User Manual

- Output for Plasma Models - Terminal Elimination Constant (λz)
- Output for Plasma Model - Area Under the Curve (AUC)
- Outputs for Plasma Model - Mean Residence Time (MRT)

Output for Plasma Models - Terminal Elimination Constant (?z)

Summary Table for Terminal Elimination Constant (λ_z)

Parameters	CDISC Term	IV Bolus	IV Infusion	EV	Validate λ_z	Validate τ	Observed C_{last}	Predicted C_{last}
MRT_{last}	MRTIVLST	✓	✓	✗	-	-	✓	✗

Note: Rows highlighted in blue represent the default output, while the remaining rows are optional.

??????????$_z$?

□□□□□□□□□ lambda$_z$□□□ λ_z□□□□□□□□□□□□□□□□ -
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□□□□□□□□□□□□□□□ MRT □□□□□□□□□□□□□□□□□



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4. □□□□



□□	□□	□ λ_z □□□
$AUC_{0-\infty}$	$AUC_{last} + C_{last}/\lambda_z$	□□□□
$AUMC_{0-\infty}$	$AUMC_{last} + t_{last}\cdot C_{last}/\lambda_z + C_{last}/\lambda_z^2$	□□□□
$\%AUC_{ext}$	$(C_{last}/\lambda_z) / AUC_{0-\infty} \times 100\%$	□□□□
CL/F	$Dose / AUC_{0-\infty}$	□□□□
V_z/F	$Dose / (AUC_{0-\infty} \cdot \lambda_z)$	□□□□
MRT_{∞}	$AUMC_{0-\infty} / AUC_{0-\infty}$	□□□□
MRT'_{∞}	$AUMC'_{0-\infty} / AUC_{0-\infty}$	□□□□

□□ $AUC_{0-\infty}$ □ $AUMC_{0-\infty}$ □□□□□□□□□ λ_z □□□□□□□□ $AUC_{0-\infty}$□ V_z/F □ MRT_{∞}□□□ CL/F □□□□□ λ_z □□□□□□ CL/F□ V_z/F□ MRT_{∞} □□□□□□□□□□

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□□□□□□□□□□□□□□□□□□□□□□□□ λ_z □□□□□□□□□□□□□□□□□□

□□ (h)	□□ (ng/mL)	ln(□□)
0.25	820	6.709
0.5	650	6.477
1	480	6.174
2	320	5.768
4	180	5.193
6	110	4.700
8	75	4.317
12	42	3.738
24	12	2.485
36	3.5	1.253
48	1.0	0.000

□ 12–48 h □□□□□□□□ $\lambda_z \approx 0.1154/h$□ $t_{1/2} \approx 6.01$ h□□□□□□□□ 6–48 h□ λ_z □□□ 0.1179/h□ +2.2%□□ adjusted R^2 □□□□□ 0.998 □□□□ C_{pred}/C_{last} □ 0.98 □□ 0.95 □□□□□□□□□ ——□□ adjusted R^2 □□□□□□□ λ_z □□□

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1. λ_z □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□
2. □□□□□□□□ < 3 □□□□□□□□□□□ < 2 □ $t_{1/2}$□□□ λ_z □□□□□□□□□
3. □□ LLOQ □□□□□□□□□□□□□□□□□□□□□□□□□□□□
4. □□□□□□□□□□□□□□□□□□□□
5. adjusted R^2 □□□□□□□□ λ_z □□□□□□□□□□□□□□□□□□□
6. □□ AUC □□□□□□ $AUC_{0-\infty}$□ $AUMC_{0-\infty}$ □□□□□□□□□□□□□□□
7. □□□□□ λ_z □□□□□□□□□□□□□□□□□ k_e□
8. □□□□□□□□□□□□□□□□□□□□

Output for Plasma Model - Area Under the Curve (AUC)

????????AUC?

□□□□□□□□ Area Under the Curve□ AUC
□□□□□□□□



□□□

?? AUC ??

□□	□□	□□□□
AUC_{0-t}	□□□□□□□□□□□□□□□	□□□□□□□□□□□□
$AUC_{0-\infty}$	□□□□□□□□□□□□	□□□□□□□□□□□□□□□
AUC_{τ}	□□□□□□□□□□□□□	□□□□□□□□□□□□□
$AUC_{0-tlast}$	□□□ t_{last} □□□	□□□□□□□□□□□□

BLQ ???????

BLQ □□□□□□□□ AUC □□□□□□□□□□□□□

1. □□□□□□□□□□ 0□
2. □□□□□□ BLQ □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□ 0 □□□□
3. □□□□□□□□□□□□□ BLQ □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□
4. □□□□□□□□□ BLQ □□□□□□□□□□□□
5. □□□□□□□□□□□□□ BLQ □□□□□□□ AUC_{0-t} □□□□□□□□□ λ_z □□□
6. □□□

AUC ???????

□□	□□	□□□□
CL/F	Dose / $AUC_{0-\infty}$	□□□□□
CL	Dose / $AUC_{0-\infty}$	□□□□□□□□□□
V_z/F	Dose / ($AUC_{0-\infty}$ · λ_z)	□□ AUC □ λ_z
MRT_{∞}	$AUMC_{0-\infty}$ / $AUC_{0-\infty}$	□□ AUC □ AUMC
□□□□□□□□	(AUC_T/$Dose_T$) / (AUC_R/$Dose_R$)	□□ AUC □□
□□□□□□□□	(AUC_{po}/$Dose_{po}$) / (AUC_{iv}/$Dose_{iv}$)	□□□□□□□ AUC

□□ CL/F □ AUC □□□□□ AUC □□□□□□□ CL/F □□□□□□□□□□□□□ $AUC_{0-\infty}$ □□□□□□□□□ CL/F□ V_z/F □ MRT_{∞} □□□□□□□□□□

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□□ (h)	□□ (ng/mL)	□□□□□□ (ng·h/mL)
0	—	—
0.25	820	—
0.5	650	183.75
1	480	282.50
2	320	400.00
4	180	500.00
6	110	290.00
8	75	185.00
12	42	234.00
24	12	324.00
36	3.5	93.00
48	1.0	27.00

□□□□□□□□□□□□ $AUC_{0–48h}$□□ $\lambda_z = 0.1154/h$□ $C_{last} = 1.0$ ng/mL□□□□□□□



□□ $AUC_{0–\infty}$ □ $AUC_{0–48h}$ □□ 8.67 ng·h/mL
□□□□□□□□□□□□

$AUC_{0-\infty}$ □□□□□□□ λ_z□□ λ_z □□□□□□ $AUC_{0-\infty}$□ CL/F□ V_z/F □ MRT_{∞} □□□□□□□□□□□□□□
$AUC_{0-\infty}$ □□□□□□□□ λ_z □□□□□□ adjusted R^2□□□□□□□□□□□□□□□□□□□□

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- Rowland M, Tozer TN. *Clinical Pharmacokinetics and Pharmacodynamics*.
- CDISC Pharmacokinetics Data Standards.
- EMA Guideline on Reporting of Pharmacokinetic Studies.
- FDA Bioanalytical Method Validation Guidance.

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□□□□□ AUC □□□□□□□□□□□□□□□□□□□□ C_{last} □□□□□□□□□□□ t_{last} □□□□□□□□
BLQ□ LLOQ□□□□□□□□□□□□□□□□□□□

Outputs for Plasma Model - Mean Residence Time (MRT)

Summary Table for Mean Residence Time (MRT)

Parameters	CDISC Term	IV Bolus	IV Infusion	EV	Validate λ_z	Validate τ	Observed C_{last}	Predicted C_{last}
MRT_{last}	MRTIVLST	✓	✓	✗	-	-	✓	✗
MRT_{last}	MRTEVLST	✗	✗	✓	-	-	✓	✗
MRT_{∞}	MRTIVIFO	✓	✓	✗	✓	-	✓	✗
MRT_{∞}	MRTEVIFO	✗	✗	✓	✓	-	✓	✗
MRT'_{∞}	MRTIVIFP	✓	✓	✗	✓	-	✗	✓
MRT'_{∞}	MRTEVIFP	✗	✗	✓	✓	-	✗	✓

Note: Rows highlighted in blue represent the default output, while the remaining rows are optional.

MRT_{last}

MRT_{last} is defined as the mean residence time based on observed data only, which is generally used when λ_z fitting fails or is unreliable. It is a robust, non-extrapolated metric.

For IV Bolus,



For IV Infusion, MRT_{last} is adjusted by subtracting half the infusion duration (T_i),



For Extravascular, MRT_{last} follows the same derivation as IV Bolus, however, it represents not only the process of distribution and elimination but also absorption,



$MRT_{?}$

MRT_{∞} is defined as the mean residence time extrapolated to infinite per observed C_{last}, which requires a valdiate λ_z.

For IV Bolus,



For IV Infusion,



For Extravascular,



$MRT'_{?}$

MRT'_{∞} is defined as the mean residence time extrapolated to infinite per predicted C_{last}, which is used for sensitivity analysis when C_{last} is considered as outlier.

During the derivation, replace C_{last} with C_{pred} (including AUC_{pred} and $AUMC_{pred}$ accordingly).