

How to Create Variables Related to Age

Joyce Gui and Shaoan Yu
Merck & Company, Rahway, NJ

ABSTRACT

A derived variable not explicitly included in a domain model is permissible to be used in the supplemental qualifiers (SUPPQUAL) for that domain for clinical data submission to FDA per the CDISC V3.1 Submission Data Standards Implementation Guide. However, one critical problem is the efficient creation of a consistent set of Study Data Tabulation Model (SDTM)-derived data that support the analysis of the safety or efficacy of the product. This paper will discuss how to define and derive the variable age at event start to meet the CDISC standards. To illustrate some of the derivations, business logic and SAS® code will be provided.

Introduction

SDTM applies to all data across all phases of clinical trial development and generally refers to "collected" data. Some variables, such as the age of the subject when the trial begins (Age at Subject Reference Start Date/Time) and the age of the subject when an AE begins (Age at AE Start), are not explicitly mentioned in a domain but support the data analysis. These variables can be considered to be included in SUPPQUAL for submission.

This paper will provide a comprehensive approach to create the age at event start variable along with the business logic and the SAS code.

The common rule is for all age results to be rounded-down to the nearest integer. The time, if collected, will not be used in the calculation.

1. Age at Subject Reference Start Date/Time (AGE, AGEU)

The Age at Subject Reference Start Date/Time (AGE) can be defined as the actual difference between the Subject Reference Start Date/Time (DM.RFSTDTC) and Date of Birth (DM.BRTHDTC). The unit of the AGE (AGEU) can be DAYS, WEEKS, MONTHS, or YEARS based on the nature of the trials. It is either specified by the sponsor or derived based on a defined rule. If the DM.BRTHDTC is null, AGE and AGEU cannot be derived. If DM.RFSTDTC is null, the first Visit Date (SV.SVSTDTC) will be used in place of the Subject Reference Start Date/Time.

The rules for deriving AGEU when it is not specified are:

- a. When Actual Calendar Days from Date of Birth to Event Start Date is less than 7, AGEU will be DAYS;

- b. When Actual Calendar Days from Date of Birth to Event Start Date is greater than or equal to 7 and Actual Calendar Months from Date of Birth to Event Start Date is less than 2, AGEU will be WEEKS;
- c. When Actual Calendar Months from Date of Birth to Event Start Date is greater than or equal to 2 but less than or equal to 23, AGEU will be MONTHS;
- d. When Actual Calendar Months from Date of Birth to Event Start Date is greater than 23, AGEU will be YEARS.

2. Age at AE Start (AEAGE, AEAGEU)

The Age at AE start can be defined as the actual difference between AE Start Date (AE.AESTDTC) and Date of Birth (DM.BRTHDTC). AEAGEU will be AGEU if it is specified; Otherwise AEAGEU will be derived based on the rules defined for AGEU in part 1 Age at Subject Reference Start Date/Time.

The business logic:

Assume that the Date of Birth (DM.BRTHDTC) and AE Start Date (AE.AESTDTC) are not null.

- a. When AGEU = DAYS, AEAGE will be the Actual Calendar Days from Date of Birth to AE Start Date. i.e., $AEAGE = AESTDTC - BRTHDTC$.
- b. When AGEU = WEEKS, AEAGE will be the Actual Calendar Days from Date of Birth to AE Start Date / 7. i.e., $AEAGE = (AESTDTC - BRTHDTC) / 7$.
- c. When AGEU = MONTHS, AEAGE will be the Actual Calendar Months from Date of Birth to AE Start Date. i.e., Months between Date of Birth and AE Start Date.
- d. When AGEU = YEARS, AEAGE will be the Actual Calendar Years from Date of Birth to AE Start Date.

Input Data:

Date of Birth (DM.BRTHDTC), AE Start Date (AE.AESTDTC), Age Unit (AGEU)

Derivation Steps:

- a. Convert the ISO 8601 format BRTHDTC and AESTDTC to numeric format-Macro %DTCtoDTN will facilitate this conversion.
- b. Find days, months, years between BRTHDTC and AESTDTC-Macro %actdif will facilitate this conversion.
- c. Derive AEAGE and AEAGEU based on the rules.

When calculating the difference in years between two dates, the traditional method is to use (event end date – event start date)/365.25; use floor function to return the largest integer that is less than or equal to the difference between the two dates. In most cases, this works fine, but when the two dates have the same month and day, a discrepancy occurs. For example, if BIRTHDTC=1937-04-03, AESTDTC=2007-04-03, the floor (AESTDTC-BIRTHDTC)/365.25) will return a value of 69, but the actual age at AE start

is 70. Therefore, the YRDIF function will be used in deriving the Age at event start to avoid a discrepancy.

Sample Code:

Input Dataset ONE:

BRTHDTC	AESTDTC	AGEU
(Date/Time of Birth)	(Start Date/Time of Adverse Event)	(Age Units)
1976-12-20	2007-12-20	YEARS
1966-09-06	2007-12-14	YEARS
2007-01-15	2007-12-15	MONTHS
2007-01-15	2008-01-23	WEEKS
1956-06-20	2008-02-15	
2007-08-01	2007-08-26	DAYS
1951-11-15	2007-08-26	
1951-11-15	2007-11-13	YEARS
1978-12-26	2007-12-26	YEARS
1972-09-11	2007-09-06	

```

data two;
  set one;
  %DTCToDTN(BRTHDTC);
  %DTCToDTN(AESTDTC);
  %actdif(AESTDTN, BRTHDTN);
run;

data aeage;
  set two;

  if not missing(AESTDTN) and not missing(BRTHDTN)
    then do;
    ***deriving AEAGE, AEAGEU based on the business logic defined in 2.***;
    .....
  end;
run;

```

Output Dataset:

BRTHDTC	AESTDTC	AGEU	AEAGE	AEAGEU
(Date/Time of Birth)	(Start Date/Time of Adverse Event)	(Age Units)	(Age at AE Start)	(Age Unit at AE Start)
1976-12-20	2007-12-20	YEARS	30	YEARS
1966-09-06	2007-12-14	YEARS	41	YEARS
2007-01-15	2007-12-15	MONTHS	11	MONTHS
2007-01-15	2008-01-23	WEEKS	53	WEEKS
1956-06-20	2008-02-15		51	YEARS
2007-08-01	2007-08-26	DAYS	25	DAYS
1951-11-15	2007-08-26		55	YEARS
1951-11-15	2007-11-13	YEARS	55	YEARS
1978-12-26	2007-12-26	YEARS	29	YEARS
1972-09-11	2007-09-06		34	YEARS

Macros Used in Sample Code:

I. %DTCToDTN(dtcvar)

```
%macro DTCToDTN(dtcvar);  
    SASdate = input(&dtcvar, is8601da.);  
    format SASdate is8601da.;  
%mend DTCToDTN;
```

This macro converts the complete character date in ISO 8601 format to SAS numeric date format. Parameter dtcvar can be any character date in ISO 8601 format (i.e. AESTDTC, BRTHDTC, EXSTDTC, etc.)

II. %ACTDIF (edate, sdate)

This macro is to be used to calculate the actual calendar day, month, and year difference between the event start date and the event end date.

Parameter sdate is the event start date and edate is the event end date; both dates should be in numeric format.

```
%macro actdif(edate, sdate);  
***Calculate actual calendar days between two dates***;  
    • use datdif function to calculate calendar days between  
      event start date and end date  
  
***Calculate actual calendar months between two dates***;  
    • use day, year and month functions to calculate whole and  
      partial months between event start and end dates. Sum the  
      total from the whole and partial months.  
  
***Calculate actual calendar years between two dates***;  
    • use yrdif and floor functions to calculate calendar years  
      between event start and end  
%mend actdif;
```

Conclusion

There are many ways to create variables. This paper presents a comprehensive way to create variables that are related to Age. It is important to define clear and consistent business logic that can be applied across different studies for future adaptation as a business standard throughout the pharmaceutical industry.

References

Merck & Co., Clinical Data Repository Standards Business Rules/Database Derivations version 4.2

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Contact Information

Your comments and questions are valued and encouraged. Please contact the authors at:

Joyce Gui
Merck & Co
RY34-A320
216 E. Lincoln Ave
Rahway, New Jersey 07065
Phone: 732-594-2139
Email: joyce_gui@merck.com

Shaoan Yu
Merck & Co
RY34-A320
216 E. Lincoln Ave
Rahway, New Jersey 07065
Phone: 732-594-0865
Email: shaoan_yu@merck.com