



**GLOSSARY USED FOR THE ASEAN COMMON TECHNICAL
DOSSIER (ACTD) AND ASEAN COMMON TECHNICAL
REQUIREMENT (ACTR)**

GLOSSARY USED IN ACTD AND ACTR (Adopted from ASEAN CTD)

The definitions used in this glossary have been developed for the ASEAN Common Technical Dossier (ACTD) and Common Technical Requirements (ACTR). They are not necessarily meaningful outside the scope of the specific parts of ACTD and ACTR to which they refer.

Accelerated Testing [from Q1AR]/Ref: ACTD – Q...

Studies designed to increase the rate of chemical degradation or physical change of a drug substance or drug product by using exaggerated storage conditions as part of the formal stability studies.

(Data from these studies, in addition to long term stability studies, can be used to assess longer term chemical effects at non-accelerated conditions and to evaluate the effect of short term excursions outside the label storage conditions such as might occur during shipping. Results from accelerated testing studies are not always predictive of physical changes; see also Stability and related terms)

Acceptance Criteria [from Q6B]/Ref: ACTD – Q...

Numerical limits, ranges or other suitable measure which the drug substance or drug product or materials at other stages of their manufacture should meet for acceptance of the results of analytical procedures.

Accuracy [from Q2A]/Ref: ACTD – Q...

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found.

Active Pharmaceutical Ingredient (API) [from WHO]

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

Adverse Drug Reaction (ADR) [from WHO]/Ref: ACTD – E...

A response to a medicine that is noxious and unintended, and which occurs at doses normally used in man.

(In this definition, it is of importance to note that it concerns the response of a patient, in which individual factors may play an important role, and that the phenomenon is noxious. An unexpected therapeutic response for example, may be a side effect but not an adverse reaction; see also Adverse Event, Side Effect).

From WHO Drug Monitoring Programme web site, www.who-umc.org

Adverse Event (AE) [from WHO]/Ref: ACTD – E...

An adverse event or experience is any untoward medical occurrence that may present during treatment with a medicine but which does not necessarily have a causal relationship with this treatment.

(The basic point here is the coincidence in time without any suspicion of a causal relationship; see also Adverse Reaction, Side Effect).

From WHO Drug Monitoring Programme web site, www.who-umc.org

Analytical Procedure [from Q2A]/Ref: ACTD – Q...

The way of performing the analysis; it should describe in detail the steps necessary to perform each analytical test.

(This may include but is not limited to the sample, the reference standard and the reagents preparations, use of the apparatus, generation of the calibration curve, use of the formulae for the calculation, etc).

Aneuploidy [from S2A]/Ref: ACTD – S...

Numerical deviation of the modal number of chromosomes in a cell or organism.

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Applicant [from WHO]

The company, corporate, or legal entity in the field of pharmaceuticals who submits an application for marketing authorisation of a pharmaceutical product, an update to an existing marketing authorisation, or a variation to an existing marketing authorisation.

Approval (in relation to Institutional Review Boards) [from E6]/Ref: ACTD – E...

The affirmative decision of the IRB that the clinical trial has been reviewed and may be conducted at the institution site within the constraints set forth by the IRB, the institution, Good Clinical Practice (GCP), and the applicable regulatory requirements.

Audit [from E6]/Ref: ACTD – E...

A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial activities were conducted, and the data were recorded, analysed and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

Audit Certificate [from E6]/Ref: ACTD – E...

A declaration of confirmation by the auditor that an audit has taken place.

Audit Report [from E6]/Ref: ACTD – E...

A written evaluation by the sponsor's auditor of the results of the audit.

Audit Trail [from E6]/Ref: ACTD – E...

Documentation that allows reconstruction of the course of events.

ASEAN Common Technical Dossier (ACTD)

The part of marketing authorisation application dossier that is common to all ASEAN member countries.

ASEAN Common Technical Requirements (ACTR)

A set of written materials intended to guide applicants to prepare application dossiers in a way that is consistent with the expectations of all ASEAN Drug Regulatory Authorities (DRA).

Batch [from WHO]

A defined quantity of starting material, packaging material or product processed in a single process or a series of processes so that it can be expected to be homogeneous.

(In the case of continuous manufacture, the batch must correspond to a defined fraction of production, characterised 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 [from WHO]

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

Batch Records [from WHO]

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.

Base Substitution [from S2A]/Ref: ACTD – S...

The substitution of one or more base(s) for another in the nucleotide sequence. This may lead to an altered protein.

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Bioavailability [from WHO]

The rate and extent of availability of an active drug substance or metabolite from a dosage form as determined by its concentration/time curve in the systemic circulation or by its excretion in urine or other body fluid.

Bioequivalence [from WHO]

Two pharmaceutical products are bioequivalent if they are pharmaceutically equivalent or alternatives and their bioavailabilities after administration in the same molar dose are similar to such a degree that their effects can be expected to be essentially the same.

Biological Activity [from Q6B]/Ref: ACTD – Q...

The specific ability or capacity of the product to achieve a defined biological effect. Potency is the quantitative measure of the biological activity.

Biological Product [from WHO]

Any product of biological origin, prepared with biological processes, derived from human blood and plasma, or manufactured by biotechnology, consisting of substances of higher molecular weight whose purity, potency, and composition cannot readily and reliably be determined by chemical or physicochemical analysis.

(Examples of this group include vaccines, blood products, modified animal tissues, high molecular weight hormones, allergens, and the products of genetic engineering or other newer biotechnological techniques. This definition does not include antibiotics and substances that, although of biological origin, are of low molecular weight and can be isolated as pure substances, such as purified steroids and alkaloids. Biological products cannot usually be approved only on the basis of in vitro comparison with a comparator product. Different brands may have the same use, for example pertussis vaccine, but each must independently have been shown to be safe and effective. Data on plasma concentrations of the “active substance” are also usually unhelpful because it is unclear whether precisely the same entity is being measured. These products cannot therefore be approved without safety and efficacy data; see also Biotechnological Product).

Biotechnological Product [from WHO]

Any product prepared with genetic engineering or other newer biotechnological techniques.

(All biotechnological products fall into the definition of Biological Products; see also Biological Product).

Blinding/Masking [from E6]/Ref: ACTD – E...

A procedure in which one or more parties involved in the trial is kept unaware of the treatment assignment(s).

(Single blinding usually refers to the subject[s] being unaware and double blinding usually refers to the subject[s], investigator[s], monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment[s]).

Bracketing [from Q1AR]/Ref: ACTD – Q...

The design of a stability schedule such that only samples on the extremes of certain design factors, e.g., strength, package size, are tested at all time points as in a full design.

(The design assumes that the stability of any intermediate level is represented by the stability of the extremes tested. Where a range of strengths is to be tested, bracketing is applicable if the strengths are identical or very closely related in composition [e.g., for a tablet range made with different compression weights of a similar basic granulation, or a capsule range made by filling different plug fill weight of the same basic composition into different size capsule shell]. Bracketing can be applied to different container sizes or different fills in the same container closure system).

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Bridging Data Package [from E5]/Ref: ACTD – E...

Selected information from the Complete Clinical Data Package that is relevant to the population of the new region, including pharmacokinetic data, and any preliminary pharmacodynamic and dose-response data and, if needed, supplemental data obtained from bridging study in the new region that allow extrapolation of the foreign safety and efficacy data to the population of the new region.

Bridging Study [from E5]/Ref: ACTD – E...

A supplemental study performed in the new region to provide pharmacodynamic or clinical data on efficacy, safety, dosage and dose regimen in the new region that will allow extrapolation of the foreign clinical data to the new region.

(Such studies could include additional pharmacokinetic information).

Calibration [from WHO]/Ref: ACTD – Q...

The set of operations which establishes under specified conditions, the relationship between values indicated by measuring instrument or measuring system, or values represented by a material measure, and the corresponding known values of a reference standard.

(Limit for acceptance of the results of measurement should be established).

Case Report Form (CRF) [from E6]/Ref: ACTD – E...

A printed, optical or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject

Cell Proliferation [from S2A]/Ref: ACTD – S...

The ability of cells to divide and to form daughter cells.

Cell Substrate [from Q5D]/Ref: ACTD – Q...

Microbial cells or cell lines derived from human or animal sources that possess the full potential for generation of the desired biotechnological/biological products for human in-vivo or ex-vivo use.

Certificate of Pharmaceutical Product (CPP) [from WHO]

A certificate of pharmaceutical product of the type defined in the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce.

Change Control [from WHO]

A formal system by which qualified representatives of appropriate disciplines review proposed or actual changes that might affect an established status.

(The intent is to determine the need for action that would ensure and document that the system is maintained in a validated state).

Clastogen [from S2A]/Ref: ACTD – S...

An agent that produces structural changes in chromosomes, usually detectable by light microscopy.

Climatic Zones [from WHO]

The four zones into which the world is classified based on the prevailing annual climatic conditions, i.e.,

- Zone I : temperate
- Zone II : sub-tropical, with possible high humidity
- Zone III : hot and dry
- Zone IV : hot and humid

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Clinical Trial/Study Report [from E6]/Ref: ACTD – E...

A written study description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical descriptions, presentations, and analyses are fully integrated into a single report.

(See the ICH Guideline for Structure and Content of Clinical Study Reports).

Clinical Trial/Study [from E6]/Ref: ACTD – E...

Any investigation in human subjects intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy.

Cloning Efficiency [from S2A]/Ref: ACTD – S...

The efficiency of single cells to form clones.

(Usually measured after seeding low numbers of cells in a suitable environment).

Commitment batches [from Q1AR]/Ref: ACTD – Q...

Production batches of a drug substance or drug product for which the stability studies are initiated or completed post approval through a commitment made in the registration application.

Comparator (Product) [from E6]/Ref: ACTD – E...

- a) A pharmaceutical product with which the new product is intended to be interchangeable in clinical practice.
(The reference product would normally be the innovator product for which efficacy, safety and quality have been established. Where the innovator product is not available the product which is the market leader may be used as a reference product, provided it has been authorised for marketing and its efficacy, safety and quality has been established and documented).
- b) An investigational or marketed product (i.e. active control), or placebo, used as a reference in a clinical trial. (See also Reference Product).

Complete Clinical Data Package [from E5]/Ref: ACTD – E...

A clinical data package intended for registration containing clinical data that fulfil the regulatory requirements of the new region and containing pharmacokinetic data relevant to the population in the new region.

Compliance (in relation to trials) [from E6]/Ref: ACTD – E...

Adherence to all the trial-related requirements, Good Clinical Practice (GCP) requirements, and the applicable regulatory requirements.

Concurrent Validation (from PIC)

Validation carried during routine production of products intended for sale.

Confidentiality [from E6]/Ref: ACTD – E...

Prevention of disclosure, to other than authorised individuals, of a sponsor's proprietary information or of a subject's identity.

Container-Closure System [from Q1AR]/Ref: ACTD – Q...

The sum of packaging components that together contain and protect the dosage form. This includes primary packaging components and secondary packaging components, if latter are intended to provide additional protection to the drug product. A packaging system is equivalent to a container closure system.

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Container Labelling [from WHO]

All information that appear on any part of a container, including that on any outer packaging such as a carton.

Contaminants [from Q6B]/Ref: ACTD – Q...

Any adventitiously introduced materials (e.g. chemicals, biochemical, or microbial species) not intended to be part of the manufacturing process, drug substance, or drug product.

Contract [from E6]/Ref: ACTD – E...

A written, dated, and signed agreement between two or more involved parties that sets out any arrangement on delegation and distribution of tasks and obligations and if appropriate, on financial matters. A protocol may serve as the basis of a contract.

Contract Research Organisation (CRO) [from E6]/Ref: ACTD – E...

A person or an organisation (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions.

Coordinating Committee [from E6]/Ref: ACTD – E...

A committee that a sponsor may organise to coordinate the conduct of a multi-centre trial.

Coordinating Investigator [from E6]/Ref: ACTD – E...

An investigator assigned the responsibility for the coordination of investigators at different centres participating in a multi-centre trial.

Country of Origin

Country where the final dosage form has been manufactured, and/or batch release takes place or from where products are shipped to importing country. There are situations where it is not possible to identify one country of origin but rather several countries of origin. This may entail obtaining more than one CPP.

(Note: This definition is to be understood in relation to the practical implementation of the WHO Certification Scheme as applicable in the context of drug registration procedures).

Critical Manufacturing Process [from ASEAN GMP]

A manufacturing process that may cause variation which affects the quality of the pharmaceutical product.

Culture Confluency [from S2A]/Ref: ACTD – S...

A quantification of the cell density in a culture (cell proliferation is usually inhibited at high degrees of confluency).

Cytogenetic Evaluation [from S2B]/Ref: ACTD – S...

Chromosome structure analysis in mitosis or meiosis by light microscopy.

Degradation Products [from Q6B]/Ref: ACTD – Q...

Molecular variants resulting from changes in the desired product or product-related substances brought about over time and/or by the action of, e.g. light, temperature, pH, water, or by reaction with an excipient and/or the immediate container/closure system. Such changes may occur as a result of manufacture and/or storage (e.g. deamidation, oxidation, aggregation, proteolyses). Degradation products may be either product-related substances, or product-related impurities.

Detection Limit [from Q2A]/Ref: ACTD – Q...

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value.

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Direct Access (in relation to clinical trials) [from E6]/Ref: ACTD – E...

Permission to examine, analyse, verify and reproduce any record and report that are important in the evaluation of a clinical trial. Any party (e.g. domestic and foreign regulatory authorities, sponsors, monitors and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and sponsors' proprietary information.

DNA Adduct [from S2B]/Ref: ACTD – S...

(Covalent) binding of chemicals to DNA.

DNA Repair [from S2B]/Ref: ACTD – S...

Reconstitution of damaged DNA sequence.

DNA Strand Breaks [from S2B]/Ref: ACTD – S...

Single or double strand scissions in the DNA.

Dosage [from E5]

The quantity of a medicine given per administration or per day.

Dosage Form [from Q1AR]

A pharmaceutical product type (e.g. tablet, capsule, solution, cream) that contains a drug substance generally, but not necessarily, in association with excipients.

Dose Regimen [from E5]/Ref: ACTD – E...

The route, frequency and duration of administration of the dose of a medicine over a period of time.

Drug [from WHO]

Any substance or pharmaceutical product for human or veterinary use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient.

Drug Product [from WHO]

See Pharmaceutical Product.

Drug Substance [from Q1AR]

The unformulated drug substance that may subsequently be formulated with excipients to produce the dosage form.

(See also Active Pharmaceutical Ingredient)

Effectiveness [from WHO]

Measure of the effect a medicine is supposed to have in the normal clinical setting. It reflects the impact of its use in the community.

Efficacy [from WHO]

Ability of a medicine to bring about the intended beneficial effect on individuals in a defined population with a given medical problem, under ideal conditions of use.

Ethnic Factors [from E5]/Ref: ACTD – E...

The word ethnically is derived from the Greek word "ethnos", meaning nation or people. Ethnic factors are factors relating to populations grouped according to common traits and customs. Ethnic factors that can influence drug safety and efficacy may be classified as either intrinsic or extrinsic:

- **Extrinsic Ethnic Factors:** Factors associated with the environment and culture in which a person resides. They tend to be less genetically and more culturally and behaviourally determined.

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(Examples of extrinsic factors include the social and cultural aspects of a region such as medical practice, diet, use of tobacco, use of alcohol, exposure to pollution and sunshine, socio-economic status, compliance with prescribed medications, and, particularly important to the reliance on studies from a different region, practices in clinical trial design and conduct).

- **Intrinsic Ethnic Factors:** Factors that help to define and identify a sub-population and may influence the ability to extrapolate clinical data between regions.

(Examples of intrinsic factors include genetic polymorphism, age, gender, height, weight, lean body mass, body composition, and organ dysfunction).

Excipient [from Q6B]/Ref: ACTD – Q...

An ingredient, added intentionally to the drug substance, which should not have pharmacological properties in the quantity used.

Expiry Date [from Q1AR]/Ref: ACTD – Q...

The date placed on the container label of a drug product designating the time prior to which a batch of the product is expected to remain within the approved shelf-life specification if stored under defined conditions.

(After the expiry date, there is no guarantee that the product will remain within the approved specifications and therefore, it may be unsuitable for use and should not be used).

Extensive Product Testing [from WHO]

The final testing of the product to an extent greater than that required in routine quality control.

(This is one of the most practical forms of process validation, mainly for non-sterile products).

Extrapolation of Foreign Clinical Data [from E5]/Ref: ACTD – E...

The generalisation and application of the safety, efficacy and dose response data generated in a population of a foreign region to the population of a new region.

Finished Product [from WHO]

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

Stability Studies [from Q1AR]/Ref: ACTD – Q...

Long-term and accelerated (and intermediate) studies undertaken on primary and/or commitment batches according to a prescribed stability protocol to establish or confirm the re-test period of a drug substance or shelf life of a drug product.

Formula [from WHO]

The composition of a dosage form, including the characteristics of its raw materials.

Frameshift Mutation [from S2A]/Ref: ACTD – S...

A mutation (change in the genetic code) in which one base or two adjacent bases are added (inserted) or deleted to the nucleotide sequence of a gene.

(This may lead to an altered or truncated protein).

Gene Mutation [from S2A]/Ref: ACTD – S...

A detectable permanent change within a single gene or its regulating sequences. The changes may be point mutations, insertions and deletions.

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Generic Product (GP) [from WHO]

A pharmaceutical product usually intended to be interchangeable with the innovator product, which is usually manufactured without a licence from the innovator company and marketed after expiry of the patent or other exclusivity rights.

(The term generic product has somewhat different meanings in different jurisdiction. Use of this term is therefore avoided as much as possible, and the term multisource pharmaceutical product is used instead. Generic products may be marketed either under the approved nonproprietary name or under a brand [proprietary] name. They may be marketed in dosage forms and/or strengths different from those of the innovator products).

Genetic Endpoint [from S2A]/Ref: ACTD – S...

The precise type or type class of genetic change investigated (e.g. gene mutations, chromosomal aberrations, DNA-repair, DNA-adduct formation, etc.).

Genetic Toxicity, Genotoxicity [from S2A]/Ref: ACTD – S...

A broad term that refers to any deleterious change in the genetic material regardless of the mechanism by which the change is induced.

Good Clinical Practice (GCP) [from E6]/Ref: ACTD – E...

A standard for the design, conduct, performance, monitoring, auditing, recording analysis, and reporting of clinical trials that provides assurance that data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

ICH (International Conference for Harmonization) Regions [from E5]/Ref: ACTD –E...

The region that includes European Union, Japan, and The United States of America.

Immediate Release Dosage Form [from WHO]

A dosage form that is intended to release all active substance on administration, with no enhanced delayed or extended release effect.

Impartial Witness [from E6]/Ref: ACTD – E...

A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.

Impermeable Containers [from QIAR]/Ref: ACTD – Q...

Containers that provide a permanent barrier to the passage of gases or solvents, e.g., sealed aluminium tubes for semi-solids, sealed glass ampoules for solutions.

Impurity [from Q6B]/Ref: ACTD – Q...

Any component present in the drug substance or drug product which is not the desired product, a product-related substance, or excipient including buffer components. It may be either process-or product-related.

Independent Ethics Committee (IEC) [from E6]/Ref: ACTD – E...

An independent body (a review board or a committee, institutional, regional, national or supranational) constituted of medical/scientific professionals and non-medical/non-scientific members whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial and to provide public assurance of that protection, by among other things, reviewing and approving/providing favourable opinion on the trial protocol, the suitability of the investigator(s), facilities, and the methods and material to be used in obtaining and documenting informed consent of the trials subjects.

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(The legal status, composition, function, operation and regulatory requirements pertaining to Independent Ethics Committee may differ among countries, but should allow the Independent Ethics Committee to act in agreement with GCP as described in the current relevant guideline).

Independent Data-Monitoring Committee (IDMC) (Data and Safety Monitoring Board, Monitoring Committee, Data Monitoring Committee)[from E6]/Ref: ACTD – E...

An independent data-monitoring committee that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a trial.

Informed Consent [from E6]/Ref: ACTD – E...

A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate.

(Informed consent is documented by means of a written, signed and dated informed consent form).

In-house Primary Reference Material [from Q6B]/Ref: ACTD – Q...

An appropriately characterised material prepared by the manufacturer from a representative lot(s) for the purpose of biological assay and physicochemical testing subsequent lots, and against which in-house working reference material is calibrated.

In-house Working Reference Material [from Q6B]/Ref: ACTD – Q...

A material prepared similarly to the primary reference material that is established solely to assess and control subsequent lots for the individual attribute in question.

(It is always calibrated against the in-house primary reference material).

Innovator Pharmaceutical Product [from WHO]

The innovator pharmaceutical product is generally that which was first authorised for marketing (normally as a patented product) on the basis of documentation of efficacy, safety and quality (according to requirements at the time of the authorisation).

(When a substance has been available for many years, it may not be possible to identify an innovator pharmaceutical product).

Installation Qualification (IQ) [from WHO]

The performance and documentation tests to ensure that equipment (such as machines, measuring equipment, utilities, manufacturing areas) used in a manufacturing process is appropriately selected, correctly installed and works in accordance with established specifications.

Institution (medical) [from E6]/Ref: ACTD – E...

Any public/private entity or agency or medical/dental facility where clinical trials are conducted.

Institutional Review Board (IRB) [from E6]/Ref: ACTD – E...

An independent body constituted of medical, scientific and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trial protocol and amendments and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

Interchangeable Pharmaceutical Product [from WHO]

A product that is therapeutically equivalent to a reference product.

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Interim Clinical Trial/Study Report [from E6]/Ref: ACTD – E...

A report of intermediate results and their evaluations based on analyses performed during the course of a trial.

Intermediate Precision [from Q2A]/Ref: ACTD – Q...

Intermediate precision expresses within-laboratories variations: different days, different analysts, different equipment, etc.

Internal Environmental Monitoring Program [from ASEAN]

A defined and documented programme which describes the routine particulate and microbiological monitoring of processing and manufacturing areas, and includes corrective action plan when action levels are exceeded.

Investigational Product [from E6]/Ref: ACTD – E...

A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Investigator [from E6]/Ref: ACTD – E...

A person responsible for conducting the clinical trial at the trial site. If the trial is conducted by a team of individuals at the trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

(See also Sub-investigator).

Laboratory Scale Batches [from WHO]

Batches produced at the research and early development laboratory stage.

(They may be of very small size [e.g. 1/100 to 1/1000 times production batch size]).

Letter of Authorisation [from WHO]

A letter from the manufacturer or product owner authorising the local agent to be the registration holder and to be responsible for all matters pertaining to the registration of the product.

Linearity [from Q2A]/Ref: ACTD – Q...

The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample.

Long Term Real Time Testing (in relation to Stability) [from Q1AR]/Ref: ACTD – Q...

Stability studies under the recommended storage condition for the re-test period or shelf life proposed (or approved) for labelling.

Major Variation (MaV) [from WHO]

Variation to an authorised pharmaceutical product affecting one or more of the following aspects:

- route of administration,
- strength, posology
- indications or
- that does not fall within the definition of minor variation.

(Applications for major variations usually require the submission of data necessary to establish quality, safety and efficacy of the new formulation resulting from the variation; see also Variation, Minor Variation)

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Manufacture [from WHO]

All operations of purchase of materials and products, production, quality control, release, storage, shipment (from storage related to manufacturing site) of finished products, and related controls.

Manufacturer [from WHO]

A company that carries out at least one step of production as well as the final release of the finished product.

Marketing Authorisation

An official document issued by the competent drug regulatory authority for the purpose of marketing or free distribution of a product after evaluation for safety, efficacy and quality.

(It must set out, inter alia, the name of the product, the pharmaceutical dosage form, the quantitative formula [including excipients] per unit dose [using INNs or national generic names where they exist], the shelf-life and storage conditions, and packaging characteristics. It specifies the information on which authorisation is based [e.g. "The product(s) must conform with all the details provided in the application and as modified in subsequent correspondence"]. It also contains the product information approved for health professionals and the public, the sales category, the name and address of the holder of the authorisation, and the period of validity of the authorisation).

Marketing Authorization Holder [from WHO]

The company or corporate or legal entity in the field of pharmaceuticals whose name the marketing authorisation has been granted. This party is responsible for all aspects of the product, including quality and compliance with the conditions of marketing authorisation. The authorised holder must be subjected to legislation in the country that issued the marketing authorisation, which normally means being physically located in that country.

Also known as Product Licence Holder.

Mass Balance [from QIAR]/Ref: ACTD – Q...

The process of adding together the assay value and levels of degradation products to see how closely these add up to 100% of the initial value, with due consideration of the margin of analytical error.

Master Cell Bank (MCB) [from Q5A]/Ref: ACTD – Q...

An aliquot of a single pool of cells which generally has been prepared from the selected cell clone under defined condition, dispensed into multiple containers and stored under defined condition.

(The MCB is used to derive all working cell banks. The testing performed on a new MCB [from a previous initial cell clone, MCB or WCB] should be the same as for the MCB, unless justified).

Master Formula [from WHO]

A document or a 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 finished product as well as the processing instruction, including in-process control.

Matrixing (in relation to Stability) [from QIAR]/Ref: ACTD – Q...

The design of a stability schedule such that a selected subset of the total number of possible samples for all factor combinations is tested at a specified time point.

(At a subsequent time point, another subset of samples for all factor combinations is tested. The design assumes that the stability of each subset of samples tested represents the stability of all samples at a given time point; the differences in the samples for the same drug product should be identified as, for example, covering different batches, different strengths, different sizes of the same container closure system, and possibly in some cases, different container closure systems).

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Medicinal Product

See Pharmaceutical Product.

Micronucleus [from S2A]/Ref: ACTD – S...

Particle in a cell that contains microscopically detectable nuclear DNA, and might contain a whole chromosome(s) or a broken centric or acentric part(s) of chromosome(s).

(The size of a micronucleus is usually defined as being less than 1/5 but more than 1/20 of the main nucleus).

Minor Variation (MiV) [from WHO]

Variation to an authorised pharmaceutical product not affecting one or more of the following aspects:

- route of administration,
- strength, posology
- indications, and
- active substance(s)

(Applications for minor variations usually require the submission of data necessary to establish quality of the new formulation resulting from the variation; see also Variation, Major Variation)

Mitotic Index [from S2A]/Ref: ACTD – S...

Percentage of cells in the different stages of mitosis amongst the cells not in mitosis (interphase) in a preparation (slide).

Multicenter Trial [from E6]/Ref: ACTD – E...

A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.

Multisource (Generic) Pharmaceutical Product [from WHO]

Multisource pharmaceutical products are pharmaceutically equivalent products that may or may not be therapeutically equivalent.

(Multisource pharmaceutical products that are therapeutically equivalent are interchangeable).

National Regulatory Authority (NRA)/Certifying Authority [from WHO]

A national body that administers the full spectrum of drug regulatory activities, including at least all of the following functions:

- marketing authorisation of new products and variation of existing products;
- quality control laboratory testing;
- adverse drug reaction monitoring;
- provision of drug information and promotion of rational drug use;
- Good Manufacturing Practice (GMP) inspections and licensing of manufacture, wholesalers and distribution channels;
- enforcement operations; and
- monitoring of drug utilisation.

New Active Substance [from WHO]

New chemical or biological API not previously authorised for marketing for any pharmaceutical use in the country in question.

(Those provisionally authorised at the time of the initial market inventory are not new active substances; see also new chemical entity, new chemical or biological API, new molecular entity, well-established drug, well established product, well established fixed-dose drug combination).

New Chemical Entity (NCE) [from WHO]

See New Active Substance.

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New Chemical or Biological API [from WHO]

See New Active Substance.

New Molecular Entity [from Q1AR]/Ref: ACTD – Q...

A new salt, ester, or non-covalent-bond derivative of an approved drug substance.

(It is considered as a new molecular entity for the purpose of stability testing; see New Active Substance).

Numerical Chromosome Changes [from S2B]/Ref: ACTD – S...

Chromosome numbers different from the original haploid or diploid set of chromosomes; for cell lines, chromosome numbers different from the modal chromosome set.

Operation Qualification (OQ) [from WHO GMP]

Documented verification that the system or sub-system performs as intended throughout all anticipated operating ranges.

Original Medical Record

See Source Documents.

Package Insert [from WHO]

A document defining information that may be supplied with a pharmaceutical product by the marketing authorisation holder.

(The content of the product package insert is approved by the NRA at the time market authorisation is issued; see also Patient Information Leaflet).

Patient Information Leaflet (PIL)

A document defining information intended for the patient that may be supplied with a pharmaceutical product by the marketing authorisation holder.

(The content of the PIL is approved by the NRA at the time market authorisation is issued; see also Package Insert)

Parent-Child/Foetus Report [from E2B]/Ref: ACTD – E...

Report in which the administration of medicines to a parent results in a suspected reaction/event in a child/foetus.

Performance Qualification (PQ) [from WHO]

Documented evidence that a process step, a total integrated process system, or an analytical method performs as intended and that it produces an in-process material, or product, or test result that consistently meets appropriate specifications and the requirements defined in the protocol.

(It is important that clear and specific acceptance criteria are established for each critical parameter).

Pharmaceutical Equivalence [from WHO]

Two products are pharmaceutically equivalent if they contain the same amount of the same active substance(s) in the same dosage form; if they meet the same or comparable standards; and if they are intended to be administered by the same route.

(Pharmaceutical equivalence does not necessarily imply therapeutic equivalence, as differences in the excipients and/or the manufacturing process can lead to differences in product performance).

Pharmaceutical Product

Any preparation for human use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient.

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Pharmacodynamic Study [from E5]/Ref: ACTD – E...

A study of a pharmacological or clinical effect of the medicine in individuals to describe the relation of the effect to dose or drug concentration.

(A pharmacodynamic effect can be a potentially adverse effect [e.g. anticholinergic effect with a tricyclic antidepressant], a measure of activity thought to be related to its clinical benefit [e.g. various measures of beta blockade, effect on ECG intervals, inhibition of ACE or of angiotensin I or II response], a short term desired effect, often a surrogate endpoint [e.g. blood pressure, cholesterol], or the ultimate intended clinical benefit [e.g. effects on pain, depression, sudden death]).

Pharmacokinetic Study [from E5]/Ref: ACTD – E...

A study of how a pharmaceutical product is handled by the body, usually involving measurement of blood concentrations of the product and its metabolite(s) (sometimes concentrations in urine or tissues) as a function of time.

(Pharmacokinetic studies are used to characterise absorption, distribution, metabolism and excretion of a pharmaceutical product, either in a blood or in other pertinent locations. When combined with pharmacodynamic measures [a PK/PD study], it can characterize the relation of blood concentrations to the extent and timing of pharmacodynamic effects).

Pilot Scale Batch [from QIAR]/Ref: ACTD – Q...

A batch of a drug substance or drug product manufactured by a procedure fully representative of and simulating that to be applied to a full production scale batch.

(For solid oral dosage forms, a pilot scale is generally at a minimum, one-tenth that of a full production scale or 100,000 tablets or capsules, whichever is the larger unless otherwise justified).

Plasmid [from S2A]/Ref: ACTD – S...

A genetic element additional to the normal bacterial genome.

(A plasmid might be inserted into the host chromosome or form an extrachromosomal element).

Point Mutations [from S2A]/Ref: ACTD – S...

Changes in the genetic code usually confined to a single DNA base pair.

Polychromatic Erythrocyte [from S2A]/Ref: ACTD – S...

An immature erythrocyte in an intermediate stage of development that still contains ribosomes and as such, can be distinguished from mature normochromatic erythrocytes (lacking ribosomes) by stains selective for ribosomes.

Population Pharmacokinetic Methods [from E5]/Ref: ACTD – E...

A population-based evaluation of measurements of systemic drug concentrations, usually two or more per patient under steady state conditions, from all, or a defined subset of, patients who participate in clinical trials.

Potency [from Q6B]/Ref: ACTD – Q...

The measure of biological activity using a suitably quantitative biological assay (also called potency assay or bioassay), based on the attribute of the product which is linked to the relevant biological properties.

Precision [from Q2A]/Ref: ACTD – Q...

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions.

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(Precision may be considered at three levels: repeatability, intermediate precision and reproducibility. Precision should be investigated using homogeneous, authentic samples. However, if it is not possible to obtain a homogeneous sample, it may be investigated using artificially prepared samples or a sample solution. The precision of an analytical procedure is usually expressed as the variance, standard deviation or coefficient of variation of a series of measurements).

Primary Batch [from QIAR]/Ref: ACTD – Q...

A batch of a drug substance or drug product used in a stability study, from which stability data are submitted in a registration application for the purpose of establishing a re-test period or shelf-life, respectively.

(A primary batch of a drug substance should be at least a pilot scale batch. For a drug product, two of the three batches should be at least pilot scale batch, and the third batch can be smaller if it is representative with regard to the critical manufacturing steps. However, a primary batch may be a production batch).

Product Owner

A person, company or entity who is the legal/registered owner of the product formulation and/or process with whom the marketing authorisation holder has a contract.

Process Related Impurities [from Q6B]/Ref: ACTD – Q...

Impurities that are derived from the manufacturing process; they may be derived from cell substances (e.g. host cell proteins, host cell DNA), cell culture (e.g. inducers, antibiotics, or media components), or downstream processing (e.g. processing reagents or column leachables).

Process Validation [from FDA]/Ref:ACTD – Q...

Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its pre-determined specifications and quality.

Product Licence Holder

See definition for Marketing Authorisation Holder.

Product-related Impurities [from Q6B]/Ref: ACTD – Q...

Molecular variants of the desired product (e.g. precursors, certain degradation products arising during manufacture and/or storage) which do not have properties comparable to those of the desired product with respect to activity, efficacy, and safety.

Product-related Substances [from Q6B]/Ref: ACTD – Q...

Molecular variants of the desired product formed during manufacture and/or storage which are active and have no deleterious effect on the safety and efficacy of the drug product.

(These variants possess properties comparable to the desired product and are not considered impurities).

Production Batch [from QIAR]/Ref: ACTD – Q...

A batch of a drug substance or drug product manufactured at production scale by using production equipment in a production facility as specified in the application.

Prospective Validation [from ASEAN GMP]

Establishing documented evidence that a process, procedure, system, equipment or mechanism used in manufacture does what it purports to do based on a pre-planned validation protocol.

Protocol (in relation to Clinical Trials) [from E6]/Ref: ACTD – E...

A document that describes the objective(s), design, methodology, statistical consideration, and organisation of a trial.

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(The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents throughout the ICH GCP Guideline. The term protocol refers to protocol and protocol amendments).

Quality Assurance (QA) [from E6 /Ref: ACTD – E...

The totality of the arrangements, including GMP, made in order to ensure that pharmaceutical products are suitable for their intended use.

Quality Control [from WHO]

Quality control is concerned with sampling, specifications and testing, and with the organisation, documentation and acceptance/rejection procedures which ensure that the necessary and relevant tests are actually carried out on starting materials, intermediates and finished products and such products are not accepted for use, sale or supply until their quality has been judged to be satisfactory.

Quantitation Limit [from Q2]/Ref: ACTD – Q...

The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy.

(The quantitation limit is a parameter of quantitative assays for low levels of compounds in sample matrices, and is used particularly in the determination of impurities and/or degradation products).

Randomisation [from E6]/Ref: ACTD – E...

The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

Recombination [from S2B]/Ref: ACTD – S...

Breakage and balanced or unbalanced rejoining of DNA.

Reference Country

Countries with established drug evaluation system as recognised by the ASEAN Drug Regulatory Authorities.

Reference Product [from WHO]

- a) A pharmaceutical product with which the new product is intended to be interchangeable in clinical practice.

(The reference product would normally be the innovator product for which efficacy, safety and quality have been established. Where the innovator product is not available, the product which is the market leader may be used as a reference product, provided it has been authorised for marketing and its efficacy, safety and quality have been established and documented).

- b) An investigational or marketed product (i.e. active control), or placebo, used as a reference in a clinical trial.

(See also Comparator Product)

Repeatability [from Q2A]/Ref: ACTD – Q...

Repeatability expresses the precision under the same operating conditions over a short interval of time.

(Repeatability is also termed intra-assay precision).

Reporter (in relation to clinical studies) [from E2B]/Ref: ACTD – E...

Reporter is the primary source of information, i.e., a person who initially reports the facts.

(This should be distinguished from the sender of the source of the message, though the reporter could also be a sender).

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Reproducibility [from Q2A]/Ref: ACTD – Q...

Reproducibility expresses the precision between laboratories.

(Collaborative studies, usually applied to standardisation of methodology).

Re-test Date [from QIAR]/Ref: ACTD – Q...

The date after which samples of the drug substance should be examined to ensure that the material is still in compliance with the specification and thus suitable for use in the manufacture of a given drug product.

Re-test Period [from QIAR]/Ref: ACTD – Q...

The period of time during which the drug substance is expected to remain within its specification and therefore, can be used in the manufacture of a given drug product, provided that the drug substance has been stored under the defined conditions.

(After this period, a batch of drug substance destined for use in the manufacture of a drug product should be re-tested for compliance with the specification and then used immediately. A batch of drug substance can be re-tested multiple times and a different portion of the batch used after each re-test, as long as it continues to comply with the specification. For most biotechnological/biological substances known to be labile, it is more appropriate to establish a shelf life than a re-test period. The same may be true for certain antibiotics).

Retrospective Validation [from ASEAN GMP]

Validation of a process for a product that has been marketed based upon accumulated manufacturing, testing and control batch data.

Revalidation [from ASEAN GMP]

A repeat of the process validation to provide an assurance that changes in the process/equipment introduced in accordance with change control procedures do not adversely affect process characteristics and product quality.

Robustness [from Q2A]/Ref: ACTD – Q...

The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

Semi-permeable Containers [from QIAR]/Ref: ACTD – Q...

Containers that allow the passage of solvent, usually water, while preventing solute loss.

(The mechanism for solvent transport occurs by adsorption onto one container surface, diffusion through the bulk of the container material, and desorption from the other surface; transport is driven by a partial-pressure gradient; examples of semi-permeable containers include plastic bags and semi-rigid, low-density polyethylene (LDPE) pouches for large volume parenterals (LVPs), and LDPE ampoules, bottles, and vials).

Sender (in relation to clinical studies) [from E2B]/Ref: ACTD – E...

The person or entity creating the message for transmission.

(Although the reporter and sender may be the same person, the function of the sender should not be confused with that of the reporter[s]).

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR) [from E6]/Ref: ACTD – E...

Any untoward medical occurrence that at any dose:

- results in death;
- is life-threatening;
- requires inpatient hospitalisation or prolongation of existing hospitalisation;

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- results in persistent or significant disability/incapacity; or
- results in a congenital anomaly/birth defect.

Shelf-life (also referred to as expiration dating period) [from Q1AR]/Ref: ACTD – Q...

The time period during which a drug product is expected to remain within the approved shelf life specification, provided that it is stored under the condition defined on the container label.

Side effect [From WHO Drug Monitoring Programme web site, www.who-umc.org]

Any unintended effect of a pharmaceutical product occurring at doses normally used in man, which is related to the pharmacological properties of the drug.

(Essential elements in this definition are the pharmacological nature of the effect, that the phenomenon is unintended, and that there is no overt overdose; see also Adverse Event, Adverse Reaction).

Source Data (in relation to clinical studies) [from E6]/Ref: ACTD – E...

All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial.

(Source data are contained in source documents, original records or certified copies).

Source Documents (in relation to clinical studies) [from E6]/Ref: ACTD – E...

Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklist, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).

Specification [from Q6B]/Ref: ACTD – Q...

A list of tests, references to analytical procedures, and appropriate acceptance criteria which are numerical limits, ranges, or other criteria for the tests described.

(It establishes the set of criteria to which a drug substance, drug product or material at other stages of its manufacture should conform to be considered acceptable for its intended use. "Conformance to specification" means that the drug substance and drug product, when tested according to the listed analytical procedures, will meet the acceptance criteria. Specifications are critical quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities as conditions of approval).

Specifications (Release) [from Q1AR]/Ref: ACTD – Q...

The specifications that determine the suitability of a drug product at the time of its release.

(See also Specification)

Specification (Shelf-life) [from Q1AR]/Ref: ACTD – Q...

The specifications that determine the suitability of a drug substance throughout its re-test period, or that a drug product should meet throughout its shelf-life.

Specificity [from Q2A]/Ref: ACTD – Q...

Specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. Typically these might include impurities, degradants, matrix, etc.

Lack of specificity of an individual analytical procedure may be compensated by other supporting analytical procedure(s).

This definition has the following implication:

Identification : To ensure the identify of an analyte.

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Purity Tests : To ensure that all the analytical procedures performed allow an accurate statement of the content of impurities of an analyte, i.e. related substances test, heavy metals, residual solvents content, etc.

Assay (Content or Potency): To provide an exact result which allows an accurate statement on the content or potency of the analyte in a sample.

Stability [from WHO]

The ability of an active substance or a drug product to retain its properties within specified limits throughout its shelf-life.

(The chemical, physical, microbiological and biopharmaceutical aspects of stability must be considered).

Standard Operation Procedures (SOPs) [from E6]/Ref: ACTD – E...

Detailed written instruction to achieve uniformity of the performance of a specific function.

Starting Material [from WHO]

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

Sterilisation [from WHO]

Validated process used to render a product free of viable organisms.

Sterility Test [from WHO]

Test performed to determine if viable microorganisms are present.

Storage Condition Tolerances (in relation to Stability) [from Q1A]/Ref: ACTD – Q...

The acceptable variations in temperature and relative humidity of storage facilities for formal stability studies.

(The equipment should be capable of controlling the storage condition within the ranges defined in the current relevant guidelines. The actual temperature and humidity when controlled, should be monitored during stability storage. Short-term spikes due to opening of doors of the storage facility are accepted as unavoidable. The effect of excursions due to equipment failure should be addressed, and reported if judged to affect stability results. Excursions that exceed the defined tolerances for more than 24 hours should be described in the study report and their effects assessed).

Stress Testing (Drug Product) [from Q1AR]/Ref: ACTD – Q...

Studies undertaken to assess the effect of severe condition on the drug product.

(Such studies include photo-stability testing; see ICH Q1B and specific testing on certain products, e.g. metered dose inhalers, creams, emulsions, and refrigerated aqueous liquid products).

Stress Testing (drug substance) [from Q1AR]/Ref: ACTD – Q...

Studies undertaken to elucidate the intrinsic stability of the drug substance. Such testing is part of the development strategy and is normally carried out under more severe conditions than those used for accelerated testing.

Sub-investigator [from E6]/Ref: ACTD – E...

Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows).

(See also Investigator)

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Subject Identification Code [from E6]/Ref: ACTD – E...

A unique identifier assigned by the investigator to each trial subject to protect the subject's identity and used in lieu of the subject's name when the investigator reports adverse events and/or other trial related data.

Summary of Product Characteristics (SPC) [from EU]

Product information as approved by the drug regulatory authority.

(The SPC serves as the source of information for health personnel as well as for consumer information on labels and leaflets of pharmaceutical products and for control of advertising; see also Package Insert, Patient Information Leaflet)

Supporting Data (in relation to Stability) [from QIAR]/Ref: ACTD – Q...

Data, other than those from formal stability studies, that support the analytical procedures, the proposed re-test period or shelf-life, and the label storage statements.

(Such data include [1] stability data on early synthetic route batches of drug substance, small scale batches of materials, investigational formulations not proposed for marketing, related formulations, and product presented in containers and closures other than those proposed for marketing; [2] information regarding test results on containers; and [3] other scientific rationales).

Survival (in the context of mutagenicity testing) [from S2A]/Ref: ACTD – S...

Proportion of the cells in a living stage among dead cells, usually determined by staining and colony counting methods after a certain treatment interval.

Transgene [from S2B]/Ref: ACTD – S...

An exogenous or foreign gene inserted into the host genome, either into somatic cells or germ line cells.

Therapeutic Equivalence [from WHO]

Two pharmaceutical products are therapeutically equivalent if they are pharmaceutically equivalent or alternatives and, after administration in the same molar dose, their effects with respect to both efficacy and safety are essentially the same, as determined from appropriate bioequivalence, pharmacodynamic, clinical or in vitro studies.

Trial Site [from E6]/Ref: ACTD – E...

The location(s) where trial-related activities are actually conducted.

Unexpected Adverse Drug Reaction [from E6]/Ref: ACTD – E...

An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g. investigator's brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product; see the ICH Guideline for Safety Data Management: Definitions and Standards for Expedited Reporting).

Unscheduled DNA Synthesis (UDS) [from S2A]/Ref: ACTD – E...

DNA synthesis that occurs at some stages in the cell cycle other than S-phase in response to DNA damage.

(It is usually associated with DNA excision repair).

Validation (from WHO GMP)

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

Validation Protocol [from Q7A]/Ref: ACTD – Q...

A written plan stating how validation will be conducted and defining acceptance criteria.

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(For example, the protocol for a manufacturing process identifies processing equipment, critical process parameters/operating ranges, product characteristics, sampling, test data to be collected, number of validation runs, and acceptable test results).

Validation Report [from ASEAN GMP]

A document in which the record, results and evaluation of a completed validation program are assembled.

(It may also contain proposals for the improvement of processes and/or equipment).

Variation [from WHO]

A change to any aspect of a pharmaceutical product, including but not limited to a change in formulation, method and site of manufacture, specifications for the finished product and ingredients, container and container labelling, and product information.

Viral Clearance [from Q5A]/Ref: ACTD – Q...

Elimination of target virus by removal of viral particles or inactivation of viral infectivity.

Virus-like Particles [from Q5A]/Ref: ACTD – Q...

Structures visible by electron microscopy which morphologically appear to be related to known viruses.

Virus Removal [from Q5A]/Ref: ACTD – Q...

Physical separation of virus particles from the intended product.

Vulnerable Subjects (in relation to clinical studies) [from E6]/Ref: ACTD – E...

Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in a case of refusal to participate.

(Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent).

Well-established Drug [from WHO]

Active pharmaceutical ingredient (API) which:

- has been marketed for at least five years in countries which undertake active post-marketing monitoring;
- has been widely used in sufficiently large numbers of patients to permit the assumption that safety and efficacy are well known; and
- has the same route of administration and strength, and the same or similar indication as in those countries.

(See also Well-established Fixed-dose Drug Combinations and Well-established Drug Products. As this definition refers to active pharmaceutical ingredients and not products, it does not take into account possible sensitivities to excipients and other factors that are relevant to therapeutic equivalence).

Well-established Drug Combinations [from WHO]

Combinations of drug which:

- have been marketed for at least five years in countries which undertake active post-marketing monitoring;
- have been widely used in sufficiently large number of patients to permit the assumption that safety and efficacy are well known; and

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- have the same route of administration and strength, and the same or similar indication as in those countries

(See also Well-established Drug and Well-established Drug Product. Because this definition refers to pharmaceutical ingredients and not products, it does not take into account possible sensitivities to excipients and other factors that are relevant to therapeutic equivalence).

Well-established Drug Products [from WHO]

Pharmaceutical products that contain well established drugs, and which:

- have been marketed for at least five years in countries which undertake active post-marketing monitoring;
- have been widely used in sufficiently large number of patients to permit the assumption that safety and efficacy are well known; and
- have the same route of administration and strength, and the same or similar indication as in those countries.

Well-established Fixed-dose Drug Combinations [from WHO]

Fixed-dose combinations of drug which:

- have been marketed for at least five years in countries which undertake active post-marketing monitoring;
- have been widely used in sufficiently large number of patients to permit the assumption that safety and efficacy are well known; and
- have the same route of administration and strength, and the same or similar indication as in those countries

(See also Well-established Drug and Well-established Drug Product. Because this definition refers to pharmaceutical ingredients and not products, it does not take into account possible sensitivities to excipients and other factors that are relevant to therapeutic equivalence).

Working Cell Bank (WCB) [from Q5A]/Ref: ACTD – Q...

The WCB is prepared from aliquots of a homogeneous suspension of cells obtained from culturing the MCB under defined culture conditions.