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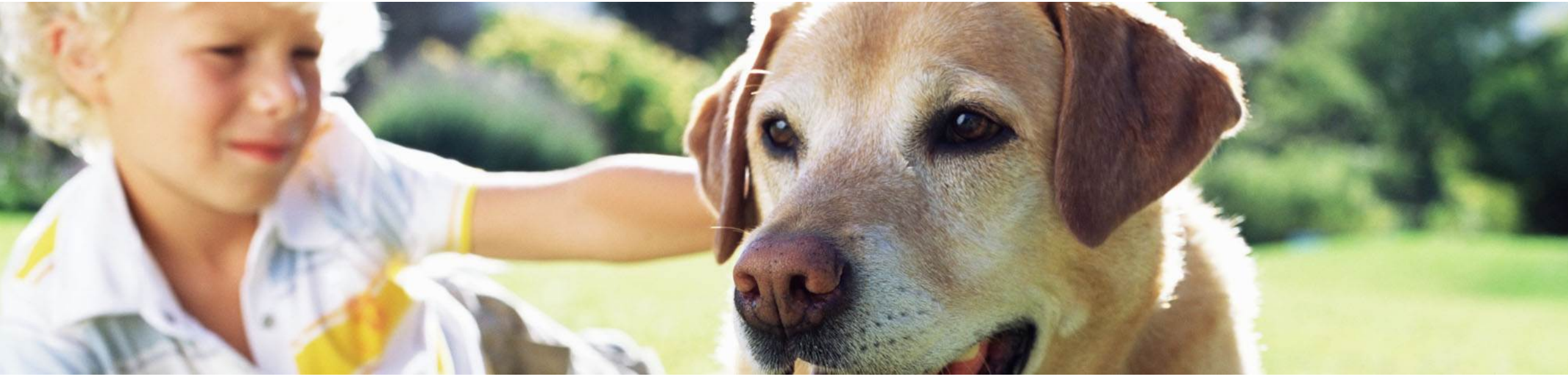

Detecting Treatment Emergent Adverse Events (TEAEs)

DH10

11Oct2017 / Matthias Lehrkamp / 1.0

PhUSE 2017

Edinburgh

- Introduction to the topic
- Interval Based Algorithm (IBA)
- Conclusion

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Introduction to the topic

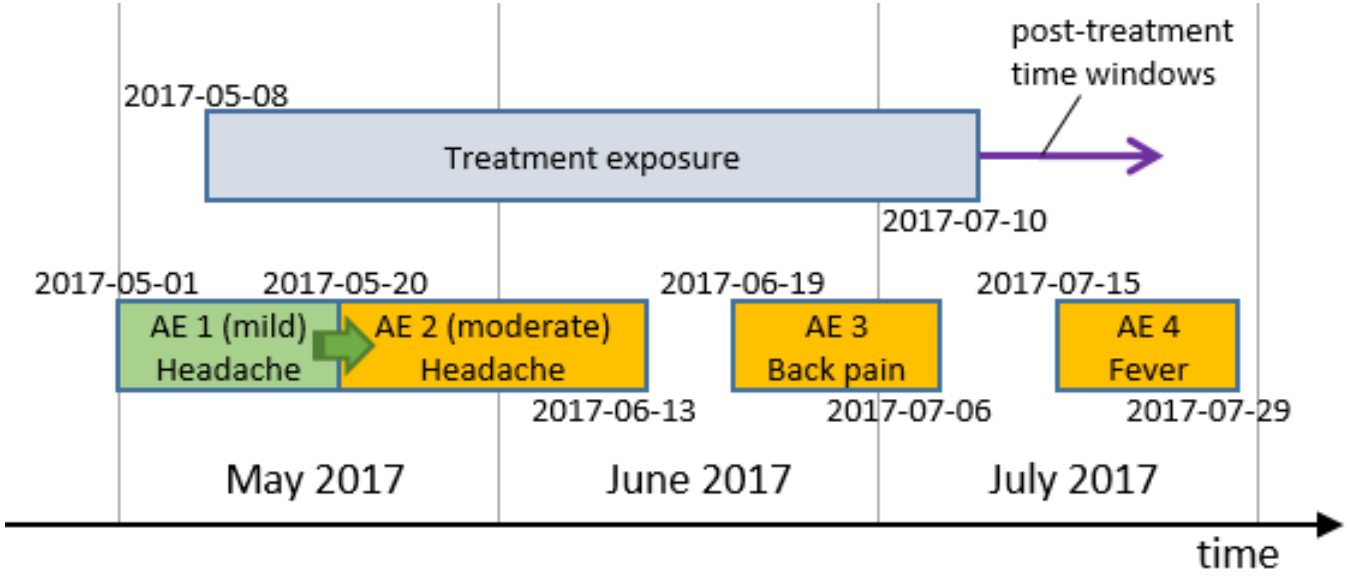
Introduction to the topic

- An algorithm was requested, based on pure SDTM variables
  - Use of SDTM date/time variables (*DTC)
  - Handling longer treatment interruptions
  - Used for analysis TEAE flags (related to a specific treatment epoch or treatment regimen, etc.)

Introduction to the topic

The definition of a TEAE is given in the GCP ICH E9 guideline

> "An event that emerges during treatment having been absent pre-treatment, or worsens relative to the pre-treatment state."



The post-treatment time window considers the time to clear the body from the drug

Introduction to the topic

AE

Unique Subject Identifier	Sequence Number	Group ID	Reported Term for the Adverse Event	Severity/ Intensity	Serious Event	Causality	Outcome of Adverse Event	Start Date/Time of Adverse Event	End Date/Time of Adverse Event
USUBJID	**AESEQ**	**AEGRPID**	**AETERM**	**AESEV**	**AESER**	**AEREL**	**AEOUT**	**AESTDTC**	**AEENDTC**
ABC-1001	1	1	Headache	MODERATE	N	NOT RELATED	NOT RECOVERED/NOT RESOLVED	2017-05	2017-05-11
ABC-1001	2	1	Headache	MILD	N	UNLIKELY RELATED	RECOVERED/RESOLVED	2017-05-11	2017-05-22
ABC-1001	3		Fever	MODERATE	N	POSSIBLY RELATED	RECOVERED/RESOLVED	2017-06-11	2017-06
ABC-1001	4		Bone pain	MODERATE	N	POSSIBLY RELATED	RECOVERED/RESOLVED	2017-07	2017-08-10
ABC-1001	5		Cold	MILD	N	POSSIBLY RELATED	RECOVERED/RESOLVED	2017-08-15	2017-09-13
ABC-1001	6	2	Back pain	MODERATE	N	POSSIBLY RELATED	NOT RECOVERED/NOT RESOLVED	2017-05	2017-08-03
ABC-1001	7	2	Back pain	MILD	N	UNLIKELY RELATED	NOT RECOVERED/NOT RESOLVED	2017-08-03	

Example data is from one subject only.
Adverse event (AE) data with 2 grouped AEs and 3 single AE records.

Introduction to the topic

AE

Unique Subject Identifier	Sequence Number	Group ID	Reported Term for the Adverse Event	Severity/ Intensity	Serious Event	Causality	Outcome of Adverse Event	Start Date/Time of Adverse Event	End Date/Time of Adverse Event
USUBJID	**AESEQ**	**AEGRPID**	**AETERM**	**AESEV**	**AESER**	**AEREL**	**AEOUT**	**AESTDTC**	**AEENDTC**
ABC-1001	1	1	Headache	MODERATE	N	NOT RELATED	NOT RECOVERED/NOT RESOLVED	2017-05	2017-05-11
ABC-1001	2	1	Headache	MILD	N	UNLIKELY RELATED	RECOVERED/RESOLVED	2017-05-11	2017-05-22
ABC-1001	3		Fever	MODERATE	N	POSSIBLY RELATED	RECOVERED/RESOLVED	2017-06-11	2017-06
ABC-1001	4		Bone pain	MODERATE	N	POSSIBLY RELATED	RECOVERED/RESOLVED	2017-07	2017-08-10
ABC-1001	5		Cold	MILD	N	POSSIBLY RELATED	RECOVERED/RESOLVED	2017-08-15	2017-09-13
ABC-1001	6	2	Back pain	MODERATE	N	POSSIBLY RELATED	NOT RECOVERED/NOT RESOLVED	2017-05	2017-08-03
ABC-1001	7	2	Back pain	MILD	N	UNLIKELY RELATED	NOT RECOVERED/NOT RESOLVED	2017-08-03	

EX

Unique Subject Identifier	Sequence Number	Name of Treatment	Dosing Frequency per Interval	Start Date/Time of Treatment	End Date/Time of Treatment
USUBJID	**EXSEQ**	**EXTRT**	**EXDOSFRQ**	**EXSTDTC**	**EXENDTC**
ABC-1001	1	A	OD	2017-05-08T08:20	2017-05
ABC-1001	2	A	OD	2017-06-15	2017-07-07
ABC-1001	3	B	OD	2017-07-21	2017-08
ABC-1001	4	B	OD	2017-08	2017-09-21

Exposure data (EX) includes 4 exposure intervals, 2 oral doses for each treatment (A & B)

Introduction to the topic

AE

Unique Subject Identifier	Sequence Number	Group ID	Reported Term for the Adverse Event	Severity/ Intensity	Serious Event	Causality	Outcome of Adverse Event	Start Date/Time of Adverse Event	End Date/Time of Adverse Event
USUBJID	**AESEQ**	**AEGRPID**	**AETERM**	**AESEV**	**AESER**	**AEREL**	**AEOUT**	**AESTDTC**	**AEENDTC**
ABC-1001	1	1	Headache	MODERATE	N	NOT RELATED	NOT RECOVERED/NOT RESOLVED	2017-05	2017-05-11
ABC-1001	2	1	Headache	MILD	N	UNLIKELY RELATED	RECOVERED/RESOLVED	2017-05-11	2017-05-22
ABC-1001	3		Fever	MODERATE	N	POSSIBLY RELATED	RECOVERED/RESOLVED	2017-06-11	2017-06
ABC-1001	4		Bone pain	MODERATE	N	POSSIBLY RELATED	RECOVERED/RESOLVED	2017-07	2017-08-10
ABC-1001	5		Cold	MILD	N	POSSIBLY RELATED	RECOVERED/RESOLVED	2017-08-15	2017-09-13
ABC-1001	6	2	Back pain	MODERATE	N	POSSIBLY RELATED	NOT RECOVERED/NOT RESOLVED	2017-05	2017-08-03
ABC-1001	7	2	Back pain	MILD	N	UNLIKELY RELATED	NOT RECOVERED/NOT RESOLVED	2017-08-03	

EX

Unique Subject Identifier	Sequence Number	Name of Treatment	Dosing Frequency per Interval	Start Date/Time of Treatment	End Date/Time of Treatment
USUBJID	**EXSEQ**	**EXTRT**	**EXDOSFRQ**	**EXSTDTC**	**EXENDTC**
ABC-1001	1	A	OD	2017-05-08T08:20	2017-05
ABC-1001	2	A	OD	2017-06-15	2017-07-07
ABC-1001	3	B	OD	2017-07-21	2017-08
ABC-1001	4	B	OD	2017-08	2017-09-21

TS

Trial Summary Parameter Short Name	Trial Summary Parameter	Parameter Value
TSPARMCD	**TSPARM**	**TSVAL**
TIMEW	Post-Treatment Time Window	7

The post-treatment time window is stored in the trial summary domain (TS) in TSVAL where TSPARAMCD='TIMEW'

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Interval Based Algorithm (IBA)

Interval Based Algorithm (IBA)

Step • : Built intervals of all date/times in which at least the year is present

AE01_DT_MINMAX

Unique Subject Identifier	Sequence Number	Group ID	Reported Term for the Adverse Event	Start Date/Time of Adverse Event	End Date/Time of Adverse Event				
USUBJID	AESEQ	AEGRPID	AETERM	AESTDTC	AEENDTC	AESTDT_MIN	AESTDT_MAX	AEENDT_MIN	AEENDT_MAX
ABC-1001	1	1	Headache	2017-05	2017-05-11	2017-05-01T00:00:00	2017-05-11T23:59:59	2017-05-11T00:00:00	2017-05-11T23:59:59
ABC-1001	2	1	Headache	2017-05-	2017-05-22	2017-05 00:00:00	2017-05 T23:59:59	2017-05-22T00:00:00	2017-05-22T23:59:59
ABC-1001	3		Fever	2017-06-1	2017-06	2017-0 00:00:00	2017- 1T23:59:59	2017-06-11T00:00:00	2017-06-30T23:59:59
ABC-1001	4		Bone pain	2017-07	017-08-10	201 01T00:00:00	20 7-31T23:59:59	2017-08-10T00:00:00	2017-08-10T23:59:59
ABC-1001	5		Cold	2017-08-15	2017	2017-08-15T00	2017-08-15T23:59:59	2017-09-13T00:00:00	2017-09-13T23:59:59
ABC-1001	6	2	Back pain	2017-05	2017-08-03	2017-05-01T00:00:00	2017-05-31T23:59:59	2017-08-03T00:00:00	2017-08-03T23:59:59
ABC-1001	7	2	Back pain	2017-08-03		2017-08-03T00:00:00	2017-08-03T23:59:59		

EX01_DT_MINMAX

Unique Subject Identifier	Sequence Number	Name of Treatment	Start Date/Time of Treatment	End Date/Time of Treatment				
USUBJID	EXSEQ	EXTRT	EXSTDTC	EXENDTC	EXSTDT_MIN	EXSTDT_MAX	EXENDT_MIN	EXENDT_MAX
ABC-1001	1	A	2017-05-08T08:20	2017-05	2017-05-08T08:20:00	2017-05-08T08:20:59	2017-05-08T08:20:00	2017-05-31T23:59:59
ABC-1001	2	A	2017-06-15	2017-07-07	2017-06-15T00:00:00	2017-06-15T23:59:59	2017-07-07T00:00:00	2017-07-07T23:59:59
ABC-1001	3	B	2017-07-21	2017-08	2017-07-21T00:00:00	2017-07-21T23:59:59	2017-08-01T00:00:00	2017-08-31T23:59:59
ABC-1001	4	B	2017-08	2017-09-21	2017-08-01T00:00:00	2017-08-31T23:59:59	2017-09-21T00:00:00	2017-09-21T23:59:59

- Straight forward imputation rules
- Each date results in an interval
- Imputation up to precision of seconds
- All time parts are numeric
- Start and end time dependencies
  *ENDT_MIN >= *STDT_MIN
  *STDT_MAX <= *ENDT_MAX

Replacements of missing date and time parts

	Earliest date/time	Last date/time
Month	1	12
Day	1	Last day of the month in the given year
Hour	0	23
Minute	0	59
Second	0	59

Interval Based Algorithm (IBA)

Step : Impute all date/times where at least the year is missing

AE03_MISSINGDT

Unique Subject Identifier	Sequence Number	Group ID	Reported Term for the Adverse Event	Start Date/Time of Adverse Event	End Date/Time of Adverse Event				
USUBJID	AESEQ	AEGRPID	AETERM	AESTDTC	AEENDTC	AESTDT_MIN	AESTDT_MAX	AEENDT_MIN	AEENDT_MAX
ABC-1001	1	1	Headache	2017-05	2017-05-11	2017-05-01T00:00:00	2017-05-11T23:59:59	2017-05-11T00:00:00	2017-05-11T23:59:59
ABC-1001	2	1	Headache	2017-05-11	2017-05-22	2017-05-11T00:00:00	2017-05-11T23:59:59	2017-05-22T00:00:00	2017-05-22T23:59:59
ABC-1001	3		Fever	2017-06-11	2017-06	2017-06-11T00:00:00	2017-06-11T23:59:59	2017-06-11T00:00:00	2017-06-30T23:59:59
ABC-1001	4		Bone pain	2017-07	2017-08-10	2017-07-01T00:00:00	2017-07-31T23:59:59	2017-08-10T00:00:00	2017-08-10T23:59:59
ABC-1001	5		Cold	2017-08-15	2017-09-13	2017-08-15T00:00:00	2017-08-15T23:59:59	2017-09-13T00:00:00	2017-09-13T23:59:59
ABC-1001	6	2	Back pain	2017-05	2017-08-03	2017-05-01T00:00:00	2017-05-31T23:59:59	2017-08-03T00:00:00	2017-08-03T23:59:59
ABC-1001	7	2	Back pain	2017-08-03		2017-08-03T00:00:00	2017-08-03T23:59:59	2017-08-03T00:00:00	2017-09-21T23:59:59

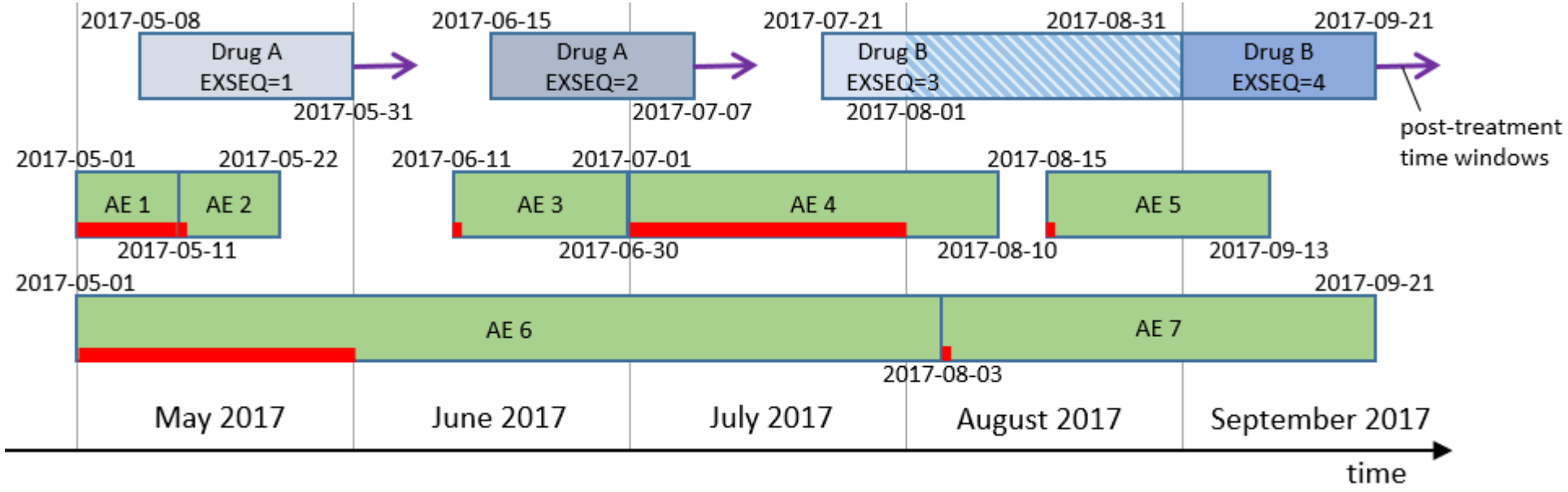
EX03_MISSINGDT

Unique Subject Identifier	Sequence Number	Name of Treatment	Dosing Frequency per Interval	Start Date/Time of Treatment	End Date/Time of Treatment				
USUBJID	EXSEQ	EXTRT	EXDOSFRQ	EXSTDTC	EXENDTC	EXSTDT_MIN	EXSTDT_MAX	EXENDT_MIN	EXENDT_MAX
ABC-1001	1	A	OD	2017-05-	2017-05	2017-05-08T08:20:00	2017-05-08T08:20:59	2017-05-08T08:20:00	2017-05-31T23:59:59
ABC-1001	2	A	OD	2017-06-15	2017-07-07	2017-06-15T00:00:00	2017-06-15T23:59:59	2017-07-07T00:00:00	2017-07-07T23:59:59
ABC-1001	3	B	OD	2017-07-21	2017-08	2017-07-21T00:00:00	2017-07-21T23:59:59	2017-08-01T00:00:00	2017-08-31T23:59:59
ABC-1001	4	B	OD	2017-08	2017-09-21	2017-08-01T00:00:00	2017-08-31T23:59:59	2017-09-21T00:00:00	2017-09-21T23:59:59

- Date/times are considered as completely missing
- Interval is build by all imputed values from step 1
- Subjects with only missing date/time values are excluded from further processing.
  →All AE are counted as TEAE

Interval Based Algorithm (IBA)

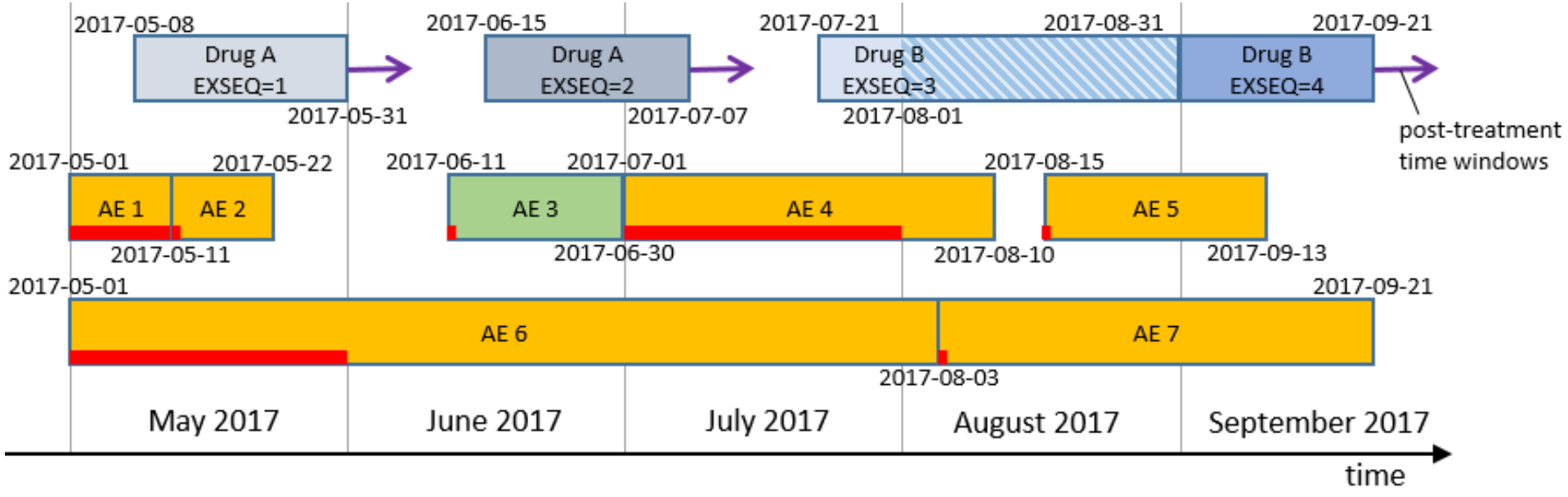
Step : Join the AE and the exposure data and determine treatment emergent for each single AE



Boxes: time from *STDT_MIN to *ENDT_MAX
Red line: AE start interval (AESTDT_MIN to AESTDT_MAX)

Interval Based Algorithm (IBA)

Step : Join the AE and the exposure data and determine treatment emergent for each single AE



Boxes: time from *STDT_MIN to *ENDT_MAX
Red line: AE start interval (AESTDT_MIN to AESTDT_MAX)
TEAE: an AE start interval (red line) overlaps any exposure interval

```
aestdt_min <= exendt_max + timew*24*60*60 AND aestdt_max >= exstdt_min
```

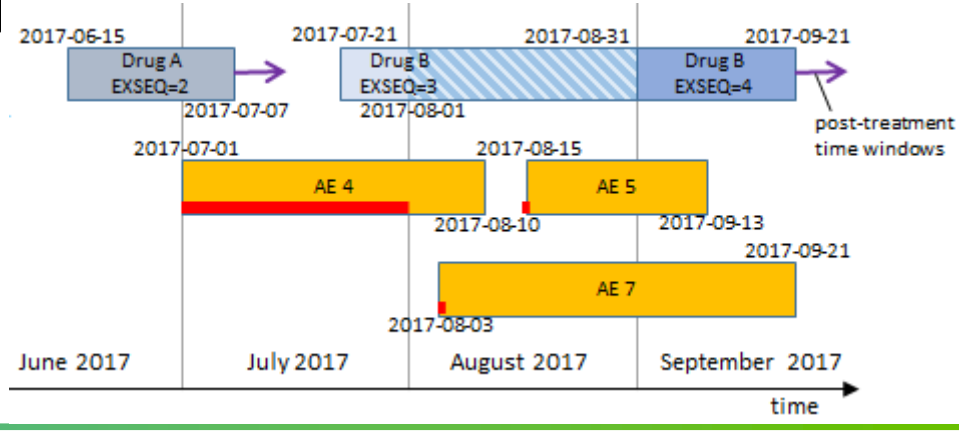
Interval Based Algorithm (IBA)

Step : Clean up duplicate AE records within the same treatment epoch

TEAE03_TEAEFLAG

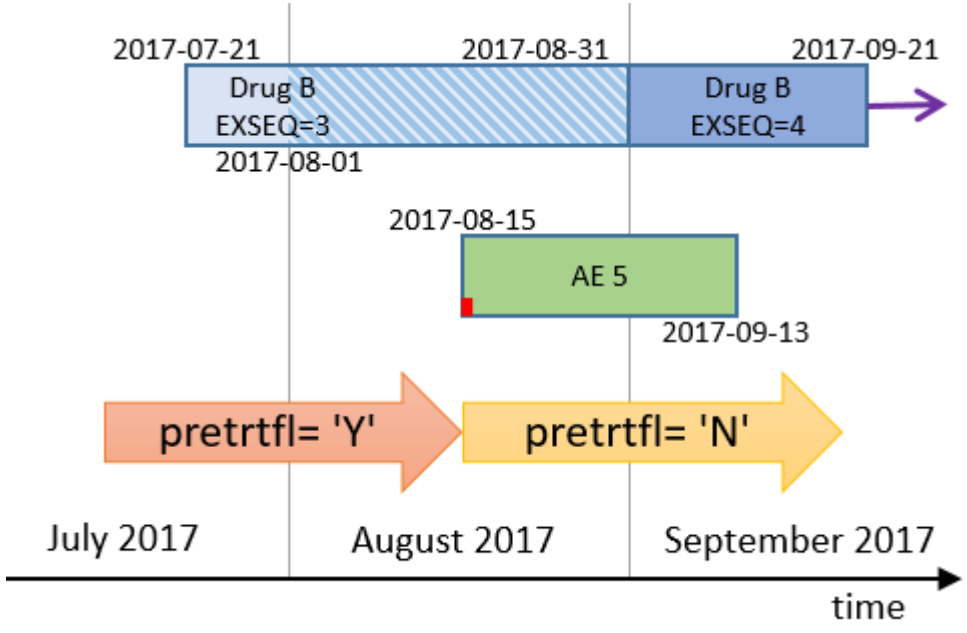
AE data							EX data			
Unique Subject Identifier	Sequence Number	Group ID	Reported Term for the Adverse Event	Start Date/Time of Adverse Event	End Date/Time of Adverse Event	Treatment Emergent Analysis Flag	Sequence Number	Name of Treatment	Start Date/Time of Treatment	End Date/Time of Treatment
USUBJID	AESEQ	AEGRPID	AETERM	AESTDTC	AEENDTC	TRTEMFL	EXSEQ	EXTRT	EXSTDTC	EXENDTC
ABC-1001	1	1	Headache	2017-05	2017-05-11	Y	1	A	2017-05-08T08:20	2017-05
ABC-1001	2	1	Headache	2017-05-11	2017-05-22	Y	1	A	2017-05-08T08:20	2017-05
ABC-1001	3		Fever	2017-06-11	2017-06	N	.			
ABC-1001	4		Bone pain	2017-07	2017-08-10	Y	2	A	2017-06-15	2017-07-07
ABC-1001	4		Bone pain	2017-07	2017-08-10	Y	3	B	2017-07-21	2017-08
ABC-1001	5		Cold	2017-08-15	2017-09-13	Y	3	B	2017-07-21	2017-08
ABC-1001	5		Cold	2017-08-15	2017-09-13	Y	4	B	2017-08	2017-09-21
ABC-1001	6	2	Back pain	2017-05	2017-08-03	Y	1	A	2017-05-08T08:20	2017-05
ABC-1001	7	2	Back pain	2017-08-03		Y	3	B	2017-07-21	2017-08
ABC-1001	7	2	Back pain	2017-08-03		Y	4	B	2017-08	2017-09-21

- AEs may be present in multiple lines (see AESEQ in 4, 5, and 7)
- Different treatments must be kept (AESEQ=4)
- Same treatments must be cleaned (AESEQ=5 and 7) (closest exposure start to the AE start, exposure before AE start has priority)



Interval Based Algorithm (IBA)

Step : Clean up duplicate AE records within the same treatment epoch




```
/* Selection of one exposure observation by aeseq and extrt */
DATA teae06_cleaned;
  SET teae05_sorted;
  BY usubjid aeseq extrt pretrtfl exstdt_min exseq;
  * indicator if a record is already selected;
  RETAIN teaeselectedfl;
  LENGTH teaeselectedfl $1;
  IF FIRST.extrt THEN teaeselectedfl='N';
  /* select the last exposure interval before AE start */
  IF teaeselectedfl='N'
     AND pretrtfl='Y' AND LAST.pretrtfl THEN DO;
    teaeselectedfl= 'Y';
    OUTPUT;
  END;
  /* select the first exposure interval after AE start */
  ELSE IF teaeselectedfl='N'
          AND pretrtfl='N' AND FIRST.pretrtfl THEN DO;
    teaeselectedfl= 'Y';
    OUTPUT;
  END;
RUN;
```

Interval Based Algorithm (IBA)

Step : Check grouped AEs and correct the TEAE flag for AEs that have not worsened

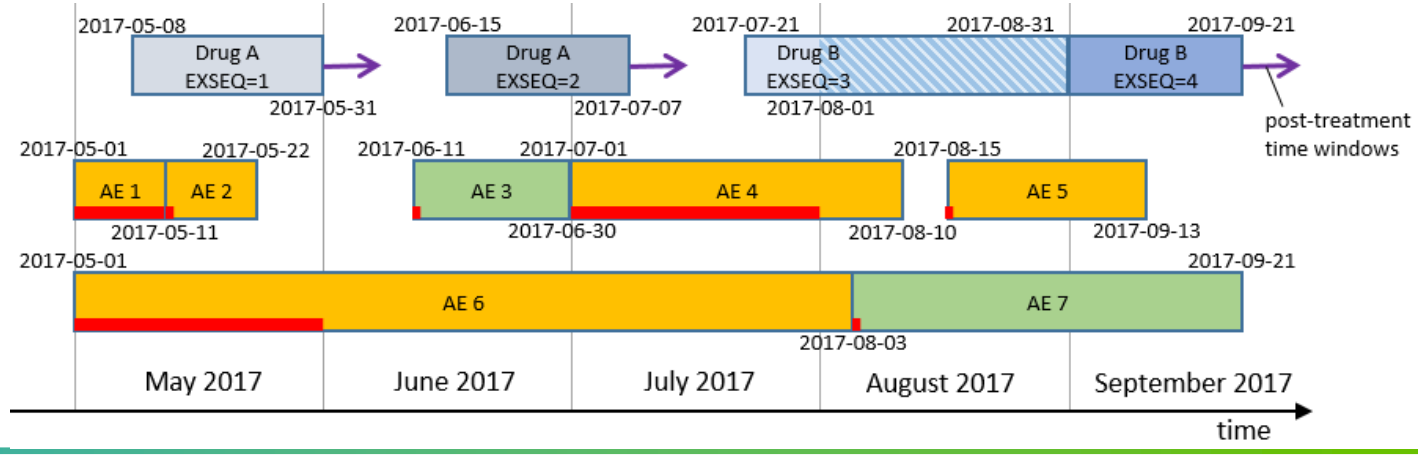
TEAE09_SORTED

AE data								EX data			
Unique Subject Identifier	Sequence Number	Group ID	Reported Term for the Adverse Event	Severity/ Intensity	Start Date/Time of Adverse Event	End Date/Time of Adverse Event	Treatment Emergent Analysis Flag	Sequence Number	Name of Treatment	Start Date/Time of Treatment	End Date/Time of Treatment
USUBJID	AESEQ	AEGRPID	AETERM		AESTDTC	AEENDTC	TRTEMFL	EXSEQ	EXTRT	EXSTDTC	EXENDTC
ABC-1001	1	1	Headache	MODERATE	2017-05	2017-05-11	Y	1	A	2017-05-08T08:20	2017-05
ABC-1001	2	1	Headache	MILD	2017-05-11	2017-05-22	Y	1	A	2017-05-08T08:20	2017-05
ABC-1001	3		Fever	MODERATE	2017-06-11	2017-06	N	.			
ABC-1001	4		Bone pain	MODERATE	2017-07	2017-08-10	Y	2	A	2017-06-15	2017-07-07
ABC-1001	4		Bone pain	MODERATE	2017-07	2017-08-10	Y	3	B	2017-07-21	2017-08
ABC-1001	5		Cold	MILD	2017-08-15	2017-09-13	Y	4	B	2017-08	2017-09-21
ABC-1001	6	2	Back pain	MODERATE	2017-05	2017-08-03	Y	1	A	2017-05-08T08:20	2017-05
ABC-1001	7	2	Back pain	MILD	2017-08-03		N	4	B	2017-08	2017-09-21

Interval Based Algorithm (IBA)

Step : Check grouped AEs and correct the TEAE flag for AEs that have not worsened

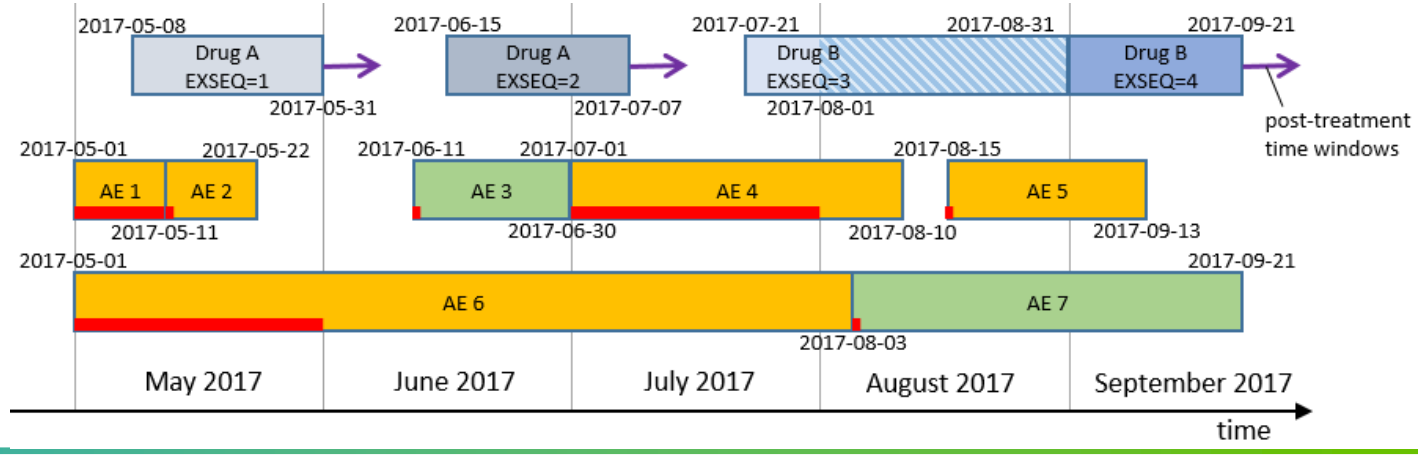
```
* Check that grouped AE have the same AETERM;
IF last_aeterm ~= aeterm THEN PUT 'WARNING: Found grouped AEs with different AE terms! ` _ALL_;
* Check if AEOUT condition is fulfilled;
IF last_aeout NOT IN('RECOVERING/RESOLVING' 'NOT RECOVERED/NOT RESOLVED')
  THEN PUT 'WARNING: AE records belongs together but the previous one has no outcome '
           'with ''RECOVERING/RESOLVING'' or ''NOT RECOVERED/NOT RESOLVED''. '
           usubjid= aegrpid= aeterm= last_aeout= aeout=;
* Update TEAE to non-TEAE when all of the following conditions are meet;
   /* previous related AE is non-treatment emergent or the treatment has changed */
IF     ( trtemfl = 'N' OR last_extrt ~= extrt )
   /* intensity/grade not worsened */
   AND last_aesev >= aesev > ' '
   /* not changed to a serious event */
   AND ( last_aeser = aeser OR  aeser = 'N' )
   /* AE is not drug-related */
   AND aerel IN('N' 'NOT RELATED'
                'UNLIKELY RELATED') THEN DO;
  trtemfl= 'N';
END;
```



Interval Based Algorithm (IBA)

Step : Check grouped AEs and correct the TEAE flag for AEs that have not worsened

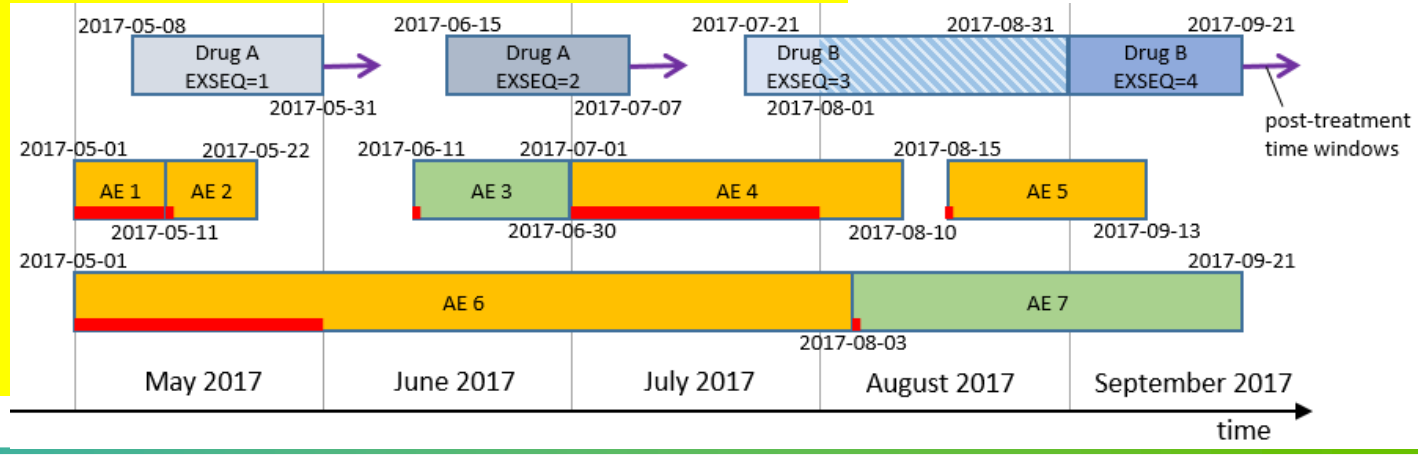
```
* Check that grouped AE have the same AETERM;
IF last_aeterm ~= aeterm THEN PUT 'WARNING: Found grouped AEs with different AE terms! ' _ALL_;
* Check if AEOUT condition is fulfilled;
IF last_aeout NOT IN('RECOVERING/RESOLVING' 'NOT RECOVERED/NOT RESOLVED')
  THEN PUT 'WARNING: AE records belongs together but the previous one has no outcome '
           'with ''RECOVERING/RESOLVING'' or ''NOT RECOVERED/NOT RESOLVED''. '
           usubjid= aegrpid= aeterm= last_aeout= aeout=;
* Update TEAE to non-TEAE when all of the following conditions are meet;
   /* previous related AE is non-treatment emergent or the treatment has changed */
IF     ( trtemfl = 'N' OR last_extrt ~= extrt )
   /* intensity/grade not worsened */
   AND last_aesev >= aesev > ' '
   /* not changed to a serious event */
   AND ( last_aeser = aeser OR  aeser = 'N' )
   /* AE is not drug-related */
   AND aerel IN('N' 'NOT RELATED'
                'UNLIKELY RELATED') THEN DO;
  trtemfl= 'N';
END;
```



Interval Based Algorithm (IBA)

Step : Check grouped AEs and correct the TEAE flag for AEs that have not worsened

```
* Check that grouped AE have the same AETERM;
IF last_aeterm ~= aeterm THEN PUT 'WARNING: Found grouped AEs with different AE terms! ' _ALL_;
* Check if AEOUT condition is fulfilled;
IF last_aeout NOT IN('RECOVERING/RESOLVING' 'NOT RECOVERED/NOT RESOLVED')
  THEN PUT 'WARNING: AE records belongs together but the previous one has no outcome '
           'with ''RECOVERING/RESOLVING'' or ''NOT RECOVERED/NOT RESOLVED''. '
           usubjid= aegrpid= aeterm= last_aeout= aeout=;
* Update TEAE to non-TEAE when all of the following conditions are meet;
   /* previous related AE is non-treatment emergent or the treatment has changed */
IF     ( trtemfl = 'N' OR last_extrt ~= extrt )
   /* intensity/grade not worsened */
   AND last_aesev >= aesev > ' '
   /* not changed to a serious event */
   AND ( last_aeser = aeser OR  aeser = 'N' )
   /* AE is not drug-related */
   AND aerel IN('N' 'NOT RELATED'
                'UNLIKELY RELATED') THEN DO;
  trtemfl= 'N';
END;
```



Interval Based Algorithm (IBA)

Step 6: Store all necessary data in ADAE

ADAE01_TEAE

AE data							TEAE09_SORTED				
Unique Subject Identifier	Sequence Number	Group ID	Reported Term for the Adverse Event	Severity/ Intensity	Start Date/Time of Adverse Event	End Date/Time of Adverse Event	Treatment Emergent Analysis Flag	Sequence Number	Name of Treatment	Start Date/Time of Treatment	End Date/Time of Treatment
USUBJID	AESEQ	AEGRPID	AETERM		AESTDTC	AEENDTC	TRTEMFL	EXSEQ	EXTRT	EXSTDTC	EXENDTC
ABC-1001	1	1	Headache	MODERATE	2017-05	2017-05-11	Y	1	A	2017-05-08T08:20	2017-05
ABC-1001	2	1	Headache	MILD	2017-05-11	2017-05-22	Y	1	A	2017-05-08T08:20	2017-05
ABC-1001	3		Fever	MODERATE	2017-06-11	2017-06	N	.			
ABC-1001	4		Bone pain	MODERATE	2017-07	2017-08-10	Y	2	A	2017-06-15	2017-07-07
ABC-1001	4		Bone pain	MODERATE	2017-07	2017-08-10	Y	3	B	2017-07-21	2017-08
ABC-1001	5		Cold	MILD	2017-08-15	2017-09-13	Y	4	B	2017-08	2017-09-21
ABC-1001	6	2	Back pain	MODERATE	2017-05	2017-08-03	Y	1	A	2017-05-08T08:20	2017-05
ABC-1001	7	2	Back pain	MILD	2017-08-03		N	4	B	2017-08	2017-09-21

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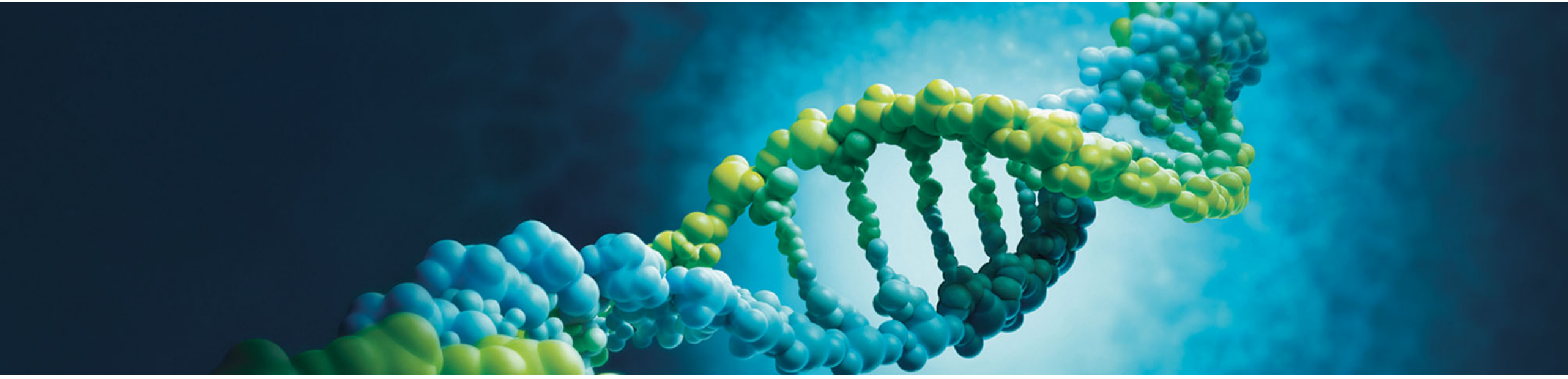
Conclusion

Conclusion

- The IBA is a stable straightforward algorithm to detect TEAEs

  → imputation of date/time values are done <u>without</u> dependencies between different datasets
  → based on pure SDTM
- The algorithm provides the ability to deal with longer treatment interruptions
- It is a good practice to discuss all special cases with the study team on a regular basis
  - AEs which persists while the treatment is changed
  - complete missing dates
  - AEs leading to death
  - data issues related to AE and exposure data

Science For A Better Life



Thank you!

Hopefully the TEAE detection runs more stable than ever before

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Get the last day of a month

Replacements of missing date and time parts

	Earliest date/time	Last date/time
Month	1	12
Day	1	Last day of the month in the given year
Hour	0	23
Minute	0	59
Second	0	59

Imputed year and month

```
* Last day of the month in the given year;
aestdt_max_day= day(intnx('month', input(cats(put(aestdt_year,z4.)
                                              ,'-',put(aestdt_max_month,z2.)
                                              ,'-01')
                                              ,is8601da.)
                                              ,0,'E'));
```

Interval function to get the last day of the month

Interval Based Algorithm (IBA)

How to parse an IS8601 formatted date?

Date/time example: 2017-03-21T15:35:51

```
DATA ae01_dt_minmax;
  SET sdtm.ae;
  * set regular expression ID for is8601dt format;
  prxid= prxparse('/^(\d{4}|-)(-(\d{2}|-)(-(\d{2}|-)(T(\d{2}|-)(:(\d{2}|-)(:(\d{2}))?)?)?)?)? *$/');
  *** impute the start date/time ***;
  * check that date/time value is not missing;
  IF NOT missing(aestdtc) THEN DO;
    * extract the date/time parts;
    IF prxmatch(prxid,aestdtc) THEN DO;
      aestdt_year= input(prxposn(prxid,1,aestdtc),?? 4.);
      aestdt_min_month= input(prxposn(prxid,3,aestdtc),?? 2.);
      aestdt_min_day= input(prxposn(prxid,5,aestdtc),?? 2.);
      aestdt_min_hour= input(prxposn(prxid,7,aestdtc),?? 2.);
      aestdt_min_minute= input(prxposn(prxid,9,aestdtc),?? 2.);
      aestdt_min_second= input(prxposn(prxid,11,aestdtc),?? 2.);
    END;
    ...
```

Interval Based Algorithm (IBA)

How to parse an IS8601 formatted date?

Date/time example: 2017-03-21T15:35:51

```
DATA ae01_dt_minmax;
  SET sdtm.ae;
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  prxid= prxparse('/^(\d{4}|-)(-(\d{2}|-)(-(\d{2}|-)(T(\d{2}|-)(:(\d{2}|-)(:(\d{2}))?)?)?)?)? *$/');
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      aestdt_min_hour= input(prxposn(prxid,7,aestdtc),?? 2.);
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      aestdt_min_second= input(prxposn(prxid,11,aestdtc),?? 2.);
    END;
    ...
```