

Making PK Analysis Easier: The New ADaM Data Standard ADNCA

Peter Schaefer
VCA-Plus, Inc
(using material developed by the ADNCA team)

Overview



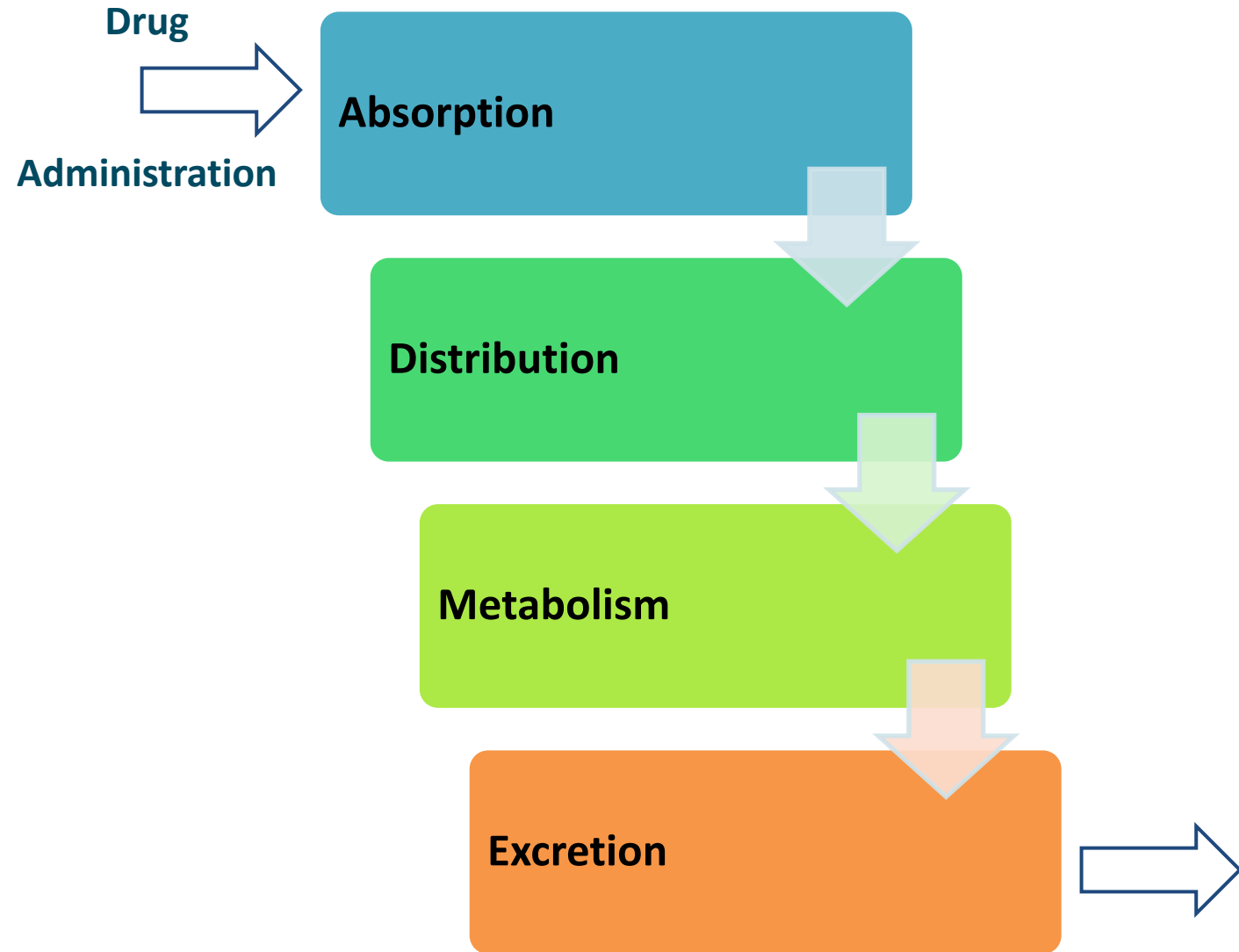
- Why is ADNCA?
- Concentration-Time Profiles
- Dosing
- Timing
- Flags

Non-compartmental PK Analysis (NCA)

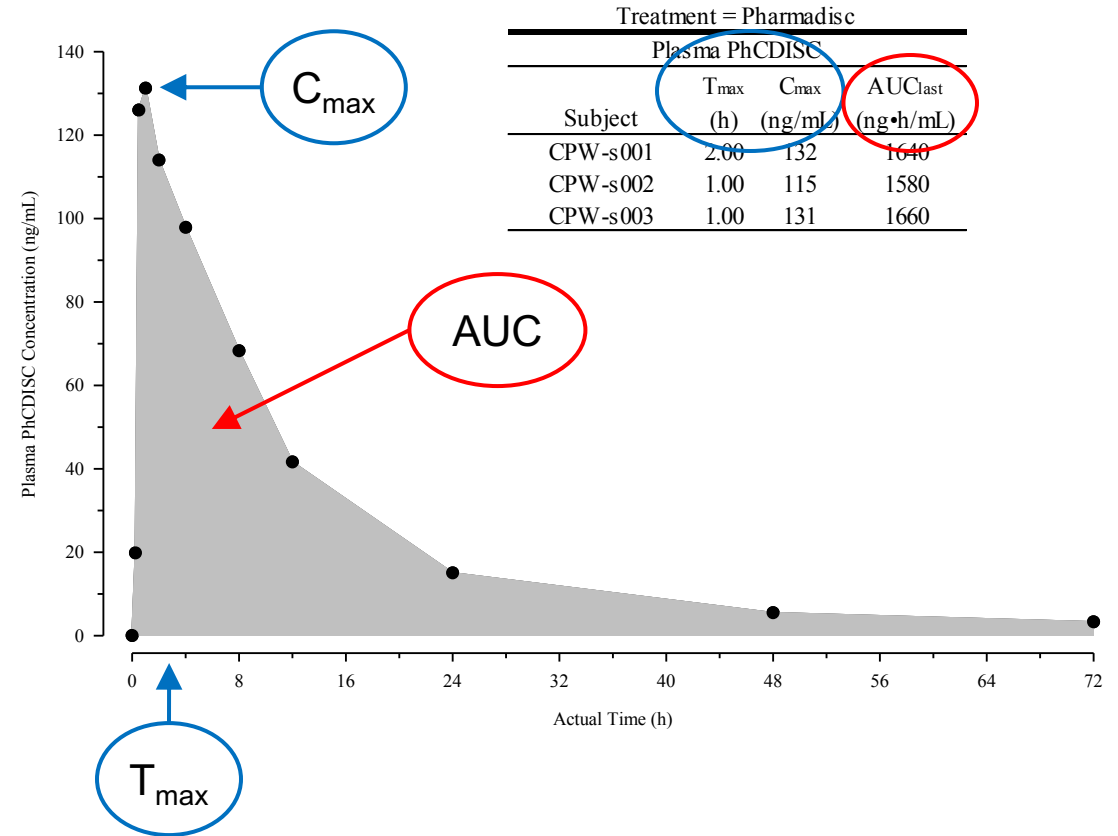
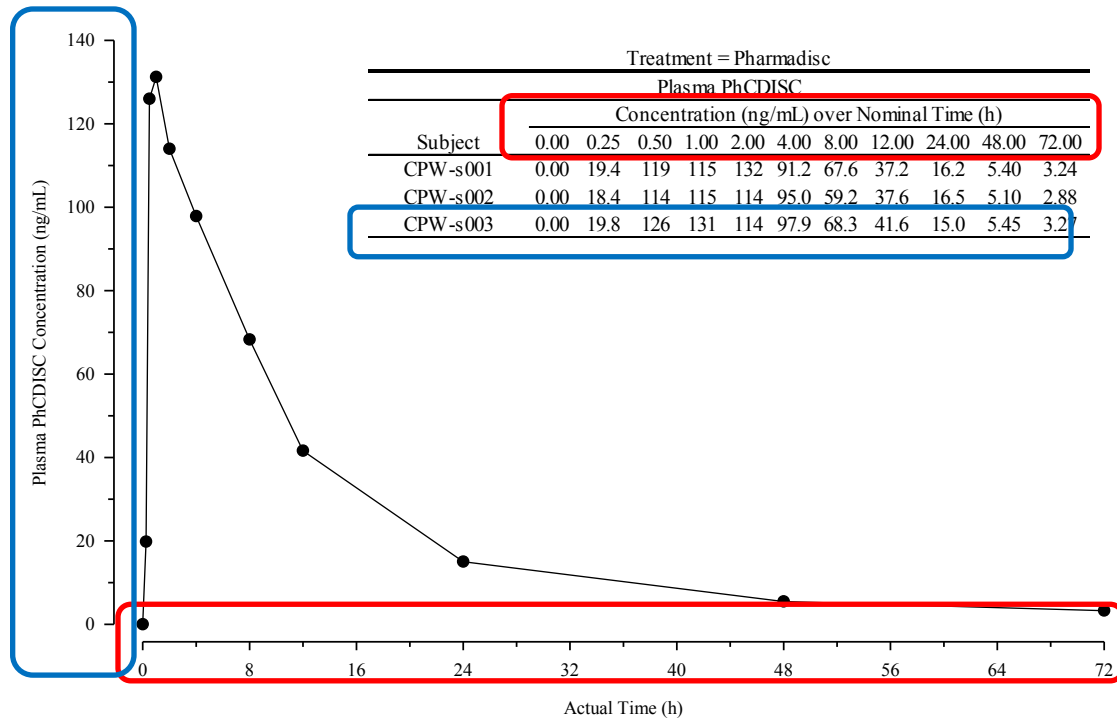
- Pharmacokinetics (PK) analysis to assess what happens to the drug after administration
- Rather simple and still widely used
- Based on concentration-time profiles for subjects
- Requires additional data (dosing, covariates, flags)

Pharmacokinetic Process Model

- **Absorption**: How the drug moves into the bloodstream.
- **Distribution**: How the drug moves through the body – including to the site of the desired effect.
- **Metabolism**: How the drug breaks down into different, often simpler substances.
- **Excretion**: How the drug and metabolites leave the body.



Concentration-Time Profiles and PK Parameters



Data for Noncompartmental PK Analysis

Profile Data

- Concentration-time profiles uniquely identified by 'key' variables such as study id, treatment id, subject id, ...

Subject Data

- Per subject demographics (such as age, race, etc.), additional findings (such as weight, alcohol usage, smoking habits, etc.) or subject characteristics (for example, skin type, genetic disposition, or other relevant conditions)

Dosing Data

- Dose amount with Dose time parameters (dosing interval for multiple doses, duration of IV administration, etc.), using the same key variables as observations

ADNCA

- Standardized analysis datasets derived from SDTM-PC, other SDTM domains (DM, EX, ...), and ADaM datasets (ADSL)
- Should support various software used for parameter calculations
- Extensions should support non-compartmental PK analyses, PK and PD data review
- Utilizes BDS but adds special features
- Potential to be used for TFL generation
- Should replace ADPC

Concentration-Time Profiles

Date Time
"as numbers"

Time

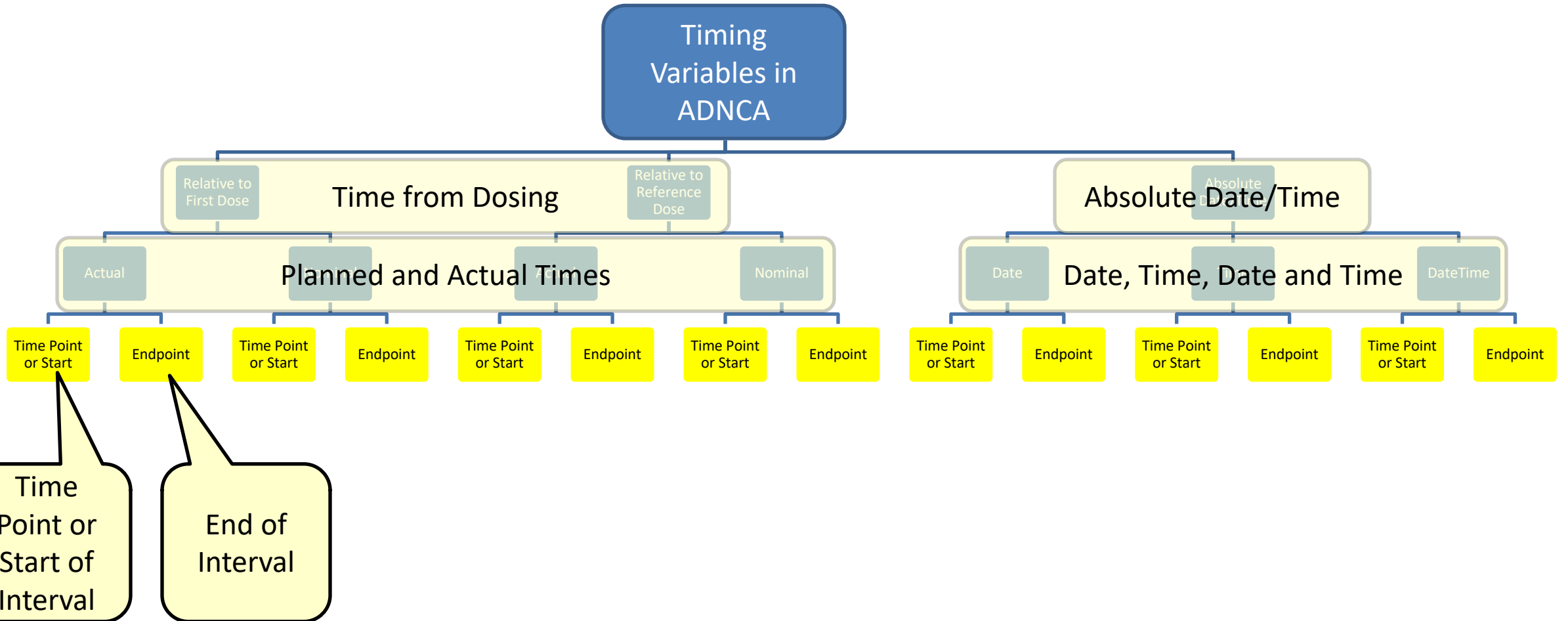
Concentration

Row	USUBJID	ADTM	ARRELTM	NRRELTM	MRRELTM	RRELTMU	APERIOD	ATPT	AVAL	PCSTRESU
1	STD1-56-001	42828.33680556	-0.083	0	0	h	1	Predose	0	ug/L
2	STD1-56-001	42828.36180556	0.5167	0.5	0.5167	h	1	0.5 H	383	ug/L
3	STD1-56-001	42828.38194444	1	1	1	h	1	1 H	533	ug/L
4	STD1-56-001	42828.42361111	2	2	2	h	1	2 H	455	ug/L
5	STD1-56-001	42828.50694444	4	4	4	h	1	4 H	443	ug/L
6	STD1-56-001	42828.67708333	8.083	8	8.083	h	1	8 H	356	ug/L
7	STD1-56-001	42828.84027778	12	12	12	h	1	12 H	320	ug/L
8	STD1-56-001	42829.33680556	23.917	24	23.917	h	1	24 H	190	ug/L

Timing Variables

- Discrete time points (plasma/blood samples, PO or IV bolus dosing) or intervals (urine samples, IV infusion dosing)
- Relative timing variables to be based off reference points commonly used in PK analysis (for example, first or most recent dose)
- Absolute timing variables for date / time values in software useable format, i.e., not ISO8601 string but numeric value based on reference time point

Timing Variables



Flags

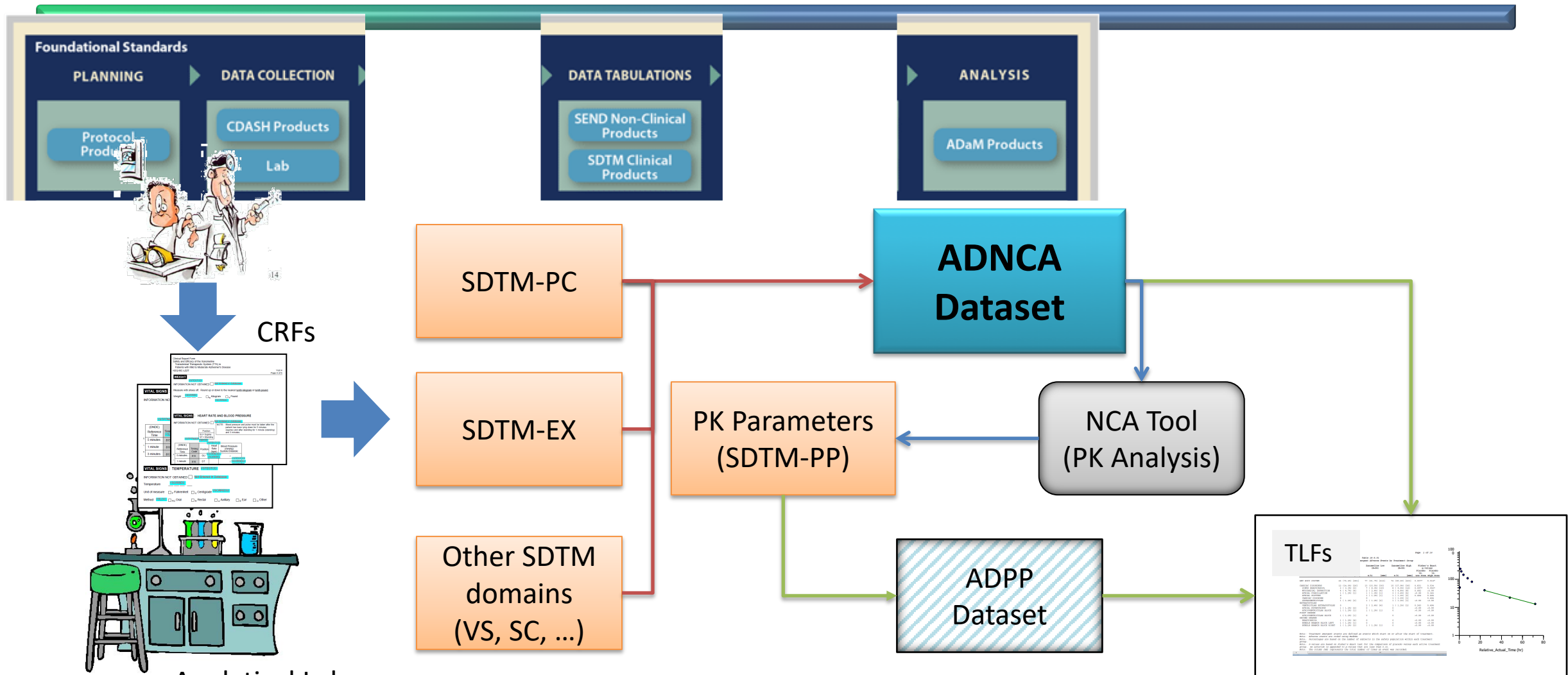


- Used to include/exclude relevant data for analysis
 - Typically an additional variable with more details
- Subject- and record-level exclusion flags
- Special conditions (meals, vomiting)
- Metabolite flag
- Some flag settings could be determined by PK scientist after initial NCA (for example, exclusions)

Flags

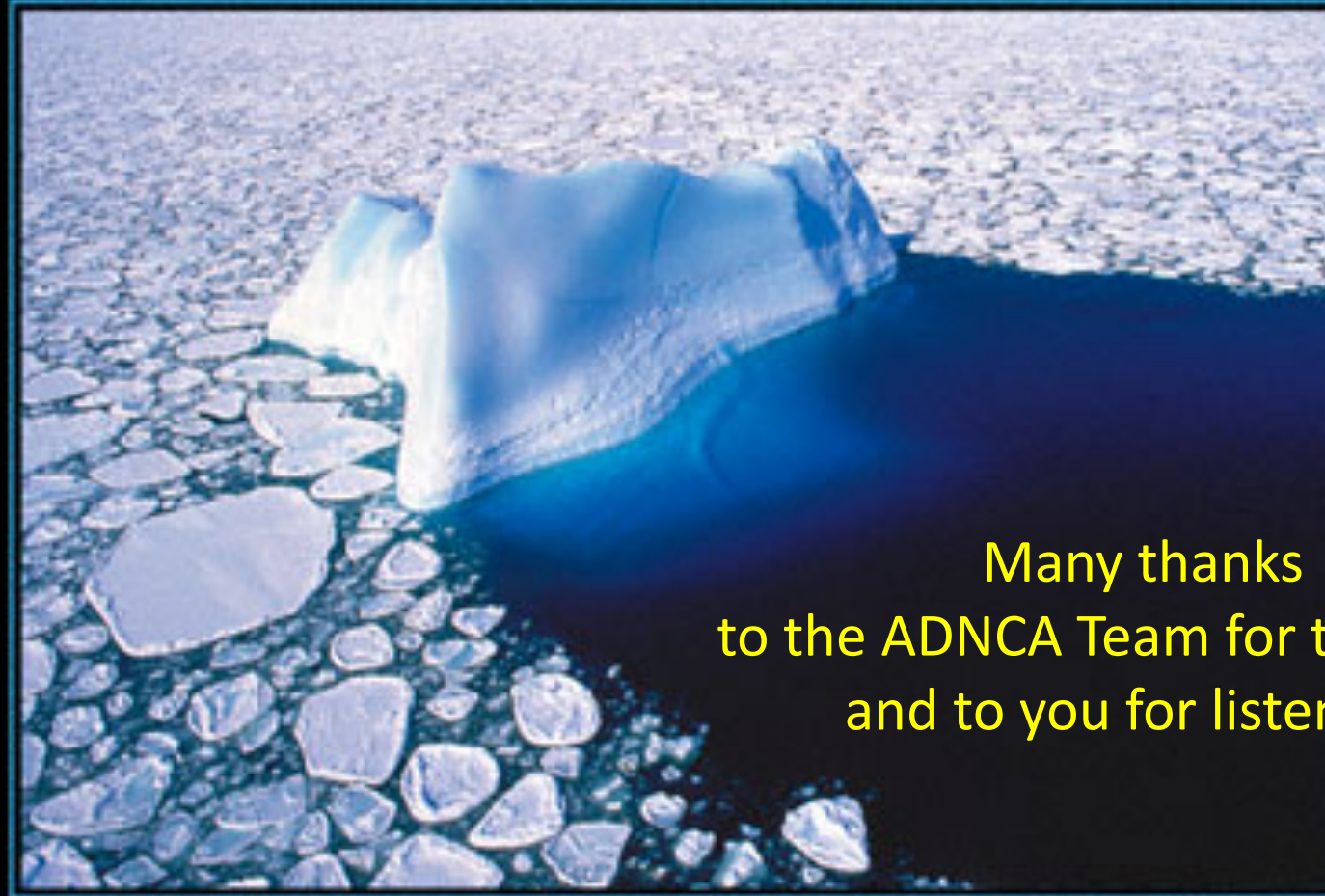
Condition	Flag Variables	Description
Exclusion	PKEFL, REXSUBJ PKERFL, REXRE	Subject- and record level exclusion flag and reason for exclusion. Likely a flag that is set after some initial data analysis
Vomiting	VOMITFL, VRELTM	Flag to indicate vomiting related to dosing with timing data
Meals	MEALFL, MRELTM	Flag to indicate a meal within the defined time window of dosing
Metabolite	METABFL	“Y” indicates that the analyte is a metabolite and not the parent drug. Allows to adjust the NCA algorithm for metabolites from IV Bolus administration

My ADNCA Vision



Summary

- ADNCA is BDS plus some additions
- ADNCA will enable streamlined data preparation, analysis, and review
- ADNCA will be coming soon – watch out for public review as one of the next steps



Many thanks
to the ADNCA Team for their work
and to you for listening!

PROBLEMS

NO MATTER HOW GREAT AND DESTRUCTIVE YOUR PROBLEMS MAY SEEM NOW,
REMEMBER, YOU'VE PROBABLY ONLY SEEN THE TIP OF THEM.