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Robust Programming Strategies for Exposure ADaM Datasets

Robust ADaM datasets for drug exposure are essential to ensure reliable safety and efficacy analyses in clinical trials with protocol-specified treatments. Tailored data and logic checks can safeguard ADaM dataset development.

USUBJID	APERIOD	ASPER	ASPERC	TRTP	TRTA	ECDOSP	EXDOSE	DOSEU	ASTDT	AENDT	COMPL	ADURN
1002	1	1	TRT	IP B 20mg	IP B 20mg	280	280	mg	11AUG2025	25AUG2025	100	15
1002	1	2	WAS	IP B 20mg	IP B 20mg	.	.		26AUG2025	22SEP2025	.	28
1002	2	1	TRT	IP A 10mg	IP A 10mg	140	130	mg	23SEP2025	06OCT2025	92.9	14
1002	2	2	WAS	IP A 10mg	IP A 10mg	.	.		07OCT2025	01NOV2025	.	26

Treatment period-based exposure ADaM dataset

USUBJID	PARAM	PARAMCD	AVAL	AVALC
301	Total dose (mg)	DOSTOT	2000	
301	Number of administrations	DOSNUM	20	
301	Time at risk (days)	ATRISKD	127	
301	Overall compliance >= 80%	COMPLFL		Y

Parameter-based exposure ADaM dataset

Process flow: exposure ADaM dataset derivation

Input datasets

- identify needed datasets
- read in datasets

data availability

- ☑ completeness of key variables, e.g., EXTRT, ECDOSE
- ☑ no partial or missing date(time)s

coherent treatment

- ☑ plausible combinations of, e.g., dose, unit, route, and treatment values

plausible/allowed values

- ☑ ECTRT and EXTRT have sponsor-defined values
- ☑ plausible EXDOSE and ECDOSE values – consider potential dose reductions

duplicates

- ☑ no exact duplicates
- ☑ none within relevant variable combinations, e.g., USUBJID, ECTRT, ECOCCUR, ECSTDTC

Data processing and transformation

- merge SDTM datasets
- delete data not needed
- manipulate variables, e.g., create numeric date variables

coherent treatment

- ☑ EX, EC and DA records can be linked plausibly
- ☑ (after unblinding) all records consistent with DM.ACTARM
- ☑ plausible mapping of combination treatments
  - combination treatment
- ☑ medication code list merged correctly to EX, EC and/or DA
  - blinded trial

dates and relative days

- ☑ exposure start/end date(time)s plausible in relation to DM reference dates
- ☑ EXSTDTC ≤ EXENDTC

treatment periods and gaps

- ☑ washout periods have minimum length
  - cross-over trial

plausible/allowed values

- ☑ compliance matches amount of dispensed, returned and/or administered medication
  - compliance data collected in CRF
- ☑ doses in EX calculated correctly from EC
  - collected unit of treatment differs from protocol-specified unit

Derivation of exposure variables and ADaM dataset creation

treatment periods and gaps

- ☑ washout periods do not run into next treatment period
  - cross-over trial
- ☑ plausible treatment gaps
- ☑ treatment interruptions may have a minimum length and do not include treatment start/stop date(time)s
- ☑ no overlapping treatment periods
  - multiple treatment administrations

duplicates

- ☑ no exact duplicates
- ☑ none within relevant variable combinations, e.g., USUBJID, PARAMCD

dates and relative days

- ☑ ASTDT ≤ AENDT
- ☑ correct reference date used for relative days
- ☑ no missing or partial dates as per sponsor rules with flags for imputed variables
- ☑ each participant has an active exposure record with ADY = 1
- ☑ no ADY < 1
  - reference start date = first day of treatment

plausible/allowed values

- ☑ plausible (combinations of) variable values, e.g., PARAM, AVAL
- ☑ coherent treatment phases and periods
  - multiple treatment phases
- ☑ coherent summary metrics

coherent treatment

- ☑ plausible combinations of dose, unit and treatment values

number of records

- ☑ record counts per USUBJID do not exceed the plausible maximum

Cross-checks against other ADaM datasets

coherent treatment

- ☑ ADSL.ACTARM/TRTxxA/TRTSEQA match exposure records
- ☑ consistency between exposure ADaM datasets

dates and relative days

- ☑ ADSL.TRTSDT = earliest exposure start date
- ☑ all exposure dates ≥ ADSL.ENRLDT/RFICDT/RANDDT
  - randomized controlled trial
- ☑ ADSL.TRTEDT = last administration date
- ☑ all exposure dates ≤ ADSL.EOSDT/DTHDT
- ☑ if specified, ADSL.APxxEDT includes REP but cut off at ADSL.DTHDT/ EOSDT
  - residual effect period specified

treatment periods and gaps

- ☑ unexpectedly short treatment durations/ low number of treatment administrations match disposition data
  - multiple treatment administrations

plausible/allowed values

- ☑ participants with ADSL.TRTFL/SAFFL = „Y" have active treatment record(s)
- ☑ ADxx.ONTRTFL = „Y" observations fall into active treatment period (+ REP)
- ☑ plausible ADSL.TRCMP values comply with exposure records
  - compliance analysed

☑ important check ☑ check condition

Conclusion

Implementing systematic checks enhances transparency and trust in the final exposure ADaM dataset, though it can be time-consuming. A risk-based checking strategy ensures efficiency by focusing on critical and error-prone process steps such as derivation of treatment periods or complex exposure parameters.

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