

# **Implementation of Imputation Rules and Creating Analysis Flags Following CDISC Guidelines**

Venkata N Madhira  
Sr. Statistical Programmer  
Consultant at Shionogi Inc, NJ, USA

**PhUSE US Connect 2019**

# Topics

- Imputation rules (generic) for Partial adverse events start and end dates.
- Flag for first occurrence of an event in a row of consecutive occurrences.
- Conditional Imputations for missing analysis value.
- Pick the first response from sustained response (until end of the study).

# Imputation rules (generic) for Partial adverse events start and end date.

|    | SUBJID | AETERM | AESTDTC    | AEENDTC    | TRTSDT    | ASTDT     | ASTDTF | AENDT     | AENDTF |
|----|--------|--------|------------|------------|-----------|-----------|--------|-----------|--------|
| 1  | 001    | Nausea | 2018-02-16 | 2018-02-16 | 15FEB2018 | 16FEB2018 |        | 16FEB2018 |        |
| 2  | 001    | cough  | 2018-02    | 2018-02-20 | 15FEB2018 | 15FEB2018 | D      | 20FEB2018 |        |
| 3  | 001    | Nausea | 2018-02-21 | 2018-02-22 | 15FEB2018 | 21FEB2018 |        | 22FEB2018 |        |
| 4  | 001    | Nausea | 2018-02-21 | 2018-02    | 15FEB2018 | 21FEB2018 |        | 28FEB2018 | D      |
| 5  | 001    | fever  | 2018-02-25 | 2018-02-26 | 15FEB2018 | 25FEB2018 |        | 26FEB2018 |        |
| 6  | 001    | fever  | 2018-03-14 | 2018-03-16 | 15FEB2018 | 14MAR2018 |        | 16MAR2018 |        |
| 7  | 001    | cough  | 2018-03    | 2018-04-03 | 15FEB2018 | 01MAR2018 | D      | 03APR2018 |        |
| 8  | 001    | ache   | 2018       | 2018-03-05 | 15FEB2018 | 15FEB2018 | M      | 05MAR2018 |        |
| 9  | 001    | ache   | 2018       | 2018-02-15 | 15FEB2018 | 15FEB2018 | M      | 15FEB2018 |        |
| 10 | 002    | ache   | 2018-03    | 2018-03-15 | 12MAR2018 | 12MAR2018 | D      | 15MAR2018 |        |
| 11 | 002    | ache   | 2018-03-17 | 2018-03    | 12MAR2018 | 17MAR2018 |        | 31MAR2018 | D      |
| 12 | 002    | ache   | 2018-10-15 | 2019-02    | 12MAR2018 | 15OCT2018 |        | 28FEB2019 | D      |
| 13 | 002    | fever  | 2018-03-30 | 2018-04    | 12MAR2018 | 30MAR2018 |        | 30APR2018 | D      |
| 14 | 002    | fever  | 2018-05-20 | 2018       | 12MAR2018 | 20MAY2018 |        | 31DEC2018 | M      |
| 15 | 002    | cough  | 2018-03    | 2018       | 12MAR2018 | 12MAR2018 | D      | 31DEC2018 | M      |
| 16 | 003    | fever  | 2018-04    | 2018-04    | 11APR2018 | 11APR2018 | D      | 30APR2018 | D      |
| 17 | 003    | fever  | 2018-06-15 | 2018-06-20 | 11APR2018 | 15JUN2018 |        | 20JUN2018 |        |
| 18 | 003    | fever  | 2018-07    | 2018-08-10 | 11APR2018 | 01JUL2018 | D      | 10AUG2018 |        |
| 19 | 004    | Nausea | 2018-04    |            | 15APR2018 | 15APR2018 | D      | .         |        |
| 20 | 004    | Nausea | 2019       |            | 15APR2018 | 01JAN2019 | M      | .         |        |

ASTDTF : Analysis Start Date Imputation Flag

AENDTF : Analysis End Date Imputation Flag

# Snippet of Code

```
/*--- Missing day part of Start Date Imputation---*/

if nmiss(st_y,st_m) eq 0 and missing(st_d) then do;
    if (st_y eq year(trtsdt)) and (st_m eq month(trtsdt)) and (ifn(length(aeendtc) eq 10,
trtsdt <= aendt_num, ifn(length(AEENDTC) eq 7, year(trtsdt) <= en_y and month(trtsdt) <= en_m,
    ifn(length(AEENDTC) eq 4, year(trtsdt) <= en_y, missing(en_y)))) ) then do;

        st_d=day(trtsdt); ASTDTF="D";
    end;
else do;
    st_d=1; ASTDTF="D";
end;

/*--- Missing Month and/or Day part of End date Imputation ---*/

if missing(en_d) and nmiss(en_y, en_m) eq 0 then do;
    AENDT=intnx("month", intnx("month", aendt_num, -1, "e"), +1, "e" );
    AENDTF="D";
end;

else if nmiss(en_m, en_d) eq 2 and ^missing(en_y) then do;
    AENDT=input(strip(put(en_y,best.))||"-"||"12-31", yymmdd10.);
    AENDTF="M";
end;
```

# Flag for first occurrence of an event in a row of consecutive occurrences.

- Consecutive AVAL greater than or equal to 25 in each SUBJID within PARAM

| SUBJID | PARAM  | VISIT  | AVAL | ANL01FL |
|--------|--------|--------|------|---------|
| 001    | PARAM1 | Visit1 | 23   |         |
| 001    | PARAM1 | Visit2 | 31   | Y       |
| 001    | PARAM1 | Visit3 | 29   |         |
| 001    | PARAM1 | Visit4 | 28   |         |
| 001    | PARAM1 | Visit5 | 24   |         |
| 001    | PARAM1 | Visit6 | 24   |         |
| 001    | PARAM1 | Visit7 | 24   |         |

| SUBJID | PARAM  | VISIT   | AVAL | ANL01FL |
|--------|--------|---------|------|---------|
| 038    | PARAM1 | Visit1  | 20   | Y       |
| 038    | PARAM1 | Visit2  | 29   |         |
| 038    | PARAM1 | Visit3  | 27   |         |
| 038    | PARAM1 | Visit4  | 28   |         |
| 038    | PARAM1 | Visit5  | 25   |         |
| 038    | PARAM1 | Visit6  | 28   |         |
| 038    | PARAM1 | Visit7  | 27   |         |
| 038    | PARAM1 | Visit8  | 28   |         |
| 038    | PARAM1 | Visit9  | 26   |         |
| 038    | PARAM1 | Visit10 | 26   |         |
| 038    | PARAM1 | Visit11 | 29   |         |
| 038    | PARAM1 | Visit12 | 27   |         |

| SUBJID | PARAM  | VISIT   | AVAL | ANL01FL |
|--------|--------|---------|------|---------|
| 002    | PARAM1 | Visit1  | 31   | Y       |
| 002    | PARAM1 | Visit2  | 30   |         |
| 002    | PARAM1 | Visit3  | 28   |         |
| 002    | PARAM1 | Visit4  | 26   |         |
| 002    | PARAM1 | Visit5  | 25   |         |
| 002    | PARAM1 | Visit6  | 27   |         |
| 002    | PARAM1 | Visit7  | 25   |         |
| 002    | PARAM1 | Visit8  | 27   |         |
| 002    | PARAM1 | Visit9  | 25   |         |
| 002    | PARAM1 | Visit10 | 25   |         |
| 002    | PARAM1 | Visit11 | 24   |         |
| 002    | PARAM1 | Visit12 | 24   |         |
| 002    | PARAM1 | Visit13 | 20   |         |
| 002    | PARAM1 | Visit14 | 22   |         |
| 002    | PARAM1 | Visit15 | 28   | Y       |
| 002    | PARAM1 | Visit16 | 28   |         |
| 002    | PARAM1 | Visit17 | 29   |         |
| 002    | PARAM1 | Visit18 | 25   |         |
| 002    | PARAM1 | Visit19 | 21   |         |

# Conditional Imputations for missing analysis value.

|    | SUBJID | AVISITN | AVAL |
|----|--------|---------|------|
| 1  | 1      | 1       | 1    |
| 2  | 1      | 2       | 1    |
| 3  | 1      | 3       | .    |
| 4  | 1      | 4       | 1    |
| 5  | 1      | 5       | 0    |
| 6  | 1      | 6       | 0    |
| 7  | 1      | 7       | .    |
| 8  | 1      | 8       | 0    |
| 9  | 1      | 9       | 0    |
| 10 | 1      | 10      | .    |
| 11 | 1      | 11      | 1    |
| 12 | 1      | 12      | .    |
| 13 | 1      | 13      | 1    |
| 14 | 1      | 14      | .    |
| 15 | 1      | 15      | .    |
| 16 | 1      | 16      | 1    |
| 17 | 2      | 1       | 1    |
| 18 | 2      | 2       | 1    |
| 19 | 2      | 3       | .    |
| 20 | 2      | 4       | .    |
| 21 | 2      | 5       | 1    |
| 22 | 2      | 6       | 0    |
| 23 | 2      | 7       | 0    |
| 24 | 2      | 8       | .    |
| 25 | 2      | 9       | 0    |
| 26 | 2      | 10      | .    |
| 27 | 2      | 11      | .    |
| 28 | 2      | 12      | 1    |
| 29 | 2      | 13      | 1    |
| 30 | 2      | 14      | .    |
| 31 | 2      | 15      | 1    |

|    | SUBJID | AVISITN | AVAL | IMP01FL |
|----|--------|---------|------|---------|
| 1  | 1      | 1       | 1    |         |
| 2  | 1      | 2       | 1    |         |
| 3  | 1      | 3       | 1 Y  |         |
| 4  | 1      | 4       | 1    |         |
| 5  | 1      | 5       | 0    |         |
| 6  | 1      | 6       | 0    |         |
| 7  | 1      | 7       | 0 Y  |         |
| 8  | 1      | 8       | 0    |         |
| 9  | 1      | 9       | 0    |         |
| 10 | 1      | 10      | 0 Y  |         |
| 11 | 1      | 11      | 1    |         |
| 12 | 1      | 12      | 1 Y  |         |
| 13 | 1      | 13      | 1    |         |
| 14 | 1      | 14      | 0 Y  |         |
| 15 | 1      | 15      | 0 Y  |         |
| 16 | 1      | 16      | 1    |         |
| 17 | 2      | 1       | 1    |         |
| 18 | 2      | 2       | 1    |         |
| 19 | 2      | 3       | 0 Y  |         |
| 20 | 2      | 4       | 0 Y  |         |
| 21 | 2      | 5       | 1    |         |
| 22 | 2      | 6       | 0    |         |
| 23 | 2      | 7       | 0    |         |
| 24 | 2      | 8       | 0 Y  |         |
| 25 | 2      | 9       | 0    |         |
| 26 | 2      | 10      | 0 Y  |         |
| 27 | 2      | 11      | 0 Y  |         |
| 28 | 2      | 12      | 1    |         |
| 29 | 2      | 13      | 1    |         |
| 30 | 2      | 14      | 1 Y  |         |
| 31 | 2      | 15      | 1    |         |

AVAL values:  
 1(= response yes)  
 and 0 (= response no)

# Pick the first response from sustained response (until end of the study).

|    | SUBJID | AVAL | AVISITN |
|----|--------|------|---------|
| 1  | 1      | 1    | 1       |
| 2  | 1      | 1    | 2       |
| 3  | 1      | .    | 3       |
| 4  | 1      | 1    | 4       |
| 5  | 1      | 0    | 5       |
| 6  | 1      | 0    | 6       |
| 7  | 1      | 0    | 7       |
| 8  | 2      | 1    | 1       |
| 9  | 2      | 1    | 2       |
| 10 | 2      | .    | 3       |
| 11 | 2      | .    | 4       |
| 12 | 2      | 1    | 5       |
| 13 | 2      | 1    | 6       |
| 14 | 2      | 1    | 7       |
| 15 | 3      | 0    | 1       |
| 16 | 3      | 0    | 2       |
| 17 | 3      | 1    | 3       |
| 18 | 3      | 1    | 4       |
| 19 | 3      | 1    | 5       |
| 20 | 3      | 1    | 6       |
| 21 | 3      | 1    | 7       |
| 22 | 3      | 1    | 8       |
| 23 | 3      | 1    | 9       |
| 24 | 4      | 1    | 1       |
| 25 | 4      | 0    | 2       |
| 26 | 4      | 1    | 3       |
| 27 | 4      | 0    | 4       |
| 28 | 4      | 0    | 5       |
| 29 | 4      | 1    | 6       |
| 30 | 4      | 1    | 7       |
| 31 | 4      | 1    | 8       |

AVAL values:

1(= response yes)  
and 0 (= response  
no)



|   | SUBJID | AVAL | AVISITN |
|---|--------|------|---------|
| 1 | 2      | 1    | 5       |
| 2 | 3      | 1    | 3       |
| 3 | 4      | 1    | 6       |

# CONCLUSION

The examples given in this presentation are helpful for the programmers to understand the imputation rules (generic) for adverse events (start and end) partial dates, some of the analysis flags derivations following CDISC guidelines.

# Acknowledgement

- I would like to thank Malla Reddy Boda, Associate Director, Shionogi Inc, for his review and invaluable comments.

Thank You

# CONTACT INFORMATION

Venkata N Madhira

E-mail: [venkatanmadhira@gmail.com](mailto:venkatanmadhira@gmail.com)

Sr. Statistical Programmer, Consultant at Shionogi Inc, NJ, USA

Harish Yeluguri

E-mail: [harish.yeluguri@gmail.com](mailto:harish.yeluguri@gmail.com)

Sr. Statistical Programmer, Consultant at Shionogi Inc, NJ, USA

Prabhakara Rao Burma

E-mail: [prsas85@gmail.com](mailto:prsas85@gmail.com)

Principal Clinical SAS Analyst, Acerta Pharma, CA, USA

Questions ?

# References

- Analysis Data Model Implementation Guide Version 1.1
- SAS<sup>®</sup> Certification Prep Guide Advanced Programming for SAS<sup>®</sup> 9
- <https://www.lexjansen.com/wuss/2012/28.pdf>
- <https://www.phusewiki.org/docs/2006/P011.pdf>
- [https://www.sas.com/storefront/aux/en/splongitudinal/58176\\_excerpt.pdf](https://www.sas.com/storefront/aux/en/splongitudinal/58176_excerpt.pdf)
- SAS<sup>®</sup> and all other SAS<sup>®</sup> Institute Inc. product or service names are registered trademarks or trademarks of SAS<sup>®</sup> Institute Inc. in the USA and other countries. <sup>®</sup> indicates USA registration. Other brand and product names are trademarks of their respective companies.