

A Macro to Mark Invalid PK Data Observations for Exclusion

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ABSTRACT

This paper describes a macro for identifying and marking observations in a SAS® PK dataset, containing dosing and related PK sampling observations, as invalid and marking them with a an exclusion code and exclusion reason text. This paper is intended for SAS programmers with a basic or higher level of expertise and familiarity with PK data.

INTRODUCTION

PK observations in a SAS data set contain study drug dose administration or PK sampling analysis data. This macro checks the PK observations and finds and marks observations for exclusion from analysis tables and figures due to confirmed or possible invalid data. Examples of such invalid data are: a pre-dose sample having a later time than the dose to which it refers, duplicated observations, excessive difference between a nominal time and its corresponding actual time, and no doses recorded for a given patient. The macro uses a flag variable with a code identifying the exclusion criteria met and a text string containing a description of the exclusion. Exclusions have an order of precedence where an observation meets two or more of the criteria. As well as setting the exclusion flag and text, a note of the exclusion and its description is written to the SAS log file with the observation numbers `_n_` and the BY variables (sort key) and their values. Observations not matching any of the exclusion criteria (the 'normal' situation) have a flag that is missing and a blank text.

EXAMPLE OF PK DATA

An example of some observations of PK data is shown below. There are two types of PK observation, *dosing*, and concentration *sampling*. These are indicated with an Event ID flag named EVID, 1 for a dosing observation and 0 for a PK sample, usually a blood draw. A dose administration of PK sample collection is referred to as an Event. The date and time of the event is EVNTSDTM, a SAS internal numeric datetime. The Dosing Cycle for this study is 21 days (504 hours)

PATNUM	COHORT	EVID	DOSE	DOSEUNIT	DOSEID	DOSETYPE	DOSETIME	DOSEAMT	DOSEAMTUNIT	DOSEAMT2	DOSEAMT2UNIT	DOSEAMT3	DOSEAMT3UNIT	DOSEAMT4	DOSEAMT4UNIT	DOSEAMT5	DOSEAMT5UNIT	DOSEAMT6	DOSEAMT6UNIT	DOSEAMT7	DOSEAMT7UNIT	DOSEAMT8	DOSEAMT8UNIT	DOSEAMT9	DOSEAMT9UNIT	DOSEAMT10	DOSEAMT10UNIT	DOSEAMT11	DOSEAMT11UNIT	DOSEAMT12	DOSEAMT12UNIT	DOSEAMT13	DOSEAMT13UNIT	DOSEAMT14	DOSEAMT14UNIT	DOSEAMT15	DOSEAMT15UNIT	DOSEAMT16	DOSEAMT16UNIT	DOSEAMT17	DOSEAMT17UNIT	DOSEAMT18	DOSEAMT18UNIT	DOSEAMT19	DOSEAMT19UNIT	DOSEAMT20	DOSEAMT20UNIT	DOSEAMT21	DOSEAMT21UNIT	DOSEAMT22	DOSEAMT22UNIT	DOSEAMT23	DOSEAMT23UNIT	DOSEAMT24	DOSEAMT24UNIT	DOSEAMT25	DOSEAMT25UNIT	DOSEAMT26	DOSEAMT26UNIT	DOSEAMT27	DOSEAMT27UNIT	DOSEAMT28	DOSEAMT28UNIT	DOSEAMT29	DOSEAMT29UNIT	DOSEAMT30	DOSEAMT30UNIT	DOSEAMT31	DOSEAMT31UNIT	DOSEAMT32	DOSEAMT32UNIT	DOSEAMT33	DOSEAMT33UNIT	DOSEAMT34	DOSEAMT34UNIT	DOSEAMT35	DOSEAMT35UNIT	DOSEAMT36	DOSEAMT36UNIT	DOSEAMT37	DOSEAMT37UNIT	DOSEAMT38	DOSEAMT38UNIT	DOSEAMT39	DOSEAMT39UNIT	DOSEAMT40	DOSEAMT40UNIT	DOSEAMT41	DOSEAMT41UNIT	DOSEAMT42	DOSEAMT42UNIT	DOSEAMT43	DOSEAMT43UNIT	DOSEAMT44	DOSEAMT44UNIT	DOSEAMT45	DOSEAMT45UNIT	DOSEAMT46	DOSEAMT46UNIT	DOSEAMT47	DOSEAMT47UNIT	DOSEAMT48	DOSEAMT48UNIT	DOSEAMT49	DOSEAMT49UNIT	DOSEAMT50	DOSEAMT50UNIT	DOSEAMT51	DOSEAMT51UNIT	DOSEAMT52	DOSEAMT52UNIT	DOSEAMT53	DOSEAMT53UNIT	DOSEAMT54	DOSEAMT54UNIT	DOSEAMT55	DOSEAMT55UNIT	DOSEAMT56	DOSEAMT56UNIT	DOSEAMT57	DOSEAMT57UNIT	DOSEAMT58	DOSEAMT58UNIT	DOSEAMT59	DOSEAMT59UNIT	DOSEAMT60	DOSEAMT60UNIT	DOSEAMT61	DOSEAMT61UNIT	DOSEAMT62	DOSEAMT62UNIT	DOSEAMT63	DOSEAMT63UNIT	DOSEAMT64	DOSEAMT64UNIT	DOSEAMT65	DOSEAMT65UNIT	DOSEAMT66	DOSEAMT66UNIT	DOSEAMT67	DOSEAMT67UNIT	DOSEAMT68	DOSEAMT68UNIT	DOSEAMT69	DOSEAMT69UNIT	DOSEAMT70	DOSEAMT70UNIT	DOSEAMT71	DOSEAMT71UNIT	DOSEAMT72	DOSEAMT72UNIT	DOSEAMT73	DOSEAMT73UNIT	DOSEAMT74	DOSEAMT74UNIT	DOSEAMT75	DOSEAMT75UNIT	DOSEAMT76	DOSEAMT76UNIT	DOSEAMT77	DOSEAMT77UNIT	DOSEAMT78	DOSEAMT78UNIT	DOSEAMT79	DOSEAMT79UNIT	DOSEAMT80	DOSEAMT80UNIT	DOSEAMT81	DOSEAMT81UNIT	DOSEAMT82	DOSEAMT82UNIT	DOSEAMT83	DOSEAMT83UNIT	DOSEAMT84	DOSEAMT84UNIT	DOSEAMT85	DOSEAMT85UNIT	DOSEAMT86	DOSEAMT86UNIT	DOSEAMT87	DOSEAMT87UNIT	DOSEAMT88	DOSEAMT88UNIT	DOSEAMT89	DOSEAMT89UNIT	DOSEAMT90	DOSEAMT90UNIT	DOSEAMT91	DOSEAMT91UNIT	DOSEAMT92	DOSEAMT92UNIT	DOSEAMT93	DOSEAMT93UNIT	DOSEAMT94	DOSEAMT94UNIT	DOSEAMT95	DOSEAMT95UNIT	DOSEAMT96	DOSEAMT96UNIT	DOSEAMT97	DOSEAMT97UNIT	DOSEAMT98	DOSEAMT98UNIT	DOSEAMT99	DOSEAMT99UNIT	DOSEAMT100	DOSEAMT100UNIT	DOSEAMT101	DOSEAMT101UNIT	DOSEAMT102	DOSEAMT102UNIT	DOSEAMT103	DOSEAMT103UNIT	DOSEAMT104	DOSEAMT104UNIT	DOSEAMT105	DOSEAMT105UNIT	DOSEAMT106	DOSEAMT106UNIT	DOSEAMT107	DOSEAMT107UNIT	DOSEAMT108	DOSEAMT108UNIT	DOSEAMT109	DOSEAMT109UNIT	DOSEAMT110	DOSEAMT110UNIT	DOSEAMT111	DOSEAMT111UNIT	DOSEAMT112	DOSEAMT112UNIT	DOSEAMT113	DOSEAMT113UNIT	DOSEAMT114	DOSEAMT114UNIT	DOSEAMT115	DOSEAMT115UNIT	DOSEAMT116	DOSEAMT116UNIT	DOSEAMT117	DOSEAMT117UNIT	DOSEAMT118	DOSEAMT118UNIT	DOSEAMT119	DOSEAMT119UNIT	DOSEAMT120	DOSEAMT120UNIT	DOSEAMT121	DOSEAMT121UNIT	DOSEAMT122	DOSEAMT122UNIT	DOSEAMT123	DOSEAMT123UNIT	DOSEAMT124	DOSEAMT124UNIT	DOSEAMT125	DOSEAMT125UNIT	DOSEAMT126	DOSEAMT126UNIT	DOSEAMT127	DOSEAMT127UNIT	DOSEAMT128	DOSEAMT128UNIT	DOSEAMT129	DOSEAMT129UNIT	DOSEAMT130	DOSEAMT130UNIT	DOSEAMT131	DOSEAMT131UNIT	DOSEAMT132	DOSEAMT132UNIT	DOSEAMT133	DOSEAMT133UNIT	DOSEAMT134	DOSEAMT134UNIT	DOSEAMT135	DOSEAMT135UNIT	DOSEAMT136	DOSEAMT136UNIT	DOSEAMT137	DOSEAMT137UNIT	DOSEAMT138	DOSEAMT138UNIT	DOSEAMT139	DOSEAMT139UNIT	DOSEAMT140	DOSEAMT140UNIT	DOSEAMT141	DOSEAMT141UNIT	DOSEAMT142	DOSEAMT142UNIT	DOSEAMT143	DOSEAMT143UNIT	DOSEAMT144	DOSEAMT144UNIT	DOSEAMT145	DOSEAMT145UNIT	DOSEAMT146	DOSEAMT146UNIT	DOSEAMT147	DOSEAMT147UNIT	DOSEAMT148	DOSEAMT148UNIT	DOSEAMT149	DOSEAMT149UNIT	DOSEAMT150	DOSEAMT150UNIT	DOSEAMT151	DOSEAMT151UNIT	DOSEAMT152	DOSEAMT152UNIT	DOSEAMT153	DOSEAMT153UNIT	DOSEAMT154	DOSEAMT154UNIT	DOSEAMT155	DOSEAMT155UNIT	DOSEAMT156	DOSEAMT156UNIT	DOSEAMT157	DOSEAMT157UNIT	DOSEAMT158	DOSEAMT158UNIT	DOSEAMT159	DOSEAMT159UNIT	DOSEAMT160	DOSEAMT160UNIT	DOSEAMT161	DOSEAMT161UNIT	DOSEAMT162	DOSEAMT162UNIT	DOSEAMT163	DOSEAMT163UNIT	DOSEAMT164	DOSEAMT164UNIT	DOSEAMT165	DOSEAMT165UNIT	DOSEAMT166	DOSEAMT166UNIT	DOSEAMT167	DOSEAMT167UNIT	DOSEAMT168	DOSEAMT168UNIT	DOSEAMT169	DOSEAMT169UNIT	DOSEAMT170	DOSEAMT170UNIT	DOSEAMT171	DOSEAMT171UNIT	DOSEAMT172	DOSEAMT172UNIT	DOSEAMT173	DOSEAMT173UNIT	DOSEAMT174	DOSEAMT174UNIT	DOSEAMT175	DOSEAMT175UNIT	DOSEAMT176	DOSEAMT176UNIT	DOSEAMT177	DOSEAMT177UNIT	DOSEAMT178	DOSEAMT178UNIT	DOSEAMT179	DOSEAMT179UNIT	DOSEAMT180	DOSEAMT180UNIT	DOSEAMT181	DOSEAMT181UNIT	DOSEAMT182	DOSEAMT182UNIT	DOSEAMT183	DOSEAMT183UNIT	DOSEAMT184	DOSEAMT184UNIT	DOSEAMT185	DOSEAMT185UNIT	DOSEAMT186	DOSEAMT186UNIT	DOSEAMT187	DOSEAMT187UNIT	DOSEAMT188	DOSEAMT188UNIT	DOSEAMT189	DOSEAMT189UNIT	DOSEAMT190	DOSEAMT190UNIT	DOSEAMT191	DOSEAMT191UNIT	DOSEAMT192	DOSEAMT192UNIT	DOSEAMT193	DOSEAMT193UNIT	DOSEAMT194	DOSEAMT194UNIT	DOSEAMT195	DOSEAMT195UNIT	DOSEAMT196	DOSEAMT196UNIT	DOSEAMT197	DOSEAMT197UNIT	DOSEAMT198	DOSEAMT198UNIT	DOSEAMT199	DOSEAMT199UNIT	DOSEAMT200	DOSEAMT200UNIT	DOSEAMT201	DOSEAMT201UNIT	DOSEAMT202	DOSEAMT202UNIT	DOSEAMT203	DOSEAMT203UNIT	DOSEAMT204	DOSEAMT204UNIT	DOSEAMT205	DOSEAMT205UNIT	DOSEAMT206	DOSEAMT206UNIT	DOSEAMT207	DOSEAMT207UNIT	DOSEAMT208	DOSEAMT208UNIT	DOSEAMT209	DOSEAMT209UNIT	DOSEAMT210	DOSEAMT210UNIT	DOSEAMT211	DOSEAMT211UNIT	DOSEAMT212	DOSEAMT212UNIT	DOSEAMT213	DOSEAMT213UNIT	DOSEAMT214	DOSEAMT214UNIT	DOSEAMT215	DOSEAMT215UNIT	DOSEAMT216	DOSEAMT216UNIT	DOSEAMT217	DOSEAMT217UNIT	DOSEAMT218	DOSEAMT218UNIT	DOSEAMT219	DOSEAMT219UNIT	DOSEAMT220	DOSEAMT220UNIT	DOSEAMT221	DOSEAMT221UNIT	DOSEAMT222	DOSEAMT222UNIT	DOSEAMT223	DOSEAMT223UNIT	DOSEAMT224	DOSEAMT224UNIT	DOSEAMT225	DOSEAMT225UNIT	DOSEAMT226	DOSEAMT226UNIT	DOSEAMT227	DOSEAMT227UNIT	DOSEAMT228	DOSEAMT228UNIT	DOSEAMT229	DOSEAMT229UNIT	DOSEAMT230	DOSEAMT230UNIT	DOSEAMT231	DOSEAMT231UNIT	DOSEAMT232	DOSEAMT232UNIT	DOSEAMT233	DOSEAMT233UNIT	DOSEAMT234	DOSEAMT234UNIT	DOSEAMT235	DOSEAMT235UNIT	DOSEAMT236	DOSEAMT236UNIT	DOSEAMT237	DOSEAMT237UNIT	DOSEAMT238	DOSEAMT238UNIT	DOSEAMT239	DOSEAMT239UNIT	DOSEAMT240	DOSEAMT240UNIT	DOSEAMT241	DOSEAMT241UNIT	DOSEAMT242	DOSEAMT242UNIT	DOSEAMT243	DOSEAMT243UNIT	DOSEAMT244	DOSEAMT244UNIT	DOSEAMT245	DOSEAMT245UNIT	DOSEAMT246	DOSEAMT246UNIT	DOSEAMT247	DOSEAMT247UNIT	DOSEAMT248	DOSEAMT248UNIT	DOSEAMT249	DOSEAMT249UNIT	DOSEAMT250	DOSEAMT250UNIT	DOSEAMT251	DOSEAMT251UNIT	DOSEAMT252	DOSEAMT252UNIT	DOSEAMT253	DOSEAMT253UNIT	DOSEAMT254	DOSEAMT254UNIT	DOSEAMT255	DOSEAMT255UNIT	DOSEAMT256	DOSEAMT256UNIT	DOSEAMT257	DOSEAMT257UNIT	DOSEAMT258	DOSEAMT258UNIT	DOSEAMT259	DOSEAMT259UNIT	DOSEAMT260	DOSEAMT260UNIT	DOSEAMT261	DOSEAMT261UNIT	DOSEAMT262	DOSEAMT262UNIT	DOSEAMT263	DOSEAMT263UNIT	DOSEAMT264	DOSEAMT264UNIT	DOSEAMT265	DOSEAMT265UNIT	DOSEAMT266	DOSEAMT266UNIT	DOSEAMT267	DOSEAMT267UNIT	DOSEAMT268	DOSEAMT268UNIT	DOSEAMT269	DOSEAMT269UNIT	DOSEAMT270	DOSEAMT270UNIT	DOSEAMT271	DOSEAMT271UNIT	DOSEAMT272	DOSEAMT272UNIT	DOSEAMT273	DOSEAMT273UNIT	DOSEAMT274	DOSEAMT274UNIT	DOSEAMT275	DOSEAMT275UNIT	DOSEAMT276	DOSEAMT276UNIT	DOSEAMT277	DOSEAMT277UNIT	DOSEAMT278	DOSEAMT278UNIT	DOSEAMT279	DOSEAMT279UNIT	DOSEAMT280	DOSEAMT280UNIT	DOSEAMT281	DOSEAMT281UNIT	DOSEAMT282	DOSEAMT282UNIT	DOSEAMT283	DOSEAMT283UNIT	DOSEAMT284	DOSEAMT284UNIT	DOSEAMT285	DOSEAMT285UNIT	DOSEAMT286	DOSEAMT286UNIT	DOSEAMT287	DOSEAMT287UNIT	DOSEAMT288	DOSEAMT288UNIT	DOSEAMT289	DOSEAMT289UNIT	DOSEAMT290	DOSEAMT290UNIT	DOSEAMT291	DOSEAMT291UNIT	DOSEAMT292	DOSEAMT292UNIT	DOSEAMT293	DOSEAMT293UNIT	DOSEAMT294	DOSEAMT294UNIT	DOSEAMT295	DOSEAMT295UNIT	DOSEAMT296	DOSEAMT296UNIT	DOSEAMT297	DOSEAMT297UNIT	DOSEAMT298	DOSEAMT298UNIT	DOSEAMT299	DOSEAMT299UNIT	DOSEAMT300	DOSEAMT300UNIT	DOSEAMT301	DOSEAMT301UNIT	DOSEAMT302	DOSEAMT302UNIT	DOSEAMT303	DOSEAMT303UNIT	DOSEAMT304	DOSEAMT304UNIT	DOSEAMT305	DOSEAMT305UNIT	DOSEAMT306	DOSEAMT306UNIT	DOSEAMT307	DOSEAMT307UNIT	DOSEAMT308	DOSEAMT308UNIT	DOSEAMT309	DOSEAMT309UNIT	DOSEAMT310	DOSEAMT310UNIT	DOSEAMT311	DOSEAMT311UNIT	DOSEAMT312	DOSEAMT312UNIT	DOSEAMT313	DOSEAMT313UNIT	DOSEAMT314	DOSEAMT314UNIT	DOSEAMT315	DOSEAMT315UNIT	DOSEAMT316	DOSEAMT316UNIT	DOSEAMT317	DOSEAMT317UNIT	DOSEAMT318	DOSEAMT318UNIT	DOSEAMT319	DOSEAMT319UNIT	DOSEAMT320	DOSEAMT320UNIT	DOSEAMT321	DOSEAMT321UNIT	DOSEAMT322	DOSEAMT322UNIT	DOSEAMT323	DOSEAMT323UNIT	DOSEAMT324	DOSEAMT324UNIT	DOSEAMT325	DOSEAMT325UNIT	DOSEAMT326	DOSEAMT326UNIT	DOSEAMT327	DOSEAMT327UNIT	DOSEAMT328	DOSEAMT328UNIT	DOSEAMT329	DOSEAMT329UNIT	DOSEAMT330	DOSEAMT330UNIT	DOSEAMT331	DOSEAMT331UNIT	DOSEAMT332	DOSEAMT332UNIT	DOSEAMT333	DOSEAMT333UNIT	DOSEAMT334	DOSEAMT334UNIT	DOSEAMT335	DOSEAMT335UNIT	DOSEAMT336	DOSEAMT336UNIT	DOSEAMT337	DOSEAMT337UNIT	DOSEAMT338	DOSEAMT338UNIT	DOSEAMT339	DOSEAMT339UNIT	DOSEAMT340	DOSEAMT340UNIT	DOSEAMT341	DOSEAMT341UNIT	DOSEAMT342	DOSEAMT342UNIT	DOSEAMT343	DOSEAMT343UNIT	DOSEAMT344	DOSEAMT344UNIT	DOSEAMT345	DOSEAMT345UNIT	DOSEAMT346	DOSEAMT346UNIT	DOSEAMT347	DOSEAMT347UNIT	DOSEAMT348	DOSEAMT348UNIT	DOSEAMT349	DOSEAMT349UNIT	DOSEAMT350	DOSEAMT350UNIT	DOSEAMT351	DOSEAMT351UNIT	DOSEAMT352	DOSEAMT352UNIT	DOSEAMT353	DOSEAMT353UNIT	DOSEAMT354	DOSEAMT354UNIT	DOSEAMT355	DOSEAMT355UNIT	DOSEAMT356	DOSEAMT356UNIT	DOSEAMT357	DOSEAMT357UNIT	DOSEAMT358	DOSEAMT358UNIT	DOSEAMT359	DOSEAMT359UNIT	DOSEAMT360	DOSEAMT360UNIT	DOSEAMT361	DOSEAMT361UNIT	DOSEAMT362	DOSEAMT362UNIT	DOSEAMT363	DOSEAMT363UNIT	DOSEAMT364	DOSEAMT364UNIT	DOSEAMT365	DOSEAMT365UNIT	DOSEAMT366	DOSEAMT366UNIT	DOSEAMT367	DOSEAMT367UNIT	DOSEAMT368	DOSEAMT368UNIT	DOSEAMT369	DOSEAMT369UNIT	DOSEAMT370	DOSEAMT370UNIT	DOSEAMT371	DOSEAMT371UNIT	DOSEAMT372	DOSEAMT372UNIT	DOSEAMT373	DOSEAMT373UNIT	DOSEAMT374	DOSEAMT374UNIT	DOSEAMT375	DOSEAMT375UNIT	DOSEAMT376	DOSEAMT376UNIT	DOSEAMT377	DOSEAMT377UNIT	DOSEAMT378	DOSEAMT378UNIT	DOSEAMT379	DOSEAMT379UNIT	DOSEAMT380	DOSEAMT380UNIT	DOSEAMT381	DOSEAMT381UNIT	DOSEAMT382	DOSEAMT382UNIT	DOSEAMT383	DOSEAMT383UNIT	DOSEAMT384	DOSEAMT384UNIT	DOSEAMT385	DOSEAMT385UNIT	DOSEAMT386	DOSEAMT386UNIT	DOSEAMT387	DOSEAMT387UNIT	DOSEAMT388	DOSEAMT388UNIT	DOSEAMT389	DOSEAMT389UNIT	DOSEAMT390	DOSEAMT390UNIT	DOSEAMT391	DOSEAMT39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DRUG - Study Drug Identifier
 VISIT - Planned Visit Test (e.g. 'SCREENING', 'CYCLE 1 DAY 1', 'WEEK 2 DAY 1')
 CYCLE - Dosing Cycle, periods of a set number of days
 DAY - Day within the cycle 1 though cycle length in days
 VISITDY - Day of visit. Day 1 is the first day of the study.
 ATPT - Sampling Analysis Time Point (e.g. '30 MIN POSTDOSE', '2 HOURS POST DOSE'). This can be blank.
 ATPFN - Sampling Analysis Time Point sequence number (e.g. 1='PRE-DOSE', 2='30 MIN POSTDOSE')
 NRELTM1 - Nominal Relative Time of Sample or Dose, ie: planned dose timepoint in the study
 ARELTM1 - Actual Relative Time of Sample or Dose, relative to the start of the study
 ETMU - Elapsed Time Units, units of measurement for NRELTM1 and ARELTM1 (e.g. 'day','hr')
 EVNTSDTM - Event date/time, numeric SAS internal datetime. A character version named EVNTSDTC is needed to run the EXCLSET macro.
 EVNTDAY - Day in the study the event took place
 ASTYP - Analyte Identifier
 ASTYPU - Analyte concentration units of measurement (e.g. ug/mL)
 NOMAMT - Planned dose amount
 ACTAMT - Actual dose amount administered
 ACTAMTU - Actual dose amount units of measurement
 AVAL - Sampling analyte concentration numeric result (missing when result is 'BLQ')
 AVALC - Sampling analyte concentration character result (e.g. '12.4','105','BLQ')
 AVALU - Result concentration units of measurement (e.g. ug/mL)
 LLOQ - Lowest level of analyte concentration that is readable (Equal to BLQ)

REASONS FOR EXCLUDING OBSERVATIONS

There are several causes of erroneous PK data which may result in inaccurate reporting on tables, and figures. Most involve the dose or analyte amount and the date or time of the dosing or sampling event. The decision to exclude a PK observation is based on a combination of study specific criteria and the opinion of the Lead Scientist as to whether the accuracy of tabulated or plotted results is compromised. Here is a list of the main sources of error:

PILLS ORAL DOSING ERRORS

Patient forgot to or refused to take their medicine

Patient took their medicine too early or too late, actual dose time ARELTM1 not close to the planned dose time NRELTM1

Patient took their medicine before instead of after, or after instead of before, a meal (affects rate of absorption in the gastrointestinal tract)

Patient did not take all of their pills or took too many pills or took incorrect strength pills (incorrect dose amount – ACTAMT did not match planned dose amount NAMT)

Adverse event. (e.g. Patient could not swallow the medicine or vomited after taking the medicine)

Dose amount or time omitted or not recorded correctly on the Case Report Form (CRF)

IVF INJECTION ERRORS

Patient missed their appointment or refused treatment

Patient determined as unable to have the infusion or injection (e.g. failed a drug test, feeling unwell)

Infusion/Injection site reaction/infection

Infusion Interruption or discontinuation (e.g. Adverse Event, problem with IV system)

Incorrect dose amount or incorrect concentration administered (e.g. recorded as ug instead of mg)

Dose amount or time omitted or not recorded correctly on the CRF

DATE AND TIME ERRORS

Date or time not recorded (missing)

Month and Day transposed

Time rounded to nearest 5 or 10 minutes or nearest hour

Different time sources (e.g. wall-clock slow, investigators watch fast)

Improper am/pm conversion to military time

Missing month or day or missing minutes

Non-date or time characters

Too large or too small a time range or window or end date or time before start date or time

HANDLING EXCLUSIONS

These exact details do not need to be specified, what is important is what is recorded (or not recorded) on the CRF. Each exclusion case is assigned a code, usually a sequence number or letter, and an explanatory text. PK observations marked for exclusion are *not* included in tables or graphs, because the results shown may be visibly distorted. Observations marked for exclusion *are* shown on listings, the applicable row of the listing is subscripted with the exclusion code, (or sequentially as a, b, c...) and the corresponding text is shown as a footnote on each page of the listing. Footnotes may include text for exclusions that did not occur, indicating the exclusion condition has been taken into consideration when checking the data. This provides a means of auditing the listed data and correlating it with other (non-PK) listings such as Adverse Events, Patient Disposition, and Missed Doses.

COMMON EXCLUSION CASES

Listed below are the main reasons for excluding observations. The order of precedence is important, for example a non BLQ pre-dose result is a specific case of a Missing or Invalid Result. These events are listed in order of precedence, once an exclusion condition is matched no further exclusion checks are performed.

PATIENT HAS NO RECORDED DOSE

If a given patient has no record of receiving a dose of the study medication any PK sample observations for this patient have no meaning.

PATIENT HAS NO POST-DOSE SAMPLES

A profile of the level of an analyte related to the study medication cannot be produced so the preceding dose observation should be excluded. A related pre-dose observation, if any, is still kept.

PRE-DOSE SAMPLE AFTER DOSE

This is a case of events occurring in an incorrect order. The cause can be an incorrect or incomplete time entered on the CRF. In this example the time of the PREDOSE sample was incorrectly recorded as 12:35 instead of 11:49.

P	C	V	C	S	A	E	R	R	E	V	E	A	N	A	C	A	A	L	L	O					
A	O	I	Y	I	T	L	L	E	T	N	A	S	O	C	T	A	V	V	L						
T	H	E	D	I	A	T	L	L	E	S	T	S	T	M	T	A	A	V	V	L					
N	O	V	R	S	Y	D	T	T	P	T	T	T	D	D	T	Y	A	A	M	V	A	A	L	L	O
U	R	I	U	I	L	A	D	P	T	M	M	M	T	A	Y	P	M	M	T	A	L	L	O		
M	T	D	G	T	E	Y	Y	T	N	1	1	U	M	Y	P	U	T	T	U	L	C	U	Q		
601	A5	1	TC8	CYCLE 2 DAY 1	2	1	22			504.0	503.33 hr	07APR2021:12:22	22			22	22 mg	.	.						
601	A5	0	TC8	CYCLE 2 DAY 1	2	1	22	PREDOSE	1	504.0	502.78 hr	07APR2021:12:35	22	R55	ug/mL				. BLQ	ug/mL	60				
601	A5	0	TC8	CYCLE 2 DAY 1	2	1	22	30 MIN POST	2	504.5	505.27 hr	07APR2021:12:46	22	R55	ug/mL				621	621	ug/mL	60			

NON-BLQ PRE-DOSE RESULT

The very first pre-dose sample, before the very first dose of the study medication, should have no measurable amount of any related analytes. Subsequent doses should, generally, have pre-dose samples with less than the lowest detectable amount of analyte(s), though in some studies a higher amount of pre-dose concentration is valid for the second and subsequent doses. This problem may arise due to incorrect or incomplete dates and times on the CRF, or an incorrectly recorded result. In this example a result, AVAL, is 27 and AVALC is '27', not 'BLQ' or 'LTR' at the very first PRE-DOSE, when no analyte should be present. For the second and subsequent doses PRE-DOSE AVAL can be non-missing but should be below a maximum limit dependent on the study, dose, and time since the prior dose. In some studies all PREDOSE results have to be BLQ.

P	C	V	C	S	A	R	A	R	E	N	V	E	A	N	A	C	A	A	L						
A	O	V	Y	I	A	T	L	L	E	S	T	S	T	M	T	A	A	V	V	L					
N	O	V	R	S	Y	D	T	T	P	T	T	T	D	D	T	Y	A	A	M	V	A	A	L	O	
U	R	I	U	I	L	A	D	P	T	M	M	M	T	A	Y	P	M	M	T	A	L	L	L	O	
M	T	D	G	T	E	Y	Y	T	N	1	1	U	M	Y	P	U	T	T	U	L	C	U	O	Q	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	PREDOSE	1	0.0	-2.12	hr	17MAR2021:10:55	1	R55	ug/mL			27	27	ug/mL	60
601	A5	1	TC8	CYCLE	1	DAY	1	1	1	1			0.0	0.00	hr	17MAR2021:13:02	1			16	16	mg			
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	30 MIN POST	2	0.5	0.55	hr	17MAR2021:13:35	1	R55	ug/mL			455	455	ug/mL	60

MISSING OR INVALID RESULT

A given sample result is missing or not in the expected range. In the following example the result (AVAL/AVALC) at the '30 MIN POST' timepoint is too small, there is a post-dose BLQ result preceding a non-BLQ post dose result, and the result at '4HR POST' is too large (may have been recorded in incorrect units).

P	C	V	C	S	A	R	A	R	E	N	V	E	A	N	A	C	A	A	L							
A	O	V	Y	I	A	T	L	L	E	S	T	S	T	M	T	A	A	V	V	L						
N	O	V	R	S	Y	D	T	T	P	T	T	T	D	D	T	Y	A	A	M	V	A	A	L	O		
U	R	I	U	I	L	A	D	P	T	M	M	M	T	A	Y	P	M	M	T	A	L	L	L	O		
M	T	D	G	T	E	Y	Y	T	N	1	1	U	M	Y	P	U	T	T	U	L	C	U	O	Q		
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	PREDOSE	1	0.0	-2.12	hr	17MAR2021:10:55	1	R55	ug/mL					BLQ	ug/mL	60
601	A5	1	TC8	CYCLE	1	DAY	1	1	1	1			0.0	0.00	hr	17MAR2021:13:02	1			16	16	mg				
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	30 MIN POST	2	0.5	0.55	hr	17MAR2021:13:35	1	R55	ug/mL					BLQ	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	2 HR POST	3	2.0	1.85	hr	17MAR2021:14:53	1	R55	ug/mL			442	442	ug/mL	60	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	4 HR POST	4	4.0	3.90	hr	17MAR2021:16:56	1	R55	ug/mL			419200	419200	ug/mL	60	

EXCESSIVE DIFFERENCE BETWEEN NOMINAL AND ACTUAL TIMES

Since correct dosing and sampling times are critical for accurate reporting the actual dose time or sample time should approximate to the corresponding nominal time. This is particularly significant within the first 72 hours of a dose, when a small time difference is a relatively large percentage of the elapsed time since dosing. For example, a deviation of four hours on the first day after dosing is much more significant than a deviation of that same number of hours a week after dosing. A maximum allowable deviation is normally specified in the Study Protocol. This issue does not apply to nominal times that are not chronological times, such as UNSCHEDULED, EARLY TERMINATION, and FOLLOW-UP, though follow-up at time intervals (e.g. FOLLOW-UP 3 MONTHS, FOLLOW-UP 6 MONTHS) must be in the appropriate order of sequence. Serious mismatches between the actual and nominal time can result in observations being out of sequence. The example below shows the '4HR POST' observation having an incorrectly recorded event date of April 17 2021, instead of March 17 2021. This results in an Actual Relative Time of 747 hours and 54 minutes instead of 3 hours and 54 minutes (an additional 31 days x 24 hours). The nominal time for the visit is 4 hours, hence there is a difference between the nominal and actual times of 743 hours and 54 minutes instead of just six minutes (16:56-13:02).

P	C	V	C	S	A	R	A	R	E	N	V	E	A	N	A	C	A	A	L							
A	O	V	Y	I	A	T	L	L	E	S	T	S	T	M	T	A	A	V	V	L						
N	O	V	R	S	Y	D	T	T	P	T	T	T	D	D	T	Y	A	A	M	V	A	A	L	O		
U	R	I	U	I	L	A	D	P	T	M	M	M	T	A	Y	P	M	M	T	A	L	L	L	O		
M	T	D	G	T	E	Y	Y	T	N	1	1	U	M	Y	P	U	T	T	U	L	C	U	O	Q		
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	PREDOSE	1	0.0	-2.12	hr	17MAR2021:10:55	1	R55	ug/mL					BLQ	ug/mL	60
601	A5	1	TC8	CYCLE	1	DAY	1	1	1	1			0.0	0.00	hr	17MAR2021:13:02	1			16	16	mg				
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	30 MIN POST	2	0.5	0.55	hr	17MAR2021:13:35	1	R55	ug/mL			455	455	ug/mL	60	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	2 HR POST	3	2.0	1.85	hr	17MAR2021:14:53	1	R55	ug/mL			442	442	ug/mL	60	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	8 HR POST	5	8.0	8.22	hr	17MAR2021:21:15	1	R55	ug/mL			417	417	ug/mL	60	
601	A5	0	TC8	CYCLE	1	DAY	2	1	2	2	24 HR POST	6	24.0	24.13	hr	18MAR2021:13:10	2	R55	ug/mL			380	380	ug/mL	60	
601	A5	0	TC8	CYCLE	1	DAY	3	1	3	3	48 HR POST	7	48.0	47.75	hr	19MAR2021:12:47	3	R55	ug/mL			348	348	ug/mL	60	
601	A5	0	TC8	CYCLE	1	DAY	8	1	8	8	POSTDOSE	8	168.0	172.05	hr	24MAR2021:17:05	8	R55	ug/mL			223	223	ug/mL	60	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	4 HR POST	4	4.0	747.50	hr	17APR2021:16:56	31	R55	ug/mL			428	428	ug/mL	60	

DUPLICATED DATES OR TIMES

Two dosing or sampling results recorded as being at the same time. Incomplete or missing times, for example the minutes missing from two samples taken within the same hour. Missing times can be imputed from other times, such as the time of the preceding or following sample.

P	C	V	C	I	A	R	R	E	N	A	S	N	A	C	A	A	L	O	Q							
A	O	V	C	I	A	R	R	E	N	A	S	N	A	C	A	A	L	O	Q							
T	H	E	D	I	Y	D	T	T	P	T	T	D	D	T	Y	A	A	M	V	A	A	L	L	O	L	
N	O	V	R	S	Y	D	T	T	P	T	T	D	D	T	Y	A	A	M	V	A	A	L	L	O	L	
U	R	I	U	I	L	A	D	P	T	M	M	M	T	A	Y	P	M	M	T	A	L	L	O	L	O	
M	T	D	G	T	E	Y	Y	T	N	1	1	U	M	Y	P	U	T	T	U	L	C	U	L	O	Q	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	PREDOSE	1	0.0	-2.12	hr	17MAR2021:10:55	1	R55	ug/mL			. BLQ	ug/mL	60		
601	A5	1	TC8	CYCLE	1	DAY	1	1	1	1			0.0	0.00	hr	17MAR2021:13:02	1			16	16	mg			.	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	30 MIN	POST	2	0.5	0.55	hr	17MAR2021:13:35	1	R55	ug/mL			455	455	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	2 HR	POST	3	2.0	1.85	hr	17MAR2021:14:53	1	R55	ug/mL			442	442	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	4 HR	POST	4	4.0	3.90	hr	17MAR2021:16:56	1	R55	ug/mL			428	428	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	8 HR	POST	5	8.0	3.90	hr	17MAR2021:16:56	1	R55	ug/mL			417	417	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	2	1	2	2	24 HR	POST	6	24.0	24.13	hr	18MAR2021:13:10	2	R55	ug/mL			380	380	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	3	1	3	3	48 HR	POST	7	48.0	47.75	hr	19MAR2021:12:47	3	R55	ug/mL			348	348	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	8	1	8	8	POSTDOSE	8	168.0	172.05	hr	24MAR2021:17:05	8	R55	ug/mL			223	223	ug/mL	60	

DUPLICATED VISIT AND NOMINAL TIME POINT

Two sampling observations have the same VISIT text and Timepoint text. (They will also have the same calculated nominal times).

P	C	V	C	I	A	R	R	E	N	A	S	N	A	C	A	A	L	O	Q							
A	O	V	C	I	A	R	R	E	N	A	S	N	A	C	A	A	L	O	Q							
T	H	E	D	I	Y	D	T	T	P	T	T	D	D	T	Y	A	A	M	V	A	A	L	L	O	L	
N	O	V	R	S	Y	D	T	T	P	T	T	D	D	T	Y	A	A	M	V	A	A	L	L	O	L	
U	R	I	U	I	L	A	D	P	T	M	M	M	T	A	Y	P	M	M	T	A	L	L	O	L	O	
M	T	D	G	T	E	Y	Y	T	N	1	1	U	M	Y	P	U	T	T	U	L	C	U	L	O	Q	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	PREDOSE	1	0.0	-2.12	hr	17MAR2021:10:55	1	R55	ug/mL			. BLQ	ug/mL	60		
601	A5	1	TC8	CYCLE	1	DAY	1	1	1	1			0.0	0.00	hr	17MAR2021:13:02	1			16	16	mg			.	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	30 MIN	POST	2	0.5	0.55	hr	17MAR2021:13:35	1	R55	ug/mL			455	455	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	2 HR	POST	3	2.0	1.85	hr	17MAR2021:14:53	1	R55	ug/mL			442	442	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	4 HR	POST	4	4.0	3.90	hr	17MAR2021:16:56	1	R55	ug/mL			428	428	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	8 HR	POST	5	8.0	8.22	hr	17MAR2021:21:15	1	R55	ug/mL			417	417	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	2	1	2	2	24 HR	POST	6	24.0	24.13	hr	18MAR2021:13:10	2	R55	ug/mL			380	380	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	2	1	3	3	24 HR	POST	6	24.0	47.75	hr	19MAR2021:12:47	3	R55	ug/mL			348	348	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	8	1	8	8	POSTDOSE	8	168.0	172.05	hr	24MAR2021:17:05	8	R55	ug/mL			223	223	ug/mL	60	

DATE, TIME, OR VISIT MISSING

The date or time is blank or has non-date time characters, or there is no VISIT text. Timepoint text can be missing for samples taken a significant time after the dose was administered, for example, one hour is a significant fraction of the first few hours after dosing, but is not a significant fraction of several days.

Sample timepoint text should be missing for dosing observations. Missing timepoint text where there is supposed to be timepoint text will impact the calculated nominal time causing it to differ significantly from the actual time.

P	C	V	C	I	A	R	R	E	N	A	S	N	A	C	A	A	L	O	Q							
A	O	V	C	I	A	R	R	E	N	A	S	N	A	C	A	A	L	O	Q							
T	H	E	D	I	Y	D	T	T	P	T	T	D	D	T	Y	A	A	M	V	A	A	L	L	O	L	
N	O	V	R	S	Y	D	T	T	P	T	T	D	D	T	Y	A	A	M	V	A	A	L	L	O	L	
U	R	I	U	I	L	A	D	P	T	M	M	M	T	A	Y	P	M	M	T	A	L	L	O	L	O	
M	T	D	G	T	E	Y	Y	T	N	1	1	U	M	Y	P	U	T	T	U	L	C	U	L	O	Q	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	PREDOSE	1	0.0	-2.12	hr	17MAR2021:10:55	1	R55	ug/mL			. BLQ	ug/mL	60		
601	A5	1	TC8	CYCLE	1	DAY	1	1	1	1			0.0	0.00	hr	17MAR2021:13:02	1			16	16	mg			.	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	30 MIN	POST	2	0.5	. hr		1	R55	ug/mL			455	455	ug/mL	60	
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1			3	2.0	1.85	hr	17MAR2021:14:53	1	R55	ug/mL			442	442	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	4 HR	POST	4	4.0	3.90	hr	17MAR2021:16:56	1	R55	ug/mL			428	428	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	8 HR	POST	5	8.0	8.22	hr	17MAR2021:21:15	1	R55	ug/mL			417	417	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	1	1	1	1	24 HR	POST	6	24.0	24.13	hr	18MAR2021:13:10	2	R55	ug/mL			380	380	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	3	1	3	3	48 HR	POST	7	48.0	47.75	hr	19MAR2021:12:47	3	R55	ug/mL			348	348	ug/mL	60
601	A5	0	TC8	CYCLE	1	DAY	8	1	8	8	POSTDOSE	8	168.0	172.05	hr	24MAR2021:17:05	8	R55	ug/mL			223	223	ug/mL	60	

MACRO CODE

This macro, EXCLSET, takes as input a PK dataset (INDS) like the one shown in the example and a variable which is a character representation of the event date and time in the format “yyyymmddThh:mm” (e.g. EVNTSDTM stored as EVNTSDTC with a length of \$25). and may or may not include the seconds in the time part. The contents of the input dataset (INDS) are unchanged except for the observation sort order and the addition of the two variables EXCLFLN and EXCLREAS. EXCLFLN is the exclusion code number and is 0 if no exclusions apply. EXCLREA is the corresponding exclusion reason text and is blank if no exclusions apply. The order of precedence of exclusion causes is the sequential order of the exclusion codes, if two or more exclusions apply to the same observation only the first is specified.

```
%macro exclset(inds=,          /* Input dataset name */
               patid=usubjid,  /* Patient ID, character or numeric */
               drugid=,        /* Drug name (character) or numeric id */
               areltml=afrlt,  /* Actual relative time from first dose */
               nreltml=nfrlt,  /* Nominal relative time from first dose */
               tpttxt=,        /* Sample timepoint text (e.g. '1HR POST')*/
               actamt=amt,     /* Actual dose amount administered */
               resultn=aval,   /* Sample concentration result (numeric) */
               resultc=avalc); /* Sample concentration result (character)*/
```

```
%local reastxt1 reastxt2 reastxt3 reastxt4 reastxt5 reastxt6 reastxt7
reastxt8 reastxt9 ulimit tfract;
```

```
%let reastxt1=Patient has No Recorded Doses for the Drug;
%let reastxt2=Patient has No Post Dose samples;
%let reastxt3=Pre-dose Sample After Dose;
%let reastxt4=Post-dose Sample Before Dose;
%let reastxt5=Non-BLQ First Pre-dose;
%let reastxt6=Missing Post-dose Result or Result Outside of Expected Range;
%let reastxt7=Excess Nominal and Actual Relative Dates or Times Difference;
%let reastxt8=Duplicated Sample Nominal Time;
%let reastxt9=Duplicated Sample Actual Time;
```

```
%let ulimit=300*&actamt; /* Upper limit of dose amount */
%let tfract=0.25; /* Maximum variance between actual and nominal time */
```

```
data &inds; /* Indicate predose=1, dose=2, postdose=3, and if BLQ/LTR */
  set &inds;
  prepost=3-evid-2*(index(upcase(&tpttxt),'PRE')>0 or
  upcase(&tpttxt)='PRIOR TO DOSE');
  fblqn=(upcase(&resultc) in ('BLQ','BQL','LTR','QNS') or
  index(&resultc,'<')>0);
run;
```

```
proc sort data=&inds; /* Get the date+time of the next scheduled dose */
  by &patid &drugid descending &nreltml descending prepost;
run;
```

```
data &inds;
  set &inds;
  by &patid &drugid descending &nreltml descending prepost;
  retain nxtreltm 0;
```

```

    if first.&drugid then do;
        nxtreltm=.;
    end;
    if prepost=2 then do;
        nxtreltm=areltm1;
    end;
run;

proc sort data=&inds; /* Get the date+time of the prior scheduled dose */
    by &patid &drugid &nreltm1 prepost;
run;

data &inds;
    set &inds;
    by &patid &drugid &nreltm1 prepost &areltm1;
    retain prireltm 0;
    if first.&drugid then do;
        prireltm=.;
    end;
    if prepost=2 then do;
        prireltm=areltm1;
    end;
run;

proc sort data=&inds;
    by &patid &drugid descending evid descending &actamt;
run;

data &inds; /* Indicate if patient had no measurable doses */
    set &inds;
    by &patid &drugid descending evid descending &actamt;
    retain f1 0;
    if first.&drugid then do;
        f1=(evid=0 or (evid=1 and &actamt le 0));
    end;
run;

proc sort data=&inds;
    by &patid &drugid descending prepost descending &resultn;
run;

data &inds; /* Indicate if patient had no measureable post dose samples */
    set &inds;
    by &patid &drugid descending prepost descending &resultn;
    retain f2 0;
    if first.&drugid then do;
        f2=(prepost in (1,2) or (prepost=3 and &resultn le 0));
    end;
run;

proc sort data=&inds;
    by &patid &drugid &nreltm1 prepost &areltm1;
run;

data &inds(drop=i f1-f9 fblqn prepost nxtreltm prireltm);
    set &inds;
    by &patid &drugid &nreltm1 prepost &areltm1;

```

```

array excflags {9} f1 f2 f3 f4 f5 f6 f7 f8 f9;
length exclrea $200;
excflags{3}=(prepost=1)*(&areltm1>nxtreltm.);
excflags{4}=(prepost=3)*(&areltm1 le prireltm or prireltm=.);
excflags{5}=(prepost=1)*(prireltm=.)*(fblqn=0);
excflags{6}=(prepost=3)*(&resultn=. or &resultn ge &ulimit or fblqn=1);
excflags{7}=((&areltm1>(&nreltm1*(1+&tfrac)))+
 (&areltm1<(&nreltm1*(1-&tfrac))))*(&nreltm1 ne 0);
excflags{8}=(first.prepost=0);
excflags{9}=(first.&drugid=0 and prepost=lag(prepost) and
 &areltm1=lag1(&areltm1));
exclfln=0;
do i=1 to dim(excflags);
  if exclfln=0 and excflags{i}=1 then do;
    exclfln=i;
    exclrea=scan("&reastxt1!&reastxt2!&reastxt3!&reastxt4!&reastxt5!
    &reastxt6!&reastxt7!&reastxt8!&reastxt9",exclfln,'!');
  end;
end;
run;

%mend exclset;

```

EXAMPLE LISTING OUTPUT

In the example listing segments below patient 601 has all valid observations. Patient 613 had a PREDOSE sample and a 30 MIN POST sample taken but there is no recording of the dose given, that is no non-missing dose amount in the drug expose data (An observation should be present in the Exposure as Collected (EC) data showing the dose was scheduled but not performed). Patient 619 only had a PRE-DOSE sample taken, there were no Post Dose samples recorded. If this patient had not had a dose the exclusion code would have been 'a' instead of 'b'. Patient 633 has a PRE-DOSE sample collection time later than the dose time (and the first post-dose time). Patient 640 has a non-BLQ sample result at the very first PRE-DOSE sample, where a BLQ result would be expected. Patient 653 has a missing result and a result not in the expected range, below LLOQ (60 ug/mL). Patient 662 has an actual relative sample collection time (2.57 hours) that deviates significantly from the nominal (planned) collection time of 30 minutes. Patient 669 has observations with duplicated VISIT and TIMEPOINT texts. Patient 672 has a duplicated actual relative sample collection time.

Listing Of PK Concentration at PK Sampling Timepoints
Protocol: TC8-001

Treatment	Subject Number	Administered Dose (mg)	Visit and Timepoint	Nominal Time (hr) from First Dose	Actual Time (hr) from First Dose	R55-Analyte Serum Concentration (ug/mL)
Cohort A5	601	16	CYCLE 1 DAY 1 PREDOSE	0.0	-2.12	BLQ
			CYCLE 1 DAY 1 30 MIN POST	0.5	0.55	455
			CYCLE 1 DAY 1 2 HR POST	2.0	1.85	442
			CYCLE 1 DAY 1 4 HR POST	4.0	3.90	428
			CYCLE 1 DAY 1 8 HR POST	8.0	8.22	417
			CYCLE 1 DAY 2 24 HR POST	24.0	24.13	380
			CYCLE 1 DAY 3 48 HR POST	48.0	47.75	348
			CYCLE 1 DAY 8 POSTDOSE	168.0	172.05	223

Listing Of PK Concentration at PK Sampling Timepoints
 Protocol: TC8-001

Treatment	Subject Number	Administered Dose (mg)	Visit and Timepoint	Nominal Time (hr) from First Dose	Actual Time (hr) from First Dose	R55-Analyte Serum Concentration (ug/mL)
		22	CYCLE 2 DAY 1 PREDOSE	504.0	502.78	BLQ
			CYCLE 2 DAY 1 30 MIN POST	504.5	505.27	621
			CYCLE 2 DAY 8 POSTDOSE	672.0	674.95	240
		22	CYCLE 3 DAY 1 PREDOSE	1008.0	1004.08	BLQ
			CYCLE 3 DAY 1 30 MIN POST	1008.5	1004.77	625
			CYCLE 3 DAY 8 POSTDOSE	1176.0	1176.66	272
		22	CYCLE 4 DAY 1 PREDOSE	1512.0	1515.48	BLQ
			CYCLE 4 DAY 1 30 MIN POST	1512.5	1516.52	622
			CYCLE 4 DAY 8 POSTDOSE	1680.0	1675.85	264
Cohort A5	613	.	CYCLE 1 DAY 1 PREDOSE	0.0	-0.66	BLQ (a)
			CYCLE 1 DAY 1 30 MIN POST	0.5	0.48	BLQ (a)
Cohort A5	619	16	CYCLE 1 DAY 1 PREDOSE	0.0	-0.44	BLQ (b)
Cohort A5	633	16	CYCLE 1 DAY 1 PREDOSE	0.0	1.14	BLQ (c)
			CYCLE 1 DAY 1 30 MIN POST	0.5	0.49	438
			CYCLE 1 DAY 1 2 HR POST	2.0	2.07	417
Cohort A5	640	16	CYCLE 1 DAY 1 PREDOSE	0.0	-0.39	79 (d)
			CYCLE 1 DAY 1 30 MIN POST	0.5	0.50	458
			CYCLE 1 DAY 1 2 HR POST	2.0	2.02	440
Cohort A5	653	16	CYCLE 1 DAY 1 PREDOSE	0.0	-0.31	BLQ
			CYCLE 1 DAY 1 30 MIN POST	0.5	0.68	. (e)
			CYCLE 1 DAY 1 2 HR POST	2.0	1.94	23 (e)
Cohort A5	662	16	CYCLE 1 DAY 1 PREDOSE	0.0	-0.35	BLQ
			CYCLE 1 DAY 1 30 MIN POST	0.5	2.57	441 (f)
			CYCLE 1 DAY 1 2 HR POST	2.0	2.02	444
Cohort A5	669	16	CYCLE 1 DAY 1 PREDOSE	0.0	-0.38	BLQ
			CYCLE 1 DAY 1 30 MIN POST	0.5	0.45	450
			CYCLE 1 DAY 1 2 HR POST	2.0	1.98	437
			CYCLE 1 DAY 1 2 HR POST	2.0	4.07	422 (g)
Cohort A5	672	16	CYCLE 1 DAY 1 PREDOSE	0.0	-0.59	BLQ
			CYCLE 1 DAY 1 30 MIN POST	0.5	0.45	450
			CYCLE 1 DAY 1 2 HR POST	2.0	0.45	437 (h)

Limit of Quantitation = 60.0 ug/mL

BLQ = Below Limit of Quantitation, LTR = Lower than Reportable, N/A = Not Applicable,

N/C = Not Calculable

(a) No recorded valid doses for the patient

(b) No post-dose PK samples recorded for this patient

(c) Pre-dose has a sample collection time later than the dose time

(d) Non-BLQ Pre-dose PK sample

(e) Missing result or result not in expected range

(f) Actual sample collection time deviates significantly from the corresponding nominal time

(g) Duplicated Visit and Timepoint in the same dosing cycle

(h) Duplicated actual sample collection time

CONCLUSIONS

This macro code is a quick method of flagging PK data observations which may distort the accuracy of tables and figures produced from these data. The flagged observations should be included in listings with the reason for the exclusion, so these observations can be identified easily. This macro also ensures consistency when applied to a group of related studies. The included example code is not exhaustive and exact specifications are often study dependent and subject to change by the Lead Scientist.

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RECOMMENDED READING

- Paturi, Durga Kalyani, May 2022, "Paper AP-146, Merging Pharmacokinetic (PK) Sample Collection and Dosing Information for PK Analysis Based on Study Design and Lessons Learned" Proceedings of Pharmasug 2022, Austin, TX. Available at: <https://www.pharmasug.org/proceedings/2022/AP/PharmaSUG-2022-AP-146.pdf>
- Veramed, 5th Floor Regal House, 70 London Road, Twickenham, London, TW1 3QS, UK. September 24, 2020. "Four Mistakes to avoid when getting started in programming with Pharmacokinetic (PK) data". Available at: <https://www.veramed.co.uk/guide/4-mistakes-pk>

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