Understanding Timing Variables: Basic and Applications in SDTM

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Meet the Speaker

Junseok Park

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Junseok Park’s professional journey spans over 15 years, encompassing diverse therapeutic areas across all phases of clinical trials.

Junseok Park serves as the Team Manager for Data Management at CMIC Korea with expertise in managing clinical data and databases.

He holds certifications as a Certified Clinical Data Manager and CDISC Tabulate, along with being a Certified Advanced Programmer for SAS9, specializing in SDTM work.

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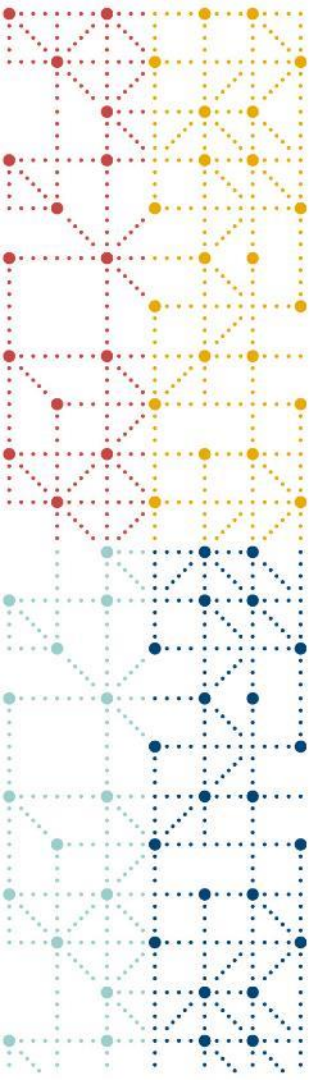
- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

Agenda

1. Model Fundamentals
2. Timing Variable in SDTM/SDTMIG
3. Conclusion



Model Fundamentals

- Observations and Variables
- Roles of Variable
- General Observation Class

Fundamentals of the SDTM

Observations and Variables

Variable = column, field

STUDYID	DOMAIN	USUBJID	BRTHDTC	AGE	SEX	RACE
CDISC-KR	DM	CDISC-KR-01-001	1960-01-01	64	M	ASIAN
CDISC-KR	DM	CDISC-KR-01-002	1970-01-10	54	F	ASIAN
CDISC-KR	DM	CDISC-KR-01-003	1980-01-31	44	M	ASIAN

Domain: defined as a collection of logically related observations with a common topic.

Observation: can be described by a series of variables, corresponding to a row in a dataset. (= row, record)

Fundamentals of the SDTM

Roles of Variable in SDTM

- **Identifier** : such as those that identify the study, subject, domain, and sequence number of the record
- **Topic** : which specify the focus of the observation (such as the name of a lab test)
- **Timing** : which describe the timing of the observation (such as start date and end date)
- **Qualifier** : which include additional illustrative text or numeric values that describe the results or additional traits of the observation (such as units or descriptive adjectives)
- **Rule** : which express an algorithm or executable method to define start, end, and branching or looping conditions in the Trial Design model

Fundamentals of the SDTM

General Observation Class

- **Intervention class** : captures investigational, therapeutic, and other treatments that are administered to the subject
  - E.g. Concomitant/Prior Medications, Exposure, etc.

- **Events class** : captures planned protocol milestones and incidents independent of planned study
  - E.g. Disposition, Adverse Events, Medical History, etc.

- **Findings class** :captures the observations resulting from planned evaluations
  - E.g. Laboratory Test Results, Vital Signs, etc.

Timing Variable in SDTM/SDTMIG

- Formats for Date/Time Variables
- Date/Time Precision
- Intervals of Time and Use of Duration for --DUR Variables
- Use of the "Study Day" Variables
- Use of Relative Timing Variables
- All Observation Classes-Timing Variables in SDTM
- Others

Timing Variable in SDTM/SDTMIG

CO – Assumptions

1. The Comments special purpose domain provides a solution for submitting free-text comments related to data in one or more SDTM domains (as described in Section 8.5, Relating Comments to a Parent Domain) or collected on a separate CRF page dedicated to comments. Comments are generally not responses to specific questions; instead, comments usually consist of voluntary, free-text or unsolicited observations.
2. The CO dataset accommodates three sources of comments:
   a. Those unrelated to a specific domain or parent record(s), in which case the values of the variables RDOMAIN, IDVAR, and IDVARVAL are null. CODTC should be populated if captured. See example, Row 1.
   b. Those related to a domain but not to specific parent record(s), in which case the value of the variable RDOMAIN is set to the DOMAIN code of the parent domain and the variables IDVAR and IDVARVAL are null. CODTC should be populated if captured. See example, Row 2.
   c. Those related to a specific parent record or group of parent records, in which case the value of the variable RDOMAIN is set to the DOMAIN code of the parent record(s) and the variables IDVAR and IDVARVAL are populated with the key variable name and value of the parent record(s). Assumptions for populating IDVAR and IDVARVAL are further described in Section 8.5, Relating Comments to a Parent Domain. CODTC should be null because the timing of the parent record(s) is inherited by the comment record. See example, Rows 3-5.
3. When the comment text is longer than 200 characters, the first 200 characters of the comment will be in COVAL, the next 200 in COVAL1, and additional text stored as needed to COVALn. See example, Rows 3-4.

   Additional information about how to relate comments to parent SDTM records is provided in Section 8.5, Relating Comments to a Parent Domain.
4. The variable COREF may be null unless it is used to identify the source of the comment. See example, Rows 1 and 5.
5. Any Identifier variables and Timing variables may be added to the CO domain, but the following qualifiers would generally not be used in CO: --GRPID, --REFID, --SPID, VISIT, VISITNUM, VISITDY, TAETORD, --TPT, --TPTNUM, --ELTM, --TPTREF, --RFTDTC.

sufficient precision to permit assignment of an observation to an EPOCH on the basis of date/time data alone. If it is not possible to determine theEPOCH of an observation, then EPOCH should be null. Methods for assigning EPOCH values can be described in the Define-XML document.

Since EPOCH is a study-design construct, it is not applicable to Interventions or Events that started before the subject's participation in the study, nor to Findings performed before their participation in the study. For such records, EPOCH should be null. Note that a subject's participation in a study includes screening, which generally occurs before the reference start date, RFSTDTC, in the DM domain.

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	Observation		8601	
--ENDTC	End Date/Time of Observation	Char	ISO 8601	End date/time of the observation.
--DY	Study Day of Visit/Collection/Exam	Num		Actual study day of visit/collection/exam expressed in integer days relative to the sponsor-defined RFSTDTC in Demographics.

Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Formats for Date/Time Variables

- **Format**
  - International Standards Organization(ISO) 8601
  - YYYY-MM-DDThh:mm:ss(.n+)?(((+|-)hh:mm)|Z)?

    Time Designator
  - Others
    - [-] (hyphen): to separate the time Elements "year" from "month" and "month" from "day" and to represent missing date components.
    - [:] (colon): to separate the time Elements "hour" from "minute" and "minute" from "second"
    - [/] (solidus): to separate components in the representation of date/time intervals
    - [P] (duration designator): precedes the components that represent the duration

Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Date/Time Precision

- **Precision**: referred to by ISO 8601 as "completeness" or "representations with reduced accuracy"

Right Truncation

Collected (CDASH)	Precision	ISO 8601 Date/Time
15-Dec-2003, 13:14:17	-	2003-12-15T13:14:17
15-Dec-2003, 13:14	Unknown seconds	2003-12-15T13:14
15-Dec-2003	Unknown time	2003-12-15
Dec-2003	Unknown day, time	2003-12
2003	Unknown month, day, time	2003

Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Date/Time Precision

- **Precision**: referred to by ISO 8601 as "completeness" or "representations with reduced accuracy"

Clinical Data Acquisition Standards Harmonization

Hypen

Collected (CDASH)	Level of Uncertainty	ISO 8601 Date/Time
15-Dec-2003, 13:15:17	-	2003-12-15T13:15:17
15-Dec-2003, ??:15	Unknown hour with known minutes	2003-12-15T-:15
15-Dec-????	Unknown year with known month and day	---12-15
??-???-????. 7:15	Unknown date with known hour and minute	-----T07:15

Timing Variable in SDTM/SDTMIG

- Why You Need Both(CDISC Articles)
  - **SDTM**: Machine-readable: Dates/Times: ISO 8601, 1 variable, YYYY-MM-DDThh:mm:ss Duration: P1M3D
  - **CDASH**: Human-readable: Dates/Times: 2 or more variables, DD- MMM-YYYY, HH:MM:SS Duration: 1 month, 3 days

  - Rationale: SDTM machine-readable formats for variables, such as dates, are good for data reusability, but are not user-friendly for data capture. There is more chance for error when people record data in unfamiliar formats.

Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Intervals of Time and Use of Duration for --DUR Variables

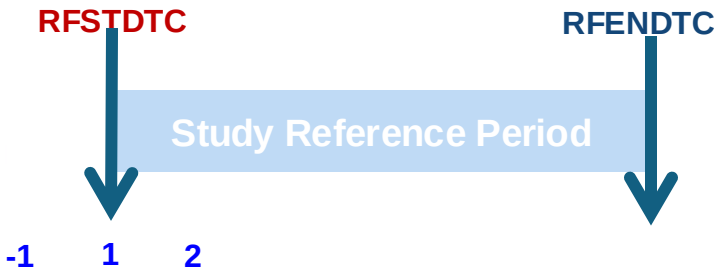
- **Intervals**
  - YYYY-MM-DDThh:mm:ss/YYYY-MM-DDThh:mm:ss
- **Duration**
  - PnYnMnDTnHnMnS
  - If both --STDTC and --ENDTC are collected, durations can be calculated by the difference in these two values, and need not be in the submission dataset

Duration as originally recorded	ISO 8601 Duration
14 Days 7 Hours 57 Minutes	P14DT7H57M
5 Days 12¼ Hours	P5DT12.25H

Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Use of the "Study Day" Variables

- **Study Day**
  - describe the relative day of the observation starting with the reference date as Day 1.
  - determined by comparing the date/time variables (--DTC, --STDTC, and --ENDTC) to the Subject Reference Start Date (RFSTDTC from the Demographics domain).
  - --DY = (date portion of --DTC) - (date portion of RFSTDTC) + 1 if --DTC is on or after RFSTDTC
  - --DY = (date portion of --DTC) - (date portion of RFSTDTC) if --DTC precedes RFSTDTC



RFSTDTC: 2005-10-13

AE dataset

AETERM	AESTDTC	AEENDTC	AESTDY	AEENDY
HEADACHE	2005-10-13	2005-10-13	1	1
Back pain	2005-10-21		9	

Timing Variable in SDTM/SDTMIG

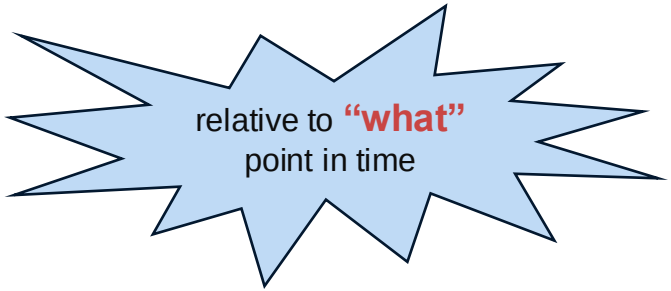
Actual and Relative Time Assumptions-Use of Relative Timing Variables

- **Relative Timing Variables**

STUDY	SITE	SUBJECT

Medical History	
Were any medical conditions or events reported?	○ Yes ○ No
Date of Collection	

No.	Medical condition/diagnosis	Start date	Ongoing	End date
1.			○ Yes ○ No	

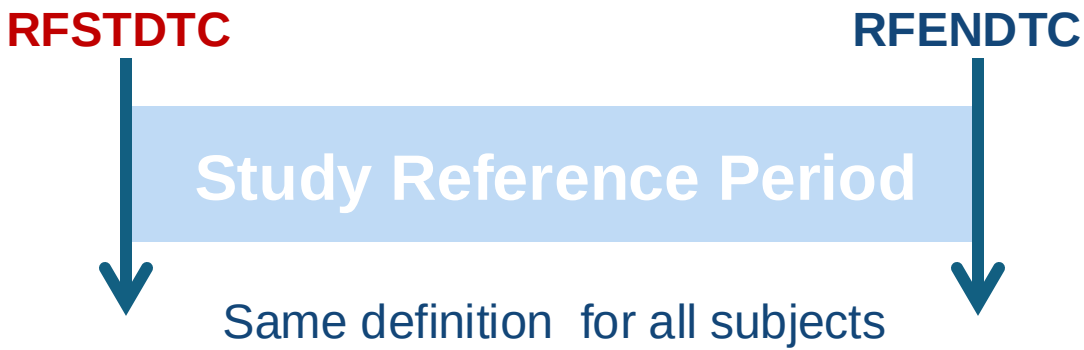


Adverse Event				
Were any adverse events experienced?			○ Yes	○ No
No.	Adverse event	Start date	End date	Ongoing
1.				○ Yes ○ No

Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Use of Relative Timing Variables

- **Relative Timing Variables**
  - **Study Reference Period**
    - Continuous period of time defined by from RFSTDTC to RFENDTC, for each subject in the DM dataset.
    - --STRF is used to identify the start of an observation relative to the sponsor-defined Study Reference Period.
    - --ENRF is used to identify the end of an observation relative to the sponsor-defined Study Reference Period.



Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Use of Relative Timing Variables

- **Example I**

Adverse Event				
Were any adverse events experienced?			● Yes ○ No	
No.	Adverse event	Start date	End date	Ongoing
1.	Headache	01-Sep-2023		● Yes ○ No

AE dataset

AETERM	AESTDTC	AEENDTC	AEENRF
Headache	2023-09-01		AFTER

Means that the event **did not end** before or during the Study Reference Period.

Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Use of Relative Timing Variables

- **Relative Timing Variables**
  - **Reference Time Point**
    - --STRTPT is used to identify the start of an observation relative to the sponsor-defined Reference Time Point.
    - --STTPT: sponsor-defined Reference Time Point

    - --ENRTPT is used to identify the end of an observation relative to the sponsor-defined Reference Time Point.
    - --ENTPT: sponsor-defined Reference Time Point

Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Use of Relative Timing Variables

- **Example II**

STUDY	SITE	SUBJECT
CDISC-KR	01	001
Medical History		
Were any medical conditions or events reported?	● Yes ○ No	
Date of Collection	01-Dec-2023	

No.	Medical condition/diagnosis	Start date	Ongoing	End date
1.	Headache	01-Sep-2023	● Yes ○ No	

MH dataset

MHTERM	MHDTC	MHSTDTC	MHENRTPT	MHENTPT
Headache	2023-12-01	2023-09-01	ONGOING	2023-12-01

Timing Variable in SDTM/SDTMIG

Actual and Relative Time Assumptions-Use of Relative Timing Variables

- **Terminology**

Code	Codelist Code	Codelist Extensible (Yes/No)	Codelist Name	CDISC Submission Value	CDISC Synonym(s)
C66728		No	Relation to Reference Period	STENRF	Relation to Reference Period
C38008	C66728		Relation to Reference Period	AFTER	
C25629	C66728		Relation to Reference Period	BEFORE	
C184710	C66728		Relation to Reference Period	BEFORE/DURING	
C25456	C66728		Relation to Reference Period	COINCIDENT	
C25490	C66728		Relation to Reference Period	DURING	
C49640	C66728		Relation to Reference Period	DURING/AFTER	
C53279	C66728		Relation to Reference Period	ONGOING	Continuous
C17998	C66728		Relation to Reference Period	UNKNOWN	U; UNK; Unknown

--STRF/--ENRF (Study Reference Period)	**--STRTPT/--ENRTPT** (Reference Time Point)	**Notes**
BEFORE		
DURING	X	interval of time rather than a point in time
DURING/AFTER	X	interval of time rather than a point in time
AFTER		
UNKNOWN		
X	**COINCIDENT**	relative to a point in time rather than an interval of time
X	**ONGOING**	relative to a point in time rather than an interval of time

Timing Variable in SDTM/SDTMIG

All Observation Classes-Timing Variables

Variable Name	Variable Label	Type	Format	Description
--DTC	Date/Time of Collection	Char	ISO 8601	**Collection** date and time of an observation.
--STDTC	Start Date/Time of Observation	Char	ISO 8601	**Start** date/time of an observation.
--ENDTC	End Date/Time of Observation	Char	ISO 8601	**End** date/time of the observation.
--DY	Study Day of Visit/Collection/Exam	Num		**Actual study day** of visit/collection/exam expressed in integer days relative to the sponsor-defined RFSTDTC in Demographics.
--STDY	Study Day of Start of Observation	Num		**Actual study day** of start of observation expressed in integer days relative to the sponsor-defined RFSTDTC in Demographics.
--ENDY	Study Day of End of Observation	Num		**Actual study day** of end of observation expressed in integer days relative to the sponsor-defined RFSTDTC in Demographics.

Timing Variable in SDTM/SDTMIG

All Observation Classes-Timing Variables

Variable Name	Variable Label	Type	Format	Description
--STRF	Start Relative to Reference Period	Char		Identifies the **start** of the observation as being before, during, or after the **sponsor-defined reference period**. The sponsor-defined reference period is a continuous period of time defined by a discrete starting point and a discrete ending point represented by RFSTDTC and RFENDTC in Demographics.
--ENRF	End Relative to Reference Period	Char		Identifies the **end** of the observation as being before, during or after the **sponsor-defined reference period**. The sponsor-defined reference period is a continuous period of time defined by a discrete starting point and a discrete ending point represented by RFSTDTC and RFENDTC in Demographics.
--STRTPT	Start Relative to Reference Time Point	Char		Identifies the **start** of the observation as being before or after the **sponsor-defined reference time point** defined by variable --STTPT.
--STTPT	Start Reference Time Point	Char		Description or date/time in ISO 8601 or other character format of the **sponsor-defined reference point** referred to by --STRTPT. Examples: **"2003-12-15" or "VISIT 1"**.
--ENRTPT	End Relative to Reference Time Point	Char		Identifies the end of the observation as being before or after the **sponsor-defined reference time point** defined by variable --ENTPT.
--ENTPT	End Reference Time Point	Char		Description or date/time in ISO 8601 or other character format of the **sponsor-defined reference point** referred to by --ENRTPT. Examples: **"2003-12-25" or "VISIT 2".**

Timing Variable in SDTM/SDTMIG

- **Others- Actual and Relative Time Assumptions-Date and Time Reported in a Domain Based on Findings**

Collection Type	--DTC	--STDTC	--ENDTC
Single-Point Collection	O	✖	
Interval Collection	O		O

- **Others- Reference(SDTM and SDTMIG Conformance Rules)**

Rule ID	Class	Domain	Variable	Rule
CG0236	FND	ALL	--DTC	--DTC is date/time of specimen collection or observation, not date/time of recording/acquisition
CG0237	EVT, INT	ALL	--DTC	--DTC is date/time of recording/data acquisition

Timing Variable in SDTM/SDTMIG

- **Others- Domain Assumptions**

CO – Assumptions

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   Additional information about how to relate comments to parent SDTM records is provided in Section 8.5, Relating Comments to a Parent Domain.
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Conclusion

Conclusion

- Timing variables (SDTM Table 2.2.5) are an essential component of all SDTM subject-level domain datasets.

- All domains based on the three general observation classes should have at least one Timing variable.

- Timing variables are available for use in any domain based on one of the 3 general observation classes, except where restricted in the assumptions for the standard domain models in the implementation guides

Thank You!