Collection of terms, symbols, equations, and explanations of common pharmacokinetic and pharmacodynamic parameters and some statistical functions

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1.1 Parameters obtained from concentrations in plasma or serum

1.1.1 Parameters after single dosing

Symbol	Unit / Dimension / Dimension	Definition	Calculation
AUC **$AUC_{(0-\infty)}$**	Amount·time/ volume	Area under the concentration-time curve from zero up to ∞ with extrapolation of the terminal phase	$\mathrm{AUC}=AUC_{(0-t_z)}+\frac{C_z}{\lambda_z}$, C_z may be measured ($C_{z,obs}$) or calculated ($C_{z,calc}$)
$AUC_{(0-t)}$, **AUC_t**	Amount·time/ volume	Area under the concentration-time curve from zero up to a definite time t $\mathrm{AUC}_{(0-t)}=\sum_{i=1}^{n-1} AUC_{(t_i-t_{i+1})}$ with $t_1=0$ and $t_n=t$, Concentrations C_i measured at times t_i, i=1,…,n.	According to the **linear trapezoidal rule**: $AUC_{(t_i-t_{i+1})}=\frac{1}{2}\cdot(C_i+C_{i+1})\cdot(t_{i+1}-t_i)$ or according to the **log-linear trapezoidal rule**: $AUC_{(t_i-t_{i+1})}=\frac{(C_i-C_{i+1})\cdot(t_{i+1}-t_i)}{(\ln C_i-\ln C_{i+1})}$ (the logarithmic trapezoidal rule is used for the descending part of the concentration-time curve, i.e. if $C_i>1.001*C_{i+1}>0$)
$AUC_{(0-tz)}$	Amount·time/ volume	Area under the concentration-time curve from zero up to the last concentration ≥LOQ (C_z)	See $AUC_{(0-t)}$
AUC_{extrap} %	%	Area under the concentration-time curve extrapolated from t_z to ∞ in % of the total AUC	$\mathrm{AUC}_{extrap}\,\%=\frac{AUC\text{-}AUC_{(0-t_z)}}{AUC}\cdot 100$
AUMC	Amount·$(time)^2$/ volume	Area under the first moment of the concentration-time curve from zero up to ∞ with extrapolation of the terminal phase	$\mathrm{AUMC}=\mathrm{AUMC}_{(0-t_z)}+\frac{t_z\cdot C_z}{\lambda_z}+\frac{C_z}{\lambda_z^2}$, C_z may be measured ($C_{z,obs}$) or calculated ($C_{z,calc}$)
$AUMC_{(0-t)}$	Amount·$(time)^2$/ volume	Area under the first moment of the concentration-time curve from zero up to a definite time t $\mathrm{AUMC}(0-t)=\sum_{i=1}^{n-1} AUMC(t_i\text{-}t_{i+1})$ with $t_1=0$ and $t_n=t$. Concentrations C_i measured at times t_i, i=1,…,n.	$\mathrm{AUMC}_{(t_i-t_{i+1})}$ $=\frac{1}{6}(t_{i+1}-t_i)(t_{i+1}(C_i+2C_{i+1})+t_i(2C_i+C_{i+1}))$ (linear trapezoidal rule) $=\frac{C_i t_i-C_{i+1}t_{i+1}}{B}+\frac{C_i-C_{i+1}}{B^2}$ with $B=\frac{\ln C_i-\ln C_{i+1}}{t_{i+1}-t_i}$ (log-linear trapezoidal rule)
$AUMC_{(0-tz)}$	Amount·$(time)^2$/ volume	Area under the first moment of the concentration-time curve from zero to the last quantifiable concentration	See $AUMC_{(0-t)}$
$AUMC_{extrap}$ %	%	Area under the first moment of the concentration-time curve extrapolated from t_z to ∞ in % of the total AUMC	$\mathrm{AUMC}_{extrap}\,\%=\frac{AUMC\text{-}AUMC_{(0-t_z)}}{AUMC}\cdot 100$

Symbol	Unit / Dimension	Definition	Calculation
C_p or **C**	Amount/ volume	Plasma concentration	
C_s or **C**	Amount/ volume	Serum concentration	
C_u	Amount/ volume	Unbound plasma concentration	
CL	Volume/ time or volume/ time/ kg	Total plasma, serum or blood clearance of drug after intravenous administration	$CL = \frac{D_{iv}}{AUC}$
CL / f	Volume/ time or volume/ time/ kg	Apparent total plasma or serum clearance of drug after oral administration	$CL / f = \frac{D_{po}}{AUC}$
CL_{int}	Volume/ time or volume/ time/ kg	Intrinsic clearance – maximum elimination capacity of the liver	
$CL_{H,b}$	Volume/ time or volume/ time/ kg	Hepatic blood clearance, product of hepatic blood flow and extraction ratio	$CL_H = Q_H \cdot E_H$
CL_{CR}	Volume/ time or volume/ time/ kg	Creatinine clearance	Measured or Cockcroft & Gault formula
CL_m	Volume/ time	Metabolic clearance	
$C_{z,\ calc}$	Amount/ volume	Predicted last plasma or serum concentration	Calculated from a log-linear regression through the terminal part of the curve
C_z or **$C_{z,\ obs}$**	Amount/ volume	Last analytically quantifiable plasma or serum concentration above LOQ	directly taken from analytical data
C_{max}	Amount/ volume	Observed maximum plasma or serum concentration after administration	directly taken from analytical data
D	Amount	Dose administered	
f	-	Fraction of the administered dose systemically available	$f = \frac{AUC_{po} \cdot D_{iv}}{AUC_{iv} \cdot D_{po}}$
F	%	Absolute bioavailability, systemic availability in %	$F = f \cdot 100$
f_{rel}	-	Fraction of the administered dose in comparison to a standard (not iv)	$f_{rel} = \frac{AUC \cdot D_{STD}}{AUC_{STD} \cdot D}$ STD = Standard
F_{rel}	%	Relative bioavailability in %	$F_{rel} = f_{rel} \cdot 100$
f_a	-	Fraction of the extravascularly administered dose actually absorbed	For orally administered drugs: $f = f_a*(1-E_H)$
f_m	-	Fraction of the bioavailable dose which is metabolized	
f_u	-	Fraction of unbound (not protein-bound or free) drug in plasma or serum	$f_u = C_u / C$
HVD	Time	Half-value duration (time interval during which concentrations exceed 50% of C_{max})	
λ_z	$(Time)^{-1}$	Terminal rate constant (slowest rate constant of the disposition)	negative of the slope of a ln-linear regression of the unweighted data considering the last concentration-time points ≥ LOQ
k_e or **k_{el}**	$(Time)^{-1}$	Elimination rate constant from the central compartment	calculated from parameters of the multiexponential fit
LOQ	Amount/ volume	Lower limit of quantification	

Symbol	Unit / Dimension	Definition	Calculation
MAT	Time	Mean absorption time	$MAT = MRT_{ev} - MRT_{iv}$ (ev = extravasal, e.g. im, sc, po)
MDT	Time	Mean dissolution time	
MRT	Time	Mean residence time (of the unchanged drug in the systemic circulation)	$MRT = \frac{AUMC}{AUC}$
MR	-	Metabolic ratio of parent drug AUC and metabolite AUC	$MR = \frac{AUC_{parent}}{AUC_{metabolite}}$
$t_{1/2}$	Time	Terminal half-life	$t_{1/2} = \frac{\ln 2}{\lambda_z}$
t_{lag}	Time	Lag-time (time delay between drug administration and first observed concentration above LOQ in plasma)	directly taken from analytical data
t_z	Time	Time p.a. of last analytically quantifiable concentration	directly taken from analytical data
t_{max}	Time	Time to reach C_{max}	directly taken from analytical data
V_{ss}	Volume or volume/kg	Apparent volume of distribution at equilibrium determined after intravenous administration	$V_{ss} = CL \cdot MRT = \frac{D \cdot AUMC}{(AUC)^2}$
V_z	Volume or volume/kg	Volume of distribution during terminal phase after intravenous administration	$V_z = \frac{D_{iv}}{AUC \cdot \lambda_z}$
V_{ss} / f	Volume or volume/kg	Apparent volume of distribution at equilibrium after oral administration	$V_{ss}/f = CL \cdot MRT = \frac{D \cdot AUMC}{(AUC)^2}$
V_z / f	Volume or volume/kg	Apparent volume of distribution during terminal phase after oral / extravascular administration	$V_z/f = \frac{D_{po}}{AUC \cdot \lambda_z}$ po instead of iv !

1.1.2 Parameters after multiple dosing (at steady state)

Symbol	Unit / Dimension	Definition	Calculation
A_{ave}	Amount	Average amount in the body at steady state	$A_{ave} = \frac{f \cdot D_M}{\lambda_z \cdot \tau}$
$AUC_{\tau,ss}$ **AUC_{SS}**	Amount·time/ volume	Area under the concentration-time curve during a dosing interval at steady state	by trapezoidal rule
AUCF%	%	Percent fluctuation of the concentrations determined from areas under the curve	$AUCF\% = 100 \cdot \frac{AUC_{(above\ C_{ave})} + AUC_{(below\ C_{ave})}}{AUC}$
$C_{av,ss}$	Amount /volume	Average plasma or serum concentration at steady state	$C_{av,ss} = \frac{AUC_{\tau,ss}}{\tau}$
$C_{max,ss}$	Amount /volume	Maximum observed plasma or serum concentration during a dosing interval at steady state	directly taken from analytical data
$C_{min,ss}$	Amount /volume	Minimum observed plasma or serum concentration during a dosing interval at steady state	directly taken from analytical data
C_{trough}	Amount /volume	Measured concentration at the end of a dosing interval at steady state (taken directly before next administration)	directly taken from analytical data
D_M	Amount	Maintenance dose	design parameter
LF	-	Linearity factor of pharmacokinetics after repeated administration	$LF = \frac{AUC_{\tau,ss}}{AUC_{sd}}$ sd = single dose
PTF %	%	Peak trough fluctuation over one dosing interval at steady state	$PTF\% = 100 \cdot \frac{C_{ss,max} - C_{ss,min}}{C_{ss,av}}$
$R_{A\ (AUC)}$		Accumulation ratio calculated from $AUC_{\tau,ss}$ at steady state and AUC_{τ} after single dosing	$R_{A\ (AUC)} = \frac{AUC_{\tau,ss}}{AUC_{\tau,sd}}$
$R_{A\ (Cmax)}$		Accumulation ratio calculated from $C_{max,ss}$ at steady state and C_{max} after single dosing	$R_{A\ (Cmax)} = \frac{C_{max,ss}}{C_{max,sd}}$ sd = single dose
$R_{A\ (Cmin)}$		Accumulation ratio calculated from $C_{min,ss}$ at steady state and from concentration at $t=\tau$ after single dose	$R_{A\ (Cmin)} = \frac{C_{min,ss}}{C_{\tau,sd}}$ sd = single dose
R_{theor}		Theoretical accumulation ratio	$R_{theor} = \frac{1}{1-2^{-\varepsilon}} = \frac{1}{1-e^{-\lambda_z \tau}}$, $\varepsilon = \frac{\tau}{t_{1/2}}$
T_{Cave}	Time	Time period during which plasma concentrations are above $C_{av,ss}$	derived from analytical data by linear interpolation
$t_{max,ss}$	Time	Time to reach the observed maximum (peak) concentration at steady state	directly taken from analytical data
τ	Time	Dosing interval	directly taken from study design

1.2 Parameters obtained from urine

Symbol	Unit / Dimension	Definition	Calculation
$Ae_{(t1-t2)}$	Amount	Amount of unchanged drug excreted into urine within time span from t_1 to t_2.	$C_{ur} * V_{ur}$
$Ae_{(0-\infty)}$	Amount	Cumulative amount (of unchanged drug) excreted into urine up to infinity after single dosing	(can commonly not be determined)
$Ae_{\tau,ss}$ **Ae_{ss}**	Amount	Amount (of unchanged drug) excreted into the urine during a dosing interval (τ) at steady state	
C_{ur}	Amount/ volume	Drug concentration in urine	
CL_R	Volume/ time or volume/ time/ amount	Renal clearance	$CL_R = \frac{Ae(0-\infty)}{AUC} \approx \frac{Ae(0-\tau)}{AUC(0-\tau)}$ after multiple dose $CL_R = \frac{Ae(0-\tau)}{AUC_{\tau,ss}}$
f_e	-	Fraction of intravenous administered drug that is excreted unchanged in urine	$f_e = \frac{A_e}{D_{iv}}$
f_e/f	-	Fraction of orally administered drug excreted into urine	$f_e / f = \frac{A_e}{D_{po}}$
F_e	%	Total urinary recovery after intravenous administration = fraction of drug excreted into urine in %	$F_e = f_e \cdot 100$
t_{mid}	Time	Mid time point of a collection interval	
V_{ur}	Volume	Volume of urine excreted	directly taken from measured lab data

2 PHARMACOKINETIC PARAMETERS OBTAINED FROM COMPARTMENTAL MODELING

Symbol	Unit / Dimensions	Definition	Calculation
A,B,C or C_i, i=1,...,n	Amount/ volume	Coefficients of the polyexponential equation	by multiexponential fitting
α, β, γ	$(Time)^{-1}$	Exponents of the polyexponential equation (slope factor)	by multiexponential fitting
λ_i	$(Time)^{-1}$	Exponent of the i^{th} (descending) exponential term of a polyexponential equation	by multiexponential fitting
AUC	Amount·time/ volume	Area under the curve (model)	iv : $AUC = \sum_{i=1}^{n}\left[\frac{C_i}{\lambda_i}\right]$ extravascular : $AUC = \sum_{i=1}^{n}\left[C_i \cdot \frac{k_a}{k_a - \lambda_i} \cdot \left(\frac{1}{\lambda_i} - \frac{1}{k_a}\right)\right]$ Note: C_i is the linear coefficient of the polyexponential equation
AUMC	Amount·$(time)^2$/ volume	Area under the first moment curve	iv : $AUMC = \sum_{i=1}^{n}\left[\frac{C_i}{\lambda_i^2}\right]$ extravascular : $AUMC = \sum_{i=1}^{n}\left[C_i \cdot \frac{k_a}{k_a - \lambda_i} \cdot \left(\frac{1}{\lambda_i^2} - \frac{1}{k_a^2}\right)\right]$ Note: C_i is the linear coefficient of the polyexponential equation
C(0)	Amount/ volume	Initial or back-extrapolated drug concentration following rapid intravenous injection	$C(0) = \sum_{i=1}^{n} C_i$ Note: C_i is the linear coefficient of the polyexponential equation
C(t)	Amount/ volume	Drug concentration at time point t	See 2.2
CL	Volume/ time	Clearance	$CL = \frac{f \cdot Dose}{AUC}$ iv: f=1
f_i	-	Fractional area, area under the various phases of disposition (λ_i) in the plasma concentration-time curve after iv dosing	$f_i = \frac{C_i / \lambda_i}{AUC}$ with $\sum_{i=1}^{n} f_i = 1$
i		Number of compartments in a multi-compartmental model	
k_0	$(Time)^{-1}$	Zero order rate constant	Design parameter or determined by multiexponential fitting
k_e or k_{el}	$(Time)^{-1}$	Elimination rate constant from the central compartment	calculated from parameters of the multiexponential fit
k_a or k_{abs}	$(Time)^{-1}$	Absorption rate constant	by multiexponential fitting
k_{ij}	$(Time)^{-1}$	Transfer rate between compartment i and j in a multi-compartmental model	by multiexponential fitting
K_m	Amount/ volume	Michaelis –Menten constant	by nonlinear fitting

Symbol	Unit / Dimensions	Definition	Calculation
MRT	Time	Mean residence time	iv: $MRT = \frac{AUMC}{AUC}$ extravascular: $MRT = \frac{AUMC}{AUC} - (t_{lag} + \frac{1}{k_a})$
$\mathbf{Q_i}$	Amount/Time	Intercompartmental clearance between central compartment and compartment i	
$\mathbf{k_0}$	Amount/Time	Zero order infusion rate	design parameter
$\mathbf{t}_{1/2, \lambda i}$	Time	Half-life associated with the i^{th} exponent of a polyexponential equation	$t_{1/2, \lambda i} = \frac{\ln 2}{\lambda_i}$
τ	Time	Infusion duration	design parameter
t	Time	Time after drug administration	
$\mathbf{V_c}$	Volume or Volume /amount	Apparent volume of the central or plasma or serum compartment	$V_c = \frac{f \cdot Dose}{\sum_{i=1}^{n} C_i}$ iv: f=1
$\mathbf{V_{max}}$	Amount/Time	Maximum metabolic rate	

2.1 Calculation of concentration-time curves

Application	Parameter	Calculation
iv bolus	concentration after bolus administration	$C_p(t) = \sum_{i=1}^{n} \left[B_i \cdot e^{-\lambda_i \cdot t} \right]$
short-term iv infusion	concentration during infusion	$C_p(t < T) = \sum_{i=1}^{n} \left[\frac{B_i}{\lambda_i} \cdot (1 - e^{-\lambda_i \cdot t}) \right]$
	peak level	$C_{max} = \sum_{i=1}^{n} \left[\frac{B_i}{\lambda_i} \cdot (1 - e^{-\lambda_i \cdot T}) \right]$
	concentration after infusion	$C_p(t) = \frac{k_0}{V_c} \sum_{i=1}^{n} \left[\frac{B_i}{\lambda_i} \cdot \left(e^{\lambda_i t^*} - 1 \right) \cdot e^{-\lambda_i t} \right]$ with t*=min(t,T)
continuous iv infusion	concentration at steady state	$C_{ss} = \frac{R_o}{CL}$
extravascular		$C_p(t) = \sum_{i=1}^{n} \left[B_i \cdot \frac{k_a}{k_a - \lambda_i} \cdot (e^{-\lambda_i \cdot tl} - e^{-k_a \cdot tl}) \right]$ $tl = t - t_{lag}$

2.2 Pharmacokinetic Equations - Collection of Equations for Compartmental Analysis

One Compartment Model, IV bolus, single dose, one elimination pathway only (assumed to be urinary excretion)	
$D \xrightarrow{i.v.} \langle X \rangle \xrightarrow{k_e} \langle U \rangle$	U - drug amount in urine
$\frac{dX}{dt} = -k_e \cdot X(t) \qquad \frac{dU}{dt} = k_e \cdot X(t)$	k_e= elimination rate constant X = drug amount in the body U =drug amount in the urine
$D = X(0) = X(t) + U(t) = U(\infty) \qquad X(t) = X(0) \cdot e^{-k \cdot t_e}$	D = dose administered X(t) = amount in plasma at time t after administration U(t) = amount in urine at time t
$C_p(t) = \frac{X(t)}{V_c}; \quad C_p(t) = C_p(0) \cdot e^{-k_e \cdot t}$ $V_c = \frac{X(0)}{C_p(0)} = \frac{D}{C_p(0)}$	C_p= Conc. in plasma after single dose k_e= negative slope of concentration-time plot in ln-linear scaling C_p (0)= intercept with y axis
$C_p(t) = \frac{D}{V_d} e^{-k_e \cdot t} \quad ; \qquad t_{1/2} = \frac{\ln(2)}{k_e}$	C_p(t) - plasma conc at any time
Urinary excretion	
$U(t) = U(\infty)(1 - e^{-k_e t}) \quad ;$ $\ln(U(\infty) - U(t)) = \ln U(\infty) - k_e \cdot t$	„Sigma-Minus Plot“ (page 21) Calc. of k_e from urine data based on ln-linear plot of $(U(\infty) - U(t))$ versus t, k_e is the negative slope, but you need <u>total amount</u> U(∞) of drug excreted into urine, which frequently is not identical to the dose administered, in contrast to the assumptions of the model
$\frac{dU}{dt} = k_e \cdot X(0) \cdot e^{-k_e \cdot t} \quad ;$ $\ln \frac{\Delta U}{\Delta t} = \ln(k_e X(0)) - k_e \cdot t_{mid}$	Other method based on urinary excretion rate (total amount of drug need not be known) $\Delta U/\Delta t$ -sampling intervals t_{mid} - mean time point of the sampling interval
$CL_R = \frac{\frac{dU}{dt}}{C_p(t)} \quad ; \quad CL_R = k_e \cdot V_c$ $\frac{\Delta U}{\Delta t} = CL_R \cdot C_p(t_{mid})$	Urinary excretion rate -described by renal clearance CL_R $C_p(t_{mid})$ = conc. in plasma at the mean time point of the urine collection interval, measured or derived by log-linear interpolation CL_R = slope of a plot $\Delta U/\Delta t$ versus $C_p(t_{mid})$
$U_t = CL_R \cdot AUC(0 - t)$ $AUC(0 - t) = \frac{C_p(0)}{k_e}(1 - e^{-k_{et} t})$	

One Compartment Model, IV Inj. and Parallel Elimination Pathways (renal, biliary, metabolic), single dose	
$k_e = k_{ren} + k_{bil} + k_{met}$	k_{ren} = rate constant of renal elimination k_{bil} = rate constant of biliary elimination k_{met} = rate constant of metabolic elimination
$\frac{dX}{dt} = -k_e X(t)$; $\frac{dU}{dt} = k_{ren} X(t)$; $\frac{dB}{dt} = k_{bil} X(t)$; $\frac{dM}{dt} = k_{met} X(t)$	X = amount in plasma U = amount in urine B = amount in bile M = amount of metabolites in plasma
$D = X(0) = X(t) + U(t) + B(t) + M(t) = U(\infty) + B(\infty) + M(\infty)$	
$C_p(t) = C_p(0) \cdot e^{-k_e t}$	Plasma concentration
$U(t) = \frac{k_{ren}}{k_e} \cdot D \cdot (1 - e^{-k_e t})$	Drug amount in urine
$U(\infty) = \frac{k_{ren}}{k_e} D$; $\frac{U(\infty)}{D} = \frac{k_{ren}}{k_e}$; $\ln(U(\infty) - U(t)) = \ln U(\infty) - k_e \cdot t$ $CL_R = k_{ren\cdot} \cdot V_c$; $CL_R^u = \frac{CL_R}{(1 - f_b)}$	Up to infinite time (t = ∞) k_e - slope can calc.from the Sigma Minus Plot (U(∞)-U(t) vs t f_b – fraction of bound drug
$B(t) = \frac{k_{bil}}{k_e} \cdot D \cdot (1 - e^{-k_e t})$; $CL_{bil} = k_{bil\cdot} \cdot V_c$	Biliary excretion can be calc. In analogous fashion assuming no reabsorption
$M(t) = \frac{k_{met}}{k_e} \cdot D \cdot (1 - e^{-k_e t})$; $CL_{met} = k_{met\cdot} \cdot V_c$ $\frac{dM_p}{dt} = k_{met} X(t) - k_e^M M_p(t)$ $C^M(t) = \frac{k_{met} D}{V_c^M (k_e^M - k_e)} (e^{-k_e t} - e^{-k_e^M t})$	Total amounts of metabolites including further excretion of metabolite into urine (k_e^M). $C^M(t)$ = concentration of the metabolite in the central circulation
$CL_{tot} = \frac{D}{AUC} = k_e \cdot V_c$; $CL_{tot} = CL_R + CL_{bil} + CL_{met}$	
D : U(∞) : B(∞) : M(∞) = k_e : k_{ren} : k_{bil} : k_{met} = CL_{tot} : CL_R: CL_{bil}: CL_{met}	after the end of all elimination into the different compartments

One Compartment, multiple IV injection (i intervals τ)	
$C_n(t) = \frac{D}{V_c} e^{-k_e t} \cdot \left(\frac{(1-e^{-nk\tau})}{(1-e^{-k\tau})} \right)$	C_n- concentration after nth administration every τ hours
$C_{ss}(t) = C_0 \cdot \frac{e^{-k_e t}}{(1-e^{-k\tau})} = C_0 \cdot R \cdot e^{-k_e t}$	During steady-state conditions (n=∞), C_0=concentration immediately after initial (first) injection = D/V_c $R = \frac{1}{1 - e^{-k_e \tau}}$
$C_{ss,max} = C_0 \cdot R = \frac{D}{V_c} \cdot \frac{1}{1-e^{-k_e \tau}}$ $C_{ss,min} = C_0 \cdot R \cdot e^{-k_e \tau} = \frac{D}{V_c} \cdot \frac{e^{-k_e \tau}}{1-e^{-k_e t}} = C_{ss,max} \cdot e^{-k_e \tau}$	= Peak = Trough
$\%Fluctuation = \frac{C_{ss,max} - C_{ss,min}}{C_{ss,max}} \cdot 100$ $Fluc. = \frac{C_{ss,max}}{C_{ss,min}} = e^{k_e \tau}$	Fluctuation depends on the relation between k_e (or $t_{1/2}$) and τ, not on the dose
$\tau = \frac{\ln\left(\frac{C_{ss,max}}{C_{ss,min}}\right)}{k_e}$	
$\bar{C}_{ss} = \frac{AUC}{\tau} = \frac{D}{CL \cdot \tau}$	Useful for calculation of the maintenance dose $\overline{C_{ss}}$ -average ss conc., weighted mean, value between C_{max} and C_{min} ; includes no inform. about fluctuations in plasma levels + no inform. about magnitude of C_{max} or C_{min}
$C_{ss,max} = \frac{D_M}{V_c} \cdot \frac{1}{1-e^{-k_e \tau}} = \frac{D_L}{V_c}$; $D_L = \frac{D_M}{1-e^{-k_e \tau}}$	D_L = loading dose required to immediately achieve the same maximum concentration as at steady state with a maintenance dose D_M every τ hours

One Compartment Model, IV Infusion, Zero Order Kinetics	
$D \xrightarrow{k_0} \rangle X \langle \xrightarrow{k_e} \rangle E \langle$	
$\frac{dX}{dt} = k_0 - k_e \cdot X(t)$	k_0- constant infusion rate
$C(t) = \frac{k_0}{k_e \cdot V_d} \cdot (1 - e^{-k_e t})$	during constant rate infusion
$C_{ss} = \frac{k_0}{k_e \cdot V_d} = \frac{k_0}{CL_{tot}}$	ss - $t = \infty$, infusion equilibrium, like ss
$R_0 = C_{ss}.CL$; $Cl_{tot} = k_e V_c$; $CL_{tot} = \frac{R_0 T}{AUC(0-T)} = \frac{D}{AUC}$	
$C_{ss} = \frac{R_0}{CL}$	Plasma concentr. at SS , CL at SS proportional to C_{ss} at SS
$C(t) = \frac{R_0}{CL}(1 - e^{-k_e t})$; $C(t) = C_{ss}(1 - e^{-k_e t})$	for example: time to reach 90% SS ? $\frac{C(t)}{C_{ss}} = 0.90 = (1 - e^{-k_e t})$; $t = \frac{(\ln 0.1)}{-k_e}$

$C_{max} = \frac{R_0}{k_e \cdot V_d} \cdot (1 - e^{-k_e T})$	C_{max} -occurs at the end of infusion, setting **t=**τ (total time of infusion)

After End of Infusion:

$C(t) = C_{max} \cdot e^{-k_e (t-T)}$	Plasma level after end of infusion with t = time after start of the infusion

Short term Infusion:

$LD = C_{ss} \cdot V_c = \frac{k_0}{k_e}$	Loading dose
Incremental LD = $V_c \cdot (C_{desired} - C_{initial})$	
$\frac{C(t)}{C_{ss}} \cdot 100 = (1 - e^{-k_e}) \cdot 100$ $1 < t_{1/2} < \tau$: $C(t_{1/2}) = \frac{C_{ss}}{2}$	Plasma level depends on infusion duration (τ) and $t_{1/2}$:

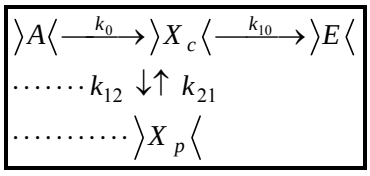
One Compartment Model, Short Term Infusion, Zero Order, multiple dose	
$C_n(t) = C_{n-1}(\tau) \cdot e^{-k_e t} + \frac{k_0}{k_e \cdot V_d}(1 - e^{-k_e t})$	$C_n(t)$ = concentration after n^{th} infusion in intervals of τ
$C_n(\tau) = \frac{k_0}{k_e \cdot V_d}(e^{-k_e(\tau - T)} - e^{-k_e \tau}) \cdot \left(\frac{1 - e^{-n k_e \tau}}{1 - e^{-k_e \tau}}\right)$	n = number of doses

One Compartment Model, Oral Administration With Resorption First Order, single dose	
$D \rightarrow \langle A \rangle \xrightarrow{k_a} \langle X \rangle \xrightarrow{k_e} \langle E \rangle$	
$\frac{dA}{dt} = -k_a A \quad ; \quad \frac{dX}{dt} = k_a A - k_e X \quad ; \quad \frac{dE}{dt} = k_e X$	A = unabsorbed drug available at resorption place E = sum of the excreted amount of drug k_a = absorp. rate constant
f D = A(t) + X(t) + E(t)= E(∞) ; $A(t) = f \cdot D \cdot e^{-k_a t}$	F = fraction of dose available for absorption
$C(t) = \frac{f \cdot D \cdot k_a}{V_d \cdot (k_a - k_e)} \cdot (e^{-k_e t} - e^{-k_a t})$ $C_{term}(t) = \frac{f \cdot D \cdot k_a}{V_d \cdot (k_a - k_e)} \cdot (e^{-k_e t})$ $\ln C_{term}(t) = \frac{f \cdot D \cdot k_a}{V_d \cdot (k_a - k_e)} - k_e t$; C(t)->C_{term}(t) for t->∞	BATEMAN-Function In most cases: $k_a > k_e$, this means that $e^{-k_a t}$ approches zero much faster than $e^{-k_e t}$ - calc. of k_e from slope of terminal phase $k_a < k_e$ - Flip-Flop, but you need an additional iv administration to distinguish this case
$C_{term}(t) - C(t) = \frac{f \cdot D \cdot k_a}{V_c \cdot (k_a - k_e)} \cdot e^{-k_a t}$ $\ln(C_{term}(t) - C(t)) = \frac{f \cdot D \cdot k_a}{V_d \cdot (k_a - k_e)} - k_a t$	k_a - feathering-method (can reasonably be used only if there are at least 4 data points in the increasing part of the concentration-time curve) substraction of C from C' (semilog. Δ(C'-C) versus t - slope -k_a)
$C(t) = \frac{f \cdot D \cdot k_a}{V_d \cdot (k_a - k_e)} \cdot (e^{-k_e (t - t_0)} - e^{-k_a (t - t_0)})$	with t_0 - lag time
$t_{\max} = \frac{\ln\left(\frac{k_a}{k_e}\right)}{k_a - k_e} = \frac{\ln(k_a) - \ln(k_e)}{k_a - k_e}$, $C_{\max} = \frac{f \cdot D \cdot k_a}{V_d} \cdot e^{-k_e t_{\max}}$	t_{max} does not depend on the bioavailability f and, since k_e commonly is substance-dependent and not preparation-dependent, reflects k_a

One Compartment Model, Oral Administration With Resorption First Order, multiple dose	
$C_n(t) = \frac{f \cdot D \cdot k_a}{V_d \cdot (k_a - k_e)} \cdot (r_e \cdot e^{-k_e t} - r_a \cdot e^{-k_a t})$ $C_{ss}(t) = \frac{f \cdot D \cdot k_a}{V_d \cdot (k_a - k_e)} \cdot \left(\frac{e^{-k_e t}}{1 - e^{-k_e \tau}} - \frac{e^{-k_a t}}{1 - e^{-k_a \tau}} \right)$	$C_n(t)$ = concentration after the n^{th} consecutive dosing in intervals τ; BATEMAN-Function expanded by accumulation factor $r_e = \frac{1 - e^{-n k_e \tau}}{1 - e^{-k_e \tau}}$; $r_a = \frac{1 - e^{-n k_a \tau}}{1 - e^{-k_a \tau}}$; n = ∞ for steady state, in most cases $r_a \approx 1$
$t_{ss,\max} = \frac{1}{k_a - k_e} \cdot \ln\left(\frac{k_a (1 - e^{-k_e \tau})}{k_e (1 - e^{-k_a \tau})} \right)$	$t_{ss,max} < t_{max}$ for $k_a > k_e$

Two Compartment Model, IV Inj (without Resorption), single dose	
$D \xrightarrow{iv} \rangle X_c \langle \xrightarrow{k_{10}} \rangle E \langle$ $\cdots\cdots k_{12} \downarrow\uparrow k_{21}$ $\cdots\cdots\cdots \rangle X_p \langle$	
$-\frac{dX_c}{dt} = k_{12} \cdot X_c + k_{10} \cdot X_c - k_{21} \cdot X_p$ $\frac{dX_p}{dt} = k_{12} \cdot X_c - k_{21} \cdot X_T \quad ; \quad \frac{dE}{dt} = k_{10} \cdot X_c$	X_c = amount in central compartment X_p = amount in peripheral comp.
$D = X(0) = X_c(0) = X_c(t) + X_p(t) + E(t) = E(\infty)$	$E(\infty)$ - Sum of drug eliminated
$C(t) = \frac{k_0}{V_C}\left[\frac{\alpha - k_{21}}{\alpha \cdot (\alpha - \beta)} \cdot (e^{\alpha t^*} - 1) \cdot e^{-\alpha t} + \frac{k_{21} - \beta}{\beta \cdot (\alpha - \beta)} \cdot (e^{\beta t^*} - 1) \cdot e^{-\beta t}\right]$	Concentration in plasma = Conc. in central compartment
$A_{iv} = \frac{(\alpha - k_{21})}{(\alpha - \beta)} \cdot \frac{D}{V_c} \quad ; \; B_{iv} = \frac{(k_{21} - \beta)}{(\alpha - \beta)} \cdot \frac{D}{V_c}$	Vc = volume of the central comp., $\alpha > k_{21} > \beta$
$\alpha = \frac{1}{2}\left(k_{12} + k_{21} + k_{10} + \sqrt{(k_{12} + k_{21} + k_{10})^2 - 4 \cdot k_{21} \cdot k_{10}}\right)$ $\beta = \frac{1}{2}\left(k_{12} + k_{21} + k_{10} - \sqrt{(k_{12} + k_{21} + k_{10})^2 - 4 \cdot k_{21} \cdot k_{10}}\right)$	α, β = Macro constants (or Hybrid constants, independent of dose, A+B proportional to dose disposition rate constants, equal for iv and oral administration
$\alpha \cdot \beta = k_{21} \cdot k_{10} \quad ; \quad \alpha + \beta = k_{12} + k_{21} + k_{10}$	k_{12}, k_{21}, k_{10} - Micro constants
$C_{term}(t) = B \cdot e^{-\beta \cdot t} \quad \rightarrow \quad \ln C_{term}(t) = \ln B - \beta \cdot t$ $C(t) - C_{term}(t) = A \cdot e^{-\alpha t} \quad \rightarrow \quad \ln(C(t) - C_{term}(t)) = \ln A - \alpha \cdot t$	$\alpha > \beta$, for elim. phase first term =0 A,B, α, β, can determined by feathering method Plot $\ln(C_{term}(t))$ vs t with slope β, intercept ln(B) Plot $\ln((C(t)-C_{term}(t)))$ vs t with slope α, intercept ln(A)
$k_{21} = \frac{A \cdot \beta + B \cdot \alpha}{A + B} \quad ; \quad k_{10} = \frac{\alpha \cdot \beta}{k_{21}} = \frac{A + B}{\frac{A}{\alpha} + \frac{B}{\beta}} \quad ;$ $k_{12} = \alpha + \beta - k_{21} - k_{10} = \frac{AB(\beta - \alpha)^2}{(A + B)(A \cdot \beta + B \cdot \alpha)}$	A,B iv $\neq$ A,B oral $k_{10} = k_{ren} + k_{met}$ $(+k_{bil} + k_{other})$ $\frac{k_{ren}}{k_{10}} = \frac{U_\infty}{E_\infty}$
$AUC_{(0-t)} = \frac{A}{\alpha}(1 - e^{-\alpha t}) + \frac{B}{\beta}(1 - e^{-\beta t}) \qquad AUC = \frac{A}{\alpha} + \frac{B}{\beta}$	AUC - by integration of the general equation for C

Two Compartment Model, IV Inj, single dose	
$D \xrightarrow{iv} \rangle X_c \langle \xrightarrow{k_{10}} \rangle E \langle$ $\cdots\cdots k_{12} \downarrow\uparrow k_{21}$ $\cdots\cdots\cdots \rangle X_p \langle$	
$X_p(t) = \frac{D \cdot k_{12}}{\beta - \alpha}\left(e^{-\alpha t} - e^{-\beta t}\right)$	X_p = drug amount in the tissues (peripheral compartment)
$t_{\max,p} = \frac{\ln\alpha - \ln\beta}{\alpha - \beta}$	$\frac{dX_p}{dt} = 0$ at $t_{max,p}$
$C_c^f(t_{\max,p}) = C(t_{\max,p}) \cdot (1 - f_b) =$ $C_p(t_{\max,p}) \cdot (1 - f_{b,p}) = C_p^f(t_{\max,p})$	Most membranes central compartment / tissue are crossed by diffusion – by unbound drug only f_b = fraction bound (to protein)
$V_c = \frac{D}{C(0)} = \frac{D}{A+B}$	V_c – volume of distribution in the central compartment
$\frac{X}{V_c} = \frac{X_c + X_p}{V_c + V_p} = (assumed)\frac{X_c}{V_c}$	Other "volume" terms are proportionality factors assuming that $C_c = C_T$, they may take on unphysiological values. Initially X_c and C_c high with X_T and C_p nearly 0. In the end frequently $C_T > C_p$. Vd = volume of distribution of the total organism – not constant in time!
$V_{d,ss} = V_{ss} = \frac{X_c + X_p}{C_{ss}} = \frac{\left(1 + \frac{k_{21}}{k_{12}}\right) \cdot X_c}{\frac{X_c}{V_c}} = \left(1 + \frac{k_{21}}{k_{12}}\right) \cdot V_c$	V_{ss} = volume of distribution at equilibrium, when flows $X_c \leftrightarrow X_T$ balance: $k_{12} \cdot X_c = k_{21} \cdot X_T$
$V_{ss} = \frac{A \cdot \beta^2 + B \cdot \alpha^2}{(A \cdot \beta + B \cdot \alpha)^2} \cdot D$	V_{ss} can also be calculated from macro constants
$V_p = V_{ss} - V_c = \frac{k_{21}}{k_{12}} V_c$; $C_p = \frac{X_p}{V_p}$	In the strictest sense only true at equilibrium
$C_{\max,p} = \frac{k_{21} \cdot D}{V_c \cdot (\beta - \alpha)} \cdot \left(e^{-\alpha \cdot t_{\max,p}} - e^{-\beta \cdot t_{\max,p}}\right)$	
$CL = \frac{\frac{dE}{dt}}{C(t)} = \frac{k_{10} \cdot X_c(t)}{C(t)} = k_{10} \cdot V_c$	
$CL = k_e \cdot V_{ss}$; $k_e = \frac{k_{10} \cdot V_c}{V_{ss}} = \frac{k_{10} \cdot k_{21}}{k_{21} + k_{12}}$	This is the definition of k_e for a two-compartment model
$AUC = \frac{A}{\alpha} + \frac{B}{\beta} = \frac{k_{21}}{\alpha \cdot \beta} \cdot \frac{D}{V_c}$; $\frac{D}{AUC} = \frac{k_{21} \cdot k_{10}}{k_{21}} V_c = k_{10} \cdot V_c = CL$	
$V_z = \frac{CL}{\beta} = \frac{D}{\beta \cdot AUC}$	V_z – volume of distribution during terminal phase, calculated based on the rate constant
$CL = k_{10} \cdot V_c = k_e \cdot V_{ss} = \beta \cdot V_z = \frac{D}{AUC}$	$V_z > V_{ss} > V_c$ – during terminal phase $X_T > X_c$

Two compartment Model single dose infusion (or zero order resorption)	
	
$k_0 = \frac{D}{T}$	Infusion of dose D during τ at constant rate k_0
$C(t) = \frac{k_0}{V_C}\left[\begin{array}{l}\frac{\alpha - k_{21}}{\alpha\cdot(\alpha-\beta)}\cdot(e^{\alpha t^*}-1)\cdot e^{-\alpha t} + \\ \frac{k_{21}-\beta}{\beta\cdot(\alpha-\beta)}\cdot(e^{\beta t^*}-1)\cdot e^{-\beta t}\end{array}\right]$	General equation for calc. of C(t) during and after infusion, t* = min(τ,t)
$C(t) = \frac{k_0}{V_C}\left[\frac{\alpha - k_{21}}{\alpha\cdot(\alpha-\beta)}\cdot(1-e^{-\alpha t}) + \frac{k_{21}-\beta}{\beta\cdot(\alpha-\beta)}\cdot(1-e^{-\beta t})\right]$	**during infusion**, t*=t ($e^{\lambda t^*}$-1)$e^{-\lambda t}$ becomes 1- $e^{-\lambda t}$
$k_0 = k_{10}\cdot A_{ss} = k_{10}\cdot C_{ss}\cdot V_c$; $C_{ss} = \frac{k_0}{k_{10}\cdot V_c} = \frac{k_0}{CL}$	For a continuing infusion, $\tau\rightarrow\infty$
$C(t) = \frac{k_0}{V_C}\left[\begin{array}{l}\frac{(\alpha - k_{21})\cdot(1-e^{-\alpha T})}{\alpha\cdot(\alpha-\beta)}\cdot e^{-\alpha(t-T)} + \\ \frac{(k_{21}-\beta)\cdot(1-e^{-\beta T})}{\beta\cdot(\alpha-\beta)}\cdot e^{-\beta(t-T)}\end{array}\right]$	**after end of infusion**, t-τ = time after end

Two compartment Model, single dose with Resorption First Order	
$\rangle A\langle \xrightarrow{k_a} \rangle X_c \langle \xrightarrow{k_{10}} \rangle E \langle$ $\cdots\cdots k_{12} \downarrow\uparrow k_{21}$ $\cdots\cdots\cdots\rangle X_p \langle$	
$C(t) = \frac{k_a \cdot F \cdot D}{V_c} \cdot \left[\frac{(k_{21}-\alpha)}{(\beta-\alpha)\cdot(k_a-\alpha)} \cdot e^{\alpha \cdot t} + \frac{(k_{21}-\beta)}{(\beta-\alpha)\cdot(k_a-\beta)} \cdot e^{-\beta \cdot t} + \frac{(k_{21}-k_a)}{(\alpha-k_a)\cdot(\beta-k_a)} \cdot e^{-k_a t} \right]$	$\frac{k_{21}-\alpha}{(\beta-\alpha)\cdot(k_a-\alpha)} + \frac{k_{21}-\beta}{(\alpha-\beta)\cdot(k_a-\beta)} = -\frac{k_{21}-k_a}{(\alpha-k_a)\cdot(\beta-k_a)}$ C-central compartment with micro constants
$C(t) = A \cdot e^{-\alpha \cdot t} + B \cdot e^{-\beta \cdot t} - (A+B) \cdot e^{-k_a t}$	C-central compartment with macro constants
$A_{IV} = \frac{D}{V_c} \cdot \frac{(k_{21}-\alpha)}{(\beta-\alpha)}$; $B_{IV} = \frac{D}{V_c} \cdot \frac{(k_{21}-\beta)}{(\alpha-\beta)}$	
$A_{oral} = \frac{k_a \cdot f}{(k_a-\alpha)} \cdot A_{iv}$; $B_{oral} = \frac{k_a \cdot f}{(k_a-\beta)} \cdot B_{iv}$ $\frac{V_c}{f} = \frac{D}{f \cdot A_{iv} + f \cdot B_{iv}}$	Without iv data only V_c/f can be determined, but based on knowledge of $f \cdot A_{iv}$ and $f \cdot B_{iv}$ the micro constants k_{10}, k_{21}, k_{12} may be derived
$C_p(t) = \frac{A \cdot k_{21}}{(k_{21}-\alpha)} \cdot e^{-\alpha t} + \frac{B \cdot k_{21}}{(k_{21}-\beta)} e^{-\beta t} - \frac{(A+B) \cdot k_{21}}{(k_{21}-k_a)} \cdot e^{-k_a t}$	C_T-deep compartment

Two compartment Model, multiple dose with Resorption First Order	
$C_n(t_x) = A \cdot \frac{(1-e^{-n\alpha\tau})}{1-e^{-\alpha\tau}} \cdot e^{-\alpha t_x} + B \frac{1-e^{-n\beta\tau}}{1-e^{-\beta\tau}} e^{-\beta t_x}$ $-(A+B) \frac{1-e^{-nk_a\tau}}{1-e^{-k_a\tau}} e^{-k_a t_x}$	C_n – concentration at time t_x after the n^{th} administration at interval τ, time after first dosing = $n \cdot \tau$

3 PHARMACODYNAMIC GLOSSARY

3.1 Definitions

Symbol	Unit / Dimension	Definition
AUEC	Arbitrary units·time	Area under the effect curve
C_e	Amount/volume	Fictive 'concentration' in the effect compartment
C_p	Amount/volume	Drug concentration in the central compartment
E	(effect unit)	Effect
E_0	(effect unit)	Baseline effect
E_{max}	(effect unit)	Maximum effect
EC_{50}	Amount/volume	Drug concentration producing 50% of maximum effect
I_{max}	(effect unit)	Maximum inhibition
I_{50}	Amount/volume	Drug concentration producing 50% of maximal inhibition
k_{eo}	$(Time)^{-1}$	Rate constant for degradation of the effect compartment
k_{in}	(effect unit) $(time)^{-1}$	Zero order constant for input or production of response
k_{out}	$(time)^{-1}$	First order rate constant for loss of response
M_{50}	Amount/volume	50% of maximum effect of the regulator
MEC	Amount/volume	Minimum effective concentration
n	-	Sigmoidicity factor (Hill exponent)
S	(effect unit)/ (amount/volume)	Slope of the line relating the effect to the concentration
t_{MEC}	Time	Duration of the minimum (or optimum) effective concentration
V_e	Volume	Fictive volume of the effect compartment

3.2 Equations: PK/PD Models

$E=E_{fixed}$ if $C \geq C_{threshold}$	fixed effect model
$E = \frac{E_{max} \cdot C}{E_{50} + C}$	E_{max} model
$E = \frac{E_{max} \cdot C^n}{E_{50}^n + C^n}$	sigmoid E_{max} model
$\frac{dR}{dt} = k_{in} - k_{out} \cdot R$	Rate of change of the response over time with no drug present
$\frac{dR}{dt} = k_{in} \cdot \left[1 - \frac{C}{IC_{50} + C}\right] - k_{out} \cdot R$ $\frac{dR}{dt} = k_{in} \cdot \left[1 - \frac{I_{max} \cdot C^n}{IC_{50} + C^n}\right] - k_{out} \cdot R$	Inhibition of build-up of response
$\frac{dR}{dt} = k_{in} - k_{out} \cdot \left[1 - \frac{I_{max} \cdot C}{IC_{50} + C}\right] \cdot R$	Inhibition of loss of response
$\frac{dR}{dt} = k_{in} \cdot \left[1 + \frac{E_{max} \cdot C}{E_{50} + C}\right] - k_{out} \cdot R$	Stimulation of build-up of response
$\frac{dR}{dt} = k_{in} - k_{out} \cdot \left[1 + \frac{E_{max} \cdot C}{E_{50} + C}\right] \cdot R$	Stimulation of loss of response

4 STATISTICAL PARAMETERS

4.1 Definitions

Symbol	Definition	Calculation
AIC	Akaike Information Criterion (smaller positive values indicate a better fit)	AIC = n·ln(WSSR) +2p n = number of observed (measured) concentrations, p = number of parameters in the model
CI	Confidence interval, e.g. 90%-CI	$CI = \bar{x} \pm t_{n-1,\alpha} \cdot SEM$
CV	Coefficient of variation in %	$CV = 100 \cdot \frac{SD}{\bar{x}}$, SD = standard deviation
Median = $\tilde{x}$	Median, value such that 50% of observed values are below and 50% above	(n+1)st value if there are 2n+1 values or arithmetic mean of nth and (n+1)st value if there are 2n values
Mean = $\bar{x}$	Arithmetic mean	$\bar{x} = \frac{1}{n}\sum_{i=1}^{n} x_i$
MSC	Model selection criterion	AIC, SC, F-ratio test, Imbimbo criterion etc.
SC	Schwarz criterion	SC = n·ln(WSSR) +p·ln(n)
SD	Standard deviation	$SD = \sqrt{Var}$
SEM	Standard error of mean	$SEM = \frac{SD}{\sqrt{n}}$
SSR	Sum of the squared deviations between the calculated values of the model and the measured values	$SSR = \sum_{i=1}^{n} \left(C_{i,obs} - C_{i,calc} \right)^2$
SS	Sum of the squared deviations between the measured values and the mean value $\bar{C}$	$SS = \sum_{i=1}^{n} \left(C_{i,obs} - \bar{C} \right)^2$ $SS = \left(\sum_{i=1}^{n} C_{i,obs}^{\,2} \right) - \frac{\left(\sum_{i=1}^{n} C_{i,obs} \right)^2}{n}$ n = number of observed (measured) concentrations use of the second formula is discouraged although mathematically identical
WSS or WSSR	Weighted sum of the squared deviations between the calculated values of the model and the measured values	$WSSR = \sum_{i=1}^{n} w_i \left(C_{i,obs} - C_{i,calc} \right)^2$
Var	Variance	$s^2 = SS/(n-1)$
$X_{25\%}$	Lower quartile (25%- quantile), value such that 25% of observed values are below and 75% above	may be calculated as median of values between minimum and the overall median
$X_{75\%}$	Upper quartile (75%- quantile)	may be calculated as median of values between the overall median and the maximum

4.2 Characterisation of log-normally distributed data

Symbol	Definition	Calculation
$\overline{X_g}$	Geometric mean of log-normally distributed data	$\overline{X}_g = \exp\left[\frac{1}{n} * \sum_{i=1}^{n} \ln(x_i)\right]$
sd_l	Standard deviation to the log-transformed data	$sd_l = \sqrt{\frac{1}{n-1} \cdot \left\{\sum_{i=1}^{n} \ln(x_i)^2 - \frac{1}{n}\left[\sum_{i=1}^{n} \ln(x_i)\right]^2\right\}}$
Scatter	Scatter-Factor	$\text{Scatter} = e^{sd_l}$
CI_g	Confidence interval of log-normally distributed data	$CI_g = \exp\left[\frac{1}{n} \cdot \sum_{i=1}^{n} \ln(x_i) \pm t_{n-1,0.05} \cdot SEM_{\ln}\right]$
CV_g	Geometric coefficient of variation in %	$CV_g = 100 \cdot \sqrt{e^{Var_{\ln}} - 1}$ [%]
$Per_{16\%}$	16% percentile of log-normally distributed data	$\text{Per}_{16\%} = \frac{\overline{X_g}}{\text{Scatter}}$
$Per_{84\%}$	84% percentile of log-normally distributed data	$\text{Per}_{84\%} = \overline{X_g} \cdot \text{Scatter}$