II GLOSSARY

**Absolute Bioavailability:** is the extent or fraction of drug absorbed upon extravascular administration in comparison to the dosage size administered.

**Absorption:** of drugs is the process of uptake of the compound from the site of administration into the systemic circulation. A prerequisite for absorption is that the drug should be in aqueous solution. The only relatively rare exception is absorption by pinocytosis.

**Accuracy:** The degree of closeness of the determined value to the nominal or known true value under prescribed conditions. This is sometimes termed trueness.

**Analyte:** A specific chemical moiety being measured, this can be an intact drug, biomolecule or its derivative, metabolite, and/or degradation product in a biological matrix.

**Analytical run (or batch):** A complete set of analytical and study samples with appropriate number of standards and QCs for their validation. Several runs (or batches) may be completed in one day, or one run (or batch) may take several days to complete.

**Bioequivalence:** It is a relative term which denotes that the drug substance in two or more identical dosage forms, reaches the systemic circulation at the same relative rate and to the same relative extent i.e. their plasma concentration-time profiles will be identical without significant statistical differences.

**Bioequivalence Requirement:** It is a requirement imposed by the Food and Drug Administration for *in vitro* and/or *in vivo* testing of specified drug products which must be satisfied as a condition of marketing.

**Biological matrix:** A discrete material of biological origin that can be sampled and processed in a reproducible manner. Examples are blood, serum, plasma, urine, feces, saliva, sputum, and various discrete tissues.

**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.

**Blood:** It consist of cellular material (99% red blood cells, with white blood cells and platelets making up the remainder), water, amino acids, proteins, carbohydrates, lipids, hormones, vitamins, electrolytes, dissolved gases, and cellular wastes. Each red blood cell
is about 1/3 hemoglobin, by volume. The primary blood gases are oxygen, carbon dioxide, and nitrogen.

**Blood-, Plasma-, or Serum-Levels:** demonstrate the drug concentration in blood, plasma or serum upon administration of a dosage form through various routes of administration. Blood, plasma, or serum-level curves are plots of drug concentration versus time on numeric or semi-log graph paper. These levels are obtained from blood samples by venopuncture in certain time intervals after administration of the drug product and chemical or microbiological analysis of the drug in the biological fluid.

**Calibration standard:** A biological matrix to which a known amount of analyte has been added or spiked. Calibration standards are used to construct calibration curves from which the concentration of analytes in QCs and in unknown study samples are determined.

**Carry over:** is a detector response observed in the blank, injected immediately after the highest calibration standard.

**Clearance:** is the hypothetical volume of distribution in mL of the un-metabolized drug which is cleared per unit time (ml/min or ml/h) by any pathway of drug removal (renal, hepatic and other pathways of elimination).

**Drug:** It is a chemical compound of synthetic, semi synthetic, natural or biological origin which interacts with human or animal cells. The interactions may be quantified, whereby these resulting actions are intended to prevent, to cure or to reduce ill effects in the human or animal body, or to detect disease-causing manifestations.

**Dosage Regimen:** It is a systematized dosage schedule for therapy, i.e. the proper dose sizes and proper dosing intervals required to produce clinical effectiveness or to maintain a therapeutic concentration in the body.

**Drug Product or Dosage Form:** It is the gross pharmaceutical form containing the active ingredient(s) [drug(s)] and vehicle substance necessary in formulating a medicament of desired dosage, desired volume and desired application form, ready for administration.

**Excretion:** is the final elimination of the drug from the body’s systemic circulation via the kidney into urine, via bile into intestines and saliva into feces, via sweat, via skin and via milk.

**First-pass Effect:** is the phenomenon that some drugs are already metabolized between the site of absorption and reaching systemic circulation. First-pass effect may occur in the
gut wall, in the mesenteric blood and/or in the liver. First-pass effect may occur upon oral and deep rectal administration.

**Internal standard:** Test compound(s) (e.g. structurally similar analog, stable labeled compound) added to both calibration standards and samples at known and constant concentration to facilitate quantification of the target analyte(s).

**Lower limit of quantification (LLOQ):** The lowest amount of an analyte in a sample that can be quantitatively determined with suitable precision and accuracy.

**Matrix effect:** The direct or indirect alteration or interference in response due to the presence of unintended analytes (for analysis) or other interfering substances in the sample.

**Metabolism:** It is the sum of all the chemical reactions for biotransformation of endogenous and exogenous substances which take place in the living cell.

**Method:** A comprehensive description of all procedures used in sample analysis.

**Pharmacokinetics:** It deals with the changes of drug concentration in the drug product and changes of concentration of a drug and/or its metabolite(s) in the human or animal body following administration, i.e., the changes of drug concentration in the different body fluids and tissues in the dynamic system of liberation, absorption, distribution, body storage, binding, metabolism, and excretion.

**Plasma:** It consists of about 92% water, with plasma proteins as the most abundant solutes. Plasma appearance is transparent with a faint straw colour. It is mainly composed of water, blood proteins (albumins, globulins, and fibrinogens), and inorganic electrolytes. It serves as transport medium for glucose, lipids, amino acids, hormones, metabolic end products, carbon dioxide and oxygen. Plasma is the largest single component of blood, making up about 55% of total blood volume.

**Precision:** The closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogenous sample under the prescribed conditions.

**Quantification range:** The range of concentration, including ULOQ and LLOQ which can be reliably and reproducibly quantified with accuracy and precision through the use of a concentration-response relationship.

**Recovery:** The extraction efficiency of an analytical process, reported as a percentage of the known amount of an analyte carried through the sample extraction and processing
steps of the 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.

**Selectivity:** The ability of the bioanalytical method to measure and differentiate the analytes in the presence of components that may be expected to be present. These could include metabolites, impurities or matrix components.

**Serum:** It refers to blood plasma in which clotting factors (such as fibrin) have been removed.

**Stability in matrix:** The chemical stability of an analyte in a given matrix under specific conditions for given time intervals. Drug stability in a biological fluid is a function of the storage conditions, the chemical properties of the drug, the matrix, and the container system. Stability evaluation is done to show that the concentration of analyte at the time of analysis corresponds to the concentration of the analyte at the time of sampling.

- **Solution stability:** The stability test for the standard stock solution of analyte done at the same temperature (room or refrigerated), container and solvent as that used in the analysis.
- **Bench top stability:** is the stability of the analyte in matrix at working temperature conditions over a short period covering the sample time, when all precautions are taken to avoid specifically known stability problems of the analyte (e.g. light sensitivity).
- **Post preparative stability (Autosampler and dry state stability):** is evaluated over the maximum time from completion of sample work-up to completion of data collection, with allowance also for potential delay in analysis due to equipment failure.
- **Freeze and Thaw stability:** This stability test is done to ensure that the sample remains stable after it is subjected to multiple freeze-thaw cycles in the process of the study.
- **Long term stability**

  This is done to assess whether the analyte is stable in the plasma matrix under the sample storage conditions for the time period required for the samples generated in a clinical study to the last date of analysis.
**Standard/Calibration curve:** The relationship between the experimental response value and the known analytical concentration.

**Therapeutic Equivalence:** This term indicates that two or more drug products that contain the same therapeutically active ingredient elicit identical pharmacologic effects and can control the disease to the same extent.

**Upper limit of quantification (ULOQ):** The highest amount of an analyte in a sample that can be quantitatively determined with precision and accuracy.

**Validation:** is a documented evidence of performance characteristics of a method, satisfying the requirements for the intended application.

**Working standard:** is an established chemical form of a substance which is characterized against reference standard used as a standard in bioanalysis.