DEFINITIONS

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, which can be intact drug, bio molecule or its derivative, metabolite, and/or degradation product in a biologic 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.

Biological matrix:

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

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 concentrations of analytes in QCs and in unknown study samples are determined.

Internal standard:

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

Limit of detection (LOD):

The lowest concentration of an analyte that the bio analytical procedure can reliably differentiate from background noise.

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.

Method:

A comprehensive description of all procedures used in sample analysis.

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.

Processed:

The final extract (prior to instrumental analysis) of a sample that has been subjected to various manipulations (e.g., extraction, dilution, concentration).

Quantification range:

The range of concentration, including ULOQ and LLOQ that 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 sample extraction and processing steps of the method.

Reproducibility:

The precision between two laboratories. It also represents precision of the method under the same operating conditions over a short period of time.

Sample:

A generic term encompassing controls, blanks, unknowns, and processed samples, as described below:

Blank:

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

Quality control sample (QC):

A spiked sample used to monitor the performance of a bio analytical 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 bio analytical method to measure and differentiate the analytes in the presence of components that may be expected to be present. These could include metabolites, impurities, degradants, or matrix components.

Stability:

The chemical stability of an analyte in a given matrix under specific conditions for given time intervals.

Standard curve (or Calibration curve):

The relationship between the experimental response value and the analytical concentration.

System suitability:

Determination of instrument performance (e.g., sensitivity and chromatographic retention) by analysis of a reference standard prior to running the analytical batch.

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

Full validation:

Establishment of all validation parameters to apply to sample analysis for the bio analytical method for each analyte.

Partial validation:

Modification of validated bio analytical methods that do not necessarily call for full revalidation.

Cross-validation:

Comparison validation parameters of two bio analytical methods.

Active Pharmaceutical Ingredient
A substance or compound that is intended to be used in the manufacture of a pharmaceutical product as a pharmacologically active compound (ingredient).

Airlock
An enclosed space with two or more doors, which is interposed between two or more rooms, e.g., of differing classes of cleanliness, for the purpose of controlling the airflow between those rooms when they need to be entered. An airlock is designed for and used by either people or goods.

Authorized Person
A person responsible for the release of batches of finished product for sale. In certain countries the batch documentation of a batch of finished product must be signed by an authorized person from the production department and the batch test results by an authorized person from the quality control department for batch release.

Batch (or Lot)
A defined quantity of starting material, packaging material, or product processed in a single process or series of processes so that it could be expected to be homogeneous. In the case of continuous manufacture, the batch must correspond to a defined fraction of the production, characterized by its intended homogeneity. It may sometimes be necessary to divide a batch into a number of sub-batches, which are later brought together to form a final homogeneous batch.

Batch Number (or Lot Number)
A distinctive combination of numbers and/or letters which specifically identifies a batch on the labels, the batch records, the certificates of analysis, etc.

Batch Numbering System
Standard operating procedure describing the details of the batch numbering.

Batch Records
All documents associated with the manufacture of a batch of bulk product or finished product. They provide a history of each batch of product and of all circumstances pertinent to the quality of the final product.

Bulk Product
Any product that has completed all processing stages up to, but not including, final packaging.

Calibration
The set of operations that establish, under specified conditions, the relationship between values indicated by an instrument or system for measuring (especially weighing), recording, and controlling, or the values represented by a material measure, and the corresponding known values of a reference standard. Limits for acceptance of the results of measuring should be established.

Clean Area
An area with defined environmental control of particulate and microbial contamination, constructed and used in such a way as to reduce the introduction, generation, and retention of contaminants within the area.

Consignment (or Delivery)
The quantity of starting material, or of a drug product, made by one manufacturer and supplied at one time in response to a particular request or order. A consignment may comprise one or more packages or containers and may include material belonging to more than one batch.

Critical Process
A process that may cause variation in the quality of the pharmaceutical product.

Cross-Contamination
Contamination of a starting material, intermediate product, or finished product with another starting material or product during production.

Finished Product
A product that has undergone all stages of production, including packaging in its final container and labelling.

In-Process Control
Checks performed during production in order to monitor and if necessary to adjust the process to ensure that the product conforms to its specifications. The control of the environment or equipment may also be regarded as a part of in-process control.

Intermediate Product
Partly processed material that must undergo further manufacturing steps before it becomes a bulk product.

Large-Volume Parenterals
Sterile solutions intended for parenteral application with a volume of 100 ml or more in one container of the finished dosage form.

Manufacture
All operations of purchase of materials and products, production, quality control, release, storage, shipment of finished products, and the related controls.

Marketing Authorization (Product Licence, Registration Certificate)
A legal document issued by the competent drug regulatory authority that establishes the detailed composition and formulation of the product and the pharmacopoeial or other recognized specifications of its ingredients and of the final product itself, and includes details of packaging, labelling, and shelf-life.

Master Formula
A document or set of documents specifying the starting materials with their quantities and the packaging materials, together with a description of the procedures and precautions required to produce a specified quantity of a finished product as well as the processing instructions, including the in-process controls.

Master Record
A document or set of documents that serve as a basis for the batch documentation (blank batch record).

Packaging
All operations, including filling and labelling, that a bulk product has to undergo in order to become a finished product. Sterile filling would not normally be regarded as part of packaging, the bulk product being the filled, but not the finally packaged, primary container.

Packaging Material
Any material, including printed material, employed in the packaging of a pharmaceutical product, excluding any outer packaging used for transportation or shipment. Packaging materials are referred to as primary or secondary according to whether or not they are intended to be in direct contact with the product.

Pharmaceutical Product
Any medicine intended for human use or veterinary product administered to food-producing animals, presented in its finished dosage form or as a starting material for use in such a dosage form, that is subject to control by pharmaceutical legislation in both the exporting state and the importing state.

Production
All operations involved in the preparation of a pharmaceutical product, from receipt of materials, through processing and packaging, to completion of the finished product.

Quality Assurance
Quality assurance is a wide-ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use. Quality assurance therefore incorporates GMP and other factors, including those outside the scope of this guide such as product design and development.

Quality Control
Quality control is the part of GMP concerned with sampling, specifications, and testing and with the organization, documentation, and release procedures which ensure that the necessary and relevant tests are actually carried out and that materials are not released for use or products released for sale or supply, until their quality has been judged to be satisfactory. Quality control is not confined to laboratory operations but must be involved in all decisions concerning the quality of the product.

Quarantine
The status of starting or packaging materials, intermediates, or bulk or finished products isolated physically or by other effective means while a decision is awaited on their release, rejection, or reprocessing.

Reconciliation
A comparison, making due allowance for normal variation, between the amount of product or materials theoretically produced or used and the amount actually produced or used.

Recovery (or Blending)
The introduction of all or part of previous batches of required quality into another batch at a defined stage of manufacture.

Reprocessing
The reworking of all or part of a batch of product of an unacceptable quality from a defined stage of production so that its quality may be rendered acceptable by one or more additional operations.

Specification
A document describing in detail the requirements with which the products or materials used or obtained during manufacture have to conform. Specifications serve as a basis for quality evaluation.

Standard Operating Procedure (SOP)
An authorized written procedure giving instructions for performing operations not necessarily specific to a given product or material but of a more general nature (e.g., equipment operation, maintenance and cleaning; validation; cleaning of premises and environmental control; sampling and inspection). Certain SOPs may be used to supplement product-specific master and batch production documentation.

Starting Material
Any substance of a defined quality used in the production of a pharmaceutical product, but excluding packaging materials.

System
A regulated pattern of interacting activities and techniques that are united to form an organized whole.

Validation
The documented act of proving that any procedure, process, equipment, material, activity, or system actually leads to the expected results.