



Automated QC Framework for Reliable ADNCA Dataset Generation with admiral

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Introduction

Automated QC Framework for Reliable
ADNCA Dataset Generation with admiral



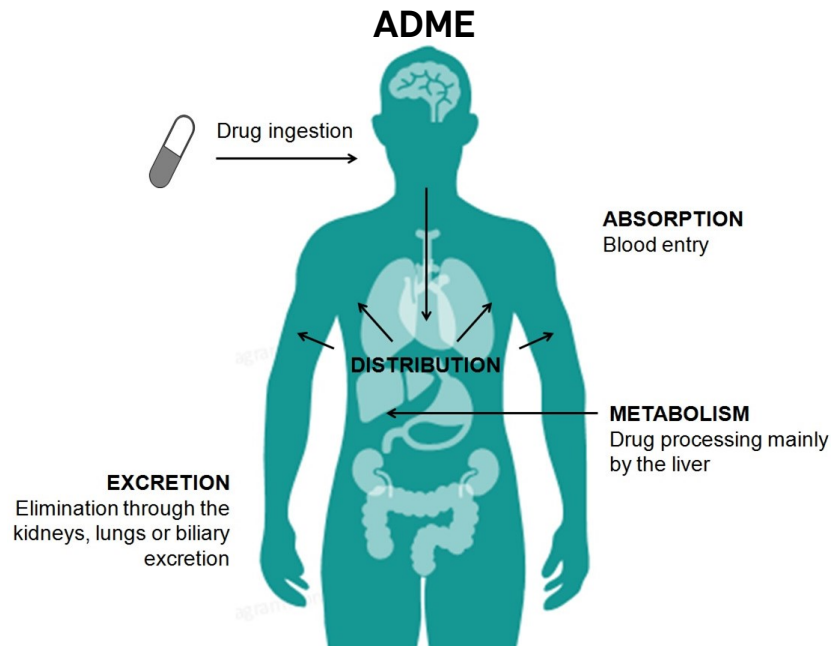
→ Pharmacokinetic analysis

Date	Version
2021-11-29	1.0 Final

Introduction

Pharmacokinetics (PK)

- Insights into **how the body acts on the drug**:
 - **A**bsorption
 - **D**istribution
 - **M**etabolism
 - **E**xcretion
- Essential to **better predict drug efficacy and safety**, and therefore improve patient outcomes.

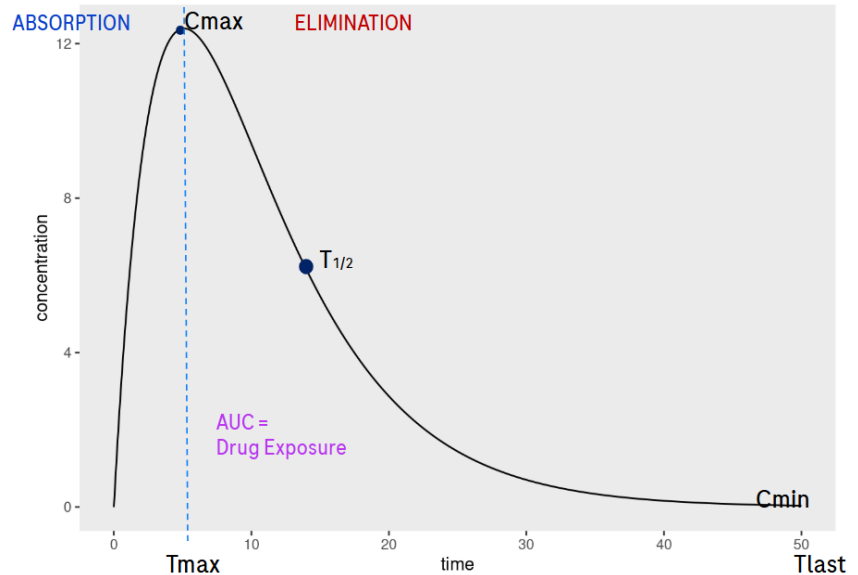


sb-peptide.com/process-development/peptide-pharmacokinetics-studies/pharmacokinetic-studies/

Introduction

Non Compartmental Analysis

- Directly estimates key **PK parameters**
(AUC, C_{max} , T_{max} , $T_{1/2}$, Clearance)
→ First step to understand **drug efficacy**
and **drug exposure**
- **Quick** and **simple**
- Relies on **log-linear regression**
- Essential for making time-critical **dosing decisions**



Context

Context

Data Scientist's challenges



Real-world clinical data (SDTM) often contains:

- **inconsistencies**
- **missing values**
- **structural issues**

that can impact NCA results.

Checking the data manually is

- **time-consuming**
- **error-prone**

Context

Goals



- **Faster** workflow
- Better **data quality**
- Better **regulatory compliance**

Automated workflow in R to ensure **reliable and early** quality control checks and **consistent** ADNCA creation.



Quality Control of SDTM Domains

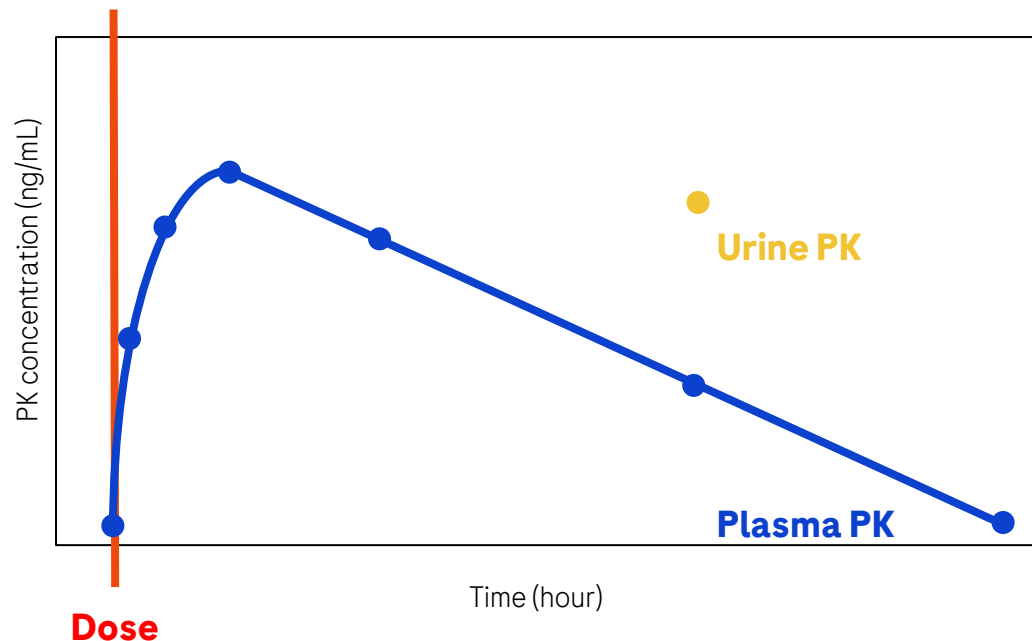
Quality Control of SDTM Domains

Study profiling



EX	Doses
PC	PK samples
VS	Vital signs
BS	Biospecimens
LB	Lab tests
..	

Subject 1: **Weight = 65 kg** **Anti-drug antibody = POSITIVE**



Need: Correct date/time, units, consistent data
To ensure accurate ADNCA creation

Quality Control of SDTM Domains

Study profiling



EX	<i>Doses</i>
PC	<i>PK samples</i>
VS	<i>Vital signs</i>
BS	<i>Biospecimens</i>
LB	<i>Lab tests</i>
..	

Automatic profiling of the study design, finding its main characteristics:

- Intravenous doses
- Urine PK samples
- Single-dose study
- Food-effect study
- etc.

→ Enables **tailored checks** and the **inclusion of the correct variables** in the final dataset.

Quality Control of SDTM Domains

Quality Control of EX (Dosing Information)



Datetime
Consistency  

EX
PC
VS
BS
LB
..

Missing clocktimes

DOMAIN	USUBJID	EXTRT	EXROUTE	VISIT	EXSTDTC	EXENDTC
EX	SUBJECT 1	DRUG 1	INTRAVENOUS	Cycle 4 Day 1	2021-04-08	2021-04-08T15:10
EX	SUBJECT 1	DRUG 1	INTRAVENOUS	Cycle 5 Day 1	2021-04-28	2021-04-28T18:00
EX	SUBJECT 1	DRUG 1	INTRAVENOUS	Cycle 6 Day 1	2021-05-19	2021-05-19T17:10

Quality Control of SDTM Domains

Quality Control of EX (Dosing Information)



Duplicate
Timepoints



EX
PC
VS
BS
LB
..

Duplicate Records

DOMAIN	USUBJID	EXTRT	EXROUTE	VISIT	EXSTDTC	EXENDTC	NDOSEDUR
EX	SUBJECT 1	DRUG 1	INTRAVENOUS	Day 4	2020-09-10T16:35	2020-09-10T17:40	1
EX	SUBJECT 1	DRUG 1	INTRAVENOUS	Day 4	2020-09-10T16:35	2020-09-10T17:40	1
EX	SUBJECT 2	DRUG 2	INTRAVENOUS	Unscheduled	2022-02-28T12:40	2022-02-28T16:38	4
EX	SUBJECT 2	DRUG 2	INTRAVENOUS	MAINTENANCE (10 months)	2022-02-28T12:40	2022-02-28T16:38	4

Quality Control of SDTM Domains

Quality Control of EX (Dosing Information)



EX
PC
VS
BS
LB
..

Study Days
Consistency



Infusion Duration
Consistency



Interrupted
Doses

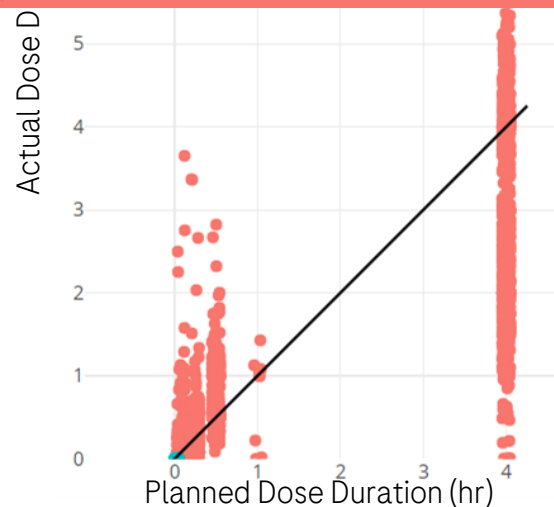


Multiple Doses per
Day



Subject ID: SUBJECT 1
Planned dose duration (hr): 1
Actual dose duration (hr): 8.83333
Visit: Day 4
Dose start time: 2020-03-18T06:55
Dose end time: 2020-03-18T15:45
Drug: DRUG 1

**Infusion
much
longer than
planned**



Quality Control of SDTM Domains

Quality Control of PC (Pharmacokinetic Concentrations)

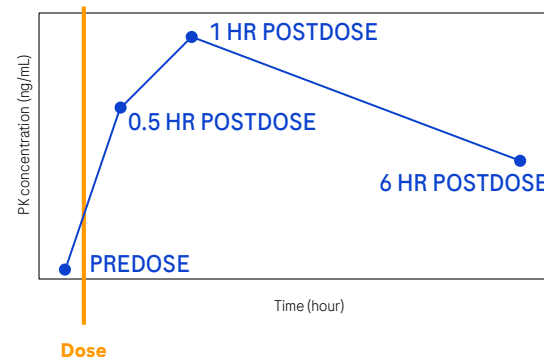
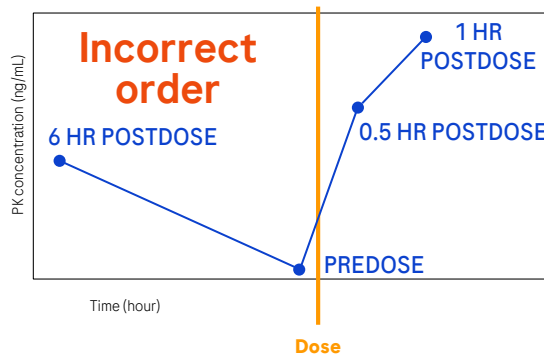


PK Sample
Inversions



EX
PC
VS
BS
LB
..

USUBJID	PCTEST	PCSPEC	VISIT	PCTPT	PCDTC	PCSTRESC
SUBJECT 1	DRUG 1	PLASMA	Cycle 3 Day 1	6 HR POSTDOSE	2021-11-15T13:05:00	34.1
SUBJECT 1	DRUG 1	PLASMA	Cycle 3 Day 1	PREDOSE	2021-11-16T08:00:00	BLQ
SUBJECT 1	DRUG 1	PLASMA	Cycle 3 Day 1	0.5 HR POSTDOSE	2021-11-16T08:35:00	41.6
SUBJECT 1	DRUG 1	PLASMA	Cycle 3 Day 1	1 HR POSTDOSE	2021-11-16T09:05:00	43.7



Quality Control of SDTM Domains

Quality Control of PC (Pharmacokinetic Concentrations)



Consistent
Units



Warning message:

Non unique units or NA values found for PCTEST/PCSPEC pairs:

A tibble: 2 × 3

	PCTEST	PCSPEC	PCSTRESU
	<chr>	<chr>	<chr>
1	DRUG 1	PLASMA	ug/mL
2	DRUG 1	PLASMA	ng/mL

**Different units for a given pair of
Analyte + Specimen**

Quality Control of SDTM Domains

Quality Control of PC (Pharmacokinetic Concentrations)



EX
PC
VS
BS
LB
..

Duplicate
Timepoints



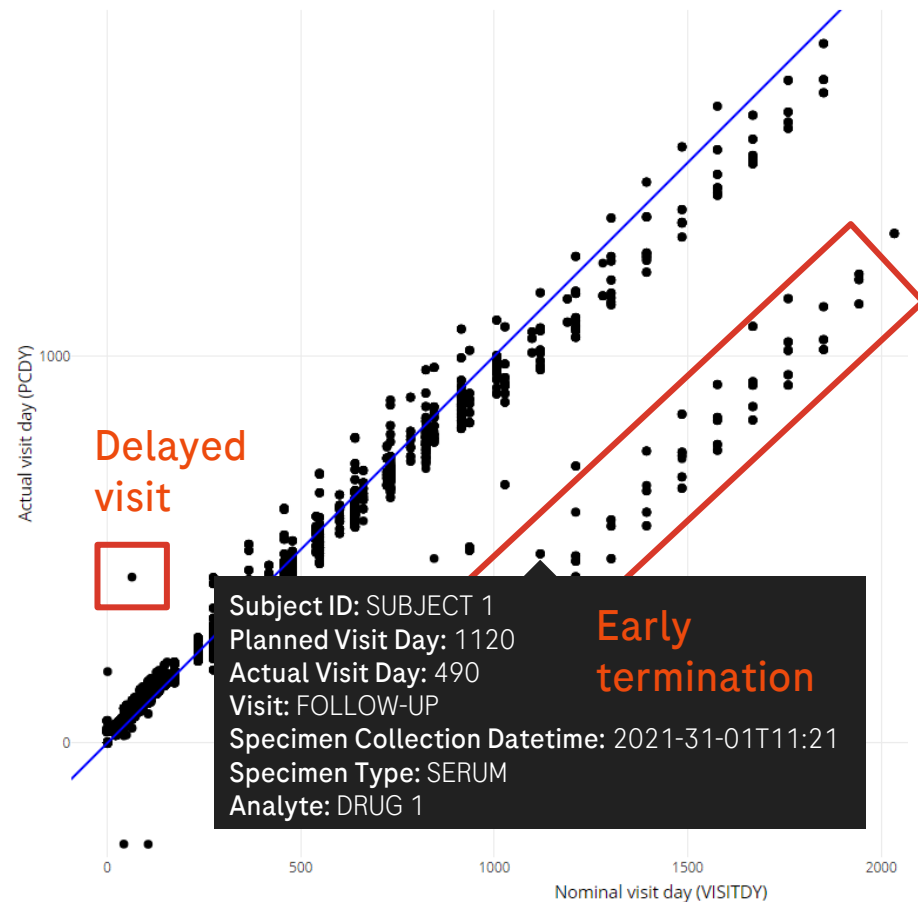
Datetime
Consistency



Study Days
Consistency



Comparison of VISITDY and PCDY



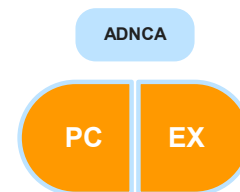
ADNCA Dataset

ADNCA Dataset

Building the dataset



- Merge PC data to EX data
- Leverage {admiral} to **derive time variables related to dosing** (time since reference dose, time since first dose)
- Derive analysis-ready flags
- Select variables to include in ADNCA **based on study design**



SDTM = Study Data Tabulation Model

eCRF = Electronic Case Report Form

ADNCA Dataset

Example of ADNCA Dataset



ADSL			PC				PC & EX	EX	
USUBJID	AGE	WEIGHT	PCSPEC	ATPT	AVAL	UNIT	AFRLT	DOSEA	ROUTE
1001	43	56	PLASMA	PREDOSE	0	ng/mL	0	500	IV
1001	43	56	PLASMA	2 HR POST INFUSION	11	ng/mL	1.8	500	IV
1001	43	56	PLASMA	4 HR POST INFUSION	23.5	ng/mL	3.5	500	IV
1001	43	56	PLASMA	6 HR POST INFUSION	20.6	ng/mL	6	500	IV
1001	43	56	PLASMA	24 HR POST INFUSION	2.2	ng/mL	25.1	500	IV
1001	43	56	URINE	24-48 HR	460.5	ng/mL	24.3	500	IV

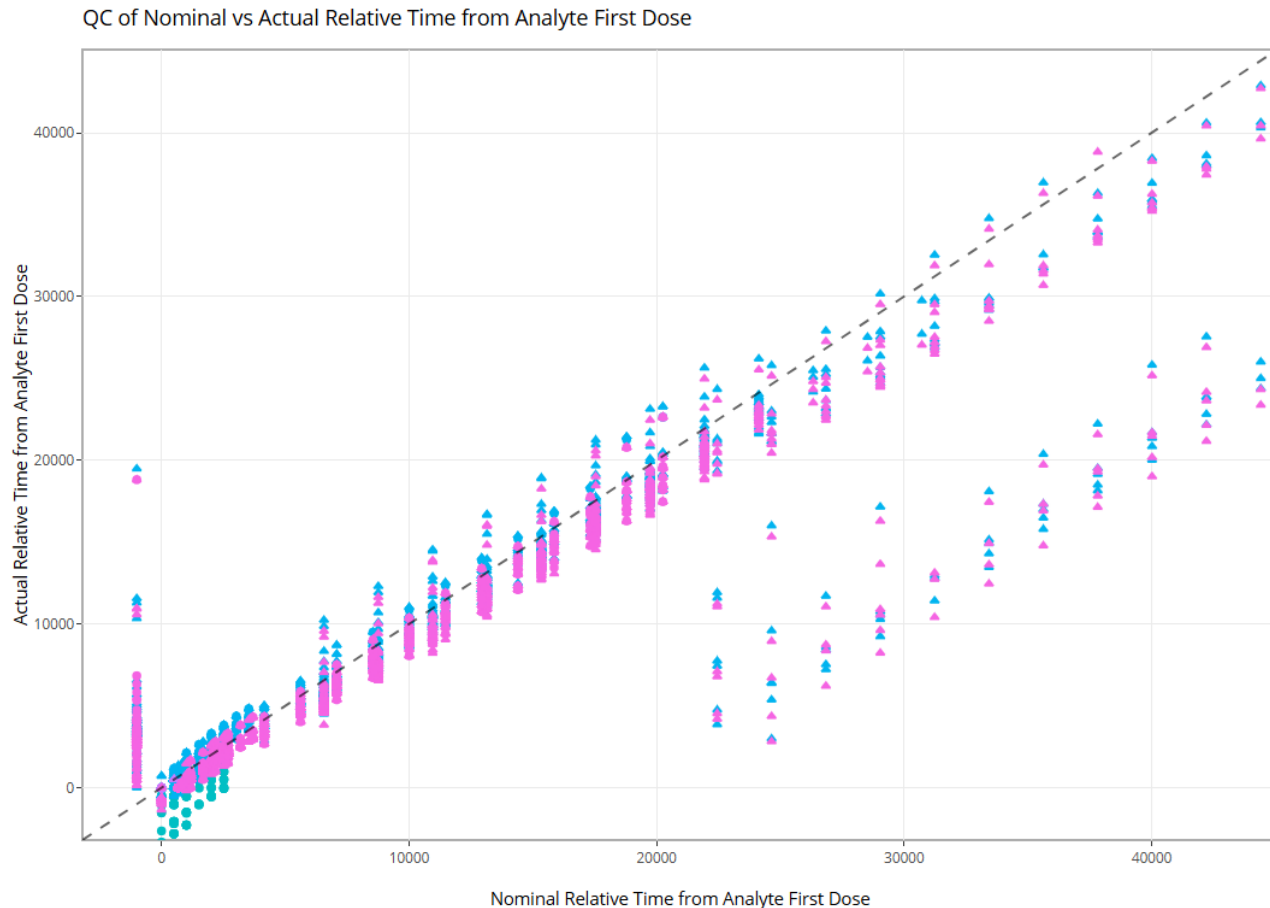
ADNCA Dataset

Quality Control of ADNCA



Final set of checks:

- Nominal vs. actual times



ADNCA Dataset

Quality Control of ADNCA



Final set of checks:

- Nominal vs. actual times
- Skipped doses
- Comparison of final ADNCA against **previous versions**

USUBJID		PCTEST	PCSPEC	PCREFID	Status	AGE	WEIGHT	ATPT	AVAL	UNIT	AFRLT	DOSEA	new_COMMENT	old_ROUTE
All		All	All	All	All	All	All	All	All	All	All	All	All	All
1	1001	Analyte 1	PLASMA	4	Row modified	43	57	6 HR POST INFUSION	20.6	ng/mL	6	500	PK sample	IV
2	1001	Analyte 1	PLASMA	5	Row modified	43	57	24 HR POST INFUSION	2.2	ng/mL	25.1	500	PK sample	IV
3	1001	Analyte 1	URINE	6	Row modified	43	57	24-48 HR	460.5	ng/mL	24.3	500	Urine sample	IV
4	1001	Analyte 1	PLASMA	7	Row added	43	57	12 HR POST INFUSION	15.1	ng/mL	12.2	500	New timepoint	
5	1002	Analyte 1	PLASMA	8	Row added	50	75	PREDOSE	0.1	ng/mL	0.1	750	New subject	
6	1001	Analyte 1	PLASMA	3	Row removed	43	56	4 HR POST INFUSION	23.5	ng/mL	3.5	500		IV
7	1001	Analyte 1	PLASMA	1	Col modified	43	56	PREDOSE	0	ng/mL	0	500	PK sample	IV
8	1001	Analyte 1	PLASMA	2	Col modified	43	56	2 HR POST INFUSION	11	ng/mL	1.8	500	PK sample	IV

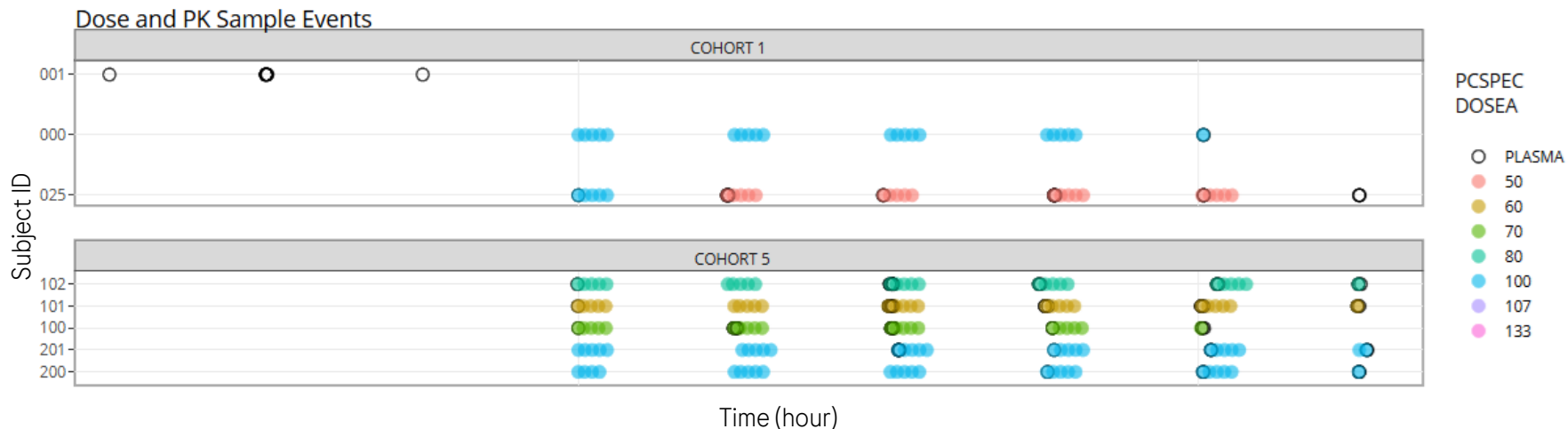
ADNCA Dataset

Quality Control of ADNCA



Final set of checks:

- Nominal vs. actual times
- Skipped doses
- Comparison of final ADNCA against **previous versions**
- Dose and PK Sample events by treatment arm



Everything is kept in a [HTML QC report](#) to be handed over to the scientist.

Future Developments

Future Developments



AI Data Bot

- Integration of the ADNCA automated code into a **LLM bot**

Generation of **ADPPK** (ADaM popPK dataset)

- More complex, more error-prone data, different dataset building rules

Conclusion

Conclusion

Improvements

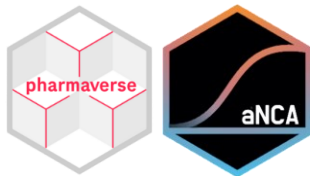


- Speed of entire process increased by **2-3 times**
- More detailed checks / find and correct errors earlier → **better data quality**
- Standardised checks and dataset structure → **better regulatory compliance**

This approach transforms a potentially error-prone task into a **transparent** and **reliable** workflow.

Conclusion

Entire Data Workflow (aNCA)



aNCA → Automation of the NCA analysis and TLG generation

If you want to know more about aNCA:

Presentation OS02: **Advancing Automated Non-Compartmental Analysis with R Shiny** on Tuesday November 18th, 11:30, Room X12

SDTM = Study Data Tabulation Model

eCRF = Electronic Case Report Form

HA = Health Authorities

Doing now what patients need next