is met. A series of

activities is "telescoping" in the sense that if one activity is performed earlier or later than scheduled, then the schedule for all the rest of the activities moves up or back accordingly.

{visit} is a visit defined in the Trial Visits table.

{order} is a positive integer assigned to an activity to be performed during a visit. {order} values may be assigned to some or all of the activities associated with a visit.

{set of visits} is a visit group defined in the Visit Groups table.

{window} is a trial window defined in the Trial Windows table. A trial window has a start, defined as {offset} before or after {anchor point} and an end, defined as {offset} before or after {anchor point}.

The following table organizes the pieces of these possible statements into columns. The columns are precursors to the variables in the Trial Activities table.

	1	2	3	4	5	6	7	8	9
1	Perform	{activity}		{offset}			after	{anchor}	
2	Perform	{activity}		{offset}			Before anticipated occurrence of	{anchor}	
3	Perform	{activity}	between	{offset 1}	and	{offset2}	Relative to	{anchor}	
4	Perform	{activity}	at each of a	{set of offsets}			relative to	{anchor}	
5	Perform	{activity}	at each of a	{periodic set of offsets}			relative to	{anchor}	
6	Perform	{activity}	at each of a					{periodic set of anchors}	
7	Perform	{activity}					during	{visit}	After activities with a higher, and before activities with a lower {order}
8	Perform	{activity}					during each of a	{set of visits}	After activities with a higher, and before activities with a lower {order}
9	Perform	{activity}					during	{window}	After activities with a higher, and before activities with a lower {order}

The contents of columns of this table:

1. "perform"
2. {activity}
3. "between" (used with a pair {offset1}, {offset2}) or "at each of" (used with an {offset group} or a {periodic set of offsets})
4. {offset} or {offset 1} or {set of offsets} or {periodic set of offsets}
5. "and" (used with a pair: {offset1}, {offset2})
6. {offset 2}
7. "after" or "before anticipated occurrence of" or "relative to" or "each of a (which go with anchors) or "during" or "during each of a" (which go with visits and windows)
8. {anchor} or {periodic set of anchors} or {visit} or {set of visits} or {window}
9. "after activities with a higher, and before activities with a lower" {order}

Column 1: Always the same, can be inferred.

Columns 2, 4, 6, 8, and 9 contain the names of entities defined in other tables, and become variables in the Trial Activities table. The words, ""after activities with a higher, and before activities with a lower" need not be represented explicitly.

Column 3: The "between" can be inferred from the presence of two offsets (in columns 4 and 6). The "at each of" can be inferred from the contents of column 4.

Column 5: The "and" can be inferred from the presence of two offsets (in columns 4 and 6).

Column 7: "After" or "before" can be conveyed by giving signs (+ or -) to the offsets in columns 4 and 6.

Columns 2, 4, 6, 8, and 9 become the "when" variables of the Trial Activity table:

Column 2 becomes ANAME, or Activity Name.

Column 4 becomes two variables:

A variable OFFSET for timings with a single offset or a range of offsets

A variable OFFGP for a group of offsets.

Column 6 becomes OFFSET2

Column 8 becomes two variables:

A variable for intervals (Visits or Windows) or groups of visits called VISWIN

A variable for anchors or groups of anchors called ANCHOR.

Column 9 becomes ORDER.

4.2 TRIAL ACTIVITIES DATASET

TRIAL ACTIVITIES

One record per activity per timing.

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be SA?	Req
ANAME	Name of Trial Activity	Char				Name given to a trial activity. Could be a finding group, a medication or medication group, an type of unplanned event or intervention, or an Other Activity like "Randomization" or "Trial Exit"	Req
OFFSET	Time relative to ANCHOR	Char	ISO 8601		Timing	Offset (in ISO 8601) relative to the part of the ANCHOR. A time point, not a time interval. Not a clock time or a date time variable. Used for points in time, left blank for interval timings.	Perm
OFFSET2	Second time relative to ANCHOR	Char	ISO 8601		Timing	Offset (in ISO 8601) relative to the part of the ANCHOR. A time point, not a time interval. Not a clock time or a date time variable. Used, in conjunction with OFFSET, when an activity is scheduled to take place within a range of times between (ANCHOR, OFFSET) and (ANCHOR, OFFSET2). OFFSET2 should be greater than OFFSET1.	Perm
OFFGRP	Offset Group Name	Char	*			The name of an Offset Group, either a Periodic Offset Group, or a non-periodic Offset Group.	Perm

VISWIN	Name Visit, Visit Group, or Window	Char	*			The name of a Visit, Visit Group, or Window	
ANCHOR	Name of Trial Anchor or Periodic Anchor Group	Char				The name of a Trial Anchor, or of a Periodic Anchor Group	
ORDER	Order of Activity	Num				Order of this activity within a Visit or Window.	Perm
ARMCD	Arm Code	Char				Short 8-character name for ARM, used for programming.	Perm
IFCOND	Condition for Performing Activity	Char				Statement of condition under which activity will be performed. Statement will start with "If". If possible, the condition will be expressed using variable names and values that would occur in the subject domains of the SDTM.	Perm

Questions

- What should the domain code for this dataset be? I have suggested SA (for Schedule of Activities).
- Should the name of this dataset be "Schedule of Activities" to match the proposed domain code?
- Does this dataset need ARM, in addition to ARMCD?

Assumptions/Conventions:

- Descriptions such as "pre-dose" which do not include an offset or range of offsets, should be used only within the context of a Visit or Window. In this context, they can be represented in the Trial Activities dataset by means of Order numbers. E.g., the pre-dose assessment in a visit could be assigned an order of 1, and the dose could be assigned an order of 2.
- When the order between activities can be inferred from their offsets, it is not necessary to also assign order numbers.

4.3 EXAMPLES OF RECORDS IN TRIAL ACTIVITIES DATASET

This section gives examples of rows in a Trial Activities Dataset. In the table, heavy lines mark activities in the same visit, as Order Variables apply to activities within a visit. Note that there are study drug activities (records) for each arm of the study.

ANAME	OFFSET	OFFSET2	OFFGRP	VISWIN	ANCHOR	ORDER	ARM	IFCOND	Notes
IE				SCREENING					
PREGTEST				SCREENING				If SEX=F and of childbearing potential	
VS2				SCREENING					
SS			DAILY						DAILY is name of an offset group used for a daily diary of symptoms
VS2				PER1DAY1		1			Three repetitions of Vital Signs, before pre-dose PK sample.
VS2				PER1DAY1		2			
VS2				PER1DAY1		3			
PKCNC				PER1DAY1		4			Pre-dose PK sample.
PLACEBO	0			PER1DAY1	PER1DOS1	5	P-5-10		Dose
DRUG5	0			PER1DAY1	PER1DOS1	5	5-P-10		Dose
DRUG5	0			PER1DAY1	PER1DOS1	5	5-10-P		Dose
PKCNC			PROFILE1	PER1DAY1	PER1DOS1				
PLACEBO			PER1D2-4		PER1DOS1		P-5-10		PER1D2-4 is an offset group that contains the offsets 1D, 2D, 3D, and so provides the timing for the Day 2, 3, and 4 doses, which are not given during a Visit.
DRUG5			PER1D2-4		PER1DOS1		5-P-10		
DRUG5			PER1D2-4		PER1DOS1		5-10-P		

PKCNC				PER1DAY5		1			Pre-dose PK sample.
PLACEBO	0			PER1DAY5	PER1DOS5	2	P-5-10		Dose
DRUG5	0			PER1DAY5	PER1DOS5	2	5-P-10		Dose
DRUG5	0			PER1DAY5	PER1DOS5	2	5-10-P		Dose
PKCNC			PROFILE2	PER1DAY5	PER1DOS5				
PKCNC				PER2DAY1		1			Pre-dose PK sample.
DRUG5	0			PER2DAY1	PER2DOS1	2	P-5-10		Dose
PLACEBO	0			PER2DAY1	PER2DOS1	2	5-P-10		Dose
DRUG10	0			PER2DAY1	PER2DOS1	2	5-10-P		Dose
PKCNC			PROFILE1	PER2DAY1	PER2DOS1				
DRUG5			PER2D2-4		PER2DOS1		P-5-10		PER2D2-4 is an offset group that contains the offsets 1D, 2D, 3D, and so provides the timing for the Day 2, 3, and 4 doses, which are not given during a Visit.
PLACEBO			PER2D2-4		PER2DOS1		5-P-10		
DRUG10			PER2D2-4		PER2DOS1		5-10-P		
PKCNC				PER2DAY5		1			Pre-dose PK sample.
DRUG5	0			PER2DAY5	PER2DOS5	2			Dose
PLACEBO	0			PER2DAY5	PER2DOS5	2			Dose
DRUG10	0			PER2DAY5	PER2DOS5	2			Dose
PKCNC			PROFILE2	PER2DAY5	PER2DOS5				
...									Items for Period 3 not shown
QS1				FOLLOWUP		1			QS1 to be done before QS2
QS2				FOLLOWUP		2			

4.4 TRIAL VISITS

This existing dataset defines another basic layer of the trial's timing structure.

One record per Planned Trial Visit

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be TV.	Req
VISIT	Visit Name	Char	*				Req
VISITNUM	Visit Sequence Number	Char					
VISITDY	Planned Study Day of Visit	Num					
ARMCD	Planned Arm Code	Char	*				
ARM	Description of Planned Arm	Char	*				
TVSTRL	Visit Start Rule	Char					

TVENRL	Visit End Rule	Char					
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Issues/Questions:

- I think TVSTRL should be populated with an Anchor and Offset. Any times when this would not work?

Assumptions/Conventions:

- One of TEENRL and TEDUR must be populated.

4.5 VISIT GROUPS

If many visits collect the same data, it may be convenient to define visit groups.

One record per visit

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be VG?	Req
VISGRP	Name of Visit Group	Char	*				Req
VISIT	Visit Name	Char					Req

Issues/Questions:

- What should the domain code for this dataset be? I have suggested VG.
- If most, but not all, of the activities for a set of visits are the same, is it okay to set up a Visit Group for those activities, but to specify additional activities visit by visit?

- Should grouping of visits be incorporated into the Trial Visits dataset, rather than being done as a separate dataset? This approach would be more similar to the approach in the Planned Activities dataset.

Assumptions/Conventions:

- Visit groups are optional.
- A visit group will only be useful if there is at least one assessment that is performed at all visits in the group.

4.6 TRIAL WINDOWS

Defines and names windows for data collection. When used in conjunction with Unplanned Interventions or Events, the record in the Trial Activities table means that all of the named type of unplanned interventions or events that occur during the window are to be recorded. When used in conjunction with Findings or Planned Interventions, the record in the Trial Activities table means that the activities are to be performed during the Window, subject to the constraints of their Order numbers.

One record per Planned Trial Window

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be TW?	Req
WINDOW	Window Name	Char	*				Req
WINDOWCD	Window Code	Char					
ARMCD	Planned Arm Code	Char	*			Used when data collection Windows depend on ARM.	Perm

ARM	Description of Planned Arm	Char	*			Used when data collection Windows depend on ARM.	Perm
STANCHOR	Anchor for start of window	Char	*			Value must be taken from Trial Anchors table.	Req
STOFFSET	Offset for start of window	Char	ISO8601			May be 0.	Req
ENANCHOR	Anchor for end of window	Char	*			Value must be taken from Trial Anchors table.	Req
ENOFFSET	Offset for end of window	Char	ISO8601			May be 0.	Req

Issues/Questions:

- What should the domain code for this dataset be? I have suggested TW.
- Do we really need both a Window Name and a Window Code?
- Evaluation Intervals that have a beginning and an end have the same structure as Windows. Should they be defined in the Trial Windows dataset, or in a separate Evaluation Intervals dataset?
- Should one dataset be used for defining Visits, Windows, and Evaluation Intervals? With perhaps a flag that indicates which records are Visits, which are Windows, which are Evaluation Intervals?

Assumptions/Conventions:

- Windows are optional.

4.7 TRIAL ANCHORS

Defines and names any anchors needed.

An anchor should be named only if it is needed to describe a time point used in the trial state machine or the trial activities table. If a time point can be described by referencing another Anchor and specifying an offset, and is not needed as a reference by some other time point, then it should not be declared as an Anchor.

The most commonly used anchors in drug trials are doses of study drug. There is often a circular relationship between doses of study drug which mark the beginning of an Epoch.

One record per anchor

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be TN?	Req
ANCHOR	Name of Anchor	Char			Identifier	Name given to an action which serves as a reference for timing of parts of the study design.	Req
ANCHDESC	Description of Anchor	Char				Description of Anchor, to include a verifiable Trial Anchor Event. Participants must be able to observe and record the time of the Trial Anchor Event.	Req

Issues/Questions:

- What should the domain code for this dataset be? I have suggested TN for Trial Anchors.

Assumptions:

-

4.8 OFFSET GROUPS

This dataset defines groups of offsets that are used together. If the group offsets is used only once in a trial, an offset group may or may not be defined. There is no need to define groups of one. Note that a reference anchor is NOT included in the Offset Group. The Offset Group and Anchor come together in the Trial Activities dataset.

One record per timepoint

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req

DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be OG?	Req
OGNAME	Name of Offset Group	Char				Name given to a group of timepoints, all of which share the same planned fixed reference.	Req
TPT	Planned Timepoint Name	Char				1. Text Description of time when an assessment will be made. 2. This is represented as an elapsed time relative to a fixed reference point, such as time of last dose. See TPTREF in Trial Assessments.	
TPTNUM	Planned Timepoint Number	Num				Numerical version of TPT to aid in sorting.	
ELTM	Elapsed Time	Char	ISO 8601			Elapsed time (in ISO 8601) format relative to the planned fixed reference. Not a clock time.	Req

Questions

- Are both TPT and TPTNUM needed? Is this where they are both defined?
- ELTM is a timing variable from SDTM. "Offset" is the terminology used throughout this document. Are "elapsed time" and "offset really the same thing; should they have a single name?

Assumptions/Conventions:

4.9 PERIODIC OFFSET GROUP

This dataset defines a group of offsets based on a common period. For example, the series of offsets {1D, 2D, 3D, ..., 28D} is a periodic offset group with a period of 1 day. A Periodic Offset Group is used in conjunction with an Anchor in the Trial Activities table, in the same way that a (non-periodic) Offset Group is used.

One record per periodic offset group

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
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STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be PO ?	Req
OGNAME	Name of Offset Group	Char				Name given to a group of timepoints, all of which share the same planned fixed reference.	Req
INOFFSET	Offset relative to Initial Anchor	Char	ISO 8601				Req
PERIOD	Period for Periodic Offset Group	Char	ISO 8601			Must be positive. May not be a range.	Req
POGENRL	End Rule for Periodic Offset Group	Char				Rule for ending the Periodic Offset Group. May be a fixed number of repetitions, or a free text description.	Req

Issues/Questions:

- Should we have a POGNUM (number of repetitions), in addition to POGENRL, the way we have DUR in addition to other ENRL's?
- I think that either Periodic Offset Groups or Periodic Anchor Groups are the natural way to express most dosing, so I haven't provided a "Frequency" or "Dosing interval" variable in the Trial Activities dataset. Is this okay?

Assumptions/Conventions:

- Periodic Offset Groups are optional.

4.10 PERIODIC ANCHOR GROUPS

Describes a set of anchors related by a common period. The first anchor in the series occurs at an initial offset relative to an initial anchor. If the initial offset is 0, the initial anchor is the first anchor in the series. The Trial Anchor Event associated with the second anchor in the series is supposed to occur at the period of the series after the time of occurrence of the first Trial Anchor Event. Each Trial Anchor Event is supposed to occur period after the time of the last Trial Anchor Event.

One record per periodic anchor group

Variable Name	Variable Label	Type	Controlled Terms or Format	Origin	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		CRF	Identifier	Unique identifier for a study within the submission.	Req
DOMAIN	Domain Abbreviation	Char	*			Two-character abbreviation for the domain, which must be PN?	Req
AGNAME	Name of Anchor Group	Char				Name given to a group of timepoints, all of which share the same planned fixed reference.	Req
INANCHOR	Anchor to which the Initial Anchor of the Periodic Group is tied					This is the same as the first anchor in the group if and only if INOFFSET=0.	
INOFFSET	Offset relative to Initial Anchor	Char	ISO 8601				Req
PERIOD	Period for Periodic Anchor Group	Char	ISO 8601			Must be positive.	Req
PAGENRL	End Rule for Periodic Anchor Group	Char				Rule for ending the Periodic Anchor Group. May be a fixed number of repetitions, or a free text description.	Req

Issues/Questions:

- Should we have a PAGNUM (number of repetitions), in addition to PAGENRL, the way we have DUR in addition to other ENRL's?
- I think Period could be a range, in which case, we probably need a PERIOD2 variable, to hold the second half of the range description.
- I have included the Initial Anchor in this group, but not in the Periodic Offset List. I think this makes sense, since this is an Anchor group, so I don't expect it to be reused with different Anchors, the way an Offset Group would be. Okay?

Assumptions/Conventions:

- Periodic Anchor Groups are optional.
- Anchors implicit in the Periodic Anchor Group do not also have to be listed in the Trial Anchors table.

5 General Issues

The following issues and questions are general, rather than related to particular datasets.

Issues/Questions:

- Do the new datasets allow description of all protocol information on scheduling of activities?
- If there are gaps, should the model be expanded to cover them? Suggestions on how to do this?
- The model now has the fourteen study-level datasets listed below to describe the "trial schema" and "schedule of activities" information in a protocol. The largest group of datasets defines ways to describe timing – are there more elegant, compact ways to model this information?
 - 3 datasets that describe the trial state machine (Trial Elements, Arm Segments, and Arms)
 - 2 datasets that describe what is done (Planned Activities and Regimens)
 - 1 dataset that allows definition of a qualifier, Evaluation Windows
 - 7 datasets that define ways to describe when things are done (Trial Visits, Trial Windows, Visit Groups, Trial Anchors, Offset Groups, Periodic Offset Groups, and Periodic Anchor Groups)
 - 1 dataset for the schedule of activities, the Trial Activities dataset

6 Feedback

Feedback on the particular Issues and Questions in this document, and on any other part of this proposal, is welcome.

Testing of the model on real protocols, and feedback on what worked and what didn't work, will be extremely valuable.