Creating a basic data structure (BDS) Exposure ADaM

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Programming workflow

Get required R packages

```
Warning: package 'pharmaversesdtm' was built under R version 4.4.2
```

```
Attaching package: 'lubridate'
```

```
The following objects are masked from 'package:base':

    date, intersect, setdiff, union
```

Read CDISC pilot SDTM and ADaM datasets

```
adsl_vars <- exprs(TRTSDT, TRTSDTM, TRTEDT, TRTEDTM)

# left join EX and adsl TRTSDT, TRTSDTM, TRTEDT, TRTEDTM on ex.STUDYID=adslSTUDYID and ex.USUB
adex <- derive_vars_merged(
   dataset=ex
  ,dataset_add = adsl
  ,new_vars = adsl_vars
  ,by_vars = exprs(STUDYID, USUBJID)
  ) # dim(adex) 591 21
```

The CDISC pilot EX domain data does not contain a dose adjustment flag or the planned dose information. For demonstration purposes, this will be added to the data.

EXADJ

- Exposure Adjustment ?

EXDOSE

- exposure dose
- from SDTM.EX.EXDOSE

EXPLDOS

- Planned Dose

```
adex <- adex %>%
  mutate(
    EXADJ = case_when(
      USUBJID == "01-701-1028" & VISIT %in% c("WEEK 2") ~ "ADVERSE EVENT",
      USUBJID == "01-701-1148" & VISIT %in% c("WEEK 2", "WEEK 24") ~ "MEDICATION ERROR",
      TRUE ~ NA_character_
    ),
    EXDOSE = case_when(
      USUBJID == "01-701-1028" & VISIT %in% c("WEEK 2") ~ 0,
      USUBJID == "01-701-1148" & VISIT %in% c("WEEK 2", "WEEK 24") ~ 0,
      TRUE ~ EXDOSE
    )
  ) %>%
  mutate(EXPLDOS = if_else(EXTRT == "PLACEBO", 0, 54))

adex %>% select(EXTRT, EXPLDOS) %>% distinct()
```

```
# A tibble: 2 x 2
  EXTRT      EXPLDOS
  <chr>        <dbl>
1 PLACEBO          0
2 XANOMELINE      54
```

Derive numeric datetime, analysis day variables

ASTDT

- Analysis Start Date
- Set to a numeric form of EX.EXSTDTC when EX.EXSTDTC consists of a full date.

AENDT

- Analysis End Date
- Set to a numeric form of EX.EXENDTC when EX.EXENDTC consists of a full date.

```
# Convert character datetime to numeric datetime
adex <- derive_vars_dt(adex, new_vars_prefix = "AST", dtc = EXSTDTC)
adex <- derive_vars_dt(adex, new_vars_prefix = "AEN", dtc = EXENDTC) # dim(adex) 591 25
adex %>% select(USUBJID,VISIT,EXSTDTC,EXENDTC,ASTDT,AENDT) %>% head()
```

```
# A tibble: 6 x 6
  USUBJID     VISIT    EXSTDTC    EXENDTC    ASTDT      AENDT
  <chr>       <chr>    <chr>      <chr>      <date>     <date>
1 01-701-1015 BASELINE 2014-01-02 2014-01-16 2014-01-02 2014-01-16
2 01-701-1015 WEEK 2   2014-01-17 2014-06-18 2014-01-17 2014-06-18
3 01-701-1015 WEEK 24  2014-06-19 2014-07-02 2014-06-19 2014-07-02
4 01-701-1023 BASELINE 2012-08-05 2012-08-27 2012-08-05 2012-08-27
5 01-701-1023 WEEK 2   2012-08-28 2012-09-01 2012-08-28 2012-09-01
6 01-701-1028 BASELINE 2013-07-19 2013-08-01 2013-07-19 2013-08-01
```

ASTDTM

AENDTM

The next examples demonstrates the datetime imputation features available in the `derive_vars_dtm()` function, where the time is imputed as “00:00:00”:

```
adex <- derive_vars_dtm(
  adex
  ,dtc = EXSTDTC
  # Impute dtc date to the first day of the month
  ,highest_imputation = "M"
  ,date_imputation = "first"
  ,new_vars_prefix = "AST"
)

adex <- derive_vars_dtm(
  adex,
  dtc = EXENDTC,
  # Impute dtc date to the last day of the month
  highest_imputation = "M",
  date_imputation = "last",
  new_vars_prefix = "AEN"
)

adex %>% select(EXSTDTC,EXENDTC,ASTDTM,AENDTM) %>% head()
```

```
# A tibble: 6 x 4
  EXSTDTC    EXENDTC    ASTDTM              AENDTM
  <chr>      <chr>      <dttm>              <dttm>
1 2014-01-02 2014-01-16 2014-01-02 00:00:00 2014-01-16 00:00:00
2 2014-01-17 2014-06-18 2014-01-17 00:00:00 2014-06-18 00:00:00
3 2014-06-19 2014-07-02 2014-06-19 00:00:00 2014-07-02 00:00:00
4 2012-08-05 2012-08-27 2012-08-05 00:00:00 2012-08-27 00:00:00
5 2012-08-28 2012-09-01 2012-08-28 00:00:00 2012-09-01 00:00:00
6 2013-07-19 2013-08-01 2013-07-19 00:00:00 2013-08-01 00:00:00
```

ASTDY

- Analysis Start Day
- ‘ASTDT-TRTSDT+1‘

AENDY

- Analysis End Day
- ‘AENDT-TRTSDT+1‘

```
adex <- derive_vars_dy(
  dataset=adex
  ,reference_date = TRTSDT
  ,source_vars = exprs(ASTDT, AENDT)
```

```
  ) # dim(adex) 591 33
adex %>% select(TRTSDT, ASTDT, ASTDY, AENDT, AENDY) %>% head()
```

```
# A tibble: 6 x 5
  TRTSDT     ASTDT      ASTDY AENDT      AENDY
  <date>     <date>     <dbl> <date>     <dbl>
1 2014-01-02 2014-01-02     1 2014-01-16    15
2 2014-01-02 2014-01-17    16 2014-06-18   168
3 2014-01-02 2014-06-19   169 2014-07-02   182
4 2012-08-05 2012-08-05     1 2012-08-27    23
5 2012-08-05 2012-08-28    24 2012-09-01    28
6 2013-07-19 2013-07-19     1 2013-08-01    14
```

EXDURD

- Duration of treatment or exposure
- 'EXDURD=AENDT - ASTDT +1'

```
adex <- adex %>%
  derive_vars_duration(
    new_var = EXDURD
    ,start_date = ASTDT
    ,end_date = AENDT
    # duration unit can be "years", "months", "weeks", "days", "hours", "minutes", "seconds"
    ,out_unit = "DAYS")

adex %>% select(ASTDT, AENDT, EXDURD) %>% head()
```

```
# A tibble: 6 x 3
  ASTDT      AENDT      EXDURD
  <date>     <date>      <dbl>
1 2014-01-02 2014-01-16     15
2 2014-01-17 2014-06-18    153
3 2014-06-19 2014-07-02     14
4 2012-08-05 2012-08-27     23
5 2012-08-28 2012-09-01      5
6 2013-07-19 2013-08-01     14
```

DOSEO

- Dose Overall (?). Refers to the actual dose of the study drug administered, standardized (e.g., per unit of body weight, such as mg/kg).
- 'EXDOSE * EXDURD'

PDOSEO

- Planned Dose Overall (?) Represents the planned dose per protocol, similarly normalized
- 'EXPLDOS * EXDURD'

```
adex <- adex %>%
  mutate(
    DOSEO = EXDOSE * EXDURD
    ,PDOSEO = EXPLDOS * EXDURD)

adex %>% select(USUBJID, EXDOSE, EXPLDOS, EXDURD, DOSEO, PDOSEO) %>% head()
```

```
# A tibble: 6 x 6
  USUBJID     EXDOSE EXPLDOS EXDURD DOSEO PDOSEO
  <chr>        <dbl>   <dbl>  <dbl> <dbl>  <dbl>
1 01-701-1015      0       0     15     0      0
2 01-701-1015      0       0    153     0      0
3 01-701-1015      0       0     14     0      0
4 01-701-1023      0       0     23     0      0
5 01-701-1023      0       0      5     0      0
6 01-701-1028     54      54     14   756    756
```

Create 1:1 mapping records

The first set of exposure records to create will be records mapped 1:1 to an existing collected exposure record in SDTM. For these records, the `AVAL` or `AVALC` would be calculated using columns that exist on the data and no summarizing of records would be necessary.

These records may be used for input into summary records or be used individually for summarization in outputs. Some examples may be exposure duration, dose administered, dose adjusted, etc. based on one exposure record in SDTM.

These records can be derived using simple `dplyr::mutate` assignments and then combined

PARAMCD

- Parameter Code

AVALC

- Analysis Value Character ?

```r
adex_durd <- adex %>%
  mutate(
    PARAMCD = "DURD",
    AVAL = EXDURD)

adex_dose <- adex %>%
  mutate(
    PARAMCD = "DOSE",
    AVAL = DOSEO)

adex_pldos <- adex %>%
  mutate(
    PARAMCD = "PLDOSE",
    AVAL = PDOSEO)

adex_adj <- adex %>%
  mutate(
    PARAMCD = "ADJ",
    AVALC = if_else(!is.na(EXADJ), "Y", NA_character_)
  )

adex_adjae <- adex %>%
  mutate(
    PARAMCD = "ADJAE",
    AVALC = if_else(EXADJ == "ADVERSE EVENT", "Y", NA_character_)
  )

adex <- bind_rows(
  adex_durd,
  adex_dose,
  adex_pldos,
  adex_adj,
  adex_adjae) %>%
  mutate(PARCAT1 = "INDIVIDUAL") # dim(adex) 2955 40

adex %>% select(USUBJID,VISIT,ASTDT,AENDT,PARAMCD,AVAL,AVALC) %>% head()
```

```
# A tibble: 6 x 7
  USUBJID     VISIT    ASTDT      AENDT      PARAMCD  AVAL AVALC
  <chr>       <chr>    <date>     <date>     <chr>   <dbl> <chr>
1 01-701-1015 BASELINE 2014-01-02 2014-01-16 DURD       15 <NA>
2 01-701-1015 WEEK 2   2014-01-17 2014-06-18 DURD      153 <NA>
3 01-701-1015 WEEK 24  2014-06-19 2014-07-02 DURD       14 <NA>
4 01-701-1023 BASELINE 2012-08-05 2012-08-27 DURD       23 <NA>
5 01-701-1023 WEEK 2   2012-08-28 2012-09-01 DURD        5 <NA>
6 01-701-1028 BASELINE 2013-07-19 2013-08-01 DURD       14 <NA>
```

Create Summary Records

Exposure is commonly analyzed by a timing interval (e.g. `APHASE`, `APERIOD`, `AVISIT`, etc.). For these types of calculations, the `derive_param_exposure()` function may be used. In addition to creating a summarized `AVAL`, the function will also compute minimum and maximum dates for the record. For example, to calculate the total dose by subject and treatment

```
adex <- derive_param_exposure(
  dataset = adex
  ,dataset_add = adex
  ,by_vars = exprs(STUDYID, USUBJID, !!!adsl_vars)
  ,input_code = "DOSE"
  ,set_values_to = exprs(
    PARAMCD = "TDOSE",
    PARCAT1 = "OVERALL",
    AVAL = sum(AVAL, na.rm = TRUE)
  )
) # dim(adex) 3209 40
```

References

Creating a BDS Exposure ADaM

ADaM Subject-level Analysis - ADSL Dataset