# Relationships Among CDISC Variables Concerning Day and Date (CDISC Variable Relationships Part 2 of 3)

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## ABSTRACT

This paper explores the relationships among the set of timing variables in CDISC domains. Many CDISC variables are related to each other and understanding relationships among variables helps both in programming and in edit checking. It is hoped that a discussion of relationships among variables, in the context of examples, will help people that are new to CDISC. This paper is one of a short series of example-focused papers devoted to exploring relationships among classes of CDISC variables.


Timing variables are the set of variables that record "time related" characteristics associated with when an event happens. Examples of time-related characteristics are: the visit when the event happened, the date that an event happened, the duration of the event, the number of days between a time point (subject entering the study, etc.), and the date of the event.

All information in this paper is contained in the CDISC Implementation Guide (IG), but it is hoped that a focused discussion of these variables might be of use to the community.

## INTRODUCTION

Examples in this paper will be developed from an imaginary study. The study involves a drug that can be administered, via skin-contact patch or a tablet and is part of a regimen that includes moderate exercise (playing in a volleyball league).

Figure 1 is shown in landscape form in an appendix to this paper. For ease of reading, it is suggested that a reader print the figures at the end of the paper and refer to them as the paper is read. The red box in Figure 1 contains cells showing the values of many of the timing variables in the study. It is hoped that this graphic will make the relationships clearer.

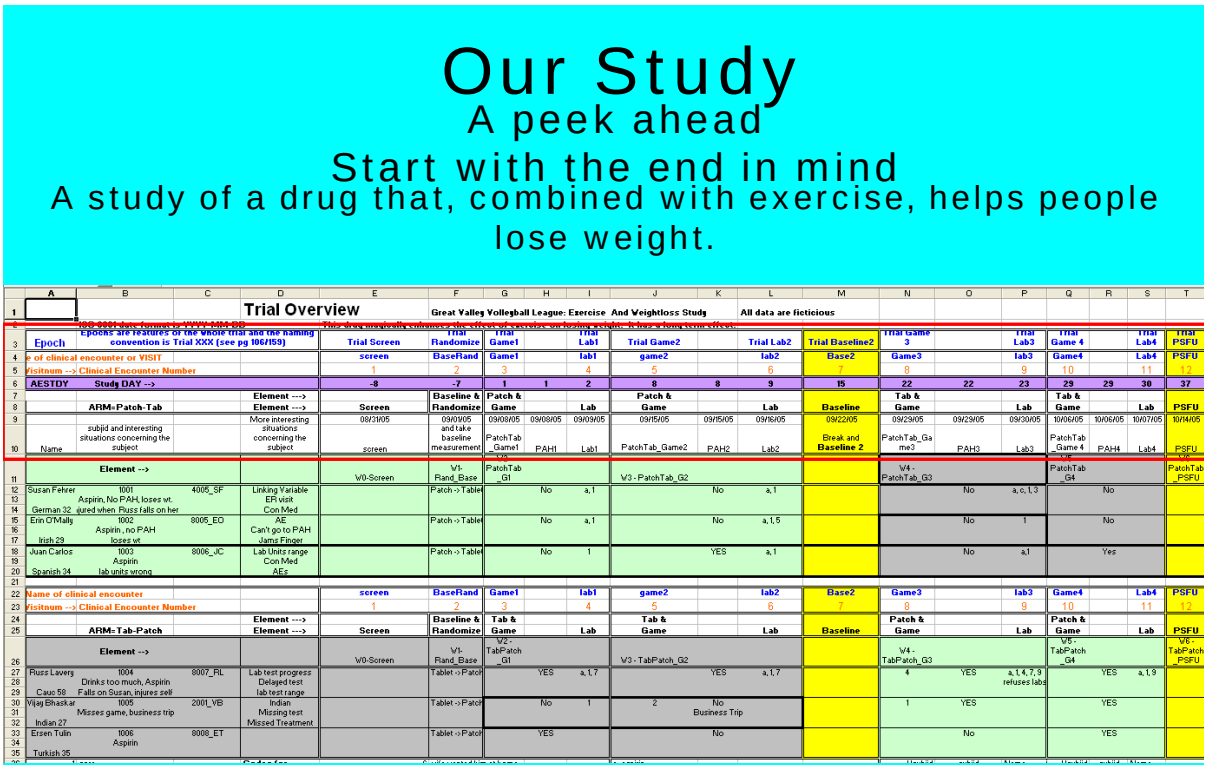


Figure 1 (Shown larger below for ease of printing)

Timing variables are in all domains and record information and relationships concerning when an event happened. Several characteristics of "when the event happened" are of interest to the researcher and CDISC has created a set of variables that can record almost any timing characteristic and time-related relationship that could be of interest to a researcher.

While timing variables appear in the many domains, two important variables, RFSTDTC and RFENDTC, are only present in the demography domain, DM. RFSTDTC, often the date-time of first treatment, is the point from which study-day is calculated. RFSTDTC and RFENDTC record the date-time when a subject enters and leaves the study and together they define the period of study participation, a time range. In addition to being used to calculate study day values they are used to create - -ENSTRF and - -ENENRF variables whose values record a relationship between and event and the start and end of the study period. Often the values are of - -ENSTRF and - -ENENRF are "BEFORE", "DURING", or "AFTER". - -ENSTRF and - -ENENRF are imprecise time measurements and are used when an exact date was not recorded.

This "BEFORE" / "DURING" / "AFTER" imprecise classification has been expanded in CDISC STDM IG v3.1.2 by the addition of four timing variables. The variables are - -STRTPT and - -ENRTPT, which define date-time points and - -STTPT and - -ENTPT which hold the evaluations made relative to these time points.

## DEFINING VISITS, ELEMENTS, EPOCHS

The CDISC Implementation Guide (IG) suggests a new and sometimes confusing structure for describing a subject's progress through a study. Much of the new structure for reporting progress through a study is to conveniently account for the differences between blinded and unblinded trials. In blinded trials, there is a need to describe subject progress without having to, without being *able* to, know what treatment the subject is receiving. In blinded studies, the schedule for both arms, treatment and control, is usually the same, if not, the treatment can be deduced from treatment pattern and the blinding is flawed. Some of the words to be used in describing subject progress through a study were created or given new meaning by CDISC and therefore bear studying. VISIT used to be the common time marker in a study. VISIT now has a new, more detailed, definition and is less important than in the past.

By CDISC definition, a visit is a clinical encounter. VISITs are defined by rules, in the "Trial Visits (TV) Domain", that describe both the start and end of the visit. Obviously, the time when a subject comes in for, and leaves from, a visit may vary slightly from the rules.

The VISIT variable is a character variable and contains human readable and meaningfully valued text. Because of this character, human readable nature, sorting by the VISIT variable is not guaranteed to order observations in a sequence that is of interest to investigators. To facilitate sorting, CDISC specified a numeric variable, VISITNUM, corresponding to VISIT and is used for sorting.

A visit can be planned or unplanned. For planned visits, the VISITNUM variable has integer values (4, 6, 23, etc.) and unplanned visits are assigned numbers with a decimal component. An unplanned visit (eg., a lab test) that occurred between planned visits 14 and 15 might have VISIT coded as "Unplanned Lab" and VISITNUM coded as 14.1 in the LB (Laboratory) Domain. What is entered into VISIT, the character-value, human-readable variable describing the clinical encounter, can be fairly free form, especially for unplanned visits. It is suggested that the sponsor attempt to establish logical standards for valuing VISIT and to apply these standards company-wide.

## ROLLING UP VISITS

A visit is an encounter between the subject and a person in the study staff, at a point in time. The encounter can be a treatment, a lab test, or a measurement. The exact characteristics of (and rules for) a visit are set in the protocol. This means that subjects will spend most of their time in a state best described as between visits, or "NOT in a visit". Consider that in our imaginary weight loss study, the administering of the drug takes only a few seconds. The volleyball game that follows drug administration takes two hours. The lab tests, scheduled for the day after the game, take 10 minutes. As a result, a subject spends the great majority of his/her time not interacting with or encountering medical personnel and is "not in visits" most of the time. This makes the description of a subject's progress awkward and produces sentences like "the subject is between Visit 4 and Visit 5".

CDISC has created a concept, and variable, called an "ELEMENT" to further describe subject progress. An ELEMENT is defined by two characteristics: 1) a period of time AND 2) what is happening to the subject at that time. An example of an element might be "first lab –scheduled for 9 Sept". ELEMENTs are *not* visits and can have different start and end points from visits. However, by CDISC definition, one element starts as another begins and subjects are *always* in an element. Since a subject is always in an element, the description of subject progress is made easier if one can use elements to describe progress.

There is freedom in defining the ELEMENT variable associated with a study. ELEMENTs and VISITs need not have the same start and end points. To make things very confusing, not only do the start and end points of visits and

elements not have to align, a visit does not have to be contained in one element. A visit can start in one element and end in another, if the investigator so defines.

Even worse than the confusion over element and visit timing, is the fact that in blinded studies elements cannot be used ***at all*** to describe subject progress. To know an element one must know two characteristics: the time period and the action taken. With blinded studies, it is usually impossible to know what is happening to the subject (treatment is blinded) during the treatment encounters. Without knowing the treatment being applied to the subject, one cannot know a subject's element at any point in time. Elements are associated with an arm and are of little use in blinded studies.

This inability to assign subjects to elements caused CDISC to create yet another way to describe a subject's progress, the EPOCH variable. An epoch is easy to confuse with an element but is a little less specific, than is an element, on what is happening to the subject. An epoch is similar to an element but is a characteristic of the trial as a whole (not of an arm) and therefore particularly useful in describing blinded studies.

A value for element might be: "Treatment # One - Drug B". Another value for element might be: "Treatment # Three - Drug A". EPOCH values for the same period might be "Trial Treatment One" and "Trial Treatment Three". The epoch simply says that the subject is getting his first treatment or her third treatment. The EPOCH variable does not specify what those treatments are. We see that elements are specific to a study arm and epochs are not tied to a study arm. Because the timing of elements and epochs usually coincide, elements and epochs are easy to confuse. Accordingly, CDISC suggests that EPOCH variables be named or valued with phrases starting with the word "Trial". A value for an ELEMENT might be "Lab 1" and the corresponding value of EPOCH might be "Trial Lab 1".

CDISC has decided that the sponsor should be very explicit in defining visits, elements, and epochs and that the information defining these terms should be included in very structured form in the submission. It was thought that the FDA reviewers and software developers would benefit from having the definitions in called Data Definition Document or DEFINE.XLS.

The order of the Data Definition Document worksheets (the group of Data Definition Document worksheets or tables) have been changed in the CDISC IG v3.1.2. The Subject Visit (SV) and Subject Elements (SE) tables were part of the Trial Design grouping of data in previous CDISC versions and are now considered to be part of the Special Purpose group of tables, with the Demography Domain.

Visits are defined in the Trial Visit table, shown in Figure 2. The investigator specifies "rules" for the start and end of the visit.

Elements are defined in the Trial Element table, shown in Figure 3. The investigator has specified start and end "rules" that are relative to previous study events and not relative to a study day. This has allowed the investigator to specify only "Lab and Game" and "Patch and Game" as values of ELEMENT, rather than "Patch and Game 1" and "Patch and Game 2".

Elements are used to define the "Study Arms" in a table called the "Trial Arms (TA) Table" shown in Figure 4 which includes the "Trial Arms" graphic, showing the use of elements and providing the opportunity to show a timing variable (TAEORD) that is not included in any other table. TAEORD is used to order the elements in the Trial Arm (TA) Table.

An arm is a planned sequence of elements. (what happens to a subject)

An arm is typically thought of as a treatment group

| | A | B | C | D | E | F | G | H | I | J |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Variable Name | STUDYID | DOMAIN | VISITNUM | VISIT | VISITDY | ARMCD | ARM | TVSTRL | TVENRL |
| 2 | Variable Label | Study Identifier | Domain Abbreviation | Visit Sequence Number | Visit Name | Planned Study Day of Visit | Arm Code (Treatment Code) | Description of Arm | Visit Start Rule | Visit End Rule |
| 3 | Type | Char | Char | Num | Char | Num | Char | Char | Char | Char |
| 4 | Controlled Terms or Format | | **TV | | | | | | | |
| 5 | Origin | CRF | Derived | CRF or Deived | CRF or Deived | CRF or Deived | Derived | Blank | Blank | Sponsor Definned / Protocol |
| 6 | Role | Identifier | Identifier | Identifier | **Topic** | Timing | Record Qualifier | Synonym Qualifier | Rule | Rule |
| 7 | Core | Req | Req | Req | Req | Perm | Exp | Perm | Perm | Perm |
| 8 | Note pages 19, 28, 90, 113, 114 | | | | | | 8 char max | | Rule describing when the Visit starts **(Should start, not does start p 113)**, in relation to the sequence of Elements,. Used only when Visits are dependent on occurrences within the study, not fixed by protocol. | Rule describing when the Visits ends, in relation to the sequence of Elements. Visit end rules may be expresses in terms of the start or end of an element, or relative to the start of the visit ( |
| 9 | | GV_VB_WL_4 | TV | 1 | Screen | -8 | PatchTab | Patch then Tab | Start of element | 1 hour post arrival |
| 10 | | GV_VB_WL_4 | TV | 2 | BASELINE & RANDOMIZE | -7 | PatchTab | Patch then Tab | 30 min pre end of Prev. elem. | 1 hour post arrival |
| 11 | | GV_VB_WL_4 | TV | 3 | TAB AND GAME | 1 | PatchTab | Patch then Tab | 1 week after start of prev elem | 2.5 hour post arrival |
| 12 | | GV_VB_WL_4 | TV | 4 | LAB | 2 | PatchTab | Patch then Tab | 1 day post start of Prev element | 1 hour post arrival |
| 13 | | GV_VB_WL_4 | TV | 5 | TAB AND GAME | 8 | PatchTab | Patch then Tab | 6 day post start of Prev element | 2.5 hour post arrival |
| 14 | | S=GV_VB_WL | TV | 6 | LAB | 9 | PatchTab | Patch then Tab | 1 day post start of Prev element | 1 hour post arrival |
| 15 | | GV_VB_WL_4 | TV | 7 | BASELINE2 | 15 | PatchTab | Patch then Tab | 6 day post start of Prev element | 1 hour post arrival |
| 16 | | GV_VB_WL_4 | TV | 8 | PATCH & GAME | 22 | PatchTab | Patch then Tab | 1 day post start of Prev element | 2.5 hour post arrival |
| 17 | | GV_VB_WL_4 | TV | 9 | LAB | 23 | PatchTab | Patch then Tab | 1 day post start of Prev element | 1 hour post arrival |
| 18 | | GV_VB_WL_4 | TV | 10 | PATCH & GAME | 29 | PatchTab | Patch then Tab | 6 day post start of Prev element | 2.5 hour post arrival |
| 19 | | GV_VB_WL_4 | TV | 11 | LAB | 30 | PatchTab | Patch then Tab | 1 day post start of Prev element | 1 hour post arrival |
| 20 | | GV_VB_WL_4 | TV | 12 | PSFU | 37 | PatchTab | Patch then Tab | 6 day post start of Prev element | 1 hour post arrival |
| 21 | | GV_VB_WL_4 | TV | 1 | Screen | -8 | TabPatch | Tab then Patch | Start of element | 1 hour post arrival |
| 22 | | GV_VB_WL_4 | TV | 2 | BASELINE & RANDOMIZE | -7 | TabPatch | Tab then Patch | 30 min pre end of Prev. elem. | 1 hour post arrival |
| 23 | | GV_VB_WL_4 | TV | 3 | PATCH & GAME | 1 | TabPatch | Tab then Patch | 1 week after start of prev elem | 2.5 hour post arrival |
| 24 | | GV_VB_WL_4 | TV | 4 | LAB | 2 | TabPatch | Tab then Patch | 1 day post start of Prev element | 1 hour post arrival |
| 25 | | GV_VB_WL_4 | TV | 5 | PATCH & GAME | 8 | TabPatch | Tab then Patch | 6 day post start of Prev element | 2.5 hour post arrival |
| 26 | | S=GV_VB_WL | TV | 6 | LAB | 9 | TabPatch | Tab then Patch | 1 day post start of Prev element | 1 hour post arrival |
| 27 | | GV_VB_WL_4 | TV | 7 | BASELINE2 | 15 | TabPatch | Tab then Patch | 6 day post start of Prev element | 1 hour post arrival |
| 28 | | GV_VB_WL_4 | TV | 8 | TAB AND GAME | 22 | TabPatch | Tab then Patch | 1 day post start of Prev element | 2.5 hour post arrival |
| 29 | | GV_VB_WL_4 | TV | 9 | LAB | 23 | TabPatch | Tab then Patch | 1 day post start of Prev element | 1 hour post arrival |
| 30 | | GV_VB_WL_4 | TV | 10 | TAB AND GAME | 29 | TabPatch | Tab then Patch | 6 day post start of Prev element | 2.5 hour post arrival |
| 31 | | GV_VB_WL_4 | TV | 11 | LAB | 30 | TabPatch | Tab then Patch | 1 day post start of Prev element | 1 hour post arrival |
| 32 | | GV_VB_WL_4 | TV | 12 | PSFU | 37 | TabPatch | Tab then Patch | 6 day post start of Prev element | 1 hour post arrival |

Figure 2

| | B | C | D | E | F | G |
|---|---|---|---|---|---|---|
| 1 | STUDYID | DOMAIN | ETCD | ELEMENT | TESTRL | TEENRL |
| 2 | Study Identifier | Domain Abbreviation | Element Code | Description of Element | Rule for Start of Element | Rule For End of Element |
| 3 | Char | Char | Char | Char | Char | Char |
| 4 | | **TE | | | | |
| 5 | CRF | Derived | Sponsor Defined | Sponsor Defined or Protocol | Sponsor Defined or Protocol | Sponsor Defined or Protocol |
| 6 | Identifier | Identifier | Record Qualifier | **TOPIC** | Rule | Rule |
| 7 | Req | Req | Req | Req | Req | Perm |
| 8 | | | 8 Char Max Abbrev | | | |
| 9 | | | 8 char name of ELEMENT. Used in transposing | TOPIC Variable for Element-- the name of the element | Expressed rule for beginning the element | Expressed rule for ending the element |
| 10 | GV_VB_WL_4 | TE | SCRN | Informed consent and screen | Inf Consent | Taking Baseline measurements |
| 11 | GV_VB_WL_4 | TE | B1R | Baseline 1: measurements & Randomizatic | Day After Inf Consent | First Dose (tab or patch) |
| 12 | GV_VB_WL_4 | TE | PTGM | Apply Patch - play game | Application of Patch | Lab test in Morning |
| 13 | GV_VB_WL_4 | TE | TBGM | Take Tablet - play game | Swallowing of Tab | Lab test in Morning |
| 14 | GV_VB_WL_4 | TE | LAB | Lab tests | Day after game | Next Dose (tab or patch) |
| 15 | GV_VB_WL_4 | TE | B2 | Baseline2: measurements | Measurement - 6 days after game2 | Next Dose (tab or patch) |
| 16 | GV_VB_WL_4 | TE | PSFU | PSFU | Arrival at P.I. Office | Leaving P.I. Office |
| 17 | | | | | | |

There are no breaks between elements.
The end of an element is the start of the next element.

An element is the basic building block of time (but not the smallest) and has:

A definition of the start of the element. The start of an element is usually the start of treatment.

A rule for ending the element. This is often the planned duration of the element.

Figure 3

An arm is a planned sequence of elements. (what happens to a subject)

An arm is typically thought of as a treatment group

| | B | C | D | E | F | G | H | I | J | K | L |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | STUDYID | DOMAIN | ARMCD | ARM | TAETORD | ETCD | ELEMENT | TABRANCH | TATRANS | EPOCH | |
| 2 | Study Identifier | Domain Abbreviation | Arm Code (Treatment Code)] | Description of Arm (Treatment Group) | Order of Element within Arm | Element Code | Description of Element | Branch | Transition Rule | Trial Epoch | |
| 3 | Char | Char | Char | Char | Num | Char | Char | Char | Char | Char | |
| 4 | | "TA | | | | | | | | | |
| 5 | CRF | Derived | Derived | Derived | Sponsor Defined | Sponsor Defined | Sponsor Defined or Protocol | Blank | Blank | Blank | |
| 6 | Identifier | Identifier | **Topic** | Synonym Qualifier | Identifier | Record Qualifier | Synonym Qualifier | Rule | Rule | Rule | |
| 7 | Req | Req | Req | Req | Perm | Perm | Perm | Exp | Exp | Perm | |
| 8 | | | If char max abbr. for ARM. Used for transposing. **If timing of visits for a trial does not depend on arm then ARMCD should be null** | If the timing of visits for a trial does not depend on which arm a subject is in, then Arm should be left blank. | Number that gives the order of the element within the arm | If char max name for element, used for transposing | Topic variable for an element | Condition subject met at a "branch" in the trial design at the end of this element. (e.g. randomized to Drug A) | If the trial design allows a subject to transition to an element other than the next element in sequence, then the condition for transitioning to those other elements and alternative Element sequences are specified in this rule | name of trial epoch with which the element of the arm is associated | |
| 9 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 1 | SCRN | Screen | | | TRIAL SCREEN | |
| 10 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 2 | B1R | BASELINE & RANDOMIZE | assign 2 Tab-Patch | | TRIAL BASELINE RANDOMIZE | |
| 11 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 3 | TBGM | TAB AND GAME | | If injured, go to element 12 | TRIAL GAME1 | |
| 12 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 4 | LAB | LAB | | | TRIAL LAB1 | |
| 13 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 5 | TBGM | TAB AND GAME | | If injured, go to element 12 | TRIAL GAME2 | |
| 14 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 6 | LAB | LAB | | | TRIAL LAB2 | |
| 15 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 7 | B2 | BASELINE2 | | | TRIAL BASELINE2 | |
| 16 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 8 | PTGM | PATCH & GAME | | If injured, go to element 12 | TRIAL GAME3 | |
| 17 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 9 | LAB | LAB | | | TRIAL LAB3 | |
| 18 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 10 | PTGM | PATCH & GAME | | If injured, go to element 12 | TRIAL GAME4 | |
| 19 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 11 | LAB | LAB | | | TRIAL LAB4 | |
| 20 | GV_VB_WL_4 | TA | TABPATCH | TAB-PATCH | 12 | PSFU | PSFU | | | TRIAL PSFU | |
| 21 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 1 | SCRN | SCREEN | | | TRIAL SCREEN | |
| 22 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 2 | B1R | BASELINE & RANDOMIZE | assign 2 Patch-Tab | | TRIAL BASELINE RANDOMIZE | |
| 23 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 3 | PTGM | PATCH & GAME | | If injured, go to element 12 | TRIAL GAME1 | |
| 24 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 4 | LAB | LAB | | | TRIAL LAB1 | |
| 25 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 5 | PTGM | PATCH & GAME | | If injured, go to element 12 | TRIAL GAME2 | |
| 26 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 6 | LAB | LAB | | | TRIAL LAB2 | |
| 27 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 7 | B2 | BASELINE2 | | | TRIAL BASELINE2 | |
| 28 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 8 | TBGM | TAB AND GAME | | If injured, go to element 12 | TRIAL GAME3 | |
| 29 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 9 | LAB | LAB | | | TRIAL LAB3 | |
| 30 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 10 | TBGM | TAB AND GAME | | If injured, go to element 12 | TRIAL GAME4 | |
| 31 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 11 | LAB | LAB | | | TRIAL LAB4 | |
| 32 | GV_VB_WL_4 | TA | PATCHTAB | PATCH-TAB | 12 | PSFU | PSFU | | | TRIAL PSFU | |
| 33 | | | | | | | | | | | |

Figure 4

The relationship between values of the EPOCH and ELEMENT variables can be seen in Figure 4.

The above “Trial Design (TD)” tables define how a study should be conducted. As we know it is a rare study in which all subjects follow the protocol exactly. A submission should also contain tables that describe the actual progress of subjects through a study. These tables are: Protocol Violations (PV), Subject Elements (SE), and Subject Visits (SV). A description of these tables is beyond the scope of this paper.

The time and date of events are recorded in the ISO 8601 format. This format can record times and duration at any desired level of precision. For a paper on the subject, please refer to “ISO 8601 – An International Standard for Date and Time Formats” by Shi Tao Yeh. It should be noted that the CDISC IG v3.1.2 has an expanded section that discusses the ISO 8601 standard.

We will only discuss ISO 8601 to a depth that allows us to understand the examples we will give. Figure 5 gives some examples of dates and durations in ISO 8601 format.

Information is recorded from left to right-- from large units of time to small. Unknown values in the middle of a value cannot be left blank, but unknown values on the far right hand side of the string may be left blank. Dates are recorded as a four digit year, then a dash, then a two digit, zero filled month, another dash, followed by a two digit, zero filled day.

If there is information on time to be recorded, a “T “is used to separate the date information from the time information. To the right of the “T” is a two digit zero filled hour that records 24-hour clock time, followed by a colon, then a two digit zero filled minute, followed by another colon, and a two zero filled digit second. Decimal seconds may also be recorded.

The separator between date units is a dash and between the time units is a colon.

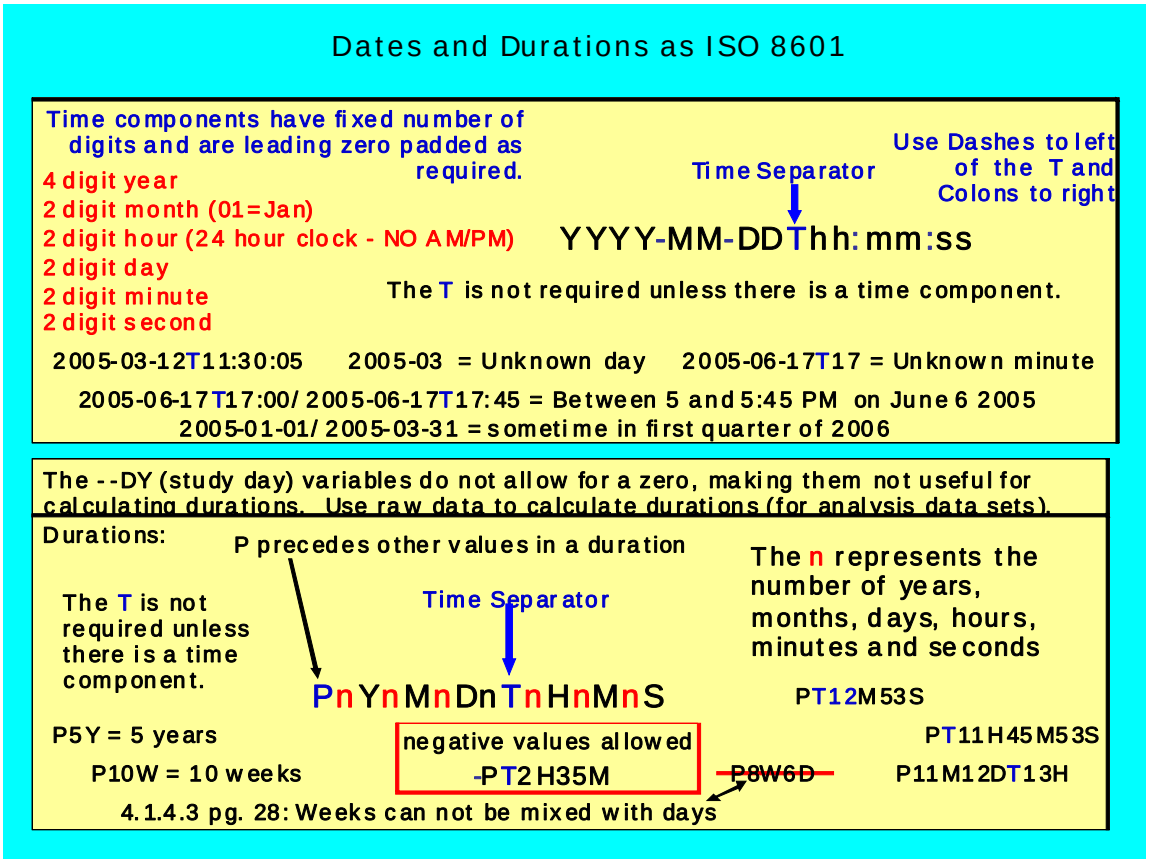


Figure 5

Figure 6 shows the relationship among some of the timing variables. We say that the information in Figure 6 is free-standing because it does not "tie in with" the data for the weight loss study shown in other figures. Also, it shows only a few of the timing variables. While these are flaws in the example, it allows us to show some of the timing variables in larger fonts as well as discuss the meaning and some special characteristics of the variables.

VISIT is character and is in human readable form. Visit names are defined in the protocol and should agree with the values in the trial tables. VISITNUM is numeric and allows for easy sorting of observations. Unplanned visits have fractional values in VISITNUM and values describing the occurrence in VISIT. VISITDY is the planned day of the visit and has values for planned visits but not for unplanned visits. Susan was called back to have tests repeated, causing an unplanned visit. LBDTC is the actual date-time of the visit in ISO 8601 format. LBDY is the actual "study day of the event" or the number of days since RFSTDTC in DM. In a well managed study, most of the visits will happen on the planned day. Unlike VISITDY, which is the planned day of the visit and can have missing values if the event is unplanned, LBDY is the actual day of the event and should always be valued.

In addition to being used to calculate study day values, RFSTDTC and RFENDTC are used to populate two variables: - -STRF and - -ENRF. These variables record whether an event occurred before, during, or after the subject was in the study. This before, during, and after study participation classification has been expanded in CDISC STDM IG v3.1.2. Two timing variables, - -STRTPT and - -ENRTPT, define new time points and the evaluation, before, during, concurrent, and after, are recorded in two variables, - -STTPT and - -ENTPT. These four variables have been added to allow the creation of new time points and the relating of data elements to these new points. These variables are not shown in any graphic.

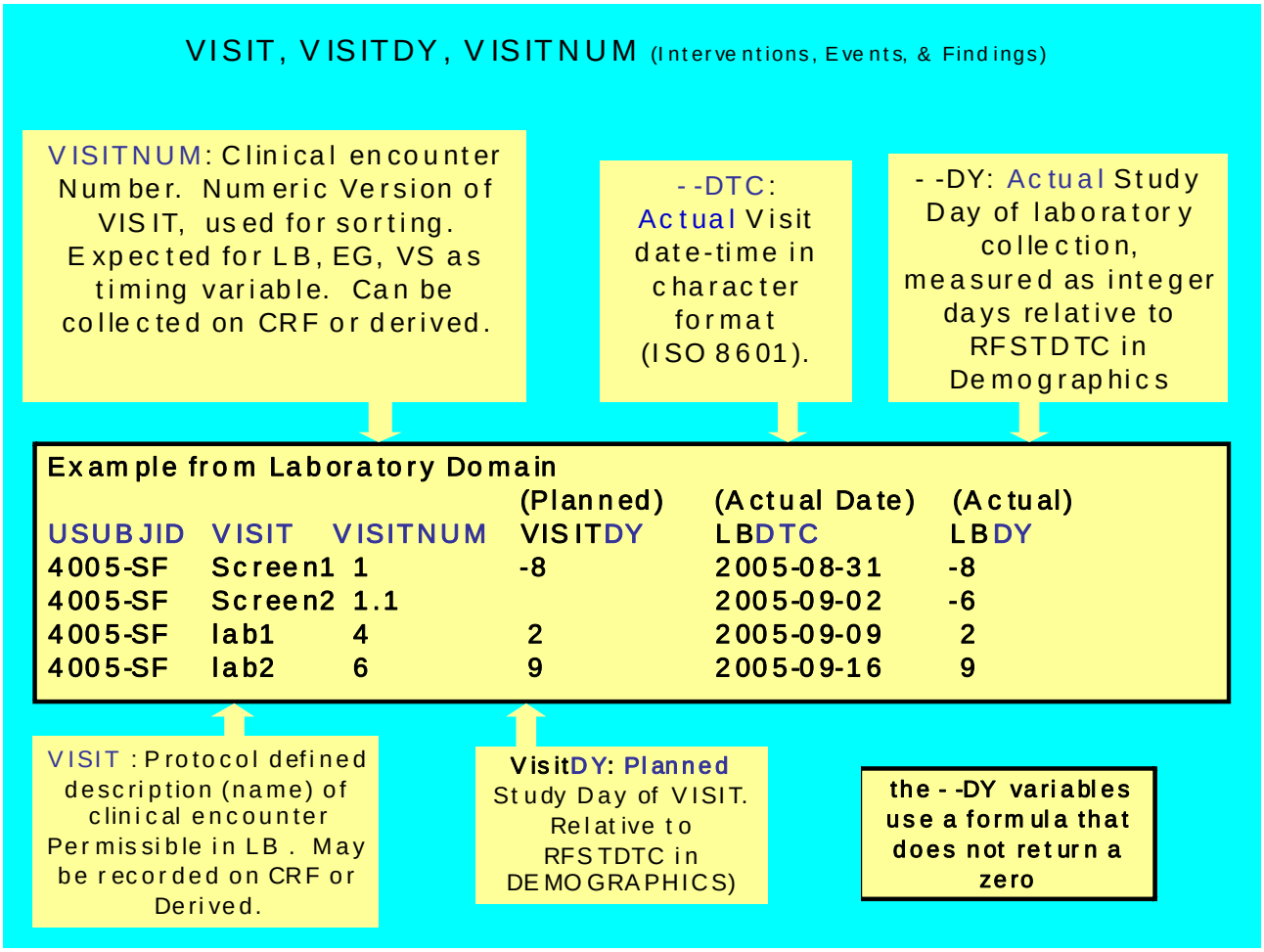


Figure 6

To support the final example and figure, we offer the following situation in the study. This example explores recording values for repeated events in the study described above. To collect an additional set of data points, the investigator asked two people to submit to additional lab tests. The investigator wanted a measure of how the stress of the volleyball game was reflected in lab tests and was able to persuade two players to be tested before, at half time and immediately after the end of the game. Results for one game (the first game played) are shown in the figure below.

The subjects were Susan and Russ.

--ELTM, --ENDTC, --TPT, --TPTNUM, --TPTREF (Interventions & Findings)

Example from Labs Domain where we measure a value before, during and after the first volleyball game. The game runs from 6PM (1800 hours) to 8PM(2000 hours).
Measure at 5PM (1700 hours), 7 PM (1900 hours) & 8PM (2000 hours).

Clin. Encounter

| | | Actual Study Day | Planned Study Day | Start of Specimen Collection | Date of Specimen Collection | End of Specimen Collection |
|---|---|---|---|---|---|---|
| USUBJID | VISIT | LBDY | VISITNUM | VISITDY | LBSTDTC | LBDTC | LBENDTC |
| 4005_SF | GLab1 | 1 | 3 | 1 | 2005-09-08T17 | 2005-09-08 | 2005-09-08T17:05 |
| 4005_SF | GLab1 | 1 | 3 | 1 | 2005-09-08T19 | 2005-09-08 | 2005-09-08T19:05 |
| 4005_SF | GLab1 | 1 | 3 | 1 | 2005-09-08T20 | 2005-09-08 | 2005-09-08T20:05 |
| 8007_RL | GLab1 | 1 | 3 | 1 | 2005-09-08T17:05 | 2005-09-08 | 2005-09-08T17:10 |
| 8007_RL | GLab1 | 1 | 3 | 1 | 2005-09-08T19:05 | 2005-09-08 | 2005-09-08T19:10 |
| 8007_RL | GLab1 | 1 | 3 | 1 | 2005-09-08T20:06 | 2005-09-08 | 2005-09-08T20:11 |

Character Sequencer

| | Numeric Sequencer | Reference Point | Elapsed Time | Optional Reference ID | Start rel. to Study | End rel. to Study | Duration | Result |
|---|---|---|---|---|---|---|---|---|
| LBTPT | LBTPTNUM | LBTPTREF | LBELTM | LBREFID | LBSTRF | LBENRF | LBDUR | LBORRES |
| PreGame | 1 | GameStart | -PT1H | Null | Null | Null | Null | 9.1 |
| MidGame | 2 | GameStart | PT1H | Null | Null | Null | Null | 6.3 |
| PostGame | 3 | GameStart | PT2H | Null | Null | Null | Null | 5.1 |
| PreGame | 1 | GameStart | -PT55M | Null | Null | Null | Null | 7.1 |
| MidGame | 2 | GameStart | PT1H5M | Null | Null | Null | Null | 7.0 |
| PostGame | 3 | GameStart | PT2H5M | Null | Null | Null | Null | 6.8 |

Figure 7

The visit was named Glab1 (G for Game– Lab1 for lab test collected during game 1). Since the VISIT had been defined as the whole experience of being dosed and playing the volleyball game, VISITNUM is valued as 3 for all three records. VISITDY is the same as the day of the first game. The Reference point for the - -DY calculation is the day of first dose. First dosing happens just before the first game, so this VISITDY has a value of 1 (zero is not allowed in any - -DY variables). LBSTDTC and LBENDTC record the start and end of dosing. LBDTC is the day of the test and should have a value when LBSTDTC and LBENDTC have values.

LBTPT is used to further identify the times for repeated events. LBTPT has human readable values and LBTPTNUM has numeric values that allow for easy sorting. Values of LBTPTNUM are allowed to repeat for different subjects as both Susan and Russ have values LBTPTNUM values =1.

LBTPTREF contains a value that is the reference point for elapsed time calculations. In this case we are recording the time of the test in reference to the start of the game. Since the first test happens before the start of the game, it has a negative elapsed time in LBELTM and a negative elapsed time is allowed by ISO 8601. The LBREFID could be used to establish a relationship between this observation and some external data source but is null in this case. It could be deleted from the data set, because it is not a required variable and is shown only to facilitate our discussion in the paper. LBSTRF and LBENRF should be null, or not included, because the actual start and end of the events were recorded in LBSTDTC and LBENDTC. LBDUR is null, because it is only has a value if it is recorded on the CRF. We offer as support of the fact LBDUR is not collected, the fact that LBSTDTC and LBENDTC are valued to allow duration to be calculated programmatically if needed for analysis data sets. The authors suggest that collecting start, end, *and* duration information will not improve the accuracy of the data, but will cause data validation errors when there is a difference between the recorded - -DUR value and the calculated duration value.

## SUMMARY

The timing variables in CDISC domains are both complex and interrelated. It is hoped that this treatment of these variables, as a group, is of use to the community.

## REFERENCES

Yeh, Shi-Tao, "ISO 8601 – An International Standard for Date and Time Formats", Proceedings of NESUG 2006 Conference, Coders Corner Paper 17, http://www.nesug.org/proceedings/nesug06/cc/cc17.pdf

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# Our Study

## A peek ahead

## Start with the end in mind

A study of a drug that, combined with exercise, helps people lose weight.

| | A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S | T |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | | | | **Trial Overview** | | **Great Valley Volleyball League: Exercise And Weightloss Study** | | | | | | **All data are ficticious** | | | | | | | | |
| 2 | | ISO 8601 date format is YYYY-MM-DD | | | This drug magically eliminates the effect of exercise on losing weight. It has a long term effect. | | | | | | | | | | | | | | | |
| 3 | **Epoch** | **Epochs are features of the whole trial and the naming convention is Trial XXX (see pg 106/159)** | | | **Trial Screen** | **Trial Randomize** | **Trial Game1** | | **Trial Lab1** | **Trial Game2** | | **Trial Lab2** | **Trial Baseline2** | **Trial Game 3** | | **Trial Lab3** | **Trial Game 4** | | **Trial Lab4** | **Trial PSFU** |
| 4 | **e of clinical encounter or VISIT** | | | | screen | BaseRand | Game1 | | lab1 | game2 | | lab2 | Base2 | Game3 | | lab3 | Game4 | | Lab4 | PSFU |
| 5 | **Visitnum -->** | **Clinical Encounter Number** | | | 1 | 2 | 3 | | 4 | 5 | | 6 | 7 | 8 | | 9 | 10 | | 11 | 12 |
| 6 | **AESTDY** | **Study DAY -->** | | | -8 | -7 | 1 | 1 | 2 | 8 | 8 | 9 | 15 | 22 | 22 | 23 | 29 | 29 | 30 | 37 |
| 7 | | | | **Element --->** | | **Baseline &** | **Patch &** | | | **Patch &** | | | | **Tab &** | | | **Tab &** | | | |
| 8 | | **ARM=Patch-Tab** | | **Element --->** | **Screen** | **Randomize** | **Game** | | **Lab** | **Game** | | **Lab** | **Baseline** | **Game** | | **Lab** | **Game** | | **Lab** | **PSFU** |
| 9 | | | | More interesting | 08/31/05 | 09/01/05 | 09/08/05 | 09/08/05 | 09/09/05 | 09/15/05 | 09/15/05 | 09/16/05 | 09/22/05 | 09/29/05 | 09/29/05 | 09/30/05 | 10/06/05 | 10/06/05 | 10/07/05 | 10/14/05 |
| 10 | Name | subjid and interesting situations concerning the subject | | situations concerning the subject | screen | and take baseline measurement | PatchTab _Game1 | PAH1 | Lab1 | PatchTab_Game2 | PAH2 | Lab2 | Break and **Baseline 2** | PatchTab_Game3 | PAH3 | Lab3 | PatchTab _Game 4 | PAH4 | Lab4 | PSFU |
| 11 | | **Element -->** | | | W0-Screen | W1-Rand_Base | PatchTab _G1 | | | W3 - PatchTab_G2 | | | | W4 - PatchTab_G3 | | | PatchTab _G4 | | | PatchTab _PSFU |
| 12 | Susan Fehrer | 1001 | 4005_SF | Linking Variable | | Patch -> Tablet | | No | a, 1 | | No | a, 1 | | | No | a, c, 1, 3 | | No | | |
| 13 | | Aspirin, No PAH, loses wt. | | ER visit | | | | | | | | | | | | | | | | |
| 14 | German 32 | jured when Russ falls on her | | Con Med | | | | | | | | | | | | | | | | |
| 15 | Erin O'Mally | 1002 | 8005_EO | AE | | Patch -> Tablet | | No | a, 1 | | No | a, 1, 5 | | | No | 1 | | No | | |
| 16 | | Aspirin , no PAH | | Can't go to PAH | | | | | | | | | | | | | | | | |
| 17 | Irish 29 | loses wt | | Jams Finger | | | | | | | | | | | | | | | | |
| 18 | Juan Carlos | 1003 | 8006_JC | Lab Units range | | Patch -> Tablet | | No | 1 | | YES | a, 1 | | | No | a,1 | | Yes | | |
| 19 | | Aspirin | | Con Med | | | | | | | | | | | | | | | | |
| 20 | Spanish 34 | lab units wrong | | AEs | | | | | | | | | | | | | | | | |
| 21 | | | | | | | | | | | | | | | | | | | | |
| 22 | **Name of clinical encounter** | | | | screen | BaseRand | Game1 | | lab1 | game2 | | lab2 | Base2 | Game3 | | lab3 | Game4 | | Lab4 | PSFU |
| 23 | **Visitnum -->** | **Clinical Encounter Number** | | | 1 | 2 | 3 | | 4 | 5 | | 6 | 7 | 8 | | 9 | 10 | | 11 | 12 |
| 24 | | | | **Element --->** | | **Baseline &** | **Tab &** | | | **Tab &** | | | | **Patch &** | | | **Patch &** | | | |
| 25 | | **ARM=Tab-Patch** | | **Element --->** | **Screen** | **Randomize** | **Game** | | **Lab** | **Game** | | **Lab** | **Baseline** | **Game** | | **Lab** | **Game** | | **Lab** | **PSFU** |
| 26 | | **Element -->** | | | W0-Screen | W1-Rand_Base | W2 - TabPatch _G1 | | | W3 - TabPatch_G2 | | | | W4 - TabPatch_G3 | | | W5 - TabPatch _G4 | | | W6 - TabPatch _PSFU |
| 27 | Russ Lavery | 1004 | 8007_RL | Lab test progress | | Tablet -> Patch | | YES | a, 1, 7 | | YES | a, 1, 7 | | 4 | YES | a, 1, 4, 7, 9 | | YES | a, 1, 9 | |
| 28 | | Drinks too much, Aspirin | | Delayed test | | | | | | | | | | | | refuses labs | | | | |
| 29 | Cauc 58 | Falls on Susan, injures self | | lab test range | | | | | | | | | | | | | | | | |
| 30 | Vijay Bhaskar | 1005 | 2001_VB | Indian | | Tablet -> Patch | | No | 1 | 2 | No | | | 1 | YES | | | YES | | |
| 31 | | Misses game, business trip | | Missing test | | | | | | | Business Trip | | | | | | | | | |
| 32 | Indian 27 | | | Missed Treatment | | | | | | | | | | | | | | | | |
| 33 | Ersen Tulin | 1006 | 8008_ET | | | Tablet -> Patch | | YES | | | No | | | | No | | | YES | | |
| 34 | | Aspirin | | | | | | | | | | | | | | | | | | |
| 35 | Turkish 35 | | | | | | | | | | | | | | | | | | | |