APPENDIX

Accuracy - The extent to which an experimentally determined value agrees with the true value.

Adverse Drug Reaction - An undesirable effect that is suspected to be associated with the use of drug by subject.

AUC (Area Under the Curve) - The area under the drug (or metabolite) concentration in plasma (or serum, or whole blood) versus time curve. The AUC symbol may be qualified by a specific time, time of last quantifiable concentration (AUC_{0-t}), or infinity ($AUC_{0-\infty}$). AUC is calculated from observed data at specific time points.

$AUC_{0-\infty}$ (AUC to infinity) - The $AUC_{0-\infty}$ is a measure of the total amount of intact drug absorbed that reaches the systemic circulation. It is calculated from the integral of total area under the concentration-time curve, from time zero to infinity. The unit of $AUC_{0-\infty}$ is a unit of drug concentration multiplied by time (e.g. µg·h/mL)

AUC_{0-t} (AUC to the time of the last quantitable concentration) - AUC_{0-t} is calculated from the data observed at specific time points by the linear trapezoidal rule.

AUC Ratio - The ratio of geometric means of the test and reference AUCs. It is calculated as the antilogarithm of the difference between the means of the logarithm (ln) of the test and reference AUCs. The C_{max} ratio should be similarly calculated.

Bioavailability - The bioavailability of a drug is the fraction (F) of rate and extent of the administered dose that reaches the systemic circulation. Bioavailability is defined as unity (or 100%) in the case of intravenous administration. After administration by other routes, bioavailability is generally reduced by incomplete absorption, first-pass metabolism, and any distribution into other tissues that occurs before the drug enters the systemic circulation. To account for differing rates of absorption into the blood, the concentration appearing in the plasma must be integrated over time to obtain an integrated total area under the plasma concentration curve (AUC).

Bioequivalence - Two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent and their bioavailabilities (rate and extent of availability) after administration in the same molar dose are similar to such a degree that their effects, with respect to both efficacy and safety, can be expected to be essentially the same. Pharmaceutical equivalence implies the same amount of the same active substance(s), in the same dosage form, for the same route of administration and meeting the same or comparable standards.

C_{max} (Maximum Plasma concentration) - C_{max} represents the maximal or the peak plasma drug concentration after drug administration. The unit for the C_{max} is a concentration unit (e.g., µg/mL, mIU/mL).

Calibration curve - Calibration curve is a general method for determining the concentration of a substance in an unknown sample by comparing the unknown to a set of standard samples of known concentration.

Calibration Standard - A biological matrix to which a known amount of analyte has been added or spiked. Calibration standard are used to construct calibration curve from which the concentrations of analytes in QCs and in unknown study samples are determined.

Clearance (Cl) - The clearance, also renal clearance or renal plasma clearance (when referring to the function of the kidney), of a substance is the inverse of the time constant that describes its removal rate from the body divided by its volume of distribution (or total body water).

Elimination Half-life ($T_{1/2}$) - The time it takes for the amount or concentration of a drug to fall to 50% of an earlier measurement; this number is a constant, regard less of concentration, for drugs eliminated by first-order kinetics (the great majority of drugs). Half-life is not a constant and therefore not particularly useful for drugs eliminated by zero-order kinetics.

Half-life is a derived parameter, completely determined by volume of distribution and clearance. Half-life can be determined graphically from a plot of the blood level versus time or from the following relationship:

$$T_{1/2} = \frac{0.0693 \times Vd}{Cl}$$

One must know both primary variables (Vd and Cl) to predict changes in half-life. Disease, age, and other variables usually alter the clearance of a drug much more than its volume of distribution.

Limit of Quantitation (LLQ) - The lowest measured concentration on the standard curve having an acceptable degree of precision and accuracy. The LLQ cannot be below the lowest nominal concentration on the same standard curve.

90% Confidence Interval - An interval about the estimated value that provides 90% assurance that it contains the true value.

Pharmaceutical equivalence - means a new drug that, in comparison with another drug, contains identical amounts of the identical medicinal ingredients, in comparable dosage forms, but that does not necessarily contain the same non-medicinal ingredients.

Pharmacokinetics - Pharmacokinetics is a branch of pharmacology dedicated to the study of the time course of substances and their relationship with an organism or system. In practice, this discipline is applied mainly to drug substances, though in principle it concerns itself with all manner of compounds residing within an organism or system, such as nutrients, metabolites, endogenous hormones, toxins, etc. So, in basic terms, while pharmacodynamics explores what a drug does to the body, pharmacokinetics explores what the body does to the drug including absorption, distribution, metabolism, and excretion.

Precision - The closeness of agreement of values obtained in the analysis of replicate samples of the same specimen, usually indicated by the percentage of coefficient of variation (%CV) which calculated as follow:

$$CV\ (\%) = \frac{S.D.}{Mean} \times 100$$

Rate of Absorption - The rate at which a drug reaches the systemic circulation after oral administration.

Relative Bioavailability (F_{rel}) - F_{rel} is the percentage or fraction of the AUC of a generic drug product as compare to the innovator reference drug.

Sample - A generic term encompassing controls, blanks, unknowns, and processed samples, as describe below:

Blank: A sample of a biological matrix to which no analytes have been added that is used to assess the specificity of the bioanalytical method.

Quality control sample (QC): A spiked sample used to monitor the performance of a bioanalytical method and to assess the integrity and validity of the results of the unknown samples analyzed in an individual batch.

Unknown: A biological sample that is the subject of the analysis.

Standard Curve - The relationship between the experimental response value and analytical concentration (also called a calibration curve).

Therapeutic Equivalence - Therapeutic equivalence means that a chemical equivalence of a drug product (i.e., containing the same amount of the same drug in the same dosage form) when administered to the same individuals in the same dosage regimen will provide essentially the same efficacy and toxicity.

Time to Reach the Maximal Plasma Concentration (T_{max}) - T_{max} corresponds to the time required to reach the maximum plasma concentration after drug administration. It is a measure of the rate of drug absorption, which exceeds it early disposition. Until a time T_{max} is reached that the rate of elimination matches the rate of absorption. The unit of T_{max} is a unit of time, e.g., h or min.

Volume of distribution (Vd) - The volume of distribution, also known as apparent volume of distribution, is a pharmacological term used to quantify the distribution of a drug throughout the body after oral or parenteral dosing. It is defined as the volume in which the amount of drug would need to be uniformly distributed in to produce the observed blood concentration.

$$Vd = \frac{\text{total amount of drug in the body}}{\text{drug blood concentration}}$$

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