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2026 Europe Interchange

THE FUTURE IS CONNECTED: STANDARDS AND AI POWERING DIGITAL TRANSFORMATION

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ADaM Implementation for Non-Compartmental Analysis: Lessons Learned from Multiple Studies

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Speakers

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Agenda

1. Non-compartmental Analysis
2. The Challenge
3. Data Journey
4. Our Solution

Non-Compartmental Analysis

What is Non-compartmental Analysis?

Non-compartmental analysis (NCA) is one class of mathematical methods for studying the level of exposure following administration of a drug and is commonly used to analyze serial drug concentration data from clinical trials by individual subjects[1].

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1. *ADaMIG_for_Non-compartmental_Analysis_Input_Data_v1.0*

Why It Matters

NCA is a cornerstone in drug development due to its versatility and directness, providing crucial insights into drug behavior without complex modeling assumptions.

Simplified & Robust

- Model-independent analysis method
- Directly based on observed drug concentration-time data

Essential Applications

- Phase I/II studies
- Bioequivalence trials
- Drug-drug interaction studies

Industry Standard

- Widely accepted by regulatory agencies
- Standardized approach for PK analysis

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NCA: Strengths & Considerations

Advantages

- Simple & Flexible
- Robust for comparisons
- Based directly on observed concentration–time data
- Industry Standards

Limitations

- Limited physiological description
- Limited predictive power
- Sensitive to λz selection
- Not ideal for sparse sampling

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NCA Delivers: Key Drug Exposure Parameters

NCA provides a comprehensive overview of drug exposure and behavior in the body through several critical pharmacokinetic parameters.

- AUC (Area Under the Curve)
- Cmax (Maximum Concentration)
- Tmax (Time to Maximum Concentration)
- Half-Life (t1/2)

NCA Data Quality Matters

High-quality NCA outputs power critical decisions in drug development — from dose selection to regulatory submissions. The value of the final analysis is only as strong as the data collected at every upstream step.

PK Parameter Accuracy

Cmax, AUC, t½ depend on precise timing and concentration data

Regulatory Confidence

SDTM/ADaM compliance ensures submission-ready outputs

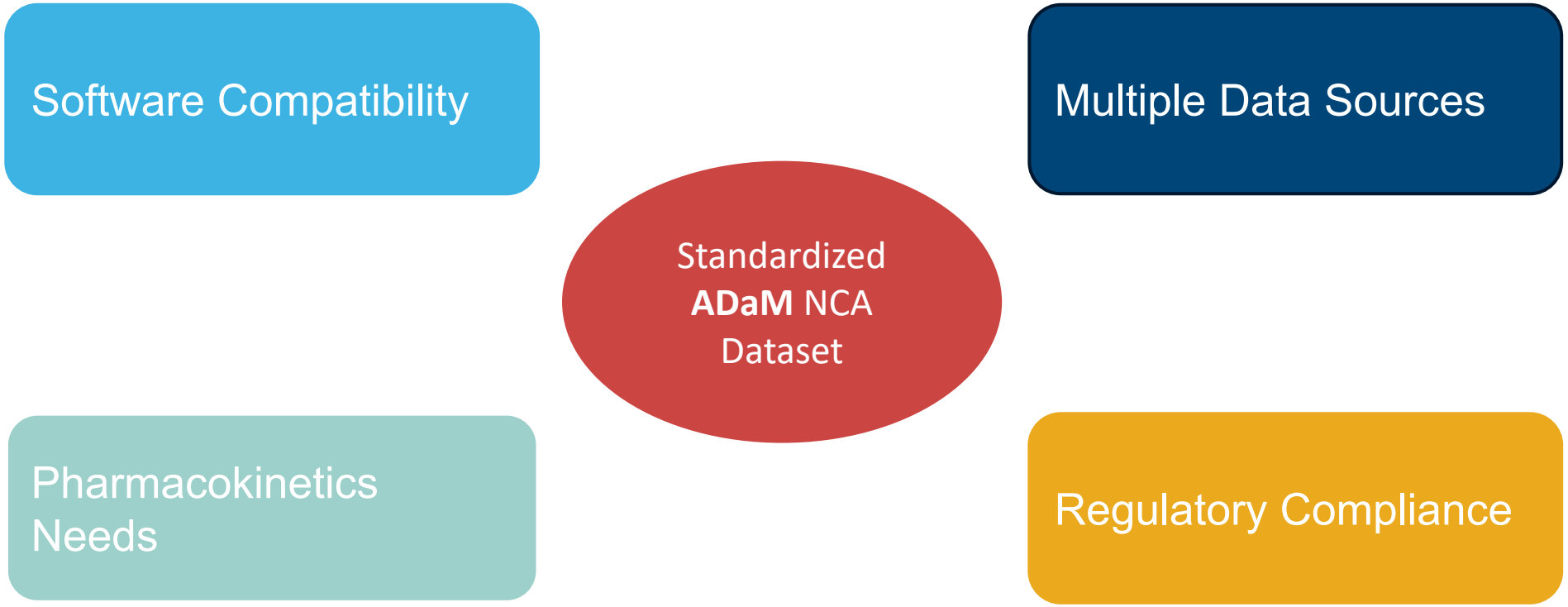
Cross-Study Comparability

Standardization allow pooling and meta-analyses

The Challenge

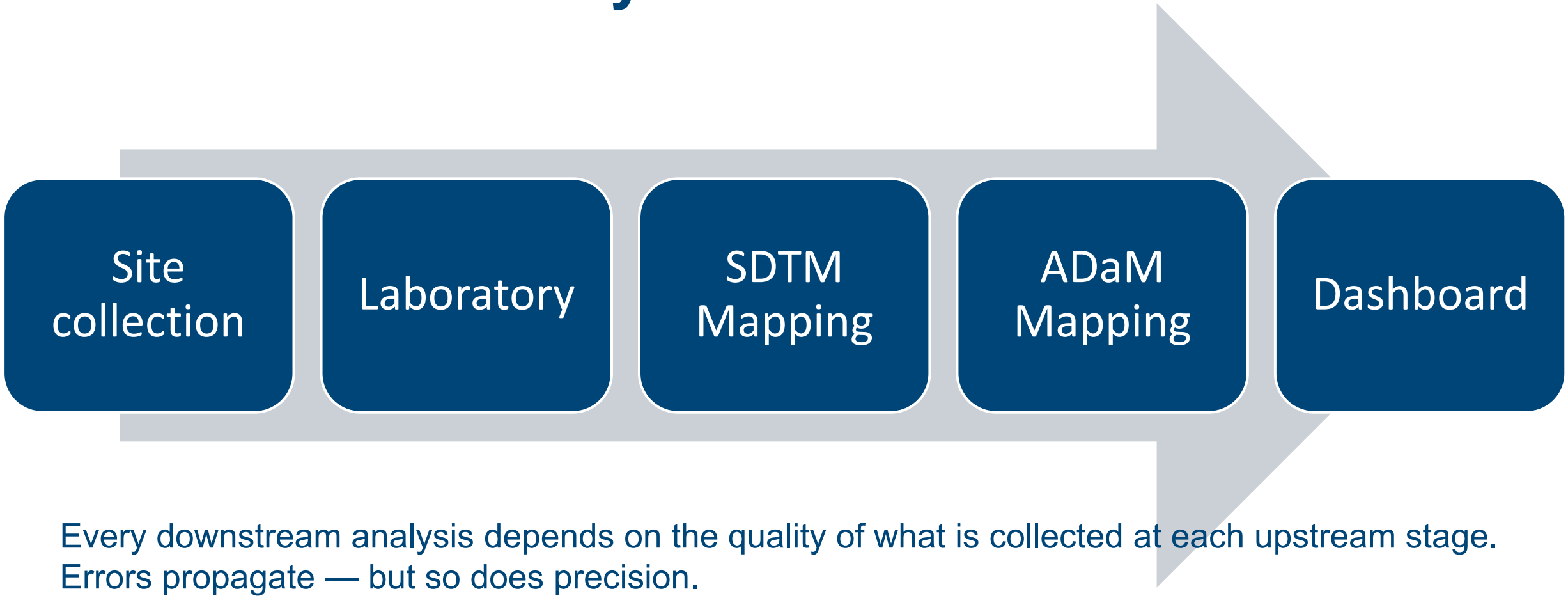
Many Studies, One Standard Result

Regardless of study design the goal is always the same: a clean, traceable, ADaM-compliant dataset ready for NCA.



Data Journey

From Patient to Analysis: The Data Flow



Every downstream analysis depends on the quality of what is collected at each upstream stage. Errors propagate — but so does precision.

Data Journey

Stage 1: Site Collection

Data Quality Starts at the Bedside

The foundation of every NCA analysis is laid at the clinical site

1	2
PK Sampling Date & Time Actual draw times must be recorded for each timepoint and subject	**Intake Records** Exact dosing time, amount, and food status captured via diary or eCRF at each visit

Even small time-recording errors at site can shift NCA parameters like Tmax and AUC significantly

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Unscheduled Sample Collection

Unscheduled samples, while potentially providing valuable insights, introduce critical considerations that extend beyond routine protocol. Their proper handling dictates their utility in analysis.

- Clinical Justification
- Logistical Precision
- Heightened Care
- Analytical Scope

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Data Journey

Stage 2: Laboratory

Lab Processing and Data Management Alignment

Bioanalytical results are only usable if they can be unambiguously linked back to the right subject, visit, and timepoint in the CRF.

Key Principle

If the lab result cannot be merged with the CRF record, it cannot be used in analysis. Reconciliation is not optional — it is the critical handoff between clinical operations and biostatistics.

→ Sample Manifest Consistency

Tube IDs and collection times on the manifest must mirror CRF entries exactly

→ Lab–DM Reconciliation

Active collaboration to resolve discrepancies before database lock

→ Blinded Study Management

Subject-level identifiers must remain consistent across CRF and LIMS under blind conditions

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Data Journey

Stage 3: SDTM

Documents: Work Plan & Data Transfer Agreement

Robust data exchange relies on clear documentation and agreed-upon specifications from the outset, guiding both scientific analysis and data management.

The NCA Work Plan

PK Scientist Responsibility

- Defines the specific NCA methodology and algorithms.
- Lists all pharmacokinetic parameters to be calculated.
- Outlines rules for handling missing data, below limit of quantification (BLQ) values, and outliers.
- Specifies criteria for terminal elimination phase estimation and fitting.

Data Transfer Agreement (DTA)

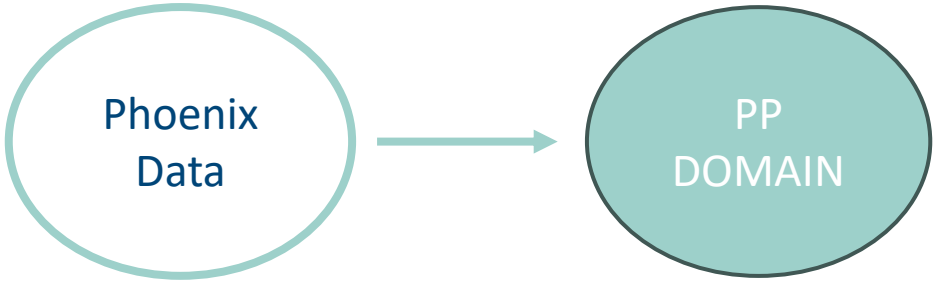
Data Manager Responsibility

- Data Format: Specifies the precise structure and content of all data files exchanged.
- Frequency: Defines how often data will be transferred (e.g., cumulative, incremental).
- Timelines: Sets expectations for delivery of both raw data and analysis results.
- CDISC Standard: Confirms the specific CDISC versions (SDTM, ADaM) to be utilized for mapping.
- Reconciliation: Establishes processes for data checks and discrepancy resolution.

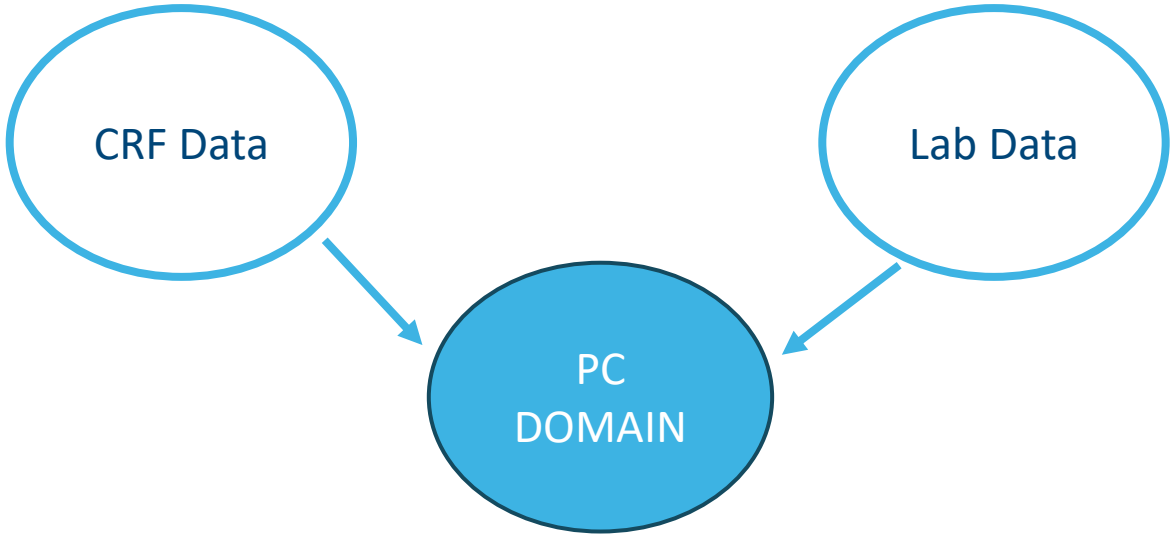
Merging the Data - SDTM

The Study Data Tabulation Model (SDTM) forms the essential backbone for PK analysis, standardizing raw data into two primary domains

- **PC - Pharmacokinetic Concentrations**
- **PP - Pharmacokinetic Parameters**



Derived PK parameters



PC is dedicated to standardizing all drug and metabolite concentration measurements, forming the backbone for subsequent PK analysis

PC Domain: Capturing PK Concentration Data

	USUBJID	PCGRPID	PCTEST	PCCAT	PCORRES	PCSTRESC	PCSTRESU
1	001-001	1_TRTxx_QD_DAY1_METxx_PLASMA	METxx	ANALYTE	NOT QUANTIFIABLE	BLQ	ng/mL
2	001-001	1_TRTxx_QD_DAY1_DRUGxx_PLASMA	DRUGxx	ANALYTE	1.12	1.12	ng/mL
3	001-001	1_TRTxx_QD_DAY1_DRUGxx_URINE	VOLUME	SPECIMEN PROPERTY	500.00	500.00	mL

	PCSPEC	PCFAST	PCDTC	PCENDTC	PCTPT	PCTPTREF	PCRFTDTC
1	PLASMA	N	2024-10-04T09:19		PREDOSE	DAY 1 DOSE	2024-10-04T09:50
2	PLASMA	N	2024-10-04T09:19		PREDOSE	DAY 1 DOSE	2024-10-04T09:50
3	URINE	N	2024-10-03T21:50	2024-10-04T09:40	PREDOSE	DAY 1 DOSE	2024-10-04T09:50

PP Domain: Capturing Derived PK Parameters

	USUBJID	PPGRPID	PPTEST	PPCAT	PPORRES	PPORRESU
1	001-001	1_TRTxx_QD_DAY1_DRUGxx_PLASMA	Max Conc	DRUGxx	89.20	ng/mL
2	001-001	1_TRTxx_QD_DAY1_DRUGxx_PLASMA	Time of CMAX Observation	DRUGxx	2.00	h

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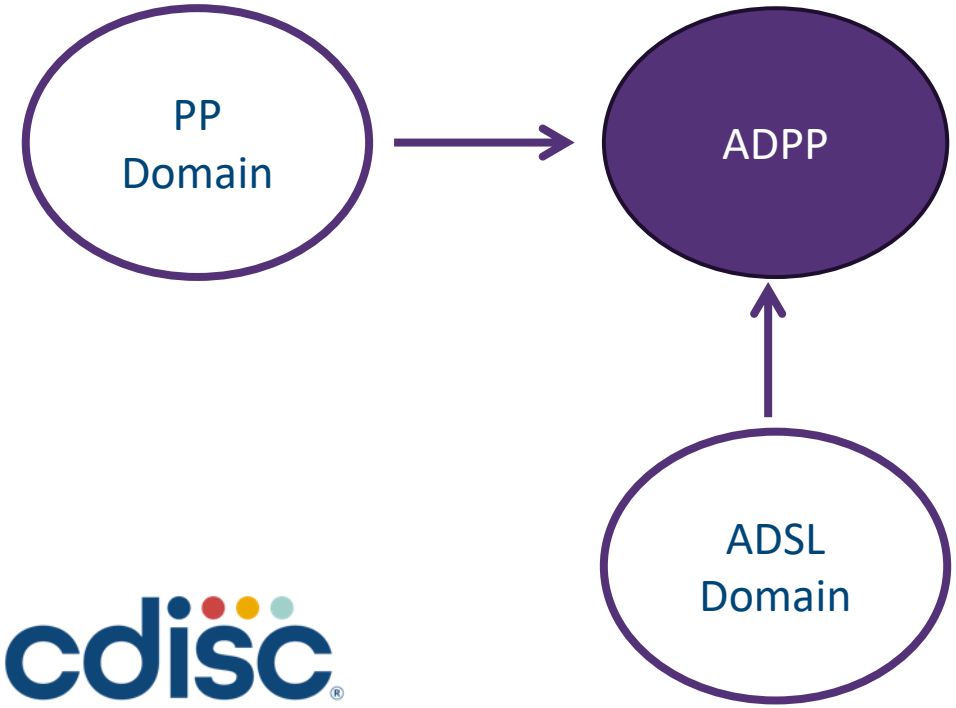
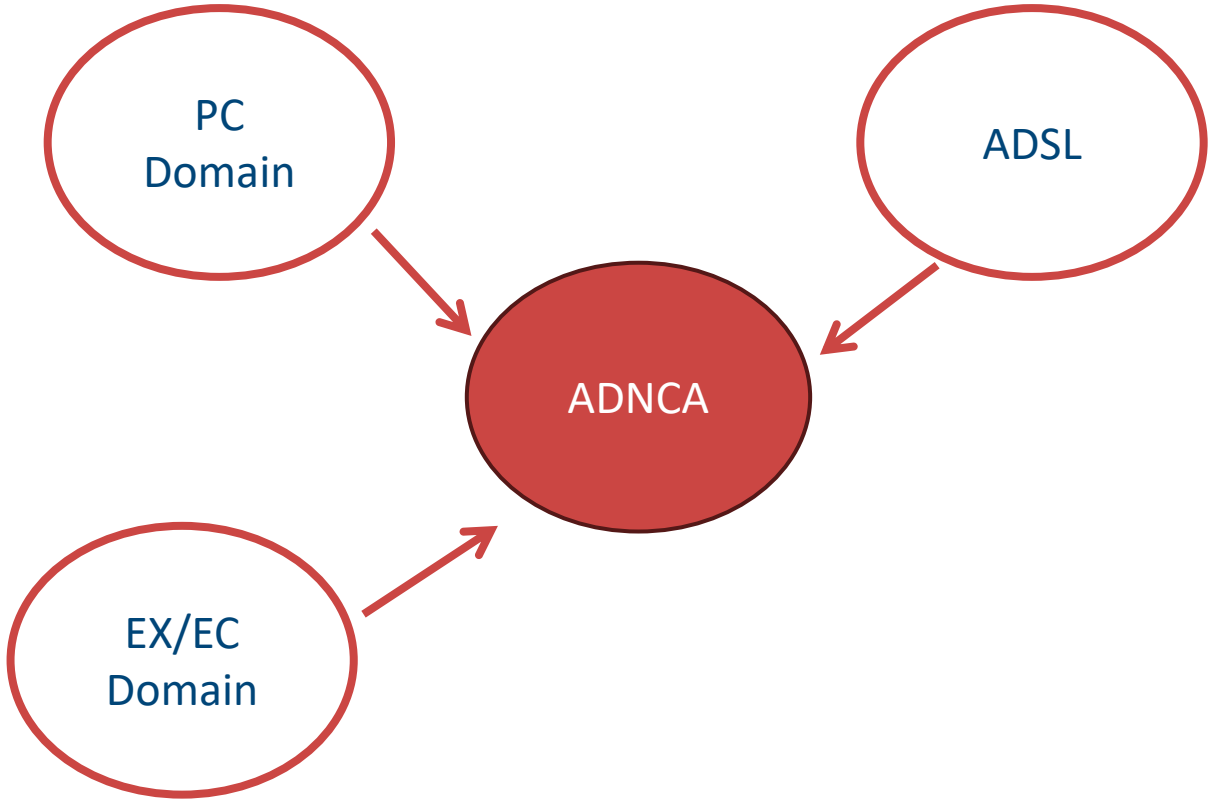
Data Journey

Stage 3: ADaM

Building Analysis-Ready Datasets for NCA

The Analysis Data Model (ADaM) transforms raw data from SDTM into a structured format optimized for NCA and other pharmacokinetic evaluations. Ensures data integrity and analytical efficiency.





What Makes ADNCA Unique - Variables

The ADNCA builds upon the foundational Basic Data Structure, integrating critical pharmacokinetic-specific extensions

Distinctive Time Management

- Nominal Relative to Reference Dose Time (**NRRLT**)
- Actual Relative to Reference Dose Time (**ARRLT**)
- Times relative to the first dose (**NEFRLT**)
- Start and end times for interval data (**NERRLT**)

Comprehensive Dose Variables

- Actual Treatment Dose(**DOSEA**)
- Treatment Dose Units (**DOSEU**)
- Time interval between doses (**TRTRINT**)
- Actual/Nominal Duration of Treatment Dose (**ADOSEDUR**)
- Reference dose time (**PCRFTDTM**)

Explicit Exclusion Management

- PK NCA Exclusion Flag (**NCAXFL**)
- Reason w for PK NCA Exclusion (**NCAwXRS**)
- PK Summary Exclusion Flag (**PKSUMXF**)

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ADNCA: A Glimpse into the Dataset

	USUBJID	PCSEQ	NCAXFL	NCA1XRS	DOSEA	DOSEU	PCRFTDT	PCRFTTM	PCRFTDTM
1	001-001	1			52000	ug	04OCT2024	09:50	04OCT24:09:50
2	001-001	2	Y	Vomiting	52000	ug	04OCT2024	09:50	04OCT24:09:50
3	001-001	3			52000	ug	04OCT2024	09:50	04OCT24:09:50

	NRRLT	NERRLT	ARRLT	MRRLT	RRLTU	AVIST	PARAMCD	PARAM	AVAL	AVALU
1	0		-0.52	0	h	Day 1	PDRUGxx	Plasma Drugxx (ng/mL)	0	ng/mL
2	0.5		0.8	0.5	h	Day 1	PDRUGxx	Plasma Drugxx (ng/mL)	1.12	ng/mL
3	0	12	-0.17	0	h	Day 1	UDRUGxx	Urine Drugxx (ng/mL)	316.64	ng/mL

	VOLUME	VOLUMEU
1		
2		
3	1600	mL

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What Makes ADNCA Unique - Structure

The NCA ADaM dataset has specific structural requirements that distinguish it from other ADaM datasets.

Duplicated Records for Analysis

Handling samples split
- PCSEQ
- BASETYPE
- PCRFTDTM

Matrix Flexibility

Plasma and urine require different
- PARAM
- PARAMCD
- VOLUME

Reporting Focus

ADNCA serves as a **computational dataset**

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ADNCA: A Glimpse into the Dataset

	USUBJID	PCSEQ	DOSEA	DOSEU	PCRFTDTM	ADTM
1	001-001	8	52000	ug	02NOV25:08:45:00	02NOV25:20:44:00
2	001-001	9	52000	ug	03NOV25:08:45:00	03NOV25:08:40:00
3	001-001	9	52000	ug	03NOV25:08:45:00	03NOV25:08:40:00

	NRRLT	ARRLT	MRRLT	RRLTU	ATPTREF	ATPT	AVAL	AVALU	ABLFL	BASE
1	12	11.98	11.98	h	Day 1	12H	38.25	ng/mL		0
2	24	23.91	23.91	h	Day 1	24H	20.45	ng/mL		0
3	0	-0.08	0	h	Day 2	Predose	20.45	ng/mL	Y	20.45

	BASETYPE	DTYPE
2	Day 1 Baseline	COPY
3	Day 2 Baseline	

Our Solution

Our Solution: A modular, Adaptable framework

Work Environment Configuration

- SDTMIG ADaMIG version
- Control terminologies
- Data read paths
- Output paths

Study Parameter Definition

- Analytical matrix
- Parent and/or metabolite compounds
- Treatment frequency
- Route of administration

Analysis Type Selection

Final or an interim analysis?

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Interim vs. Final Analysis

The approach to NCA adapts significantly depending on whether the analysis is interim or final, driven by data availability and study blinding status

Interim Analysis

- Data Source: **Laboratory data only**
- Timepoints: Relies exclusively on **nominal timepoints** for calculations.
- Blinding: Always performed **blinded** to treatment assignments.
- Purpose: Provides early insights; not for definitive conclusions.

Final Analysis

- Data Source: Integrates **Laboratory data with full CRF data**.
- Timepoints: Utilizes **actual timepoints** for precise NCA derivation.
- Blinding: Conducted **unblinded** following CRF lock and database close.
- Purpose: Delivers definitive pharmacokinetic parameters for reporting.

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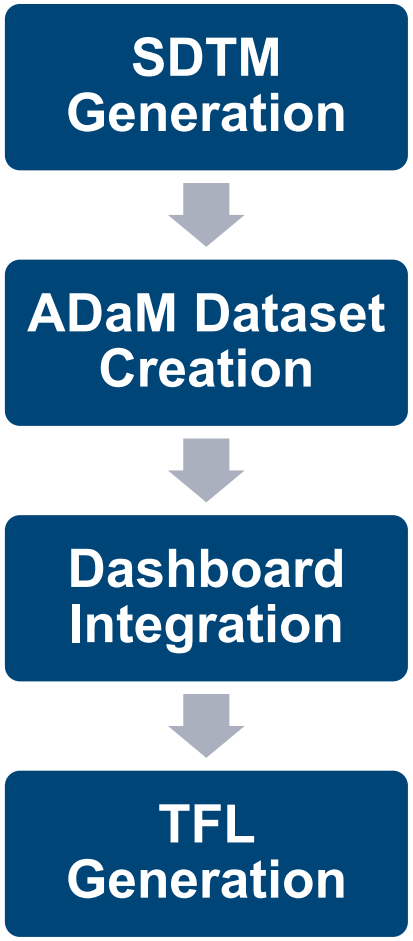
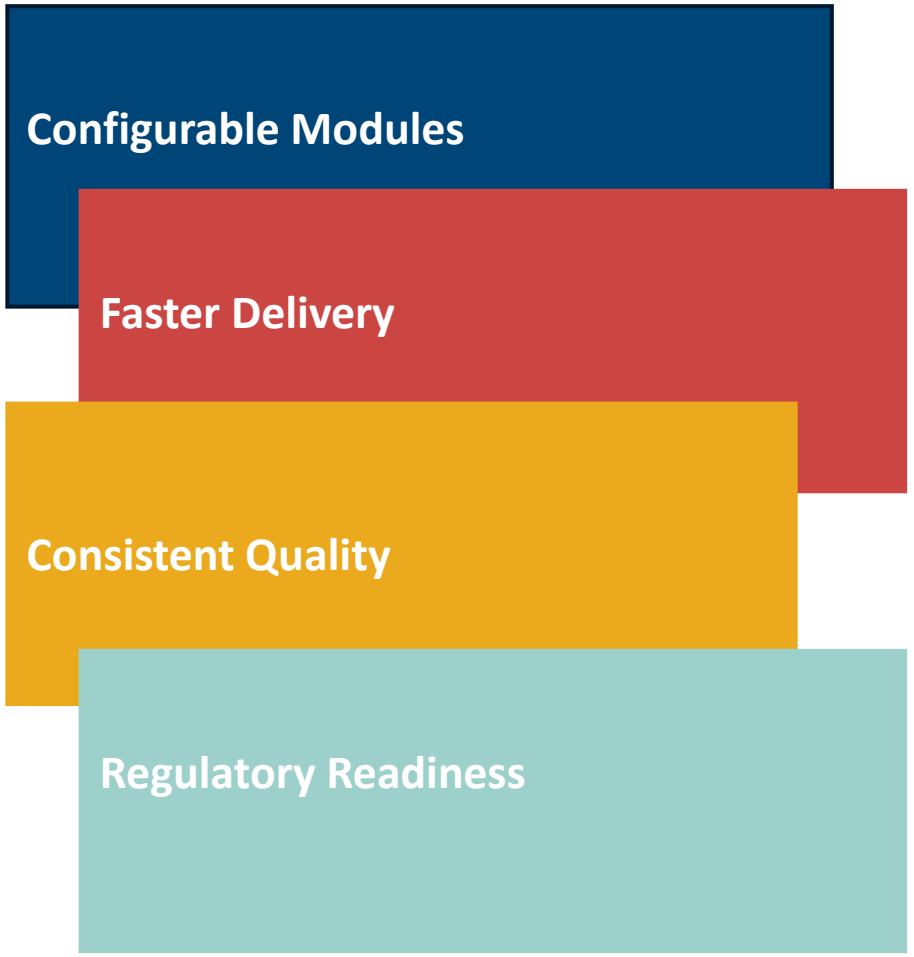
Our Solution: A modular, Adaptable framework





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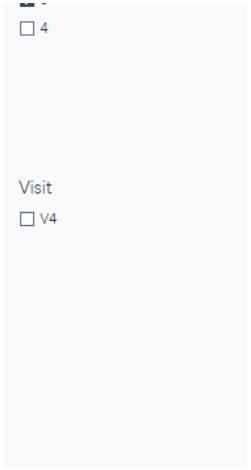
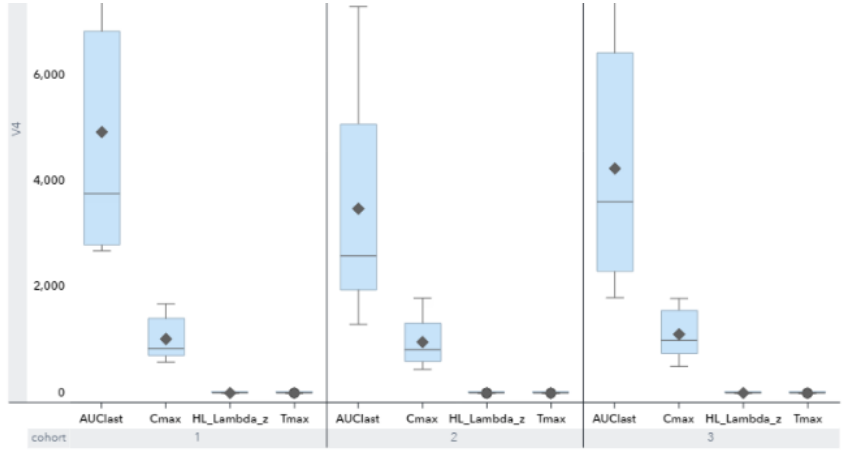
Visualizing ADNCA: Single cohort

Visualizing ADNCA: Cohort comparison



Cmax	ug/mL	V4	2	966.52	511.00	824.30	450.37	1,797.75	8	52.87%
			3	1,114.33	479.35	998.23	505.54	1,790.84	8	43.02%
HL_Lambda_z	hr	V4	1	3.41	0.58	3.37	2.85	4.00	3	16.95%
			2	2.41	0.27	2.44	1.90	2.81	7	11.24%
			3	2.39	0.39	2.42	1.84	3.03	7	16.27%
Tmax	hr	V4	1	1.84	1.01	1.96	0.92	4.00	8	54.85%
			2	1.08	0.34	0.96	0.92	1.92	8	31.58%
			3	1.13	0.37	1.00	1.00	2.03	8	32.35%



Statistical values of Concentrations per Cohort

		cohort	1			2			3		
VISIT	Time		Mean	Median	StDev	Mean	Median	StDev	Mean	Median	StDev
V4	0		0.93	0.00	2.64	0.00	0.00	0.00	0.16	0.00	0.46
	1		883.00	795.99	358.82	925.84	824.30	454.04	1,082.00	998.23	456.16
	2		881.48	783.06	387.17	760.27	531.25	530.13	892.35	843.92	450.01
	4		689.62	560.33	476.30	437.29	308.98	298.61	532.88	445.13	296.82
	8		383.96	217.81	463.19	137.66	90.46	107.99	210.30	126.74	194.29

Dose Proportional

	parameter	AUCLAST	CMAX
ratio	Fold Increase in Dose	value	value
Dose 120/Dose 30	4	0.86	1.09
Dose 120/Dose 60	2	1.22	1.15
Dose 60/Dose 30	2	0.71	0.94

Key Takeaways

Better data In, Better NCA Out

The Bigger Picture

Applying ADaM principles from the earliest stages of data handling — starting directly from bioanalytical outputs — strengthens traceability, enhances regulatory readiness, and empowers timely clinical decision-making.

From patient to parameter: every step in the chain matters.

Thank You!

Questions?