Glossary of ICH terms and definitions

Compiled by CIOMS

from the International Council for Harmonization (ICH)'s

Quality Safety Efficacy Miscellaneous

Guidelines

Council for International Organizations of Medical Sciences

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26 September 2022

About this glossary

This is a cumulative glossary of terms and definitions included in the guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). It was compiled from the PDF guidelines posted at www.ich.org as listed in the Index of Guidelines available on the ICH website.

The terms and definitions were taken from the Glossaries in the guidelines. Additional terms and definitions were identified by searching the text for occurrences of: "defined/definition", “term", and expressions such as "mean/means", "purpose", "denote", and "refers/referred". Where a definition occurs both in the main text and in the Glossary, only the latter was considered.

The terms and definitions were included verbatim. Full text for abbreviations was added, as were clarifications {in curly brackets} where considered useful. Please note that the definitions in this glossary are specific for use within the guidelines from which they were sourced.

The glossary was compiled in an Excel database, from which this PDF has been printed with automatic pagination. Page breaks may therefore occur at awkward places. For any definition at the end of a page, please check to see if it continues on the next page.

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While every effort has been made to ensure the accuracy of this glossary, we cannot give any guarantee or take responsibility for errors or omissions. Please refer to the original ICH guidelines to verify the information provided.

This glossary is freely available at: https://doi.org/10.56759/eftb6868

A

Accelerated testing

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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.

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

Studies designed to increase the rate of chemical degradation and physical change of an active pharmaceutical ingredient or finished pharmaceutical product by using exaggerated storage conditions as part of the stability testing programme. The data thus obtained, in addition to those derived from long-term stability studies, may be used to assess longer- term chemical effects under non-accelerated conditions and to evaluate the impact of short-term excursions outside the label storage conditions, as might occur during shipping. The results of accelerated testing studies are not always predictive of physical changes.

Acceptable intake

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

In the context of this guideline, an intake level that poses negligible cancer risk, or for serious/life-threatening indications where risk and benefit are appropriately balanced.

Acceptable limit

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

Maximum acceptable concentration of an impurity in a drug substance or drug product derived from the acceptable intake and the daily dose of the drug.

Acceptance criteria

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

Numerical limits, ranges, or other suitable measures for acceptance of the results of analytical procedures.

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Numerical limits, ranges, or other suitable measures for acceptance of test results.

Acceptance criterion

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

Numerical limits, ranges, or other suitable measures for acceptance of the results of analytical procedures.

Accuracy

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The degree of closeness of the measured value to the nominal or known true value under prescribed conditions (or as measured by a particular method). In this document accuracy is expressed as percent of the nominal value.

Accuracy (%) = (Measured Value/Nominal Value) × 100

Q14 Analytical Procedure Development, Glossary

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or as an accepted reference value and the value measured. (ICH Q2)

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

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. This is sometimes termed trueness.

Q2(R2) Validation of Analytical Procedures, Glossary

The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or as an accepted reference value and the value measured. (ICH Q2)

Acknowledgement Message (ICSRACK)

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

The acknowledgement message is an EDI Message with the information on the result of the acknowledgement of receipt procedure to acknowledge the receipt of one safety message and the safety report(s) contained in the safety file.[EMA]

Action Limit

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

An internal (in-house) value used to assess the consistency of the process at less critical steps.

Active Controls

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

A system consisting of hardware and software architecture, mechanisms, and algorithms that automatically adjust a process to maintain the process output within a desired range. Examples include feedforward and feedback controls.

Active pharmaceutical ingredient

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

Any substance or mixture of substances intended to be used in the manufacture of a pharmaceutical dosage form and that, when so used, becomes an active ingredient of that pharmaceutical dosage form. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease or to affect the structure and function of the body.

Active Pharmaceutical Ingredient (API) (or Drug Substance)

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Any substance or mixture of substances intended to be used in the manufacture of a drug (medicinal) product and that, when used in the production of a drug, becomes an active ingredient of the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure and function of the body.

Adequate and Well-controlled Trial

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

An adequate and well controlled trial has the following characteristics:
* a design that permits a valid comparison with a control to provide a quantitative assessment of treatment effect; * the use of methods to minimize bias in the allocation of patients to treatment groups and in the measurement and assessment of response to treatment; and * an analysis of the study results appropriate to the design to assess the effects of the treatment

Advanced cancer

S9 Nonclinical Evaluation for Anticancer Pharmaceuticals, 1.3

This guideline provides information for pharmaceuticals that are intended to treat cancer in patients with serious and life threatening malignancies. For the purpose of this guideline, this patient population is referred to as patients with advanced cancer.

Adventitious Virus

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Unintentionally introduced contaminant viruses.
{See also “Virus”}

Adverse Drug Reaction (ADR)

E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting, II.A.2

In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: All noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions.
The phrase "responses to a medicinal products" means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

Regarding marketed medicinal products, a well-accepted definition of an adverse drug reaction in the post-marketing setting is found in WHO Technical Report 498 [1972] and reads as follows: A response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for modification of physiological function.
The old term "side effect" has been used in various ways in the past, usually to describe negative (unfavourable) effects, but also positive (favourable) effects. It is recommended that this term no longer be used and particularly should not be regarded as synonymous with adverse event or adverse reaction.

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) cannot be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase ‘responses to a medicinal product’ means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, e.g. the relationship cannot be ruled out.
Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function (See the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).[ICHE6(R1)]

E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting, 2.2

Adverse drug reactions, as established by regional regulations, guidance, and practices, concern noxious and unintended responses to a medicinal product.
The phrase “responses to a medicinal product” means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility (refer to the ICH E2A guideline).
A reaction, in contrast to an event, is characterized by the fact that a causal relationship between the drug and the occurrence is suspected. For regulatory reporting purposes, if an event is spontaneously reported, even if the relationship is unknown or unstated, it meets the definition of an adverse drug reaction.

E6(R2) Good Clinical Practice (GCP), Glossary

In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase responses to a medicinal product means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.
Regarding marketed medicinal products: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function
(see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting)

Adverse Event

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).[ICHE6(R1)]

Adverse Event (AE)

E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting, 2.1

An adverse event is any untoward medical occurrence in a patient administered a medicinal product and which does not necessarily have to have a causal relationship with this treatment. An adverse event can therefore be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to this medicinal product.

E6(R2) Good Clinical Practice (GCP), Glossary

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

Adverse Event (or Adverse Experience)

E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting, II.A.1

Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.

An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

Adverse event of special interest

E2F Development Safety Update Report, Glossary

An adverse event of special interest (serious or non-serious) is one of scientific and medical concern specific to the sponsor's product or programme, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate. Such an event might warrant further investigation in order to characterise and understand it. Depending on the nature of the event, rapid communication by the trial sponsor to other parties (e.g., regulators) might also be warranted.

{Source: } Based on CIOMS VI

Alkaline elution assay

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

See DNA strand break assay.

Allometric and isometric growth

S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines, Glossary

Isometric growth occurs when proportional relationships are preserved as size changes during growth. Allometric growth is any deviation from isometric growth. With allometric growth, properties such as bone length, organ weight and body surface area can change according to an exponential function of body mass.

Alternative assay(s)

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

In vitro, ex vivo or non-mammalian in vivo assay(s) intended to predict malformations or embryo-fetal lethality; see Malformation or Embryo-Fetal Lethality (MEFL).

Amendment (to the protocol)

E6(R2) Good Clinical Practice (GCP), Glossary

See Protocol Amendment.

Analysis

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A series of analytical procedures from sample processing/dilution to measurement on an analytical instrument.

Analyte

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A specific chemical moiety being measured, including an intact drug, a biomolecule or its derivative or a metabolite in a biological matrix.

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

The chemical entity assayed in biological samples.

Analytical procedure

Q14 Analytical Procedure Development, Glossary

The analytical procedure refers to the way of performing the analysis. The analytical procedure description should include in detail the steps necessary to perform each analytical test. (ICH Q2)

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

The analytical procedure refers to 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.

Q2(R2) Validation of Analytical Procedures, Glossary

The analytical procedure refers to the way of performing the analysis. The analytical procedure description should include in detail the steps necessary to perform each analytical test. (ICH Q2)

Analytical procedure attribute

Q14 Analytical Procedure Development, Glossary

A technology specific property that should be within an appropriate limit, range, or distribution to ensure the desired quality of the measured result. For example, attributes for chromatography measurements may include peak symmetry factor and resolution. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

A technology specific property that should be within an appropriate limit, range or distribution to ensure the desired quality of the measured result. For example, attributes for chromatography measurements may include peak symmetry factor and resolution. (ICH Q14)

Analytical procedure control strategy

Q14 Analytical Procedure Development, Glossary

A planned set of controls derived from current analytical procedure understanding that ensures the analytical procedure performance and the quality of the measured result. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

A planned set of controls derived from current analytical procedure understanding that ensures the analytical procedure performance and the quality of the measured result. (ICH Q14)

Analytical procedure parameter

Q14 Analytical Procedure Development, Glossary

Any factor (including reagent quality) or analytical procedure operational step that can be varied continuously (e.g., flow rate) or specified at controllable, unique levels. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

Any factor (including reagent quality) or analytical procedure operational step that can be varied continuously (e.g., flow rate) or specified at controllable, unique levels. (ICH Q14)

Analytical procedure validation strategy

Q14 Analytical Procedure Development, Glossary

An analytical procedure validation strategy describes how to select the analytical procedure performance characteristics for validation. In the strategy, data gathered during development studies (e.g., using MODR or PAR) and system suitability tests (SSTs) can be applied to validation and an experimental scheme for future movements of parameters within an MODR/PAR can be predefined. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

An analytical procedure validation strategy describes how to select the analytical procedure performance characteristics for validation. In the strategy, data gathered during development studies (e.g., using MODR or PAR) and system suitability tests (SSTs) can be applied to validation and an experimental scheme for future movements of parameters within an MODR/PAR can be predefined. (ICH Q14)

Analytical Run (also referred to as “Run”)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A complete set of analytical and study samples with appropriate number of calibration standards and quality control samples (QCs) for their validation. Several runs may be completed in one day or one run may take several days to complete.

Analytical target profile (ATP)

Q14 Analytical Procedure Development, Glossary

A prospective summary of the performance characteristics describing the intended purpose and the anticipated performance criteria of an analytical measurement. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

A prospective summary of the performance characteristics describing the intended purpose and the anticipated performance criteria of an analytical measurement. (ICH Q14)

Anchor Calibration Standards/Anchor Points

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Spiked samples set at concentrations below the lower limit of quantification (LLOQ) or above the upper limit of quantification (ULOQ) of the calibration curve and analysed to improve curve fitting in ligand binding assays (LBAs).

Aneuploidy

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

Anonymised data and samples

E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories, 2.3.3

Anonymised data and samples are initially single or double coded but where the link between the subjects' identifiers and the unique code(s) is subsequently deleted.

Anonymous data and samples

E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories, 2.3.4

Anonymous data and samples are never labelled with personal identifiers when originally collected, neither is a coding key generated.

Anticipated efficacy/benefit

E2F Development Safety Update Report, Glossary

Efficacy/benefit that has not yet been established for the investigational drug, but which is anticipated based on knowledge of the class of drugs or data from previous clinical trials or non-clinical studies. {Source: } Based on wording of CIOMS VI definition of anticipated risk

API processes requiring validation

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, 12.12

Validation should extend to those operations determined to be critical to the quality and purity of the Active Pharmaceutical Ingredient (API).

API Starting Material

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A raw material, intermediate, or an Active Pharmaceutical Ingredient (API) that is used in the production of an API and that is incorporated as a significant structural fragment into the structure of the API. An API Starting Material can be an article of commerce, a material purchased from one or more suppliers under contract or commercial agreement, or produced in-house. API Starting Materials are normally of defined chemical properties and structure.
{See also ICH Q7 Q&As, Question 1.1:} ICH Q7 does not apply to Steps prior to the introduction of the API starting material. However, there is an expectation that an appropriate level of controls suitable for the production of the API starting material should be applied [ICH Q7, Section 1.3]. Normally, the 'API-starting material' is defined in the regulatory filing by the applicant and approved in the regulatory reviewing process. Additional guidance is provided to define and justify 'API starting material' derived from various sources [ICH Q11, Section 5]; for master cell banks, see [ICH Q5B; ICH Q5D].

Applicability domain

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

refers to the definition of the physicochemical properties of the substances that can be reliably tested in the assay and the biological mechanisms of action covered by the assay.

Applicable Regulatory Requirement(s)

E6(R2) Good Clinical Practice (GCP), Glossary

Any law(s) and regulation(s) addressing the conduct of clinical trials of investigational products.

Approval (in relation to Institutional Review Boards)

E6(R2) Good Clinical Practice (GCP), Glossary

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.

Assay qualification (for regulatory use)

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

Confirmation of the predictivity of an alternative assay(s) to identify Malformation or Embryo-Fetal Lethality (MEFL), as observed in vivo.

Assessment

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

In the context of this document, an assessment is an evaluation of all available information and does not always mean an additional test is conducted.

Audit

E6(R2) Good Clinical Practice (GCP), Glossary

A systematic and independent examination of trial related activities and documents to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed 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

E6(R2) Good Clinical Practice (GCP), Glossary

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

Audit Report

E6(R2) Good Clinical Practice (GCP), Glossary

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

Audit Trail

E6(R2) Good Clinical Practice (GCP), Glossary

Documentation that allows reconstruction of the course of events.

Authorisation versus Approval

E2C(R2) Periodic Benefit-Risk Evaluation Report, 1.3 Footnote 2

For the purpose of this document, the terms “authorisation” and “authorised” refer to clinical trials and the terms “approval” and “approved” refer to marketing applications

B

Base substitution

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

Batch

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

A defined quantity of starting material, packaging material or finished pharmaceutical product processed in a single process or series of processes so that it is expected to be homogeneous. 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. In the case of terminal sterilization, the batch size is determined by the capacity of the autoclave. In continuous manufacture, the batch must correspond to a defined fraction of the production, characterized by its intended homogeneity. The batch size can be defined either as a fixed quantity or as the amount produced in a fixed time interval.

Batch (for Bioanalysis)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A batch is comprised of quality control samples (QCs) and study samples, and possibly blanks, zero samples and calibration standards, which are handled during a fixed period of time and by the same group of analysts with the same reagents under homogenous conditions.

Batch (for Reference Standards and Reagents)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A specific quantity of material produced in a process or series of processes so that it is expected to be homogeneous within specified limits. Also referred to as “Lot”.

Batch (or Lot)

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

A specific quantity of material produced in a process or series of processes that is expected to be homogeneous within specified limits. In the case of continuous production, a batch may correspond to a defined fraction of the production. The batch size can be defined either by a fixed quantity or by the amount produced in a fixed time interval.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A specific quantity of material produced in a process or series of processes so that it is expected to be homogeneous within specified limits. In the case of continuous production, a batch may correspond to a defined fraction of the production. The batch size can be defined either by a fixed quantity or by the amount produced in a fixed time interval.

Batch Number (or Lot Number)

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A unique combination of numbers, letters, and/or symbols that identifies a batch (or lot) and from which the production and distribution history can be determined.

Bayesian Approaches

E9 Statistical Principles for Clinical Trials, Glossary

Approaches to data analysis that provide a posterior probability distribution for some parameter (e.g. treatment effect), derived from the observed data and a prior probability distribution for the parameter. The posterior distribution is then used as the basis for statistical inference.

Bias

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The tendency of a measurement process to over- or under-estimate the value of a population parameter.

Bias (Statistical & Operational)

E9 Statistical Principles for Clinical Trials, Glossary

The systematic tendency of any factors associated with the design, conduct, analysis and evaluation of the results of a clinical trial to make the estimate of a treatment effect deviate from its true value. Bias introduced through deviations in conduct is referred to as 'operational' bias. The other sources of bias listed above are referred to as 'statistical'.

Binding Reagent

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A reagent that binds to the analyte in ligand binding assay (LBA)-based bioanalytical methods.

Bioanalytical Method

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Analytical method used in the quantitative determination of analytes in biological matrices.

Bioburden

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The level and type (e.g. objectionable or not) of micro-organisms that can be present in raw materials, Active Pharmaceutical Ingredient (API) starting materials, intermediates or APIs. Bioburden should not be considered contamination unless the levels have been exceeded or defined objectionable organisms have been detected.

Biodistribution (BD)

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, 2

Biodistribution (BD) is the in vivo distribution, persistence, and clearance of a Gene Therapy (GT) product at the site of administration and in target and non-target tissues, including biofluids (e.g., blood, cerebrospinal fluid, vitreous fluid), in biologically relevant animal species.

Biodistribution (BD)

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, 2

BD is the in vivo distribution, persistence, and clearance of a GT product at the site of administration and in target and non-target tissues, including biofluids (e.g., blood, cerebrospinal fluid, vitreous fluid), in biologically relevant animal species.

Biological Activity

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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

Biological Drugs

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Drugs that are made by living organisms or cells (e.g., therapeutic proteins).

Biological Matrix

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A biological material including, but not limited to, blood, serum, plasma and urine.

Biomaterials, human

M4E(R2) CTD on Efficacy, 53.2

Human biomaterials is a term used to refer to proteins, cells, tissues and related materials derived from human sources that are used in vitro or ex vivo to assess PK properties of drug substances.
Examples include cultured human colonic cells that are used to assess permeability through biological membranes and transport processes, and human albumin that is used to assess plasma protein binding.

Biotechnological process

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, 18.11

The term “biotechnological process” (biotech) refers to the use of cells or organisms that have been generated or modified by recombinant DNA, hybridoma or other technology to produce Active Pharmaceutical Ingredients (APIs).

The APIs produced by biotechnological processes normally consist of high molecular weight substances, such as proteins and polypeptides, for which specific guidance is given in this Section. Certain APIs of low molecular weight, such as antibiotics, amino acids, vitamins, and carbohydrates, can also be produced by recombinant DNA technology.The level of control for these types of APIs is similar to that employed for classical fermentation.

Biotechnological products, biological products

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, 1.3

“Biotechnological/biological products” refers to any products prepared from cells cultivated from cell banks with the exception of microbial metabolites such as, for example, antibiotics, amino acids, carbohydrates, and other low molecular weight substances.

Blank Sample

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A sample of a biological matrix to which no analyte, no Internal Standard (IS) and no additional-alternative matrix or buffer has been added.

Blending

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, 8.4

For the purpose of this document, blending is defined as the process of combining materials within the same specification to produce a homogeneous intermediate or API. In-process mixing of fractions from single batches (e.g., collecting several centrifuge loads from a single crystallization batch) or combining fractions from several batches for further processing is considered to be part of the production process and is not considered to be blending.

Blind Review

E9 Statistical Principles for Clinical Trials, Glossary

The checking and assessment of data during the period of time between trial completion (the last observation on the last subject) and the breaking of the blind, for the purpose of finalising the planned analysis.

Blinding/Masking

E6(R2) Good Clinical Practice (GCP), Glossary

A procedure in which one or more parties to the trial are 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

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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 levels 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 weights of the same basic composition into different size capsule shells). Bracketing can be applied to different container sizes or different fills in the same container closure system.

Q1D Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products, 2.3

As defined in the glossary to the parent guideline, bracketing is the design of a stability schedule such that only samples on the extremes of certain design factors (e.g., strength, container size and/or fill) are tested at all time points as in a full design. The design assumes that the stability of any intermediate levels is represented by the stability of the extremes tested.
{Parent guideline: Q1A}

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The design of a stability schedule such that only samples at the extremes of certain design factors, e.g. strength and package size, are tested at all time points as in a full design. The design assumes that the stability of any intermediate levels 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 weights of the same basic composition into different size capsule shells). Bracketing can be applied to different container sizes or different fills in the same container-closure system (refer to ICH Q1D).

Bridging Data Package

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

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 a bridging study in the new region that will allow extrapolation of the foreign safety and efficacy data to the population of the new region.

Bridging Study

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

A bridging study is defined as 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.

C

Calibration

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The demonstration that a particular instrument or device produces results within specified limits by comparison with those produced by a reference or traceable standard over an appropriate range of measurements.

Calibration Curve

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The relationship between the instrument response (e.g., peak area, height or signal) and the concentration (amount) of analyte in the calibration standards within a given range. Also referred to as Standard Curve.

Calibration data set

Q14 Analytical Procedure Development, Multivariate glossary

A set of data with matched known characteristics and measured analytical results, that spans the desired operational range. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

A set of data with matched known characteristics and measured analytical results, that spans the desired operational range. (ICH Q2)

Calibration model

Q14 Analytical Procedure Development, Glossary

A model based on analytical measurements of known samples that relates the input data to a value for the property of interest (i.e., the model output). (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

A model based on analytical measurements of known samples that relates the input data to a value for the property of interest (i.e., the model output). (ICH Q2)

Calibration Range

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The interval between the upper and lower concentration (amounts) of analyte in the calibration standards (including these concentrations)

Calibration Standard

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A matrix to which a known amount of analyte has been added or spiked. Calibration standards are used to construct calibration curves.

Capability of a Process

Q10 Pharmaceutical Quality System, Glossary

Ability of a process to realise a product that will fulfil the requirements of that product. The concept of process capability can also be defined in statistical terms. (ISO 9000:2005)

Carry-over

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The appearance of an analyte signal in a sample from a preceding sample.

Case

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

An observation requiring investigation, and includes problems that might or might not involve individual or groups of investigative subjects.[HL7 Patient Safety]

Case Report Form (CRF)

E6(R2) Good Clinical Practice (GCP), Glossary

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 bank

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

A cell bank is a collection of appropriate containers, whose contents are of uniform composition, stored under defined conditions. Each container represents an aliquot of a single pool of cells.

Cell line

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

Type of cell population which originates by serial subculture of a primary cell population, which can be banked.

Cell proliferation

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

Cell Substrate

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Cells used to manufacture product.

Centromere/kinetochore

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Structures in chromosomes essential for association of sister chromatids and for attachment of spindle fibers that move daughter chromosomes to the poles and ensure inclusion in daughter nuclei.

Certified Copy

E6(R2) Good Clinical Practice (GCP), Glossary (Addendum)

A copy (irrespective of the type of media used) of the original record that has been verified (i.e., by a dated signature or by generation through a validated process) to have the same information, including data that describe the context, content, and structure, as the original.

Change Management

Q10 Pharmaceutical Quality System, Glossary

A systematic approach to proposing, evaluating, approving, implementing and reviewing changes. (ICH Q10)

Q3D(R2) Guideline for Elemental Impurities, Glossary

A systematic approach to proposing, evaluating, approving, implementing and reviewing changes. (ICH Q10)

Chemical Development Studies

Q3A(R2) Impurities in New Drug Substances, Glossary

Studies conducted to scale-up, optimise, and validate the manufacturing process for a new drug substance.

Chemical Drugs

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Chemically synthesised drugs.

Chemical Transformation Step

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

For Chemical Entities, a step involved in the synthesis of the chemical structure of the drug substance from precursor molecular fragments. Typically it involves C-X or C-C bond formation or breaking.

Child assent

E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population, Glossary

The affirmative agreement of a child to participate in research or to undergo a medical intervention. Lack or absence of expression of agreement or disagreement must not be interpreted as assent.

Chiral

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

Not superimposable with its mirror image, as applied to molecules, conformations, and macroscopic objects, such as crystals. the term has been extended to samples of substances whose molecules are chiral, even if the macroscopic assembly of such molecules is racemic.

Chromophore

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

The substructure of a molecule that absorbs visible or ultraviolet light.

Class

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

Class is used in this document to qualify a base level element from the Health Level 7 (HL7) standard.

Classical fermentation

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, 18.12

The term “classical fermentation” refers to processes that use microorganisms existing in nature and/or modified by conventional methods (e.g. irradiation or chemical mutagenesis) to produce Active Pharmaceutical Ingredients (APIs).

APIs produced by “classical fermentation” are normally low molecular weight products such as antibiotics, amino acids, vitamins, and carbohydrates.

Clastogen

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

An agent that produces structural breakage of chromosomes, usually detectable by light microscopy.

Climatic zone

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The zones into which the world is divided based on the prevailing annual climatic conditions (see reference to the living document “Long-term stability testing conditions as identified by WHO Member States” 4). {Footnote 4: http://www.who.int/medicines/areas/quality_safety/quality_assurance/StabilityConditionsTable2UupdatedMarch2015.pdf?ua=1, accessed 1 March 2017.

Climatic zones

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

The four zones in the world that are distinguished by their characteristic prevalent annual climatic conditions. This is based on the concept described by W. Grimm (Drugs Made in Germany, 28:196-202, 1985 and 29:39-47, 1986).

Clinical development programme

E2F Development Safety Update Report, Glossary

This refers to all clinical trials being conducted with the same investigational drug, regardless of indication or formulation.

{Source: } ICH E2F

Clinical drug development

E8(R1) General Considerations for Clinical Studies, 4.3

Clinical drug development, defined as studying the drug in humans, is conducted in a sequence that builds on knowledge accumulated from non-clinical and previous clinical studies.

Although clinical drug development is often described as consisting of four temporal phases (phases 1-4), it is important to appreciate that the phase concept is a description and not a requirement,and that the phases of drug development may overlap or be combined.

Clinical exposure

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q5.1

Mean steady state maximum concentration (Cmax,ss) associated with the maximum therapeutic dose

Clinical study

E8(R1) General Considerations for Clinical Studies, 1

For the purposes of this document, a clinical study is meant to refer to a study of one or more medicinal products in humans, conducted at any point in a product's lifecycle, both prior to and following marketing authorisation.

Clinical Trial/Study

E6(R2) Good Clinical Practice (GCP), Glossary

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. The terms clinical trial and clinical study are synonymous.

Clinical Trial/Study Report

E6(R2) Good Clinical Practice (GCP), Glossary

A written description of a trial/study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report
(see the ICH Guideline for Structure and Content of Clinical Study Reports).

Cloning efficiency

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

The efficiency of single cells to form clones. It is usually measured after seeding low numbers of cells in a suitable environment.

Closed signal

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

A signal for which an evaluation was completed during the reporting interval.
{Source:} ICH Guideline E2C(R2)

Cocktail study

M12 EWG Drug Interaction Studies , 3.1.4

A cocktail study includes the simultaneous administration of substrates of multiple enzymes and/or transporters to study subjects. A cocktail approach can simultaneously evaluate a drug's inhibition or induction potential for multiple enzymes and transporters if the study is properly designed and conducted (refer to Section 3.2.6 for additional details).

Combination product

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

A drug product which contains more than one drug substance.

Comet assay

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

See DNA strand break assay.

Commercially available chemical

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), 5.2.1

A commercially available chemical is usually one that is sold as a commodity in a pre-existing, non-pharmaceutical market in addition to its proposed use as starting material.
{See also Q11 Q&As, Question 5.5: "A definition of “custom synthesised chemical” was not provided in ICH Q11, but a custom synthesised chemical is generally understood to be one that is made specifically to a drug substance manufacturer’s requirement, either in-house or externally, or available for purchase but where the only use is for pharmaceutical manufacture. The reference to “non-pharmaceutical market” in the ICH Q11 description of commercially available chemicals is intended to preclude purchased intermediates from being claimed as commercially available chemicals."}

Commitment batches

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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.

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

Production batches of an active pharmaceutical ingredient or finished pharmaceutical product for which the stability studies are initiated or completed post-approval through a commitment made in a regulatory application.

Common adverse events

M4E Q&As (R4) Questions & Answers: CTD on Efficacy, Q2

Guidance is provided by ICH E3 Guideline. {E3, Point 12: 'Second, the more common adverse events, laboratory test changes etc. should be identified, classified in some reasonable way, compared for treatment groups, and analysed, as appropriate, for factors that may affect the frequency of adverse reactions/events, such as time dependence, relation to demographic characteristics, relation to dose or drug concentration etc.'}

Company

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Glossary

Manufacturing sites and Marketing Authorisation Holder (MAH) where relevant

Company Core Data Sheet (CCDS)

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

A document prepared by the marketing authorisation holder (MAH) containing, in addition to safety information, material related to indications, dosing, pharmacology and other information concerning the product.
{Source:} ICH Guideline E2C

Company Core Safety Information (CCSI)

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

All relevant safety information contained in the Company Core Data Sheet (CCDS) prepared by the marketing authorisation holder (MAH) and which the MAH requires to be listed in all countries where the company markets the drug, except when the local regulatory authority specifically requires a modification. It is the reference information by which listed and unlisted are determined for the purposes of periodic reporting for marketed products, but not by which expected ad unexpected are determined for expedited reporting.
{Source:} ICH Guideline E2C

Comparability Bridging Study

Q5E Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process, Glossary

A study performed to provide nonclinical or clinical data that allows extrapolation of the existing data from the drug product produced by the current process to the drug product from the changed process.

Comparability Exercise

Q5E Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process, Glossary

The activities, including study design, conduct of studies, and evaluation of data, that are designed to investigate whether the products are comparable.

Comparable

Q5E Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process, Glossary

A conclusion that products have highly similar quality attributes before and after manufacturing process changes and that no adverse impact on the safety or efficacy, including immunogenicity, of the drug product occurred. This conclusion can be based on an analysis of product quality attributes. In some cases, nonclinical or clinical data might contribute to the conclusion.

{1.2 Footnote 4}: Improvement of product quality is always desirable and encouraged. If the results of the comparability exercise indicate an improved quality suggesting a significant benefit in efficacy and/or safety, the pre- and post-change product may not be comparable. However, this result could be considered acceptable. The manufacturer is advised to consult the appropriate regional Regulatory Authority.

Comparator (Product)

E6(R2) Good Clinical Practice (GCP), Glossary

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

Complete Clinical Data Package

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

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.

Completed clinical trial

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

Clinical trial for which a final study report is available.

{Source:} ICH Guideline E2F

E2F Development Safety Update Report, Glossary

Study for which a final clinical study report is available. Note: For purposes of the Development Safety Update Report (DSUR), any clinical trial for which enrolment has begun, but for which a final clinical study report is not available, is considered to be ongoing (see “ongoing clinical trial” definition).

{Source: } CIOMS VII

Compliance (in relation to trials)

E6(R2) Good Clinical Practice (GCP), Glossary

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

Compounds Insensitive to Ethnic Factors

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

A compound whose characteristics suggest minimal potential for clinically significant impact by ethnic factors on safety, efficacy, or dose response.

Compounds Sensitive to Ethnic Factors

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

A compound whose pharmacokinetic, pharmacodynamic, or other characteristics suggest the potential for clinically significant impact by intrinsic and/or extrinsic ethnic factors on safety, efficacy, or dose response.

Computer System

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A group of hardware components and associated software, designed and assembled to perform a specific function or group of functions.

Computerized System

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A process or operation integrated with a computer system.

Concomitant toxicokinetics

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

Toxicokinetic measurements performed in the toxicity study, either in all animals or in representative subgroups or in satellite groups.

Confidentiality

E6(R2) Good Clinical Practice (GCP), Glossary

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

Confirmatory studies

Q1B Stability Testing : Photostability Testing of New Drug Substances and Products, Glossary

Confirmatory studies are those undertaken to establish photostability characteristics under standardized conditions. These studies are used to identify precautionary measures needed in manufacturing or formulation and whether light resistant packaging and/or special labeling is needed to mitigate exposure to light. For the confirmatory studies, the batch(es) should be selected according to batch selection for long-term and accelerated testings which is described in the Parent Guideline.

Conformance to specification

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary, definition of "Specification"

"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.

Conformance to specifications

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary, definition of "Specification"

"Conformance to specifications" means that the drug substance and / or drug product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria.

Conjugated Product

Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products, Glossary

A conjugated product is made up of an active ingredient (for example, peptide, carbohydrate) bound covalently or noncovalently to a carrier (for example, protein, peptide, inorganic mineral) with the objective of improving the efficacy or stability of the product.

Consistency of treatment effect

E17 General principles for planning and design of Multi-Regional Clinical Trials, Glossary

A lack of clinically relevant differences between treatment effects in different regions or subpopulations of an MRCT

Constitutive ingredients

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

Chemicals or biologic substances used as excipients, diluents, or adjuvants in a vaccine, including any diluent provided as an aid in the administration of the product and supplied separately.

Consumer

E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting, 2.6

Consumer is defined as a person who is not a healthcare professional such as a patient, lawyer, friend, or relative of a patient.

Container closure system

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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

Q3D(R2) Guideline for Elemental Impurities, Glossary

The sum of packaging components that together contain and protect the dosage form. This includes primary packaging components and secondary packaging components, if the latter are intended to provide additional protection to the drug product. A packaging system is equivalent to a container closure system. (ICH Q1A)

Container-closure system

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

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

Contaminants

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

Any adventitiously introduced materials (e.g., chemical, biochemical, or microbial species) not intended to be part of the manufacturing process of the drug substance or drug product. (ICH Q6B)

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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

Contamination

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a raw material, intermediate, or Active Pharmaceutical Ingredient (API) during production, sampling, packaging or repackaging, storage or transport.

Content Validity

E9 Statistical Principles for Clinical Trials, Glossary

The extent to which a variable (e.g. a rating scale) measures what it is supposed to measure.

Context Group

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

Defines the context of a group of documents with the same Context of Use code and Keyword code combination. Previously known as "Document Group" in Electronic Common Technical Document (eCTD) v4.0 Implementation Guide version 1.1.

Context of Use code and Keyword code combination

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

The combination includes both the code and code system for the Context of Use and Keyword in order to define the specific context group under which the documents are grouped.

Continual Improvement

Q10 Pharmaceutical Quality System, Glossary

Recurring activity to increase the ability to fulfil requirements. (ISO 9000:2005)

Continuous cell line

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

A cell line having an infinite capacity for growth. Often referred to as “immortal” and previously referred to as “established”.

Continuous Process Verification

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

An alternative approach to process validation in which manufacturing process performance is continuously monitored and evaluated. (ICH Q8)

Q8(R2) Pharmaceutical Development, Glossary (Part I)

An alternative approach to process validation in which manufacturing process performance is continuously monitored and evaluated.

Contract

E6(R2) Good Clinical Practice (GCP), Glossary

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

Contract Manufacturer

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A manufacturer performing some aspect of manufacturing on behalf of the original manufacturer. {Q7 Q&As, Question 16.2:} The term ‘outsourced activities’, as defined and described in [ICH Q10, Section 2.7, Glossary], aligns with the description of ‘contract manufacturer’ in [ICH Q7, Section 16].

Contract Research Organization (CRO)

E6(R2) Good Clinical Practice (GCP), Glossary

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

Control strategy

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

A planned set of controls, derived from current product and process understanding that ensures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control.

Q10 Pharmaceutical Quality System, Glossary

A planned set of controls, derived from current product and process understanding, that assures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. (ICH Q10)

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

A planned set of controls, derived from current product and process understanding, that assures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. (ICH Q10)

Q14 Analytical Procedure Development, Glossary

A planned set of controls, derived from current product and process understanding, that assures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. (ICH Q10)

Q2(R2) Validation of Analytical Procedures, Glossary

A planned set of controls, derived from current product and process understanding, that assures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. (ICH Q10)

Q3D(R2) Guideline for Elemental Impurities, Glossary

A planned set of controls, derived from current product and process understanding, that assures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. (ICH Q10)

Q8(R2) Pharmaceutical Development, Glossary (Part II)

A planned set of controls, derived from current product and process understanding that ensures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. (ICH Q10)

Control Threshold

Q3D(R2) Guideline for Elemental Impurities, Glossary

A limit that is applied during the assessment of elemental impurities to determine if additional control elements may be required to ensure that the PDE is not exceeded in the drug product. The limit is defined as 30% of the Permitted Daily Exposure (PDE) of the specific elemental impurity under consideration.

Controlled vocabulary

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

A controlled vocabulary is an established list of standardised terminology for use in indexing and retrieval of information.(1) (1)Refer to ICH M2 Glossary of Terms and Abbreviations (https://www.ich.org/page/m2-recommendations-technical- references)

Coordinating Committee

E6(R2) Good Clinical Practice (GCP), Glossary

A committee that a sponsor may organize to coordinate the conduct of a multicentre trial.

Coordinating Investigator

E6(R2) Good Clinical Practice (GCP), Glossary

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

Corrective Action

Q10 Pharmaceutical Quality System, Glossary

Action to eliminate the cause of a detected non-conformity or other undesirable situation. NOTE: Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence. (ISO 9000:2005)

Corrective Action and Preventive Action (CAPA)

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Glossary

System that focuses on investigating, understanding, and correcting discrepancies while attempting to prevent their occurrence

Counterfeit Medicine

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

A medicine which is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products can include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging.[WHO]13
{Footnote 13”} World Health Organisation International Medical Products Anti-Counterfeiting Task Force (IMPACT). http://www.who.int/impact/FinalBrochureWHA2008a.pdf {Link no longer valid as of 25 July 2022}

Co-validation

Q14 Analytical Procedure Development, Glossary

Demonstration that the analytical procedure meets its predefined performance criteria when used at different laboratories for the same intended purpose. Co-validation can involve all (full revalidation) or a subset (partial revalidation) of performance characteristics potentially impacted by the change in laboratories. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

Demonstration that the analytical procedure meets its predefined performance criteria when used at different laboratories for the same intended purpose. Co-validation can involve all (full revalidation) or a subset (partial revalidation) of performance characteristics potentially impacted by the change in laboratories. (ICH Q2)

Critical

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Describes a process step, process condition, test requirement, or other relevant parameter or item that must be controlled within predetermined criteria to ensure that the Active Pharmaceutical Ingredient (API) meets its specification.

Critical Process Parameter (CPP)

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Glossary

Process parameter whose variability has an impact on a critical quality attribute and therefore should be monitored or controlled to assure the process produces the desired product quality. (Q8(R2))

Q8(R2) Pharmaceutical Development, Glossary (Part II)

A process parameter whose variability has an impact on a critical quality attribute and therefore should be monitored or controlled to ensure the process produces the desired quality.

Critical Quality Attribute (CQA)

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality. (ICH Q8)

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Glossary

A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to assure the desired product quality. (Q8(R2))

Q14 Analytical Procedure Development, Glossary

A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range or distribution to ensure the desired product quality. (ICH Q8)

Q2(R2) Validation of Analytical Procedures, Glossary

A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality. (ICH Q8)

Q8(R2) Pharmaceutical Development, Glossary (Part II)

A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality.

Critical Reagent

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Critical reagents for ligand binding assays (LBAs) include binding reagents (e.g., antibodies, binding proteins, peptides) and those containing enzymatic moieties that have a direct impact on the results of the assay.

Cross Validation

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Assessment of potential bias between two bioanalytical methods or the same bioanalytical method used in different laboratories in order to determine whether reported data are comparable.

Cross-Contamination

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Contamination of a material or product with another material or product.

Cross-validation

Q14 Analytical Procedure Development, Glossary

Demonstration that two or more analytical procedures meet the same predefined performance criteria and can therefore be used for the same intended purpose. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

Demonstration that two or more analytical procedures meet the same predefined performance criteria and can therefore be used for the same intended purpose. (ICH Q2)

Culture confluency

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

A quantification of the cell density in a culture by visual inspection.

Cumulative intake

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

The total intake of a substance that a person is exposed to over time.

Cytogenetic evaluation

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Chromosome structure analysis in mitosis or meiosis by light microscopy or micronucleus analysis.

D

Daily Dose

Q3D(R2) Guideline for Elemental Impurities, Glossary

The total mass of drug product that is consumed by a patient on a daily basis.

Data

E6(R3) EWG Good Clinical Practice (GCP) - Draft principles, Draft principles; Footnote 1

For the purposes of this guideline (…) "data" reflects measurement and assessment of variable parameters relevant to specific outcomes.
{See also "Information" and "Results"}

Data lock point

E2F Development Safety Update Report, Glossary

The date (month and day) designated as the cut-off for data to be included in a Development Safety Update Report (DSUR). It is based on the Development International Birth Date (DIBD).
{Source: } CIOMS VII

Data Monitoring Committee (synonyms: Independent Data Monitoring Committee, Data and Safety Monitoring Board

E2F Development Safety Update Report, Glossary

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.
{Source: } ICH E6

Data transformation

Q14 Analytical Procedure Development, Multivariate glossary

Mathematical operation on model input data to assume better correlation with the output data and simplify the model structure. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

Mathematical operation on model input data to assume better correlation with the output data and simplify the model structure. (ICH Q14)

Datatype

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

Datatype is used in this document to qualify elements and attributes that come from a datatype in the Health Level 7 (HL7) standard.

Decision Maker(s)

Q9 Quality Risk Management, Definitions

Person(s) with the competence and authority to make appropriate and timely quality risk management decisions.

Q9(R1) EWG Quality Risk Management, Definitions

Person(s) with the competence and authority to make appropriate and timely quality risk management decisions.

Degradation Product

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

A molecule resulting from a chemical change in the drug molecule brought about over time and/or by the action of light, temperature, pH, water, or by reaction with an excipient and/or the immediate container/closure system.

Q3B(R2) Impurities in New Drug Products, Glossary

An impurity resulting from a chemical change in the drug substance brought about during manufacture and/or storage of the new drug product by the effect of, for example, light, temperature, pH, water, or by reaction with an excipient and/or the immediate container closure system.

Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products, Glossary

A molecule resulting from a change in the drug substance (bulk material) brought about over time. For the purpose of stability testing of the products described in this guideline, such changes could occur as a result of processing or storage (e.g., by deamidation, oxidation, aggregation, proteolysis). For biotechnological/biological products some degradation products may be active.

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

A molecule resulting from a chemical change in the drug molecule 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. Also called decomposition product.

Degradation Products

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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, proteolysis). Degradation products may be either product-related substances, or product-related impurities.

Degradation Profile

Q3B(R2) Impurities in New Drug Products, Glossary

A description of the degradation products observed in the drug substance or drug product.

Delayed Release

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

Release of a drug (or drugs) at a time other than immediately following oral administration.

Dermal Drugs

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

Products applied topically to the skin.

Design Space

Q10 Pharmaceutical Quality System, Glossary

The multidimensional combination and interaction of input variables (e.g., material attributes) and process parameters that have been demonstrated to provide assurance of quality. (ICH Q8)

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

The multidimensional combination and interaction of input variables (e.g., material attributes) and process parameters that have been demonstrated to provide assurance of quality. Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory post approval change process. Design space is proposed by the applicant and is subject to regulatory assessment and approval. (ICH Q8)

Q8(R2) Pharmaceutical Development, Glossary (Part I)

The multidimensional combination and interaction of input variables (e.g., material attributes) and process parameters that have been demonstrated to provide assurance of quality. Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory post approval change process. Design space is proposed by the applicant and is subject to regulatory assessment and approval.

Q8(R2) Pharmaceutical Development, Glossary (Part II)

The multidimensional combination and interaction of input variables (e.g., material attributes) and process parameters that have been demonstrated to provide assurance of quality. Working within the design space is not considered as a change. Movement out of the design space is considered to be a change and would normally initiate a regulatory post approval change process. Design space is proposed by the applicant and is subject to regulatory assessment and approval (ICH Q8).

Desired Product

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

(1) The protein which has the expected structure, or (2) the protein which is expected from the DNA sequence and anticipated post-translational modification (including glycoforms), and from the intended downstream modification to produce an active biological molecule.

Detectability

Q9 Quality Risk Management, Definitions

The ability to discover or determine the existence, presence, or fact of a hazard.

Q9(R1) EWG Quality Risk Management, Definitions

The ability to discover or determine the existence, presence, or fact of a hazard.

Detection limit

Q14 Analytical Procedure Development, Glossary

The detection limit is the lowest amount of an analyte in a sample which can be detected but not necessarily quantitated as an exact value. (ICH Q2)

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

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.

Q2(R2) Validation of Analytical Procedures, Glossary

The detection limit is the lowest amount of an analyte in a sample which can be detected but not necessarily quantitated as an exact value. (ICH Q2)

Determination

Q14 Analytical Procedure Development, Glossary

The reported value(s) from single or replicate measurements of a single sample preparation as per the validation protocol. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

The reported value(s) from single or replicate measurements of a single sample preparation as per the validation protocol. (ICH Q2)

Development International Birth Date

E2F Development Safety Update Report, Glossary

Date of first approval (or authorisation) for conducting an interventional clinical trial in any country. {Source: } CIOMS VII

Development Studies

Q3B(R2) Impurities in New Drug Products, Glossary

Studies conducted to scale-up, optimise, and validate the manufacturing process for a drug product.

Developmental toxicity

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

Any adverse effect induced prior to attainment of adult life. It includes effects induced or manifested from conception to postnatal life.

Deviation

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Departure from an approved instruction or established standard.

Q7 Q&As Questions and Answers: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Q20.1

The term ‘deviation’, as used in ICH Q7, refers to a ‘departure from an approved instruction or established standard’ that may or may not have an impact on the quality of the material. {See also "Non-conformance"}

Dilution Factor

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The magnitude by which a sample is diluted.

Dilution Integrity

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Assessment of the sample dilution procedure to confirm that the procedure does not impact the measured concentration of the analyte.

Dilution Linearity

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A parameter demonstrating that the method can appropriately analyse samples at a concentration exceeding the Upper Limit of Quantification (ULOQ) of the calibration curve without influence of prozone (hook) effect and that the measured concentrations are not affected by dilution within the calibration range in Ligand Binding Assays (LBAs).

Diploid cell line

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

A cell line having a finite in vitro lifespan in which the chromosomes are paired (euploid) and are structurally identical to those of the species from which they were derived.

Direct Access

E6(R2) Good Clinical Practice (GCP), Glossary

Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsor's 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 sponsor’s proprietary information.

Direct Phototoxicity

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

Phototoxicity induced by absorption of light by the drug or excipient

Disturbances

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

Unplanned changes to process inputs beyond normal operating range or conditions (e.g., process parameter, material property, equipment condition, or environment) that are introduced into a system.

Diversion

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

Procedure in which materials are isolated and separated from the product stream in the manufacturing process.

DNA adduct

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Product of covalent binding of a chemical to DNA.

DNA repair

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Reconstitution of the original DNA sequence after DNA damage.

DNA strand break test

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Alkaline treatment that converts certain types of DNA lesions into strand breaks that can be detected by the alkaline elution technique, measuring migration rate through a filter, or by the single cell gel electrophoresis or Comet test (in which cells embedded in a thin layer of gel on a microscope slides are subjected to electric current, causing shorter pieces of DNA to migrate out of the nucleus into a “Comet tail”). The extent of DNA migration is measured visually under the microscope on stained cells.
{Other glossary entries include the mention "See DNA strand break assay", suggesting that this term is used interchangeably with "DNA strand break test" in S2(R1).}

DNA strand breaks

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Single or double strand scissions in the DNA.

DNA-reactive

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

The potential to induce direct DNA damage through chemical reaction with DNA.

Document

M4(R4) Organisation Including the Granularity document that provides guidance on document location and paginations, Annex

A document is defined for a paper submission as a set of pages, numbered sequentially and divided from other documents by a tab (see Document Pagination and Segregation section of this Annex). A document can be equated to a file for an electronic submission.
The granularity of the paper and electronic submissions should be equivalent, although if a paper submission is updated to be an electronic submission, some changes in granularity could be introduced to facilitate on-going lifecycle management. In an electronic submission, a new file starts at the same point at which in a paper submission, a tab divides the documents.

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

Document is used in this document to identify a content file representing a document required or provided to be submitted. In the Electronic Common Technical Document (eCTD) v4.0 message a document will be represented by a document element referencing the file location and providing a title. The document element will be presented in its context of use. Since a document can be used multiple times, a documentReference element allows a document to be specified for the contextOfUse. Each time the document is used in the same submission unit, that document may have a different contextOfUse. The relationship is provided via the documentReference element. Accordingly, each Context of Use must reference a document.

Document Label

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

An abbreviated name for the document that may be assigned for each context of use.

Document Submission

Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions, Glossary

The working documents received from the PDG or one or more pharmacopoeial sources (USP, Ph. Eur., or JP) that contain the proposed pharmacopoeial text and any other support documents provided for Q4B evaluation.

Documentation

E6(R2) Good Clinical Practice (GCP), Glossary

All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records, and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken.

Dosage

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

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

Dosage form

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The form of the finished pharmaceutical product, e.g. tablet, capsule, elixir or suppository.

Dose Regimen

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

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

Double coded data and samples

E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories, 2.3.2.2

Double coded data and samples are initially labelled with a single specific code and do not carry any personal identifiers. The data and samples are then relabelled with a second code, which is linked to the first code via a second coding key.

Double-Dummy

E9 Statistical Principles for Clinical Trials, Glossary

A technique for retaining the blind when administering supplies in a clinical trial, when the two treatments cannot be made identical. Supplies are prepared for Treatment A (active and indistinguishable placebo) and for Treatment B (active and indistinguishable placebo). Subjects then take two sets of treatment; either A (active) and B (placebo), or A (placebo) and B (active).

Dropout

E9 Statistical Principles for Clinical Trials, Glossary

A subject in a clinical trial who for any reason fails to continue in the trial until the last visit required of him/her by the study protocol.

Drug

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

(See Medicinal Product)

E2E Pharmacovigilance Planning, 1.1

(…) in this guideline, the term “drug” denotes chemical entities, biotechnology-derived products, and vaccines

E8(R1) General Considerations for Clinical Studies, 1

The term "drug" should be considered synonymous with therapeutic, preventative, or diagnostic medicinal products.

Drug (Medicinal) Product

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The dosage form in the final immediate packaging intended for marketing. (Reference Q1A)

Drug approval

E8(R1) General Considerations for Clinical Studies, 1

The term “drug approval” refers to obtaining marketing authorisation for the drug.

Drug product

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

The dosage form in the final immediate packaging intended for marketing.

Drug Product (Dosage Form; Finished Product)

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

A pharmaceutical product type that contains a drug substance, generally, in association with excipients.

Drug substance

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

See Active Pharmaceutical Ingredient

Drug Substance (Bulk Material)

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

The material which is subsequently formulated with excipients to produce the drug product. It can be composed of the desired product, product-related substances, and product- and process-related impurities. It may also contain excipients including other components such as buffers.

Drug versus Pharmaceutical

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, S7B Q&As, Q1.1

Note that the word “drug(s)” in the Q&As is used interchangeably with {the} word “pharmaceutical(s)” in ICH S7B

E

Early stage entities

M3(R2) Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals, 17

compounds with limited clinical experience (i.e., Phase II studies or less)
{See also: "Late stage entities"}

EDI Message

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

An EDI Message consists of a set of segments, structured using an agreed standard, prepared in a computer readable format and capable of being automatically and unambiguously processed.[EMA]

Efficacy versus Effectiveness

E2C(R2) Periodic Benefit-Risk Evaluation Report, 2.6

Because the terms are not harmonized across regions, the terms “efficacy/effectiveness” are used in this Guideline to clarify that information from both clinical trials and everyday medical practice are within the scope of the information on benefit to be included within the PBRER. In some regions, efficacy refers to evidence of benefit from controlled clinical trials while effectiveness implies use in everyday medical practice. Conversely, in other regions, this distinction is not made.

Electronic Data Interchange (EDI)

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

A technology for exchanging structured information for the purpose of conducting business transactions.[ICH M2]

Enabler

Q10 Pharmaceutical Quality System, Glossary

A tool or process which provides the means to achieve an objective. (ICH Q10)

Enantiomeric Impurity

Q3A(R2) Impurities in New Drug Substances, Glossary

A compound with the same molecular formula as the drug substance that differs in the spatial arrangement of atoms within the molecule and is a non-superimposable mirror image.

Enantiomers

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

Compounds with the same molecular formula as the drug substance, which differ in the spatial arrangement of atoms within the molecule and are nonsuperimposable mirror images.

Endogenous Virus

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Viral entity whose genome is part of the germ line of the species of origin of the cell line and is covalently integrated into the genome of animal from which the parental cell line was derived. For the purposes of this document, intentionally introduced, non-integrated viruses such as EBV used to immortalise cell substrates or Bovine Papilloma Virus fit in this category.
{See also "Virus"}

Endpoint Subset

S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines, Glossary

A set of individual animals within a dose group that are assigned to the same endpoint

Enhanced approach

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), 1

In an enhanced approach {to developing a drug substance}, risk management and scientific knowledge are used more extensively to identify and understand process parameters and unit operations that impact critical quality attributes (CQAs) and develop appropriate control strategies applicable over the lifecycle of the drug substance which may include the establishment of design space(s).
Traditional and enhanced approaches are not mutually exclusive. A company can use either a traditional approach or an enhanced approach to drug substance development, or a combination of both. {And see 3.1.3: "These concepts apply equally to the development of the drug substance manufacturing process. "}

Enhanced Pre- and Postnatal Development Study (ePPND)

S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines, Glossary

This study design is based on biopharmaceutical experience, often in non-human primates (NHP), and is a PPND study which includes elements of the embryofetal development (EFD) study in newborns and infants instead of the fetus.

Equivalence Trial

E9 Statistical Principles for Clinical Trials, Glossary

A trial with the primary objective of showing that the response to two or more treatments differs by an amount which is clinically unimportant. This is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence margin of clinically acceptable differences.

Essential Documents

E6(R2) Good Clinical Practice (GCP), Glossary

Documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced
(see 8. Essential Documents for the Conduct of a Clinical Trial).

Established Condition (EC)

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, 3.2.1

ECs are legally binding information considered necessary to assure product quality. As a consequence, any change to ECs necessitates a submission to the regulatory authority.

Established conditions (ECs)

Q14 Analytical Procedure Development, Glossary

ECs are legally binding information considered necessary to assure product quality. As a consequence, any change to ECs necessitates a submission to the regulatory authority. (ICH Q12)

Q2(R2) Validation of Analytical Procedures, Glossary

ECs are legally binding information considered necessary to assure product quality. As a consequence, any change to ECs necessitates a submission to the regulatory authority. (ICH Q12)

Estimand

E9(R1) Addendum: Statistical Principles for Clinical Trials, Glossary

A precise description of the treatment effect reflecting the clinical question posed by the trial objective. It summarises at a population-level what the outcomes would be in the same patients under different treatment conditions being compared.

Estimate

E9(R1) Addendum: Statistical Principles for Clinical Trials, Glossary

A numerical value computed by an estimator.

Estimator

E9(R1) Addendum: Statistical Principles for Clinical Trials, Glossary

A method of analysis to compute an estimate of the estimand using clinical trial data.

Ethnic Factors

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

The word ethnicity is derived from the Greek word “ethnos”, meaning nation or people. Ethnic factors are factors relating to races or large populations grouped according to common traits and customs. Note that this definition gives ethnicity, by virtue of its cultural as well as genetic implications, a broader meaning than racial. Ethnic factors may be classified as either intrinsic or extrinsic. (Appendix A)

{From: 1. Introduction} For the purposes of this document {i.e. E5(R1)}, ethnic factors are defined as those factors relating to the genetic and physiologic (intrinsic) and the cultural and environmental (extrinsic) characteristics of a population (Appendix A {Glossary}).

{See also: "Intrinsic ethnic factors", "Extrinsic ethnic factors"}

Evidence of risk

S7B The Non-Clinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals, 2.3.7

Evidence of risk is the overall conclusion from the integrated risk assessment for a test substance to delay ventricular repolarization and prolong QT interval in humans.

Excipient

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

Anything other than the drug substance in the dosage form.

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

A substance or compound, other than the active pharmaceutical ingredient and packaging materials, that is intended or designated to be used in the manufacture of a finished pharmaceutical product.

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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

Existing active pharmaceutical ingredient

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

An active pharmaceutical ingredient that is not considered a new active substance, which has been previously approved through a finished product by a stringent regulatory authority or by the World Health Organization, but requires the filing of a dossier. This would include, for example, new product dossiers and variations to multisource products.

Expert knowledge

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

In the context of this guideline, expert knowledge can be defined as a review of pre-existing data and the use of any other relevant information to evaluate the accuracy of an in silico model prediction for mutagenicity.

Expiration date

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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, and after which it must not be used.

Expiry date

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The date given on the individual container (usually on the label) of a product up to and including which the active pharmaceutical ingredient and finished pharmaceutical product are expected to remain within specifications if stored under the long-term conditions at which stability was established. It is set for each batch by adding the shelf life to the date of manufacture.

Expiry Date (or Expiration Date)

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The date placed on the container/labels of an Active Pharmaceutical Ingredient (API) designating the time during which the API is expected to remain within established shelf life specifications if stored under defined conditions, and after which it should not be used.
{See also ICH Q7 Q&As Question 14.2:} According to the definition, material should not be used after the expiry date. The original intent of this definition in ICH Q7 was that expired API should not be used in drug product formulation. It may be acceptable to reprocess [ICH Q7, Section 14.2] or rework [ICH Q7, Section 14.3] the expired API where the API manufacturer has all related historical GMP documentation and additional stability data on the reworked or reprocessed API. There may be registration/filing considerations that are beyond the scope of ICH Q7 in addition to the GMP considerations.

Exposure

M3(R2) Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals, 19

In this document "exposure" generally means group mean Area Under the Curve (AUC).

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

Exposure is represented by pharmacokinetic parameters demonstrating the local and systemic burden on the test species with the test compound and/or its metabolites. The area under the matrix level concentration-time curve (AUC) and/or the measurement of matrix concentrations at the expected peak-concentration time Cmax, or at some other selected time C(time),are the most commonly used parameters. Other parameters might be more appropriate in particular cases.

Exposure, 10% threshold for metabolites

M3(R2) Q&As (R2) Questions & Answers: Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals, Section 2. Q2

The 10% threshold refers to when a human metabolite comprises greater than 10% of the measured total exposure to drug and metabolites, usually based on group mean Area Under the Curve (AUC) (e.g., AUC 0-inf).

Exposure, 50-fold margin

M3(R2) Q&As (R2) Questions & Answers: Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals, Section 1. Q1

Generally, the exposure margins should be calculated using the group/cohort mean Area Under the Curve (AUC) values for animals at the highest dose tested and for humans at the anticipated therapeutic exposure. In some special cases, based on prior knowledge of the compound class, exposure limits based on Maximum Plasma Concentration (Cmax) might also be appropriate (e.g., if it is suspected that the drug could cause seizures).
Using the 50-fold approach, the high dose in the toxicity studies should be selected to produce a 50-fold exposure margin over the anticipated clinical exposure at the highest dose proposed for phase II and III studies; see exception for phase III trials in the United States (Section 1.5 of ICH M3(R2)) and answers to Question 2 and Question 3. For phase I clinical trials it is recognized that the therapeutic exposure generally will be exceeded and smaller margins are appropriate (for example, see answers to Question 2 and Question 3)

Expression Construct

Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products, Glossary

The expression vector which contains the coding sequence of the recombinant protein and the elements necessary for its expression.

Expression products

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, Glossary

Molecules such as RNA and protein, produced in the cells guided by the transferred genetic materials.

Extended Release

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

Products which are formulated to make the drug available over an extended period after administration.

Extraneous Contaminant

Q3A(R2) Impurities in New Drug Substances, Glossary

An impurity arising from any source extraneous to the manufacturing process.

Extrapolation of Foreign Clinical Data

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

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

Extrinsic Ethnic Factors

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

Extrinsic ethnic factors are factors associated with the environment and culture in which a person resides. Extrinsic factors tend to be less genetically and more culturally and behaviourally determined. 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.

{See also "Ethnic factors"}

F

Failure Mode Effects Analysis (FMEA)

Q9 Quality Risk Management, Annex I.2

FMEA (see IEC 60812) provides for an evaluation of potential failure modes for processes and their likely effect on outcomes and/or product performance. Once failure modes are established, risk reduction can be used to eliminate, contain, reduce or control the potential failures. FMEA relies on product and process understanding. FMEA methodically breaks down the analysis of complex processes into manageable steps. It is a powerful tool for summarizing the important modes of failure, factors causing these failures and the likely effects of these failures.

{Reference: IEC 60812 Analysis Techniques for system reliability—Procedures for failure mode and effects analysis (FMEA).} https://webstore.iec.ch/publication/26359

Q9(R1) EWG Quality Risk Management, Annex I.2

FMEA (see IEC 60812) provides for an evaluation of potential failure modes for processes and their likely effect on outcomes and/or product performance. Once failure modes are established, risk reduction can be used to eliminate, contain, reduce or control the potential failures. FMEA relies on product and process understanding. FMEA methodically breaks down the analysis of complex processes into manageable steps. It is a powerful tool for summarizing the important modes of failure, factors causing these failures and the likely effects of these failures.
{Reference: IEC 60812:2018 Failure modes and effects analysis (FMEA and FMECA). https://webstore.iec.ch/publication/26359

Failure Mode, Effects and Criticality Analysis (FMECA)

Q9 Quality Risk Management, Annex I.3

Failure Mode Effects Analysis (FMEA) might be extended to incorporate an investigation of the degree of severity of the consequences, their respective probabilities of occurrence, and their detectability, thereby becoming a Failure Mode Effect and Criticality Analysis (FMECA; see IEC 60812). In order for such an analysis to be performed, the product or process specifications should be established. FMECA can identify places where additional preventive actions might be appropriate to minimize risks.
{Reference: IEC 60812 Analysis Techniques for system reliability—Procedures for failure mode and effects analysis (FMEA).} https://webstore.iec.ch/publication/26359

Q9(R1) EWG Quality Risk Management, Annex I.3

Failure Mode Effects Analysis (FMEA) might be extended to incorporate an investigation of the degree of severity of the consequences, their respective probabilities of occurrence, and their detectability, thereby becoming a Failure Mode Effect and Criticality Analysis (FMECA; see IEC 60812). In order for such an analysis to be performed, the product or process specifications should be established. FMECA can identify places where additional preventive actions might be appropriate to minimize risks.
{Reference: IEC 60812:2018 Failure modes and effects analysis (FMEA and FMECA) https://webstore.iec.ch/publication/26359

Fault Tree Analysis (FTA)

Q9 Quality Risk Management, Annex I.4

The FTA tool (see IEC 61025) is an approach that assumes failure of the functionality of a product or process. This tool evaluates system (or sub-system) failures one at a time but can combine multiple causes of failure by identifying causal chains. The results are represented pictorially in the form of a tree of fault modes. At each level in the tree, combinations of fault modes are described with logical operators (AND, OR, etc.). FTA relies on the experts' process understanding to identify causal factors.
{Reference: IEC 61025 - Fault Tree Analysis (FTA).} https://webstore.iec.ch/publication/4311

Q9(R1) EWG Quality Risk Management, Annex I.4

The FTA tool (see IEC 61025) is an approach that assumes failure of the functionality of a product or process. This tool evaluates system (or sub-system) failures one at a time but can combine multiple causes of failure by identifying causal chains. The results are represented pictorially in the form of a tree of fault modes. At each level in the tree, combinations of fault modes are described with logical operators (AND, OR, etc.). FTA relies on the experts' process understanding to identify causal factors.
{Reference: IEC 61025 - Fault Tree Analysis (FTA).}

Feedback / Feedforward

Q10 Pharmaceutical Quality System, Glossary

Feedback: The modification or control of a process or system by its results or effects. Feedforward: The modification or control of a process using its anticipated results or effects. (Oxford Dictionary of English. Oxford University Press; 2003) Feedback/ feedforward can be applied technically in process control strategies and conceptually in quality management. (ICH Q10)

Finished pharmaceutical product

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

A product that has undergone all stages of production, including packaging in its final container and labelling. A finished pharmaceutical product may contain one or more active pharmaceutical ingredients.

Flanking Control Regions

Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products, Glossary

Non-coding nucleotide sequences that are adjacent to the 5' and 3' end of the coding sequence of the product which contain important elements that affect the transcription, translation, or stability of the coding sequence. These regions include, e.g., promoter, enhancer, and splicing sequences and do not include origins of replication and antibiotic resistance genes.

Forced degradation testing studies

Q1B Stability Testing : Photostability Testing of New Drug Substances and Products, Glossary

Forced degradation testing studies are those undertaken to degrade the sample deliberately. These studies, which may be undertaken in the development phase normally on the drug substances, are used to evaluate the overall photosensitivity of the material for method development purposes and/or degradation pathway elucidation.

Foreign Clinical Data

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

Foreign clinical data is defined as clinical data generated outside of the new region (i.e., in the foreign region).

Formal Experimental Design

Q8(R2) Pharmaceutical Development, Glossary (Part I)

A structured, organized method for determining the relationship between factors affecting a process and the output of that process. Also known as “Design of Experiments”.

Formal knowledge management system

Q8/9/10 Q&As (R4) Q8/Q9/Q10 - Implementation, Section 5, Q5

There is no added regulatory requirement for a formal knowledge management system. However it is expected that knowledge from different processes and systems will be appropriately utilised. Note: ‘formal’ means: it is a structured approach using a recognised methodology or (IT-) tool, executing and documenting something in a transparent and detailed manner.

Formal stability studies

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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 the shelf life of a drug product.

Forward Compatibility

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

Refers to converting v3.2.2 content into v4.0 references to achieve life cycle and document reuse. This includes all xml sources index.xml, stf.xml, and regional xml. {stf: Study Tagging File; xml: Extensible Markup Language}

Fostering

S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines, Glossary

The act of nurturing or offering parental care to offspring that are not genetically related. The fully fostering technique arbitrarily mixes up litters with the intent not to have dams with their genetic pups. The minimally fostering technique retains the natural litter as intact as possible, fostering only as necessary to achieve desired litter size and sex ratio.

Frameshift mutation

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

A mutation (change in the genetic code) in which one base or two adjacent bases are added to (inserted in) or deleted from the nucleotide sequence of a gene. This can lead to an altered or truncated protein.

Frequentist Methods

E9 Statistical Principles for Clinical Trials, Glossary

Statistical methods, such as significance tests and confidence intervals, which can be interpreted in terms of the frequency of certain outcomes occurring in hypothetical repeated realisations of the same experimental situation.

Full Analysis Set

E9 Statistical Principles for Clinical Trials, Glossary

The set of subjects that is as close as possible to the ideal implied by the intention-to- treat principle. It is derived from the set of all randomised subjects by minimal and justified elimination of subjects.

Full Validation

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Establishment of all validation parameters that ensure the integrity of the method when applied to sample analysis.

Fully automated reading method

E14 Q&As (R3) The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs, Q1.2

Fully automated reading methods rely entirely upon a computer algorithm for the placement of the fiducial points and the measurement of the ECG intervals.

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q1.2

Fully automated reading methods rely entirely upon a computer algorithm for the placement of the fiducial points and the measurement of the ECG intervals.

Fully manual reading method

E14 Q&As (R3) The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs, Q1.2

When using a fully manual reading technique, a human reader is responsible for examining the ECG waveform and placing the fiducial points to mark the beginning and the end of the intervals, without the assistance of a computer algorithm.

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q1.2

When using a fully manual reading technique, a human reader is responsible for examining the ECG waveform and placing the fiducial points to mark the beginning and the end of the intervals, without the assistance of a computer algorithm.

G

GD 0

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

The day on which positive evidence of mating is detected (e.g., sperm is found in the vaginal smear / vaginal plug in rodents, or observed mating in rabbits).

Gene mutation

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

Gene therapy (GT) products

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, Glossary

Therapeutic products that mediate their effect by the expression (transcription/translation) of transferred genetic materials, or by specifically altering the target genome of human cells. This definition is for the purpose of this guideline.

Gene transfer

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, Glossary

Delivery of therapeutic genetic material into the cells using vectors (e.g. transduction for viral vectors and transfection for plasmids).

Generalisability, Generalisation

E9 Statistical Principles for Clinical Trials, Glossary

The extent to which the findings of a clinical trial can be reliably extrapolated from the subjects who participated in the trial to a broader patient population and a broader range of clinical settings.

Genetic endpoint

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

Genomic biomarker

E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories, 2.1

A measurable DNA and/or RNA characteristic that is an indicator of normal biologic processes, pathogenic processes, and/or response to therapeutic or other interventions.

E16 Biomarkers Related to Drug or Biotechnology Product Development: Context, Structure and Format of Qualification Submissions, 1.2 (Footnote 1)

ICH E15 defines a genomic biomarker as a “measurable DNA and/or RNA characteristic that is an indicator of normal biologic processes, pathogenic processes, and/or response to therapeutic or other interventions”

E18 Genomic Sampling and Management of Genomic Data, 1.3 (Footnote 1)

ICH E15 defines a genomic biomarker as a “measurable DNA and/or RNA characteristic that is an indicator of normal biologic processes, pathogenic processes, and/or response to therapeutic or other interventions”.

Genotoxic Carcinogens

Q3C(R8) Guideline for Residual Solvents, Glossary

Carcinogens which produce cancer by affecting genes or chromosomes.

Genotoxicity

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

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

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

Genotoxicity tests

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, 1.4

Genotoxicity tests can be defined as in vitro and in vivo tests designed to detect compounds that induce genetic damage by various mechanisms. These tests enable hazard identification with respect to damage to DNA and its fixation. Fixation of damage to DNA in the form of gene mutations, larger scale chromosomal damage or recombination is generally considered to be essential for heritable effects and in the multi-step process of malignancy, a complex process in which genetic changes might possibly play only a part. Numerical chromosome changes have also been associated with tumorigenesis and can indicate a potential for aneuploidy in germ cells.
Compounds that are positive in tests that detect such kinds of damage have the potential to be human carcinogens and/or mutagens. Because the relationship between exposure to particular chemicals and carcinogenesis is established for humans, whilst a similar relationship has been difficult to prove for heritable diseases, genotoxicity tests have been used mainly for the prediction of carcinogenicity. Nevertheless, because germ line mutations are clearly associated with human disease, the suspicion that a compound might induce heritable effects is considered to be just as serious as the suspicion that a compound might induce cancer. In addition, the outcome of genotoxicity tests can be valuable for the interpretation of carcinogenicity studies.

Geriatric population

E7 Studies in Support of Special Populations: Geriatrics, IV

The geriatric population is arbitrarily defined, for the purpose of this guideline, as comprising patients aged 65 years or older.
It is important, however, to seek patients in the older age range, 75 and above, to the extent possible. Protocols should not ordinarily include arbitrary upper age cutoffs. It is also important not to exclude unnecessarily patients with concomitant illnesses; it is only by observing such patients that drug-disease interactions can be detected. The older the population likely to use the drug, the more important it is to include the very old.

Global Assessment Variable

E9 Statistical Principles for Clinical Trials, Glossary

A single variable, usually a scale of ordered categorical ratings, which integrates objective variables and the investigator's overall impression about the state or change in state of a subject.

Good Clinical Practice (GCP)

E6(R2) Good Clinical Practice (GCP), Glossary

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

Group Title

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

A sender-defined keyword that may be used to further organise content under a context group.

Grouped Submission

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

A grouped submission is defined as a regulatory activity that impacts multiple dossiers, based on regulatory requirements. Implementation of grouped submission functionality may vary region to region.

H

Harm

Q9 Quality Risk Management, Definitions

Damage to health, including the damage that can occur from loss of product quality or availability.

Q9(R1) EWG Quality Risk Management, Definitions

Damage to health, including the damage that can occur from loss of product quality or availability.

Hazard

Q9 Quality Risk Management, Definitions

The potential source of harm (ISO/IEC Guide 51).
{Reference: ISO/IEC Guide 51:1999 - Safety Aspects - Guideline for their inclusion in standards.}

Q9(R1) EWG Quality Risk Management, Definitions

The potential source of harm (ISO/IEC Guide 51).
{Reference: ISO/IEC Guide 51:2014 - Safety Aspects - Guideline for their inclusion in standards.}

Hazard Analysis and Critical Control Points (HACCP)

Q9 Quality Risk Management, Annex I.5

HACCP is a systematic, proactive, and preventive tool for assuring product quality, reliability, and safety (see WHO Technical Report Series No 908, 2003 Annex 7) {See link below}. It is a structured approach that applies technical and scientific principles to analyze, evaluate, prevent, and control the risk or adverse consequence(s) of hazard(s) due to the design, development, production, and use of products.
{WHO TRS 908 Annex 7: https://apps.who.int/iris/rest/bitstreams/50525/retrieve#page=109}

HACCP consists of the following seven steps:
(1) conduct a hazard analysis and identify preventive measures for each step of the process;
(2) determine the critical control points; (3) establish critical limits;
(4) establish a system to monitor the critical control points;
(5) establish the corrective action to be taken when monitoring indicates that the critical control points are not in a state of control;
(6) establish system to verify that the HACCP system is working effectively; (7) establish a record-keeping system.

Q9(R1) EWG Quality Risk Management, Annex I.5

HACCP is a systematic, proactive, and preventive tool for assuring product quality, reliability, and safety (see WHO Technical Report Series No 908, 2003 Annex 7) {see link below}. It is a structured approach that applies technical and scientific principles to analyze, evaluate, prevent, and control the risk or adverse consequence(s) of hazard(s) due to the design, development, production, and use of products.
{WHO TRS 908 Annex 7: https://apps.who.int/iris/rest/bitstreams/50525/retrieve#page=109}
HACCP consists of the following seven steps:
(1) conduct a hazard analysis and identify preventive measures for each step of the process;
(2) determine the critical control points;
(3) establish critical limits;
(4) establish a system to monitor the critical control points;
(5) establish the corrective action to be taken when monitoring indicates that the critical control points are not in a state of control;
(6) establish system to verify that the HACCP system is working effectively;
(7) establish a record-keeping system.

Hazard Identification

Q9(R1) EWG Quality Risk Management, Definitions

The systematic use of information to identify potential sources of harm (hazards) referring to the risk question or problem description.

Hazard Operability Analysis (HAZOP)

Q9 Quality Risk Management, Annex I.6

HAZOP (see IEC 61882) is based on a theory that assumes that risk events are caused by deviations from the design or operating intentions. It is a systematic brainstorming technique for identifying hazards using so-called “guide-words”. “Guide-words” (e.g., No, More, Other Than, Part of, etc.) are applied to relevant parameters (e.g., contamination, temperature) to help identify potential deviations from normal use or design intentions. It often uses a team of people with expertise covering the design of the process or product and its application.
{Reference: IEC 61882 - Hazard Operability Analysis (HAZOP). https://webstore.iec.ch/publication/24314

Q9(R1) EWG Quality Risk Management, Annex I.6

HAZOP (see IEC 61882) is based on a theory that assumes that risk events are caused by deviations from the design or operating intentions. It is a systematic brainstorming technique for identifying hazards using so-called “guide-words”. “Guide-words” (e.g., No, More, Other Than, Part of, etc.) are applied to relevant parameters (e.g., contamination, temperature) to help identify potential deviations from normal use or design intentions. It often uses a team of people with expertise covering the design of the process or product and its application.
IEC 61882:2016 - Hazard and operability studies (HAZOP studies) – Application guide.
https://webstore.iec.ch/publication/24314

Healthcare Professional

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

Person entrusted with the direct or indirect provision of defined healthcare services to a subject of care or a population of subjects of care[ENV 1613:1995] [ISO 21574-7] EXAMPLE Qualified medical practitioner, pharmacist, nurse, social worker, radiographer, medical secretary or clerk

E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting, 2.5

Healthcare professional is defined as a medically-qualified person such as a physician, dentist, pharmacist, nurse, coroner, or as otherwise specified by local regulations.

Herbal Products

Q3A(R2) Impurities in New Drug Substances, Glossary

Medicinal products containing, exclusively, plant material and/or vegetable drug preparations as active ingredients. In some traditions, materials of inorganic or animal origin can also be present.

Q3D(R2) Guideline for Elemental Impurities, Glossary

Medicinal products containing, exclusively, plant material and/or vegetable drug preparations as active ingredients. In some traditions, materials of inorganic or animal origin can also be present.

High clinical exposure

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q5.1

Exposure (Mean steady state maximum concentration, Cmax,ss) achieved when the maximum therapeutic dose is administered in the presence of the intrinsic or extrinsic factor (e.g. organ impairment, drug-drug interaction, food effect, etc.) that has the largest effect on increasing Cmax,ss

High pharmacological activity; high toxicity

Q7 Q&As Questions and Answers: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Q4.1

While ICH Q7 does not define high pharmacological activity or toxicity, these are generally determined by evaluating relevant animal and human data collected during research and development. Important considerations in this evaluation of pharmacological activity or toxicity may include Occupational Exposure Limit (OEL), Permitted Daily Exposure (PDE), Acceptable Daily Exposure (ADE), Threshold for Toxicological Concerns (TTC), No Observed Adverse Effect Level (NOAEL) [ICH S Guidelines, ICH E2E, Section 2.1.1], and the consequences of cross-contamination [ICH Q9, Section 4.3].

Highest Non-Severely Toxic Dose (HNSTD)

S9 Nonclinical Evaluation for Anticancer Pharmaceuticals, 5

The HNSTD is defined as the highest dose level that does not produce evidence of lethality, life-threatening toxicities or irreversible findings.

Highly effective methods of birth control

M3(R2) Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals, 19

Those, alone or in combination, that result in a low failure rate (i.e., less than 1% per year) when used consistently and correctly.

Highly Water Soluble Drugs

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

Drugs with a dose/solubility volume of less than or equal to 250 mL over a pH range of 1.2 to 6.8. (Example: Compound A has as its lowest solubility at 37± 0.5°C, 1.0 mg/mL at pH 6.8, and is available in 100 mg, 200 mg, and 400 mg strengths. This drug would be considered a low solubility drug as its dose/solubility volume is greater than 250 mL (400 mg/1.0 mg/mL = 400 mL).

Hook Effect

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Suppression of response due to very high concentrations of a particular analyte. A hook effect may occur in ligand binding assays (LBAs) that use a liquid-phase reaction step for incubating the binding reagents with the analyte. Also referred to as prozone effect.

Host cells

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

See Parental cells.

I

ICH Regions

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

European Union, Japan, The United States of America.

Identifiability

E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting, 5.1

{Assessing Patient and Reporter Identifiability} The term identifiable in this context refers to the verification of the existence of a patient and a reporter.
Local data privacy laws regarding patient and reporter identifiability might apply.
One or more of the following should automatically qualify a patient as identifiable: age (or age category, e.g., adolescent, adult, elderly), gender, initials, date of birth, name, or patient identification number. In addition, in the event of second-hand reports, every reasonable effort should be made to verify the existence of an identifiable patient and reporter.

Identification Threshold

Q3A(R2) Impurities in New Drug Substances, Glossary

A limit above (>) which an impurity should be identified.

Q3B(R2) Impurities in New Drug Products, Glossary

A limit above (>) which a degradation product should be identified.

Identified data and samples

E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories, 2.3.1

Identified data and samples are labelled with personal identifiers such as name or identification numbers (e.g., social security or national insurance number).

Identified Degradation Product

Q3B(R2) Impurities in New Drug Products, Glossary

A degradation product for which a structural characterisation has been achieved.

Identified Impurity

Q3A(R2) Impurities in New Drug Substances, Glossary

An impurity for which a structural characterisation has been achieved.

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

An impurity for which a structural characterization has been achieved.

Identified risk

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

An untoward occurrence for which there is adequate evidence of an association with the medicinal product of interest.

Examples of identified risks include:

* an adverse reaction adequately demonstrated in non- clinical studies and confirmed by clinical data;
* an adverse reaction observed in well designed clinical trials or epidemiological studies for which the magnitude of the difference compared with the comparator group (placebo or active substance) on a parameter of interest suggests a causal relationship; and
* an adverse reaction suggested by a number of well documented spontaneous reports where causality is strongly supported by temporal relationship and biological plausibility, such as anaphylactic reactions or application site reactions

{Source:} ICH Guideline E2F

E2F Development Safety Update Report, Glossary

An untoward occurrence for which there is adequate evidence of an association with the medicinal product of interest. Examples of identified risks include:

* an adverse reaction adequately demonstrated in non-clinical studies and confirmed by clinical data;
* an adverse reaction observed in well-designed clinical trials or epidemiological studies for which the magnitude of the difference compared with the comparator group (placebo or active substance) on a parameter of interest suggests a causal relationship;
* an adverse reaction suggested by a number of well-documented spontaneous reports where causality is strongly supported by temporal relationship and biological plausibility, such as anaphylactic reactions or application site reactions

Immediate (primary) pack

Q1B Stability Testing : Photostability Testing of New Drug Substances and Products, Glossary

Immediate (primary) pack is that constituent of the packaging that is in direct contact with the drug substance or drug product, and includes any appropriate label.

Immediate Release

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

Allows the drug to dissolve in the gastrointestinal contents, with no intention of delaying or prolonging the dissolution or absorption of the drug.

Immunotoxicity

S8 Immunotoxicity Studies for Human Pharmaceuticals, 1.1

Immunotoxicity is, for the purpose of this guideline, defined as unintended immunosuppression or enhancement. Drug-induced hypersensitivity and autoimmunity are excluded.

Impartial Witness

E6(R2) Good Clinical Practice (GCP), Glossary

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

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

Containers that provide a permanent barrier to the passage of gases or solvents, e.g. sealed aluminium tubes for semisolids, sealed glass ampoules for solutions and aluminium/aluminium blisters for solid dosage forms (refer to 2.2.7.2).

Important identified risk, important potential risk

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

An identified risk or potential risk that could impact on the risk-benefit profile of the product or have implications for public health. What constitutes an important risk will depend upon several factors, including the impact on the individual, the seriousness of the risk, and the impact on public health. Normally, any risk that is likely to be included in the contraindications or warnings and precautions section of the product labelling should be considered important.
{Source:} ICH Guideline E2C(R2)

Important identified risk; important potential risk

E2F Development Safety Update Report, Glossary

An identified risk or potential risk that could have an impact on the risk-benefit balance of the product or have implications for public health.
{Source: } Volume 9A Rules Governing Medicinal Products in the EU

Important missing information

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

Critical gaps in knowledge for specific safety issues or populations that use the marketed product.
{Source:} ICH Guideline E2C(R2)

Important protocol deviations

E3 Q&As (R1) Questions & Answers: Structure and Content of Clinical Study Reports, Q7

Important protocol deviations are a subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being. For example, important protocol deviations may include enrolling subjects in violation of key eligibility criteria designed to ensure a specific subject population or failing to collect data necessary to interpret primary endpoints, as this may compromise the scientific value of the trial. Protocol violation and important protocol deviation are sometimes used interchangeably to refer to a significant departure from protocol requirements. The word “violation” may also have other meanings in a regulatory context. However, in Annex IVa, Subject Disposition of the ICH E3 Guideline, the term protocol violation was intended to mean only a change, divergence, or departure from the study requirements, whether by the subject or investigator, that resulted in a subject’s withdrawal from study participation. (Whether such subjects should be included in the study analysis is a separate question.)

Impurity

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

Any component of the drug substance or drug product that is not the drug substance or an excipient.

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

See ICH Q3A, ICH Q6A and ICH Q6B.

Q3A(R2) Impurities in New Drug Substances, Glossary

Any component of the new drug substance that is not the chemical entity defined as the new drug substance.

Q3B(R2) Impurities in New Drug Products, Glossary

Any component of the new drug product that is not the drug substance or an excipient in the drug product.

Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products, Glossary

Any component of the drug substance (bulk material) or drug product (final container product) which is not the chemical entity defined as the drug substance, an excipient, or other additives to the drug product.

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

(1) Any component of the new drug substance which is not the chemical entity defined as the new drug substance. (2) Any component of the drug product which is not the chemical entity defined as the drug substance or an excipient in the drug product.

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Any component present in the intermediate or Active Pharmaceutical Ingredient (API) that is not the desired entity.

Impurity Profile

Q3A(R2) Impurities in New Drug Substances, Glossary

A description of the identified and unidentified impurities present in a new drug substance.

Q3B(R2) Impurities in New Drug Products, Glossary

A description of the identified and unidentified impurities present in a drug product.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A description of the identified and unidentified impurities present in an Active Pharmaceutical Ingredient (API).

In Vitro Cell Age

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

A measure of the period between thawing of the MCB vial(s) and harvest of the production vessel measured by elapsed chronological time in culture, population doubling level of the cells or passage level of the cells when subcultivated by a defined procedure for dilution of the culture.

Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products, Glossary

Measure of time between thaw of the MCB vial(s) to harvest of the production vessel measured by elapsed chronological time in culture, by population doubling level of the cells, or by passage level of the cells when subcultivated by a defined procedure for dilution of the culture.

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

Measure of time between thaw of the Master Cell Bank (MCB) vial(s) to harvest of the production vessel measured by elapsed chronological time, by population doubling level of the cells, or by passage level of the cells when subcultivated by a defined procedure for dilution of the culture.

Inactivation

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Reduction of virus infectivity caused by chemical or physical modification.

Incurred Sample

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A sample obtained from study subjects or animals.

Incurred Sample Reanalysis (ISR)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Reanalysis of a portion of the incurred samples in a separate analytical run on a different day to determine whether the original analytical results are reproducible.

Independent {quality unit, from production}

Q7 Q&As Questions and Answers: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Q2.1

The intent of the term 'independent' is to prevent any conflict of interest and ensure unbiased decision-making regarding quality-related decisions in the organisation structure. The person in the quality unit who is responsible for final decision-making (e.g., batch release decision) should not have responsibilities for production activities [ICH Q7, Section 2.13]

Independent Data Monitoring Committee (IDMC) (Data and SafetyMonitoring Board, Monitoring Committee, Data Monitoring Committee)

E9 Statistical Principles for Clinical Trials, Glossary

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.

Independent Data-Monitoring Committee (IDMC) (Data and Safety Monitoring Board, Monitoring Committee, Data Monitoring Committee)

E6(R2) Good Clinical Practice (GCP), Glossary

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.

Independent Ethics Committee (IEC)

E6(R2) Good Clinical Practice (GCP), Glossary

An independent body (a review board or a committee, institutional, regional, national, or supranational), constituted of medical professionals and non-medical members, whose responsibility it 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 trial subjects.
The legal status, composition, function, operations and regulatory requirements pertaining to Independent Ethics Committees may differ among countries, but should allow the Independent Ethics Committee to act in agreement with GCP as described in this guideline.

Independent sample

Q14 Analytical Procedure Development, Multivariate glossary

Independent samples are samples not included in the calibration set of a multivariate model.
Independent samples can come from the same batch from which calibration samples are selected. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

Independent samples are samples not included in the calibration set of a multivariate model.
Independent samples can come from the same batch from which calibration samples are selected. (ICH Q2)

Index drugs

M12 EWG Drug Interaction Studies , 3.1.2

'Perpetrators' (inhibitors or inducers) and substrates ('victims') with well-understood and predictable pharmacokinetic and DDI properties with regard to level of inhibition, induction, or metabolic pathway are known as “index drugs”.

Indirect Phototoxicity

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

Phototoxicity due to cellular, biochemical or physiological alterations caused by the drug or excipient, but not related to photochemical reactivity of the drug or excipient (e.g., perturbation of heme homeostasis).

Individual Case Safety Report

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

The complete information provided by a reporter at a certain point in time to describe an event or incident of interest. The report can include information about a case involving one subject or a group of subjects. [27953 Human Pharmaceutical Reporting]

Information

E6(R3) EWG Good Clinical Practice (GCP) - Draft principles, Draft principles; Footnote 1

For the purpose of this guideline, the term “information” reflects meaningful organization and processing of data and documentation

{See also "Data" and "Results"}

Informed Consent

E6(R2) Good Clinical Practice (GCP), Glossary

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.

Inhalation Unit Risk

Q3D(R2) Guideline for Elemental Impurities, Glossary

The upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/L in water, or 1 µg/m3 in air. The interpretation of inhalation unit risk would be as follows if unit risk = 2 x 10-6 per µg/L, 2 excess cancer cases (upper bound estimate) are expected to develop per 1,000,000 people if exposed daily for a lifetime to 1 µg of the chemical in 1 liter of drinking water. (US Environmental Protection Agency)

In-house Primary Reference Material

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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

In-house Working Reference Material

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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.

Innovation

Q10 Pharmaceutical Quality System, Glossary

The introduction of new technologies or methodologies. (ICH Q10)

In-Process Control (or Process Control)

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Checks performed during production in order to monitor and, if appropriate, to adjust the process and/or to ensure that the intermediate or Active Pharmaceutical Ingredient (API) conforms to its specifications.

In-process tests

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

Tests which may be performed during the manufacture of either the drug substance or drug product, rather than as part of the formal battery of tests which are conducted prior to release.

Inspection

E6(R2) Good Clinical Practice (GCP), Glossary

The act by a regulatory authority(ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority(ies) to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organization’s (CRO’s) facilities, or at other establishments deemed appropriate by the regulatory authority(ies).

Institution (medical)

E6(R2) Good Clinical Practice (GCP), Glossary

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

Institutional Review Board (IRB)

E6(R2) Good Clinical Practice (GCP), Glossary

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.

Integrated risk assessment

S7B The Non-Clinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals, 2.3.6

The integrated risk assessment is the evaluation of non-clinical study results including the results from follow-up studies and other relevant information. The integrated risk assessment should be scientifically based and individualized for the test substance.

Integration Site

Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products, Glossary

The site where one or more copies of the expression construct is integrated into the host cell genome.

Intention-To-Treat Principle

E9 Statistical Principles for Clinical Trials, Glossary

The principle that asserts that the effect of a treatment policy can be best assessed by evaluating on the basis of the intention to treat a subject (i.e. the planned treatment regimen) rather than the actual treatment given. It has the consequence that subjects allocated to a treatment group should be followed up, assessed and analysed as members of that group irrespective of their compliance to the planned course of treatment.

Interaction (Qualitative & Quantitative)

E9 Statistical Principles for Clinical Trials, Glossary

The situation in which a treatment contrast (e.g. difference between investigational product and control) is dependent on another factor (e.g. centre). A quantitative interaction refers to the case where the magnitude of the contrast differs at the different levels of the factor, whereas for a qualitative interaction the direction of the contrast differs for at least one level of the factor.

Interchangeable

Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions, Glossary

Where such status is indicated, any of the official texts from JP, EP, or USP can be substituted one for the other (appropriately referenced) in the ICH regions for purposes of the pharmaceutical registration/approval process. Using any of the interchangeable methods, an analyst will reach the same accept or reject decisions irrespective of which PDG pharmacopeia is used.

Q4B FAQs Frequently Asked Questions: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions, 4

A status of "interchangeable" in the Q4B Annex means that any of the official texts from JP, Ph. Eur., or USP can be substituted one for the other (appropriately referenced) in the ICH regions for purposes of the pharmaceutical registration/approval process. Using any of the interchangeable methods, an analyst will reach the same accept or reject decisions irrespective of which Pharmacopoeial Discussion Group (PDG) pharmacopoeia is used.

Intercurrent Events

E9(R1) Addendum: Statistical Principles for Clinical Trials, Glossary

Events occurring after treatment initiation that affect either the interpretation or the existence of the measurements associated with the clinical question of interest. It is necessary to address intercurrent events when describing the clinical question of interest in order to precisely define the treatment effect that is to be estimated.

Interfering Substance

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A substance that is present in the matrix that may affect the quantification of an analyte.

Interim Analysis

E9 Statistical Principles for Clinical Trials, Glossary

Any analysis intended to compare treatment arms with respect to efficacy or safety at any time prior to the formal completion of a trial.

Interim Clinical Trial/Study Report

E6(R2) Good Clinical Practice (GCP), Glossary

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

Intermediate

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

See ICH Q7, ICH Q3A, and ICH Q5C.

Q3A(R2) Impurities in New Drug Substances, Glossary

A material produced during steps of the synthesis of a new drug substance that undergoes further chemical transformation before it becomes a new drug substance.

Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products, Glossary

For biotechnological/biological products, a material produced during a manufacturing process which is not the drug substance or the drug product but whose manufacture is critical to the successful production of the drug substance or the drug product. Generally, an intermediate will be quantifiable and specifications will be established to determine the successful completion of the manufacturing step prior to continuation of the manufacturing process. This includes material which may undergo further molecular modification or be held for an extended period of time prior to further processing.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A material produced during steps of the processing of an Active Pharmaceutical Ingredient (API) that undergoes further molecular change or purification before it becomes an API. Intermediates may or may not be isolated. (Note: this Guide only addresses those intermediates produced after the point that the company has defined as the point at which the production of the API begins.)

Intermediate precision

Q14 Analytical Procedure Development, Glossary

Intermediate precision expresses within-laboratories variations. Factors to be considered should include potential sources of variability, for example, different days, different environmental conditions, different analysts and different equipment. (ICH Q2)

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

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

Q2(R2) Validation of Analytical Procedures, Glossary

Intermediate precision expresses within-laboratories variations. Factors to be considered should include potential sources of variability, for example, different days, different environmental conditions, different analysts and different equipment. (ICH Q2)

Intermediate testing

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

Studies conducted at 30°C/65% RH and designed to moderately increase the rate of chemical degradation or physical changes for a drug substance or drug product intended to be stored long term at 25°C.

Internal Standard (IS)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A structurally similar analogue or stable isotope labelled compound added to calibration standards, quality control samples (QCs) and study samples at a known and constant concentration to facilitate quantification of the target analyte.

Internal test set

Q14 Analytical Procedure Development, Multivariate glossary

A set of data obtained from samples that have physical and chemical characteristics that span a range of variabilities similar to the samples used to construct the calibration set. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

A set of data obtained from samples that have physical and chemical characteristics that span a range of variabilities similar to the samples used to construct the calibration set. (ICH Q14)

Internal testing

Q14 Analytical Procedure Development, Multivariate glossary

Internal testing is a process of checking if unique samples processed by the model yield the correct predictions (qualitative or quantitative). Internal testing serves as means to establish the optimal number of latent variables, estimate the standard error and detect potential outliers. Internal testing is preferably done by using samples not included in the calibration set. Alternatively, internal testing can be done using a subset of calibration samples, while temporarily excluding them from the model calculation. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

Internal testing is a process of checking if unique samples processed by the model yield the correct predictions (qualitative or quantitative). Internal testing serves as means to establish the optimal number of latent variables, estimate the standard error and detect potential outliers. Internal testing is preferably done by using samples not included in the calibration set. Alternatively, internal testing can be done using a subset of calibration samples, while temporarily excluding them from the model calculation. (ICH Q2)

International Birth Date (IBD)

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

The date of the first marketing authorisation for any product containing the active substance granted to any company in any country in the world.

{Source:} ICH Guideline E2C

Inter-Rater Reliability

E9 Statistical Principles for Clinical Trials, Glossary

The property of yielding equivalent results when used by different raters on different occasions.

Interventional clinical trial

E2F Development Safety Update Report, Glossary

An interventional clinical trial is any research study that prospectively assigns people to one or more health-related interventions (e.g., preventive care, drugs, surgical procedures, behavioural treatments, etc.) to evaluate their effects on health-related outcomes.

{Source: } CIOMS VII

Intra-Rater Reliability

E9 Statistical Principles for Clinical Trials, Glossary

The property of yielding equivalent results when used by the same rater on different occasions.

Intrinsic Ethnic Factors

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

Intrinsic ethnic factors are 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.

{See also "Ethnic factors"}

In-use period

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

A period of time during which a reconstituted preparation of the finished dosage form in a multidose container, or a moisture-sensitive product in a large-format final container (e.g. high-density polyethylene (HDPE) bottles of 500) can be used after opening.

Investigational drug

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

The term investigational drug is used in this Guideline to indicate only the experimental product under study or development. Note: This term is more specific than “investigational medicinal product,” which includes comparators and placebos.

{Source:} ICH Guideline E2F

E2F Development Safety Update Report, Glossary

The term investigational drug is used in this guideline to indicate only the experimental product under study or development.
Note: This term is more specific than “investigational medicinal product” which includes comparators and placebos.
{Source: } CIOMS VII

Investigational Product

E6(R2) Good Clinical Practice (GCP), Glossary

A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization 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

E6(R2) Good Clinical Practice (GCP), Glossary

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

Investigator/Institution

E6(R2) Good Clinical Practice (GCP), Glossary

An expression meaning "the investigator and/or institution, where required by the applicable regulatory requirements".

Investigator's Brochure

E6(R2) Good Clinical Practice (GCP), Glossary

A compilation of the clinical and nonclinical data on the investigational product(s) which is relevant to the study of the investigational product(s) in human subjects
(see 7. Investigator’s Brochure).

Irradiance

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

The intensity of UV or visible light incident on a surface, measured in W/m2 or mW/cm2.

Irradiation

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

The process by which an object/subject is exposed to UV or visible radiation.

J

Juvenile Animal

S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines, Glossary

An animal in any postnatal stage not fully matured in terms of organ or system morphology and function.

Juvenile Animal Study (JAS)

S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines, Glossary

A nonclinical safety study typically conducted with the objective to provide an assessment of the toxicity profile of a pharmaceutical in juvenile animals.

K

Knowledge Management

Q10 Pharmaceutical Quality System, Glossary

Systematic approach to acquiring, analysing, storing, and disseminating information related to products, manufacturing processes and components. (ICH Q10)

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Appendix 2, Section on "Use of Knowledge in Change Management"

An effective change management system includes active knowledge management, in which information from multiple sources is integrated to identify stimuli for changes needed to improve product and/or process robustness.

Q14 Analytical Procedure Development, Glossary

A systematic approach to acquiring, analysing, storing and disseminating information related to products, manufacturing processes and components. (ICH Q10)

Q2(R2) Validation of Analytical Procedures, Glossary

A systematic approach to acquiring, analysing, storing and disseminating information related to products, manufacturing processes and components. (ICH Q10)

L

Largest time-matched mean difference between drug and placebo (baseline-adjusted)

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q4.1

Regardless of the study design, "the largest time-matched mean difference between drug and placebo (baseline-adjusted)" is determined as follows: The mean QTc for the drug (i.e., averaged across the study population) is compared to the mean QTc for placebo (averaged across the study population) at each time point. The "largest time-matched mean difference between drug and placebo" is the largest of these differences at any time point.

The term "baseline-adjusted" in ICH E14 implies that the baseline data are taken into account in the statistical analysis.

Late stage entities

M3(R2) Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals, 17

Compounds with significant clinical experience (i.e., from Phase III studies and/ or post marketing) {See also: "Early stage entities"}

Latent variables

Q14 Analytical Procedure Development, Multivariate glossary

Mathematically derived variables that are directly related to measured variables and are used in further processing. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

Mathematically derived variables that are directly related to measured variables and are used in further processing. (ICH Q2)

Legally Acceptable Representative

E6(R2) Good Clinical Practice (GCP), Glossary

An individual or juridical or other body authorized under applicable law to consent, on behalf of a prospective subject, to the subject's participation in the clinical trial.

Lifecycle

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

All phases in the life of a product from the initial development through marketing until the product's discontinuation. (ICH Q8)

Q8(R2) Pharmaceutical Development, Glossary (Part I)

All phases in the life of a product from the initial development through marketing until the product's discontinuation.

Q8(R2) Pharmaceutical Development, Glossary (Part II)

All phases in the life of a product from the initial development through marketing until the product's discontinuation (ICH Q8).

Ligand

Q3A(R2) Impurities in New Drug Substances, Glossary

An agent with a strong affinity to a metal ion.

Ligand Binding Assay (LBA)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A method to analyse an analyte of interest using reagents that specifically bind to the analyte. The analyte is detected using reagents labelled with e.g., an enzyme, radioisotope, fluorophore or chromophore. Reactions are carried out in microtitre plates, test tubes, disks, etc.

Limit of Quantitation (LoQ)

Q3D(R2) Guideline for Elemental Impurities, Glossary

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 for the determination of impurities and/or degradation products. (ICH Q2)

Linearity

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

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 testing

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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

Long-term stability studies

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

Experiments on the physical, chemical, biological, biopharmaceutical and microbiological characteristics of an active pharmaceutical ingredient or finished pharmaceutical product, during and beyond the expected shelf life and storage periods of samples under the storage conditions expected in the intended market. The results are used to establish the retest period or the shelf life, to confirm the projected retest period and shelf life, and to recommend storage conditions.

Lot

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

{See "Batch (for Reference Standards and Reagents)"}

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

See Batch

Lot Number

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

See Batch Number

Lower Limit of Quantification (LLOQ)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The lowest amount of an analyte in a sample that can be quantitatively determined using a method with predefined precision and accuracy.

Lowest-Observed Effect Level (LOEL)

Q3C(R8) Guideline for Residual Solvents, Glossary

The lowest dose of substance in a study or group of studies that produces biologically significant increases in frequency or severity of any effects in the exposed humans or animals.

Lowest-Observed-Adverse-Effect Level (LOAEL)

Q3D(R2) Guideline for Elemental Impurities, Glossary

Lowest concentration or amount of a substance (dose), found by experiment or observation, that causes an adverse effect on morphology, functional capacity, growth, development, or life span of a target organism distinguishable from normal (control) organisms of the same species and strain under defined conditions of exposure. (International Programme for Chemical Safety, IUPAC)

Lowest-Observed-Effect Level (LOEL)

Q3D(R2) Guideline for Elemental Impurities, Glossary

The lowest dose of substance in a study or group of studies that produces biologically significant increases in frequency or severity of any effects in the exposed humans or animals.

M

Malformation

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

Permanent structural deviation that generally is incompatible with or severely detrimental to normal development or survival.

Manual Adjudication (Manual Over-Read/Computer-Assisted/Semi-Automated)

E14 Q&As (R3) The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs, Q1.2

The manual adjudication approach refers to reading methods in which a computer algorithm is responsible for the initial placement of the fiducial points on the ECG waveform. A human reader subsequently reviews the algorithmic placement of the fiducial points, performing adjustments wherever the computerized measurements are considered to be inaccurate.

Manual Adjudication (Manual Over-Read/Computer-Assisted/Semi-Automated)

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q1.2

The manual adjudication approach refers to reading methods in which a computer algorithm is responsible for the initial placement of the fiducial points on the ECG waveform. A human reader subsequently reviews the algorithmic placement of the fiducial points, performing adjustments wherever the computerized measurements are considered to be inaccurate.

Manufacture

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

All operations of receipt of materials, production, packaging, repackaging, labelling, relabelling, quality control, release, storage, and distribution of Active Pharmaceutical Ingredients (APIs) and related controls.

{Q7 Q&As, Question 16.2:} Related controls' include any activities or services necessary to support production (e.g., maintenance, calibration, etc.). ICH Q7 applies to any activities performed by the original manufacturer or the company that is performing the activity on behalf of the original manufacturer.

Manufacturer

Q5E Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process, 1.2 Footnote 1

For convenience, when the term "manufacturer" is used, it is intended to include any third party having a contractual arrangement to produce the intermediates, drug substance, or drug product on behalf of the marketing authorisation holder (or the developer, if prior to market authorisation).

Manufacturing process(es)

Q5E Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process, 1.2 Footnote 2

For convenience, when the term "manufacturing process(es)" is used, it also includes facilities and equipment that might impact on critical processing parameters and, thereby, on product quality.

Manufacturing Scale Production

Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products, Glossary

Manufacture at the scale typically encountered in a facility intended for product production for marketing.

Marketing Authorisation Holder

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

An organisation, usually a biopharmaceutical firm, that holds a valid marketing authorisation for a medicinal product delivered by the Health Authority of a country.

Marketing pack

Q1B Stability Testing : Photostability Testing of New Drug Substances and Products, Glossary

Marketing pack is the combination of immediate pack and other secondary packaging such as a carton.

Mass balance

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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)

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

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

Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products, Glossary

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

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

An aliquot of a single pool of cells which generally has been prepared from the selected cell clone under defined conditions, dispensed into multiple containers and stored under defined conditions. 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 Working Cell Bank (WCB)) should be the same as for the MCB unless justified.

Material

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A general term used to denote raw materials (starting materials, reagents, solvents), process aids, intermediates, Active Pharmaceutical Ingredients (APIs) and packaging and labelling materials.

Material Traceability

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

The ability to track the distribution of materials throughout the manufacturing process.

Matrix

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

Blood, plasma, urine, serum or other fluid or tissue selected for assay.

Matrix Effect

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The direct or indirect alteration or interference in response due to the presence of unintended analytes or other interfering substances in the sample.

Matrixing

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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.

Q1D Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products, 2.4

As defined in the glossary of the parent guideline, matrixing is the design of a stability schedule such that a selected subset of the total number of possible samples for all factor combinations would be tested at a specified time point. At a subsequent time point, another subset of samples for all factor combinations would be 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.
{Parent guideline: Q1A}

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

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 finished pharmaceutical 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 (refer to ICH Q1D).

Maximally tolerated dose (MTD)

S1C(R2) Dose Selection for Carcinogenicity Studies of Pharmaceuticals, 1

The following definition of the MTD is considered consistent with those published previously by international regulatory authorities (Note 1): The top dose or maximum tolerated dose is that which is predicted to produce a minimum toxic effect over the course of the carcinogenicity study. Such an effect can be predicted from a 90-day dose range-finding study in which minimal toxicity is observed. Factors to consider are alterations in physiological function which would be predicted to alter the animal's normal life span or interfere with interpretation of the study. Such factors include: no more than 10% decrease in body weight gain relative to controls; target organ toxicity; significant alterations in clinical pathological parameters.

{The terms 'Maximum tolerated dose' and 'Maximally tolerated dose' appear to be used interchangeably in S1C(R2); see Section 3. Notes, Note 1: "This dose, sometimes called the maximum tolerated dose (MTD), ….."}

Mean kinetic temperature

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

A single derived temperature that, if maintained over a defined period of time, affords the same thermal challenge to a drug substance or drug product as would be experienced over a range of both higher and lower temperatures for an equivalent defined period. The mean kinetic temperature is higher than the arithmetic mean temperature and takes into account the Arrhenius equation. When establishing the mean kinetic temperature for a defined period, the formula of J. D. Haynes (J. Pharm. Sci., 60:927-929, 1971) can be used.

Mean Photo Effect (MPE)

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

The Mean Photo Effect (MPE) is calculated for results of the 3T3 NRU-PT. The MPE is based on comparison of the complete concentration response curves (see Organisation for Economic Co-operation and Development, Test Guideline (OECD TG) 432).

Medical Dictionary for Regulatory Activities

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

Medical Dictionary for Regulatory Activities (MedDRA) terminology for adverse event reporting used globally by the biopharmaceutical industry and regulators to promote consistent reporting and data analysis.

Medicinal Product

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

Any substance or combination of substances presented as having properties for treating or preventing disease in human beings;
Any substance or combination of substances which might be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.[ISO 11615]
Any substance or combination of substances which might be administered to human beings or animals for treating or preventing disease, with the view to making medical diagnosis or to restore, correct or modify physiological functions [ENV 13607] [Directive 65/65/EEC, modified]

Meta-Analysis

E9 Statistical Principles for Clinical Trials, Glossary

The formal evaluation of the quantitative evidence from two or more trials bearing on the same question. This most commonly involves the statistical combination of summary statistics from the various trials, but the term is sometimes also used to refer to the combination of the raw data.

Metazoan

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

Organism of multicellular animal nature.

Method operable design region (modr)

Q14 Analytical Procedure Development, Glossary

A combination of analytical procedure parameter ranges within which the analytical procedure performance criteria are fulfilled and the quality of the measured result is assured. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

A combination of analytical procedure parameter ranges within which the analytical procedure performance criteria are fulfilled and the quality of the measured result is assured. (ICH Q14)

Micronucleus

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Particle in a cell that contains nuclear DNA; it might contain a whole chromosome(s) or a broken centric or acentric part(s) of chromosome(s).

Microsampling

S3A Q&As Questions and Answers: Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure - Focus on Microsampling, 1.1 (Q1)

For the purpose of this document, microsampling is a method to collect a very small amount of blood (typically ≤50 µL) that is generally used to measure concentrations of a drug and/or its metabolites, and subsequently calculate the appropriate TK parameters. The appropriate matrices used for microsampling techniques include blood and its derived plasma or serum, which can be used in liquid or dried form for transportation, storage and subsequent analysis. Microsampling for TKs can be used in rodents and non-rodents. Microsampling in non-blood derived matrices is outside the scope of this Q&As document.

Minimal Risk Level (MRL)

Q3D(R2) Guideline for Elemental Impurities, Glossary

An estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk. (ATSDR)

Minimum Exposure Time

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

The shortest period for which a treatment step will be maintained.

Minimum Required Dilution (MRD)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The initial dilution factor by which biological samples are diluted with buffer solution for the analysis by ligand binding assays (LBAs). The MRD may not necessarily be the ultimate dilution but should be identical for all samples including calibration standards and quality control samples (QCs). However, samples may require further dilution.

Missing Data

E9(R1) Addendum: Statistical Principles for Clinical Trials, Glossary

Data that would be meaningful for the analysis of a given estimand but were not collected. They should be distinguished from data that do not exist or data that are not considered meaningful because of an intercurrent event.

Mitotic index

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

Model Maintenance

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

A set of planned activities over the product lifecycle to monitor and sustain the model's performance to continually ensure its suitability for the intended and approved purpose.

Q14 Analytical Procedure Development, Multivariate glossary

Safeguards over the lifecycle of a multivariate model to ensure continued model performance, often including outlier diagnostics and resulting actions for model redevelopment or change in the maintenance plans. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

Safeguards over the lifecycle of a multivariate model to ensure continued model performance, often including outlier diagnostics and resulting actions for model redevelopment or change in the maintenance plans. (ICH Q14)

Model validation

Q14 Analytical Procedure Development, Multivariate glossary

The process of determining the suitability of a model by challenging it with independent test data and comparing the results against prespecified criteria. For quantitative models, validation involves confirming the calibration model's performance with an independent dataset. For identification libraries, validation involves analysing samples (a.k.a., challenge samples) not represented in the library to demonstrate the discriminative ability of the library model. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

The process of determining the suitability of a model by challenging it with independent test data and comparing the results against prespecified criteria. For quantitative models, validation involves confirming the calibration model's performance with an independent dataset. For identification libraries, validation involves analysing samples (a.k.a., challenge samples) not represented in the library to demonstrate the discriminative ability of the library model. (ICH Q2)

Modelling and Simulation (M&S)

E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population, Glossary

A range of quantitative approaches, including pharmacometrics/systems pharmacology and other mathematical/statistical approaches based on physiology, pathology and pharmacology to quantitatively characterize the interactions between a drug and an organ system which could predict quantitative outcomes of the drug and/or system's behavior in future experiments. In modelling and simulation, existing knowledge is often referred to as "prior" knowledge.

Modified Release

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

Dosage forms whose drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as a solution or an immediate release dosage form. Modified release solid oral dosage forms include both delayed and extended release drug products.

Modifying Factor

Q3C(R8) Guideline for Residual Solvents, Glossary

A factor determined by professional judgment of a toxicologist and applied to bioassay data to relate that data safely to humans.

Q3D(R2) Guideline for Elemental Impurities, Glossary

An individual factor determined by professional judgment of a toxicologist and applied to bioassay data to relate that data to human safety. (ICH Q3C) (See related term Safety Factor)

Molar Extinction Coefficient (MEC)

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

Molar Extinction Coefficient (also called molar absorptivity) reflects the efficiency with which a molecule can absorb a photon at a particular wavelength (typically expressed as L mol-1 cm-1) and is influenced by several factors, such as solvent.

Monitor

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

To take a small number of matrix samples (e.g. 1-3) during a dosing interval to estimate C(time) or Cmax.

Monitoring

E6(R2) Good Clinical Practice (GCP), Glossary

The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

Monitoring Plan

E6(R2) Good Clinical Practice (GCP), Glossary (Addendum)

A document that describes the strategy, methods, responsibilities, and requirements for monitoring the trial.

Monitoring Report

E6(R2) Good Clinical Practice (GCP), Glossary

A written report from the monitor to the sponsor after each site visit and/or other trial-related communication according to the sponsor's SOPs.

Mother Liquor

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The residual liquid which remains after the crystallization or isolation processes. A mother liquor may contain unreacted materials, intermediates, levels of the Active Pharmaceutical Ingredient (API) and/or impurities. It may be used for further processing.

Multicentre Trial

E6(R2) Good Clinical Practice (GCP), Glossary

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

E9 Statistical Principles for Clinical Trials, Glossary

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

Multi-Regional Clinical Trial (MRCT)

E17 General principles for planning and design of Multi-Regional Clinical Trials, Glossary

A clinical trial conducted in more than one region under a single protocol.

Multivariate analytical procedure

Q14 Analytical Procedure Development, Multivariate glossary

An analytical procedure where a result is determined through a multivariate calibration model utilizing more than one input variable. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

An analytical procedure where a result is determined through a multivariate calibration model utilizing more than one input variable. (ICH Q2)

Multivariate Statistical Process Control

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

The application of multivariate statistical techniques to analyse complex process data with potentially correlated variables. (European Pharmacopoeia, EP)

Mutagenic impurity

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

An impurity that has been demonstrated to be mutagenic in an appropriate mutagenicity test model, e.g., bacterial mutagenicity assay.

Mutagenic potential versus Genotoxic potential

M7(R2) Q&As Questions and Answers: Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Q1.1

The terms “mutagenic potential” and “genotoxic potential” are not interchangeable. Mutagenic potential refers to the ability of a compound to induce point mutations (i.e., bacterial reverse mutation assay), while genotoxic potential refers to both mutagenic and clastogenic potential. ICH M7 focuses specifically on mutagenicity.

N

Narrow therapeutic index

M9 Q&As Questions and Answers: Biopharmaceutics Classification System-based Biowaivers , Q1.4

Drugs with a narrow therapeutic index can be defined as those drugs where small differences in dose or blood concentration may lead to dose and blood concentration dependent, serious therapeutic failures or adverse drug reactions. They are characterized by a steep drug dose- response relationship within the usual dose range or a narrow span between effective drug concentrations and concentrations associated with serious toxicity.

BCS-based biowaiver principles are not designed to take into account more stringent criteria for a biowaiver. Therefore, the BCS-based biowaiver approach is not considered a suitable surrogate for the establishment of bioequivalence of narrow therapeutic index drugs.

Negative study

E14 The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs, 2.2.2

{See "Thorough QT/QTc study"}

Neonates / Neonatal period

E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population, 4

Neonates include term, post-term and preterm newborn infants. The neonatal period for term and post-term newborn infants is defined as the day of birth plus 27 days. The neonatal period for preterm newborn infants is defined as the day of birth through the expected date of delivery plus 27 days. As the neonatal population represents a broad maturational range, the conditions that affect this population can vary considerably; therefore, it is important to carefully consider the rationale for the selection of a neonatal population or subpopulation to be studied.

Nested drug-drug interaction (DDI) study

M12 EWG Drug Interaction Studies , 3.1.1

Alternatively {to a stand-alone drug-drug interaction (DDI) study} DDIs can be evaluated as part of larger studies in patients (e.g., phase 2/3) for which DDI evaluation is not the primary objective, if the DDI evaluation is prospectively planned and appropriately designed. As such, the DDI evaluation is nested within a larger study (refer to Section 3.2.2 for more details).

Neurotoxicity

Q3C(R8) Guideline for Residual Solvents, Glossary

The ability of a substance to cause adverse effects on the nervous system.

New active pharmaceutical ingredient

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

Active pharmaceutical ingredient that has not been previously authorized as a medicine for use in humans in the country in question.

New dosage form

Q1C Stability Testing for New Dosage Forms, 2

A new dosage form is defined as a drug product which is a different pharmaceutical product type, but contains the same active substance as included in the existing drug product approved by the pertinent regulatory authority.

New drug product

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

A pharmaceutical product type, for example, tablet, capsule, solution, cream, etc., which has not previously been registered in a region or Member State, and which contains a drug ingredient generally, but not necessarily, in association with excipients.

New Drug Substance

Q3A(R2) Impurities in New Drug Substances, Glossary

The designated therapeutic moiety that has not been previously registered in a region or member state (also referred to as a new molecular entity or new chemical entity). It can be a complex, simple ester, or salt of a previously approved drug substance.

Q3B(R2) Impurities in New Drug Products, Glossary

The designated therapeutic moiety that has not been previously registered in a region or member state (also referred to as a new molecular entity or new chemical entity). It can be a complex, simple ester, or salt of a previously approved substance.

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

The designated therapeutic moiety, which has not previously been registered in a region or Member State (also referred to as a new molecular entity or new chemical entity). It may be a complex, simple ester, or salt of a previously approved drug substance.

New molecular entity

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

An active pharmaceutical substance not previously contained in any drug product registered with the national or regional authority concerned. A new salt, ester, or non-covalent-bond derivative of an approved drug substance is considered a new molecular entity for the purpose of stability testing under this guidance.

New Region

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

The region where product registration is sought.

Newly identified signal

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

A signal first identified during the reporting interval, prompting further actions or evaluation. This term could also apply to a previously closed signal for which new information becomes available in the reporting interval prompting further action or evaluation.

{Source:} ICH Guideline E2C(R2)

Nominal Concentration

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Theoretical or expected concentration.

Nonclinical biodistribution (BD)

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, 2

Nonclinical biodistribution (BD) studies entail the use of analytical methods to detect the Gene Therapy (GT) product and transferred genetic material in collected samples and can include methods to detect the expression product of the transferred genetic material.

Nonclinical biodistribution (BD) studies

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, 2

Nonclinical BD studies entail the use of analytical methods to detect the gene therapy (GT) product and transferred genetic material in collected samples and can include methods to detect the expression product of the transferred genetic material.

Biodistribution (BD) studies can be conducted as stand-alone BD studies or in conjunction with nonclinical pharmacology and toxicology studies (see Section 5.3). Therefore, in this document the term “BD study” represents either scenario.

Nonclinical safety assessment

M3(R2) Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals, 1.3

The nonclinical safety assessment for marketing approval of a pharmaceutical usually includes pharmacology studies, general toxicity studies, toxicokinetic and nonclinical pharmacokinetic studies, reproduction toxicity studies, genotoxicity studies and, for drugs that have special cause for concern or are intended for a long duration of use, an assessment of carcinogenic potential. Other nonclinical studies to assess phototoxicity, immunotoxicity, juvenile animal toxicity and abuse liability should be conducted on a case-by-case basis.

Nonclinical Study

E6(R2) Good Clinical Practice (GCP), Glossary

Biomedical studies not performed on human subjects.

Non-conformance

Q7 Q&As Questions and Answers: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Q20.1

'Non-conformance' refers to a status as a result of a failure of the material to meet specifications or appropriately established standards that impacts the quality of the material [ICH Q7, Sections 2.50, 14.30, 20]

{See also "Deviation"}

Non-endogenous Virus

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Viruses from external sources present in the Master Cell Bank.

{See also "Virus"}

Non-Inferiority Trial

E9 Statistical Principles for Clinical Trials, Glossary

A trial with the primary objective of showing that the response to the investigational product is not clinically inferior to a comparative agent (active or placebo control).

Non-interventional clinical study

E2F Development Safety Update Report, Glossary

A study where the medicinal product(s) is (are) prescribed in the usual manner in accordance with the terms of the marketing authorisation. The assignment of the patient to a particular therapeutic strategy is not decided in advance by a trial protocol but falls within current practice and the prescription of the medicine is clearly separated from the decision to include the patient in the study. No additional diagnostic or monitoring procedures are applied to the patients and epidemiological methods are used for the analysis of collected data.

{Source: } EU Directive 2001/20/EC on Clinical Trials

Non-proprietary Drug (generic) Name

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

Drug name that is not protected by a trademark, usually descriptive of its chemical structure; sometimes called a public name. International Non-proprietary Names (INN) allocated by WHO, identify pharmaceutical substances or active pharmaceutical ingredients. Each INN is a unique name that is globally recognised and is public property. A non-proprietary name is also known as a generic name. In the US, most generic drug names are assigned by the US Adopted Name Council (USAN).

Non-specific Model Virus

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

A virus used for characterisation of viral clearance of the process when the purpose is to characterise the capacity of the manufacturing process to remove and/or inactivate viruses in general, i.e., to characterise the robustness of the purification process.

{See also "Virus"}

No-Observed-Adverse-Effect Level (NOAEL)

Q3D(R2) Guideline for Elemental Impurities, Glossary

Greatest concentration or amount of a substance, found by experiment or observation, that causes no detectable adverse alteration of morphology, functional capacity, growth, development, or life span of the target organism under defined conditions of exposure.

No-Observed-Effect Level (NOEL)

Q3C(R8) Guideline for Residual Solvents, Glossary

The highest dose of substance at which there are no biologically significant increases in frequency or severity of any effects in the exposed humans or animals.

Q3D(R2) Guideline for Elemental Impurities, Glossary

The highest dose of substance at which there are no biologically significant increases in frequency or severity of any effects in the exposed humans or animals.

Notification

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Glossary

A change to an approved established condition that does not require approval prior to implementation.

No-toxic-effect dose level

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 5

In this context, a 'no-toxic-effect dose level' (deemed to be the same as 'no-observed-adverse-effect dose level') is defined as a dose level at which some pharmacological response may be observed, but at which no adverse effect is found.

Numerical chromosome changes

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

O

Ongoing clinical trial

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

Trial where enrolment has begun, whether a hold is in place or analysis is complete, but for which a final clinical study report is not available.

{Source:} ICH Guideline E2F

E2F Development Safety Update Report, Glossary

Trial where enrolment has begun, whether a hold is in place or analysis is complete, but without a final clinical study report available.
{Source: } CIOMS VII

Ongoing monitoring

Q14 Analytical Procedure Development, Glossary

The collection and evaluation of analytical procedure performance data to ensure the quality of measured results throughout the analytical procedure lifecycle. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

The collection and evaluation of analytical procedure performance data to ensure the quality of measured results throughout the analytical procedure lifecycle. (ICH Q14)

Ongoing signal

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

A signal that remains under evaluation at the Data Lock Point (DLP).
{Source:} ICH Guideline E2C(R2)

Ongoing stability study

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The study carried out by the manufacturer on production batches according to a predetermined schedule in order to monitor, confirm and extend the projected retest period (or shelf life) of the active pharmaceutical ingredient, or confirm or extend the shelf life of the finished pharmaceutical product.

Opinion (in relation to Independent Ethics Committee)

E6(R2) Good Clinical Practice (GCP), Glossary

The judgement and/or the advice provided by an Independent Ethics Committee (IEC).

Original Medical Record

E6(R2) Good Clinical Practice (GCP), Glossary

See Source Documents.

Other significant adverse events

E3 Structure and Content of Clinical Study Reports, 12

For the purpose of this guideline, "other significant adverse events" are marked haematological and other laboratory abnormalities and any adverse events that led to an intervention, including withdrawal of drug treatment, dose reduction or significant additional concomitant therapy.
{Referring to the E2A definition of} a "serious adverse event" (experience) or reaction is any untoward medical occurrence that at any dose: results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect.

Outlier diagnostic

Q14 Analytical Procedure Development, Multivariate glossary

Tests that can identify unusual or atypical data in a multivariate analytical procedure. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

Tests that can identify unusual or atypical data in a multivariate analytical procedure. (ICH Q14)

Outpatient Study

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

A clinical study in which patients are not restricted to a clinical site.

Outsourced Activities

Q10 Pharmaceutical Quality System, Glossary

Activities conducted by a contract acceptor under a written agreement with a contract giver. (ICH Q10)

P

Packaging Material

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Any material intended to protect an intermediate or Active Pharmaceutical Ingredient (API) during storage and transport.

Paediatric-First Development

S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines, Glossary

Paediatric-first development describes development for treatment of paediatric patients before any development for an adult indication.

Paediatric-Only Development

S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines, Glossary

Paediatric-only development describes development for treatment exclusively in paediatric ages (e.g., neonatal respiratory distress syndrome).

Parallelism

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Parallelism demonstrates that the serially diluted incurred sample response curve is parallel to the calibration curve. Parallelism is a performance characteristic that can detect potential matrix effects.

Parental (legal guardian) consent/permission

E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population, Glossary

Expression of understanding and agreement by fully informed parent(s) or legal guardian to permit the investigator/sponsor of a clinical study to enroll a child in a clinical investigation. The choice of the terms parental consent or parental permission in different regions may reflect local legal/regulatory and ethical considerations.

Parental cells

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

Cell to be manipulated to give rise to a cell substrate or an intermediate cell line. For microbial expression systems, it is typical to also describe the parental cells as the host cell. For hybridomas, it is typical to also describe the parental cells as the cells to be fused.

Parent-child/fetus report

E2B(R2) Maintenance of the ICH guideline on clinical safety data management : Data elements for transmission of individual case safety reports , Glossary

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

Partial Validation

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Validation based on evaluation of selected validation parameters. Applicable to methods that were changed after full validation.

Patient perspective

M4E(R2) CTD on Efficacy, 2.5.6

Patient perspective information describes the attitudes and preferences of patients with respect to the therapeutic context, benefits, and risks. Such information may be obtained directly from patients or indirectly from other stakeholders (e.g., parents and caregivers) using qualitative, quantitative, or descriptive methods.

The detailed presentation of this information, if available, should be submitted in Module 5.

Payload

M8 eCTD v4.0 Electronic Common Technical Document (eCTD) v4.0, Common Abbreviations and Terms

The payload schema is the Electronic Common Technical Document (eCTD) v4.0 base and it contains the elements in eCTD v4.0, including items from the Common Product Model and Common Message Element schema. It is organised with the following three elements in the structure: submissionUnit, submission and application.

Pediatric extrapolation

E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population, 5.1.1

“Pediatric extrapolation” is defined as an approach to providing evidence in support of effective and safe use of drugs in the pediatric population when it can be assumed that the course of the disease and the expected response to a medicinal product would be sufficiently similar in the pediatric and reference (adult or other pediatric) population.

E11A EWG Paediatric Extrapolation, 1.2

Pediatric extrapolation is defined in the ICH E11(R1) guideline as “an approach to providing evidence in support of effective and safe use of drugs in the pediatric population when it can be assumed that the course of the disease {Footnote 1} and the expected response to a medicinal product would be sufficiently similar in the pediatric [target] and reference (adult or other pediatric) population.” -- {Footnote 1} For the purposes of this document “disease” includes both “diseases” and “conditions”.

Pediatric formulations

E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population, 7 (Footnote 2)

For purposes of this document, the term “pediatric formulations” includes design considerations for the dosage form, route of administration, packaging, measuring or administration device of a pediatric medicine (drug).

Per Protocol Set (Valid Cases, Efficacy Sample, Evaluable Subjects Sample)

E9 Statistical Principles for Clinical Trials, Glossary

The set of data generated by the subset of subjects who complied with the protocol sufficiently to ensure that these data would be likely to exhibit the effects of treatment, according to the underlying scientific model. Compliance covers such considerations as exposure to treatment, availability of measurements and absence of major protocol violations.

Performance characteristic

Q14 Analytical Procedure Development, Glossary

A technology independent description of a characteristic to ensure the quality of the measured result. Typically, accuracy, precision, specificity/selectivity and range may be considered. The term was previously called VALIDATION CHARACTERISTIC. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

A technology independent description of a characteristic to ensure the quality of the measured result. Typically, accuracy, precision, specificity/selectivity and range may be considered. The term was previously called VALIDATION CHARACTERISTIC. (ICH Q2)

Performance criterion

Q14 Analytical Procedure Development, Glossary

An acceptance criterion describing a numerical range, limit or desired state to ensure the quality of the measured result. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

An acceptance criterion describing a numerical range, limit or desired state to ensure the quality of the measured result. (ICH Q14)

Performance Indicators

Q10 Pharmaceutical Quality System, Glossary

Measurable values used to quantify quality objectives to reflect the performance of an organisation, process or system, also known as “performance metrics” in some regions. (ICH Q10)

Periodic verification testing

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

Also known as periodic or skip testing in ICH Q6A.

Permitted Daily Exposure (PDE)

Q3C(R8) Guideline for Residual Solvents, Glossary

The maximum acceptable intake per day of residual solvent in pharmaceutical products. {From Point 3.1 of the guideline} The term "tolerable daily intake" (TDI) is used by the International Program on Chemical Safety (IPCS) to describe exposure limits of toxic chemicals and "acceptable daily intake" (ADI) is used by the World Health Organization (WHO) and other national and international health authorities and institutes. The new term "permitted daily exposure" (PDE) is defined in the present guideline as a pharmaceutically acceptable intake of residual solvents to avoid confusion of differing values for ADI's of the same substance.

Q3D(R2) Guideline for Elemental Impurities, Glossary

The maximum acceptable intake of elemental impurity in pharmaceutical products per day.

Pharmaceutical

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, 2

This guideline applies to all pharmaceuticals, including biopharmaceuticals, vaccines (and their novel constitutive ingredients) for infectious diseases, and novel excipients that are part of the final pharmaceutical product. For the purposes of this guideline, the term “pharmaceutical” is used to encompass all of these treatment modalities. This guideline does not apply to cellular therapies, gene therapies and tissue-engineered products.

Pharmaceutical Quality System (PQS)

Q10 Pharmaceutical Quality System, Glossary

Management system to direct and control a pharmaceutical company with regard to quality. (ICH Q10 based upon ISO 9000:2005)

Pharmacodynamic Study

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

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 (anticholinergic effect with a tricyclic), a measure of activity thought related to clinical benefit (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 (blood pressure, cholesterol), or the ultimate intended clinical benefit (effects on pain, depression, sudden death).

Pharmacogenetics (PGt)

E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories, 2.2.1.2

Pharmacogenetics (PGt) is a subset of pharmacogenomics (PGx) and is defined as: The study of variations in DNA sequence as related to drug response.

Pharmacogenomics (PGx)

E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories, 2.2.1.1

Pharmacogenomics (PGx) is defined as: The study of variations of DNA and RNA characteristics as related to drug response.

Pharmacokinetic Study

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

A study of how a medicine is handled by the body, usually involving measurement of blood concentrations of drug and its metabolite(s) (sometimes concentrations in urine or tissues) as a function of time. Pharmacokinetic studies are used to characterize absorption, distribution, metabolism and excretion of a drug, either in 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.

Pharmacopoeial Discussion Group (PDG)

Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions, Glossary

The three-party Pharmacopoeial Discussion Group consisting of representatives from the European Directorate for the Quality of Medicines (EDQM) in the Council of Europe; the Ministry of Health, Labour and Welfare (MHLW) of Japan, and the United States Pharmacopoeial Convention, Inc (USP).

Pharmacopoeial text

Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions, Glossary

The pharmacopoeial monographs, general test chapters, and analytical methods emanating from the three regional pharmacopoeias.

Pharmacovigilance

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

The science of activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.[(2) WHO; 2002;]

E2E Pharmacovigilance Planning, 1.1

This document (...) uses the WHO definition of the term ‘pharmacovigilance’ as “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems.” This definition encompasses the use of pharmacoepidemiological studies.

Photo Irritation Factor (PIF)

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

Photo Irritation Factor is calculated for results of the In vitro 3T3 Neutral Red Uptake Phototoxicity Test (3T3 NRU-PT) by comparing the IC50 values obtained with and without irradiation.

Photoallergy

S10 Photosafety Evaluation of Pharmaceuticals, 1.4

An immunologically mediated reaction to a chemical, initiated by the formation of photoproducts (e.g., protein adducts) following a photochemical reaction.

Photoproducts

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

New compounds/structures formed as a result of a photochemical reaction.

Photoreactivity

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

The property of chemicals to react with another molecule as a consequence of absorption of photons.

Photosafety assessment

S10 Photosafety Evaluation of Pharmaceuticals, 1.4

The photosafety assessment of a pharmaceutical is an integrated process that can involve an evaluation of photochemical characteristics, data from nonclinical studies and human safety information. The photosafety assessment aims to determine whether risk minimization measures are warranted to prevent adverse events in humans.

{See also the definition of "Assessment" in S10}

Photosensitization

S10 Photosafety Evaluation of Pharmaceuticals, 1.4

Photosensitization is a general term occasionally used to describe all light-induced tissue reactions. However, in order to clearly distinguish between photoallergy and phototoxicity, the term photosensitization is not used in this guideline.

Phototoxicity (photoirritation)

S10 Photosafety Evaluation of Pharmaceuticals, 1.4

An acute light-induced tissue response to a photoreactive chemical.

Pilot Plant Scale

Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products, Glossary

The production of a recombinant protein by a procedure fully representative of and simulating that to be applied on a full commercial manufacturing scale. The methods of cell expansion, harvest, and product purification should be identical except for the scale of production.

Pilot scale batch

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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.

Pilot-Plant Scale

Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products, Glossary

The production of the drug substance or drug product by a procedure fully representative of and simulating that to be applied at manufacturing scale. The methods of cell expansion, harvest, and product purification should be identical except for the scale of production.

Pilot-scale batch

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

A batch of an active pharmaceutical ingredient or finished pharmaceutical product manufactured by a procedure fully representative of and simulating that to be applied to a full production-scale batch. For example, 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 adequately justified.

Plasmid

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Genetic element additional to the normal bacterial genome. A plasmid might be inserted into the host chromosome or form an extra-chromosomal element.

Platform analytical procedure

Q14 Analytical Procedure Development, Glossary

A platform analytical procedure can be defined as a multi-product method suitable to test quality attributes of different products without significant change to its operational conditions, system suitability and reporting structure. This type of method would apply to molecules that are sufficiently alike with respect to the attributes that the platform method is intended to measure. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

A platform analytical procedure can be defined as a multi-product method suitable to test quality attributes of different products without significant change to its operational conditions, system suitability and reporting structure. This type of method would apply to molecules that are sufficiently alike with respect to the attributes that the platform method is intended to measure. (ICH Q2)

Platform Manufacturing

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

The approach of developing a production strategy for a new drug starting from manufacturing processes similar to those used by the same applicant to manufacture other drugs of the same type (e.g., as in the production of monoclonal antibodies using predefined host cell, cell culture, and purification processes, for which there already exists considerable experience).

Point mutations

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

Polychromatic erythrocyte

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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 RNA.

Polymorphic Forms

Q3A(R2) Impurities in New Drug Substances, Glossary

Different crystalline forms of the same drug substance. These can include solvation or hydration products (also known as pseudo-polymorphs) and amorphous forms.

Polymorphism

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

The occurrence of different crystalline forms of the same drug substance. This may include solvation or hydration products (also known as pseudopolymorphs) and amorphous forms.

Polyploidy

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Numerical deviation of the modal number of chromosomes in a cell, with approximately whole multiples of the haploid number. Endoreduplication is a morphological form of polyploidy in which chromosome pairs are associated at metaphase as “diplochromosomes”.

Pooled regions

E17 General principles for planning and design of Multi-Regional Clinical Trials, Glossary

Pooling some geographical regions, countries or regulatory regions at the planning stage, if subjects in those regions are thought to be similar enough with respect to intrinsic and/or extrinsic factors relevant to the disease and/or drug under study.

Pooled subpopulations

E17 General principles for planning and design of Multi-Regional Clinical Trials, Glossary

Pooling a subset of the subjects from a particular region with similarly defined subsets from other regions whose members share one or more intrinsic or extrinsic factors important for the drug development programme at the planning stage. Pooled subpopulations is assumed as ethnicity-related subgroup particular important in the MRCT setting.

Population doubling or culture growth

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

This can be calculated in different ways; one example of an appropriate formula is: Population doublings (PDs) = the log of the ratio of the final count (N) to the starting (baseline) count (Xo), divided by the log of 2. That is: PD = [log(N : Xo)] : log 2.

Population Pharmacokinetic Methods

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

Population pharmacokinetic methods are 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.

Population Representative of the New Region

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

A population that includes the major racial groups within the new region.
{See"New region"}

Positive study, positive control

E14 The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs, 2.2.2

{See "Thorough QT/QTc study"}

Possible causal relationship

E2B(R3) Q&As EWG/IWG Electronic Transmission of Individual Case Safety Reports (ICSRs), Q3.8 (011)

By definition a spontaneous report contains suspected adverse reactions (i.e., a possible causal relationship is suspected but not established). However, there is no universally accepted definition for "possible" in the scale of causality assessment.

Post-Approval Change Management Protocol (PACMP)

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, 1.3

The PACMP is a regulatory tool that provides predictability regarding the information required to support a CMC change and the type of regulatory submission based on prior agreement between the MAH and regulatory authority. Such a mechanism enables planning and implementation of future changes to ECs in an efficient and predictable manner.

Post-approval CMC commitment

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Glossary

Commitment by the Marketing Authorization Holder (MAH) to undertake specific Chemistry, Manufacturing and Controls (CMC) activities to be implemented during the commercial phase.

Postmenopausal

M3(R2) Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals, 11.2

Postmenopausal is defined as 12 months with no menses without an alternative medical cause

Potency

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

The measure of the 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.

Potential Impurity

Q3A(R2) Impurities in New Drug Substances, Glossary

An impurity that theoretically can arise during manufacture or storage. It may or may not actually appear in the new drug substance.

Potential risk

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

An untoward occurrence for which there is some basis for suspicion of an association with the medicinal product of interest but where this association has not been confirmed. Examples of potential risks include:

* non-clinical safety concerns that have not been observed or resolved in clinical studies;
* adverse events observed in clinical trials or epidemiological studies for which the magnitude of the difference, compared with the comparator group (placebo or active substance, or unexposed group), on the parameter of interest raises a suspicion of, but is not large enough to suggest, a causal relationship;
* an event which is known to be associated with other products of the same class or which could be expected to occur based on the properties of the medicinal product

{Source:} ICH Guideline E2F

E2F Development Safety Update Report, Glossary

An untoward occurrence for which there is some basis for suspicion of an association with the medicinal product of interest but where this association has not been confirmed. Examples of potential risks include:

* Non-clinical safety concerns that have not been observed or resolved in clinical studies;
* Adverse events observed in clinical trials or epidemiological studies for which the magnitude of the difference, compared with the comparator group (placebo or active substance, or unexposed group), on the parameter of interest raises a suspicion of, but is not large enough to suggest, a causal relationship;
* A signal arising from a spontaneous adverse reaction reporting system;
* An event which is known to be associated with other products of the same class or which could be expected to occur based on the properties of the medicinal product.

Precision

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The closeness of agreement (i.e., degree of scatter) among a series of measurements. Precision is expressed as the coefficient of variation (CV) or the relative standard deviation (RSD) expressed as a percentage.

%CV = (Standard Deviation/Mean) x 100

Q14 Analytical Procedure Development, Glossary

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple samplings of the same homogeneous sample under the prescribed conditions. Precision can be considered at three levels: repeatability, intermediate precision and reproducibility. The precision of an analytical procedure is usually expressed as the variance, standard deviation or coefficient of variation of a series of measurements. (ICH Q2)

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

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. 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.

Q2(R2) Validation of Analytical Procedures, Glossary

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple samplings of the same homogeneous sample under the prescribed conditions. Precision can be considered at three levels: repeatability, intermediate precision and reproducibility. The precision of an analytical procedure is usually expressed as the variance, standard deviation or coefficient of variation of a series of measurements. (ICH Q2)

Preclinical safety studies

S6(R1) Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals, 3.1

The objectives of the preclinical safety studies are to define pharmacological and toxicological effects not only prior to initiation of human studies but throughout clinical development. Both in vitro and in vivo studies can contribute to this characterisation.

Pre-dose baseline

E14 Q&As (R3) The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs, Q4.2

{Baseline} taken shortly prior to dosing

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q4.2

{Baseline} taken shortly prior to dosing

Preferred and Included Terms

E9 Statistical Principles for Clinical Trials, Glossary

In a hierarchical medical dictionary, for example MedDRA, the included term is the lowest level of dictionary term to which the investigator description is coded. The preferred term is the level of grouping of included terms typically used in reporting frequency of occurrence. For example, the investigator text “Pain in the left arm” might be coded to the included term “Joint pain”, which is reported at the preferred term level as “Arthralgia”.

Preliminary EFD (pEFD) toxicity study

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

An embryo-fetal developmental toxicity study that includes exposure over the period of organogenesis, has adequate dose levels, uses a minimum of 6 pregnant animals per group, and includes assessments of fetal survival, fetal weight, and external and soft tissue alterations (see ICH M3).

Preliminary Hazard Analysis (PHA)

Q9 Quality Risk Management, Annex I.7

PHA is a tool of analysis based on applying prior experience or knowledge of a hazard or failure to identify future hazards, hazardous situations and events that might cause harm, as well as to estimate their probability of occurrence for a given activity, facility, product or system. The tool consists of: 1) the identification of the possibilities that the risk event happens, 2) the qualitative evaluation of the extent of possible injury or damage to health that could result and 3) a relative ranking of the hazard using a combination of severity and likelihood of occurrence, and 4) the identification of possible remedial measures.

Q9(R1) EWG Quality Risk Management, Annex I.7

PHA is a tool of analysis based on applying prior experience or knowledge of a hazard or failure to identify future hazards, hazardous situations and events that might cause harm, as well as to estimate their probability of occurrence for a given activity, facility, product or system. The tool consists of: 1) the identification of the possibilities that the risk event happens, 2) the qualitative evaluation of the extent of possible injury or damage to health that could result and 3) a relative ranking of the hazard using a combination of severity and likelihood of occurrence, and 4) the identification of possible remedial measures.

Preventive Action

Q10 Pharmaceutical Quality System, Glossary

Action to eliminate the cause of a potential non-conformity or other undesirable potential situation. NOTE: Preventive action is taken to prevent occurrence whereas corrective action is taken to prevent recurrence. (ISO 9000:2005)

Primary batch

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

A batch of a drug substance or drug product used in a formal 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.

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

A batch of an active pharmaceutical ingredient (API) or finished pharmaceutical product (FPP) used in a stability study, from which stability data are submitted in a registration application for the purpose of establishing a retest period or shelf life, as the case may be. Primary batch requirements are outlined in 2.1.3 and 2.2.3 for the API and FPP, respectively.

Primary pack

Q1B Stability Testing : Photostability Testing of New Drug Substances and Products, Glossary

{See "Immediate (primary) pack"}

Primary pharmacodynamic studies

S7A Safety Pharmacology Studies for Human Pharmaceuticals, 3. Note 2

Studies on the mode of action and/or effects of a substance in relation to its desired therapeutic target are primary pharmacodynamic studies.

Primary pharmacodynamics

M4S(R2) CTD on Safety , 2.6.2.2

See ICH Guideline S7, Safety Pharmacology Studies for Human Pharmaceuticals, Note 2. p. 8, for definitions

Principal Stratification

E9(R1) Addendum: Statistical Principles for Clinical Trials, Glossary

Classification of subjects according to the potential occurrence of an intercurrent event on all treatments. With two treatments, there are four principal strata with respect to a given intercurrent event: subjects who would not experience the event on either treatment, subjects who would experience the event on treatment A but not B, subjects who would experience the event on treatment B but not A, and subjects who would experience the event on both treatments. In this document a principal stratum refers to any of the strata (or combination of strata) defined by principal stratification.

Prior approval

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Glossary

Change to an approved established condition that requires regulatory review and approval prior to implementation

Procedure

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A documented description of the operations to be performed, the precautions to be taken and measures to be applied directly or indirectly related to the manufacture of an intermediate or Active Pharmaceutical Ingredient (API).

Process Aids

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Materials, excluding solvents, used as an aid in the manufacture of an intermediate or Active Pharmaceutical Ingredient (API) that do not themselves participate in a chemical or biological reaction (e.g. filter aid, activated carbon, etc).

Process Analytical Technology (PAT)

Q8(R2) Pharmaceutical Development, Glossary (Part I)

A system for designing, analyzing, and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality.

Process Characterisation of Viral Clearance

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Viral clearance studies in which non-specific “model” viruses are used to assess the robustness of the manufacturing process to remove and/or inactivate viruses.

Process Control

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

See In-Process Control.

Process Dynamics

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

The response of a manufacturing process to changing conditions or transient events.

Process Evaluation Studies of Viral Clearance

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Viral clearance studies in which “relevant” and/or specific “model” viruses are used to determine the ability of the manufacturing process to remove and/or inactivate these viruses.

Process Robustness

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

Ability of a process to tolerate variability of materials and changes of the process and equipment without negative impact on quality. (ICH Q8)

Q8(R2) Pharmaceutical Development, Glossary (Part I)

Ability of a process to tolerate variability of materials and changes of the process and equipment without negative impact on quality.

Processed Sample

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The final sample that has been subjected to various manipulations (e.g., extraction, dilution, concentration).

Process-Related Impurities

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

Impurities that are derived from the manufacturing process. They may be derived from cell substrates (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).

Product

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

A thing or things produced by labour or effort for a specific use and marketed to satisfy a need or want. [HL7 Patient Safety]

Q5E Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process, 1.2 Footnote 3

For convenience, when the term “product” is used without modifiers, it is intended to refer to the intermediates, drug substance, and drug product.

Product Lifecycle

Q3D(R2) Guideline for Elemental Impurities, Glossary

All phases in the life of the product from the initial development through marketing until the product's discontinuation. (ICH Q9)

Q9 Quality Risk Management, Definitions

All phases in the life of the product from the initial development through marketing until the product's discontinuation.

Q9(R1) EWG Quality Risk Management, Definitions

All phases in the life of the product from the initial development through marketing until the product's discontinuation.

Product Lifecycle Management (PLCM) Document

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, 1.3

The PLCM document serves as a central repository for the Established Conditions (Ecs) and the associated reporting category for changes made to ECs. The document also captures how a product will be managed during the commercial phase of the lifecycle including relevant post-approval Chemistry, Manufacturing and Controls (CMC) commitments and Post-Approval Change Management Protocols (PACMPs)

Product Quality Review (PQR)

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Glossary

Regular periodic review of Active Pharmaceutical Ingredient (API) or drug products with the objective to verify process consistency, to highlight any trends and to identify product and process improvements

Product quality reviews

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, 2.5

Regular quality reviews of APIs should be conducted with the objective of verifying the consistency of the process. Such reviews should normally be conducted and documented annually and should include at least:

*A review of critical in-process control and critical API test results;
*A review of all batches that failed to meet established specification(s);
*A review of all critical deviations or non-conformances and related investigations;
*A review of any changes carried out to the processes or analytical methods;
*A review of results of the stability monitoring program;
*A review of all quality-related returns, complaints and recalls; and
*A review of adequacy of corrective actions.

Product Realisation

Q10 Pharmaceutical Quality System, Glossary

Achievement of a product with the quality attributes appropriate to meet the needs of patients, health care professionals, and regulatory authorities (including compliance with marketing authorisation) and internal customers requirements. (ICH Q10)

Production

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

All operations involved in the preparation of an Active Pharmaceutical Ingredient (API) from receipt of materials through processing and packaging of the API.

Production batch

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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.

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

A batch of an active pharmaceutical ingredient or finished pharmaceutical product manufactured at production scale by using production equipment in a production facility as specified in the application.

Production Cells

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Cell substrate used to manufacture product.

Product-Related Impurities

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

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.

Profile

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

To take (e.g. 4-8) matrix samples during a dosing interval to make an estimate of Cmax and/or C(time) and area under matrix concentration- time curve (AUC).

Protocol

E6(R2) Good Clinical Practice (GCP), Glossary

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

Protocol Amendment

E6(R2) Good Clinical Practice (GCP), Glossary

A written description of a change(s) to or formal clarification of a protocol.

Protocol deviation

E3 Q&As (R1) Questions & Answers: Structure and Content of Clinical Study Reports, Q7

A protocol deviation is any change, divergence, or departure from the study design or procedures defined in the protocol.

{See also "Important protocol deviations"}

Proven Acceptable Range

Q8(R2) Pharmaceutical Development, Glossary (Part II)

A characterised range of a process parameter for which operation within this range, while keeping other parameters constant, will result in producing a material meeting relevant quality criteria.

Proven acceptable range for analytical procedures (PAR)

Q14 Analytical Procedure Development, Glossary

A characterised range of an analytical procedure parameter for which operation within this range, while keeping other parameters constant, will result in an analytical measurement meeting relevant performance criteria. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

A characterised range of an analytical procedure parameter for which operation within this range, while keeping other parameters constant, will result in an analytical measurement meeting relevant performance criteria. (ICH Q14)

Provisional shelf life

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

A provisional expiry date that is based on acceptable accelerated and available long-term data for the finished pharmaceutical product to be marketed in the proposed container-closure system.

Prozone Effect

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

{See “Hook Effect”}

Purge factor

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

Purge reflects the ability of a process to reduce the level of an impurity, and the purge factor is defined as the level of an impurity at an upstream point in a process divided by the level of an impurity at a downstream point in a process. Purge factors may be measured or predicted.

Q

Q -(Q)SAR and SAR

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

(Q)SAR and SAR: In the context of this guideline, refers to the relationship between the molecular (sub) structure of a compound and its mutagenic activity using (Quantitative) Structure-Activity Relationships derived from experimental data.
{The "Q" before the term "(Q)SAR and SAR" was added for sorting purposes}

Q4B Outcome

Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions, Glossary

Produced by the Q4B evaluation process; information concerning how the evaluated pharmacopoeial text can be used. The Q4B Outcome is included as part of the topic- specific Q4B annex developed as a result of each favourable evaluation.

QT prolongation

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q5.1

An upper bound of the two-sided 90% confidence interval around the estimated maximal effect on ΔQTc less than 10 ms, as computed by the concentration-response analysis or the intersection-union test.

Qualification

Q3A(R2) Impurities in New Drug Substances, Glossary

The process of acquiring and evaluating data that establishes the biological safety of an individual impurity or a given impurity profile at the level(s) specified.

Q3B(R2) Impurities in New Drug Products, Glossary

The process of acquiring and evaluating data that establishes the biological safety of an individual degradation product or a given degradation profile at the level(s) specified.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Action of proving and documenting that equipment or ancillary systems are properly installed, work correctly, and actually lead to the expected results. Qualification is part of validation, but the individual qualification steps alone do not constitute process validation.

Qualification Threshold

Q3A(R2) Impurities in New Drug Substances, Glossary

A limit above (>) which an impurity should be qualified.

Q3B(R2) Impurities in New Drug Products, Glossary

A limit above (>) which a degradation product should be qualified.

Quality

Q10 Pharmaceutical Quality System, Glossary

The degree to which a set of inherent properties of a product, system or process fulfils requirements. (ICH Q9)

Q3D(R2) Guideline for Elemental Impurities, Glossary

The degree to which a set of inherent properties of a product, system, or process fulfills requirements(see ICH Q6A definition specifically for quality of drug substance and drug products). (ICH Q9)

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

The suitability of either a drug substance or drug product for its intended use. This term includes such attributes as the identity, strength, and purity.

Q8(R2) Pharmaceutical Development, Glossary (Part I)

The suitability of either a drug substance or drug product for its intended use. This term includes such attributes as the identity, strength, and purity (from ICH Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances).

Q8(R2) Pharmaceutical Development, Glossary (Part II)

The suitability of either a drug substance or a drug product for its intended use. This term includes such attributes as the identity, strength, and purity (ICH Q6A).

Q9 Quality Risk Management, Definitions

The degree to which a set of inherent properties of a product, system or process fulfills requirements (see ICH Q6A definition specifically for "quality" of drug substance and drug (medicinal) products.)

Q9(R1) EWG Quality Risk Management, Definitions

The degree to which a set of inherent properties of a product, system or process fulfills requirements (see ICH Q6A definition specifically for "quality" of drug substance and drug (medicinal) products.)

Quality Assurance (QA)

E6(R2) Good Clinical Practice (GCP), Glossary

All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirement(s).

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The sum total of the organised arrangements made with the object of ensuring that all Active Pharmaceutical Ingredients (APIs) are of the quality required for their intended use and that quality systems are maintained.

Quality Attribute

Q5E Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process, Glossary

A molecular or product characteristic that is selected for its ability to help indicate the quality of the product. Collectively, the quality attributes define identity, purity, potency and stability of the product, and safety with respect to adventitious agents. Specifications measure a selected subset of the quality attributes.

Quality by Design (QbD)

Q8(R2) Pharmaceutical Development, Glossary (Part II)

A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management.

Quality Control (QC)

E6(R2) Good Clinical Practice (GCP), Glossary

The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Checking or testing that specifications are met.

Quality Control Sample (QC)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A biological matrix spiked with a known quantity of analyte that is used to monitor the performance of a bioanalytical method and assess the integrity and validity of the results of the unknown samples analysed in an individual batch or run.

Quality Manual

Q10 Pharmaceutical Quality System, Glossary

Document specifying the quality management system of an organisation. (ISO 9000:2005)

Quality Objectives

Q10 Pharmaceutical Quality System, Glossary

A means to translate the quality policy and strategies into measurable activities. (ICH Q10)

Quality Planning

Q10 Pharmaceutical Quality System, Glossary

Part of quality management focused on setting quality objectives and specifying necessary operational processes and related resources to fulfil the quality objectives. (ISO 9000:2005)

Quality Policy

Q10 Pharmaceutical Quality System, Glossary

Overall intentions and direction of an organisation related to quality as formally expressed by senior management. (ISO 9000:2005)

Quality Risk Management

Q10 Pharmaceutical Quality System, Glossary

A systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle. (ICH Q9)

Q14 Analytical Procedure Development, Glossary

A systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle. (ICH Q9)

Q2(R2) Validation of Analytical Procedures, Glossary

A systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle. (ICH Q9)

Q3D(R2) Guideline for Elemental Impurities, Glossary

A systematic process for the assessment, control, communication, and review of risks to the quality of the drug product across the product lifecycle. (ICH Q9)

Q9 Quality Risk Management, Definitions

A systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle.

Q9(R1) EWG Quality Risk Management, Definitions

A systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle.

Quality Risk Management (QRM)

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

A systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle. (ICH Q9)

Quality System

Q3D(R2) Guideline for Elemental Impurities, Glossary

The sum of all aspects of a system that implements quality policy and ensures that quality objectives are met. (ICH Q10)

Q9 Quality Risk Management, Definitions

The sum of all aspects of a system that implements quality policy and ensures that quality objectives are met.

Q9(R1) EWG Quality Risk Management, Definitions

The sum of all aspects of a system that implements quality policy and ensures that quality objectives are met.

Quality Target Product Profile (QTPP)

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

A prospective summary of the quality characteristics of a drug product that ideally will be achieved to ensure the desired quality, taking into account safety and efficacy of the drug product. (ICH Q8)

Q8(R2) Pharmaceutical Development, Glossary (Part II)

A prospective summary of the quality characteristics of a drug product that ideally will be achieved to ensure the desired quality, taking into account safety and efficacy of the drug product.

Quality Unit(s)

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

An organizational unit independent of production which fulfills both Quality Assurance and Quality Control responsibilities. This can be in the form of separate QA and QC units or a single individual or group, depending upon the size and structure of the organization.

Quantitation limit

Q14 Analytical Procedure Development, Glossary

The quantitation limit is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. The quantitation limit for an analytical procedure should not be more than the reporting threshold. The quantitation limit is a parameter used for quantitative assays for low levels of compounds in sample matrices, and, particularly, is used for the determination of impurities and/or degradation products. (ICH Q2)

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

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 for the determination of impurities and/or degradation products.

Q2(R2) Validation of Analytical Procedures, Glossary

The quantitation limit is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. The quantitation limit for an analytical procedure should not be more than the reporting threshold. The quantitation limit is a parameter used for quantitative assays for low levels of compounds in sample matrices, and, particularly, is used for the determination of impurities and/or degradation products. (ICH Q2)

Quarantine

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The status of materials isolated physically or by other effective means pending a decision on their subsequent approval or rejection.

R

Racemate

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

A composite (solid, liquid, gaseous, or in solution) of equimolar quantities of two enantiomeric species. It is devoid of optical activity.

Randomization

E6(R2) Good Clinical Practice (GCP), Glossary

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.

Range

Q14 Analytical Procedure Development, Glossary

The range of an analytical procedure is the interval between the lowest and the highest reportable results in which the analytical procedure has a suitable level of precision, accuracy and response. (ICH Q2)
{See also “Reportable range”, "Working range"}

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

The range of an analytical procedure is the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations) for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity.

Q2(R2) Validation of Analytical Procedures, Glossary

The range of an analytical procedure is the interval between the lowest and the highest reportable results in which the analytical procedure has a suitable level of precision, accuracy and response. (ICH Q2)
{See also “Reportable range”, "Working range"}

Rapidly Dissolving Products

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

An immediate release solid oral drug product is considered rapidly dissolving when not less than 80% of the label amount of the drug substance dissolves within 15 minutes in each of the following media: (1) pH 1.2, (2) pH 4.0, and (3) pH 6.8.

Raw Material

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A general term used to denote starting materials, reagents, and solvents intended for use in the production of intermediates or Active Pharmaceutical Ingredients (APIs).

Reactive Oxygen Species (ROS)

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

Reactive Oxygen Species, including superoxide anion and singlet oxygen.

Reagent

Q3A(R2) Impurities in New Drug Substances, Glossary

A substance other than a starting material, intermediate, or solvent that is used in the manufacture of a new drug substance.

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

A substance, other than a starting material or solvent, which is used in the manufacture of a new drug substance.

Real Time Release Testing

Q8(R2) Pharmaceutical Development, Glossary (Part II)

The ability to evaluate and ensure the quality of in-process and/or final product based on process data, which typically include a valid combination of measured material attributes and process controls.
{See also Q8/9/10 Q&As (R4), Section 2.2 Question 9:}The term ‘Real time release’ in the Q8(R2), Step 2 document was revised to ‘Real time release testing’ in the final Q8(R2) Part II document to fit the definition more accurately and thus avoid confusion with batch release.

Real Time Release Testing (RTRT)

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), Glossary

The ability to evaluate and ensure the quality of in-process and/or final product based on process data, which typically include a valid combination of measured material attributes and process controls. (ICH Q8)

Q14 Analytical Procedure Development, Glossary

The ability to evaluate and ensure the quality of the in-process and/or final product based on process data, which typically include a valid combination of measured material attributes and process controls. (ICH Q8)

Q2(R2) Validation of Analytical Procedures, Glossary

The ability to evaluate and ensure the quality of the in-process and/or final product based on process data, which typically include a valid combination of measured material attributes and process controls. (ICH Q8)

Reanalysis

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

An additional evaluation of a previously assayed sample. Also referred to as Repeat Analysis.

Reasonable causal relationship

E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting, III.A.1

Many terms and scales are in use to describe the degree of causality (attributability) between a medicinal product and an event, such as certainly, definitely, probably, possibly or likely related or not related. Phrases such as "plausible relationship," "suspected causality," or "causal relationship cannot be ruled out" are also invoked to describe cause and effect. However, there is currently no standard international nomenclature. The expression "reasonable causal relationship" is meant to convey in general that there are facts (evidence) or arguments to suggest a causal relationship.

Receiver

E2B(R2) Maintenance of the ICH guideline on clinical safety data management : Data elements for transmission of individual case safety reports , Glossary

The intended recipient of the transmission.

Recombination

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Breakage and balanced or unbalanced rejoining of DNA.

Recovery

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

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.

Reference Information Model (RIM)

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

The HL7 information model from which all other information models, e.g. RMIMS, and messages are derived.

Reference procedure

Q14 Analytical Procedure Development, Multivariate glossary

A separate analytical procedure used to obtain the reference values of the calibration and validation samples for a multivariate analytical procedure. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

A separate analytical procedure used to obtain the reference values of the calibration and validation samples for a multivariate analytical procedure. (ICH Q2)

Reference Safety Information (RSI)

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

All relevant safety information contained in the reference product information (e.g., CCDS) prepared by the marketing authorisation holder (MAH) and which the MAH requires to be listed in all countries where the company markets the drug, except when the local regulatory authority specifically requires a modification. It is a subset of information contained within the MAH's reference product information for the Periodic Benefit-Risk Evaluation Report (PBRER) Where the reference product information is the Company Core Data Sheet (CCDS), the reference safety information is the Company Core Safety Information (CCSI).
{Source:} ICH Guideline E2C(R2)

Reference sample

Q14 Analytical Procedure Development, Multivariate glossary

A sample representative of the test sample with a known value for the property of interest, used for calibration. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

A sample representative of the test sample with a known value for the property of interest, used for calibration. (ICH Q14)

Reference Standard

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A well-characterised substance of known purity and identity used to prepare calibration and quality control samples.

Reference Standard, Primary

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A substance that has been shown by an extensive set of analytical tests to be authentic material that should be of high purity. This standard can be: (1) obtained from an officially recognised source, or (2) prepared by independent synthesis, or (3) obtained from existing production material of high purity, or (4) prepared by further purification of existing production material.

Reference Standard, Secondary

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A substance of established quality and purity, as shown by comparison to a primary reference standard, used as a reference standard for routine laboratory analysis.

Reference Standards

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

Refer to international or national standards.

Refined Message Information Model (RMIM)

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

An information structure that represents the requirements for a set of messages.

Region

E17 General principles for planning and design of Multi-Regional Clinical Trials, Glossary

A geographical region, country or regulatory region

Regional Pharmacovigilance Centre

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

A governmentally recognised centre (or integrated system) within a country with the clinical and scientific expertise to collect, collate, analyze and give advice on all information related to drug safety.

Registry

E2E Pharmacovigilance Planning, Annex, Point 2

A registry is a list of patients presenting with the same characteristic(s). This characteristic can be a disease (disease registry) or a specific exposure (drug registry).

E2F Development Safety Update Report, Glossary

A registry is a list of patients presenting with the same characteristic(s). This characteristic can be a disease (disease registry) or a specific exposure (drug registry). Both types of registries, which only differ by the type of patient data of interest, can collect a battery of information using standardised questionnaires in a prospective fashion. Commentary: Exposure (drug) registries collect information over time on populations exposed to drugs of interest and/or specific populations. Patients can be included in a cohort study to collect data on adverse events using standardised questionnaires. They can be useful for signal amplification, particularly of rare outcomes.
{Source: } ICH E2E

Regulatory Agency or Regulatory Authorities

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

Geopolitical entities have established agencies/authorities responsible for regulating products used in health care. The agencies are collectively referred to as regulatory agencies.

Regulatory Authorities

E6(R2) Good Clinical Practice (GCP), Glossary

Bodies having the power to regulate. In the ICH GCP Guideline the expression Regulatory Authorities includes the authorities that review submitted clinical data and those that conduct inspections (see 1.29). These bodies are sometimes referred to as competent authorities.

Regulatory Region

E17 General principles for planning and design of Multi-Regional Clinical Trials, Glossary

A region comprised of countries for which a common set of regulatory requirements applies for drug approval (e.g., EU).

Reintegration

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Change of the original integration of a chromatographic peak

Relative total growth (RTG)

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

This measure of cytotoxicity takes the relative suspension growth (based on cell loss and cell growth from the beginning of treatment to the second day post-treatment) and multiplies it by the relative plating efficiency at the time of cloning for mutant quantization.

Release specification

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The combination of physical, chemical, biological, and microbiological tests and acceptance criteria that determine the suitability of an active pharmaceutical ingredient or finished pharmaceutical product at the time of its release.

Relevant Genotypic and Phenotypic Markers

Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products, Glossary

Those markers permitting the identification of the strain of the cell line which should include the expression of the recombinant protein or presence of the expression construct.

Relevant Virus

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Virus used in process evaluation studies which is either the identified virus, or of the same species as the virus that is known, or likely to contaminate the cell substrate or any other reagents or materials used in the production process.

{See also “Virus”}

Repeat Analysis

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

{See “Reanalysis”}

Repeatability

Q14 Analytical Procedure Development, Glossary

Repeatability expresses the precision under the same operating conditions over a short interval of time. Repeatability is also termed intra-assay precision. (ICH Q2)

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

Repeatability expresses the precision under the same operating conditions over a short interval of time. Repeatability is also termed intra-assay precision .

Q2(R2) Validation of Analytical Procedures, Glossary

Repeatability expresses the precision under the same operating conditions over a short interval of time. Repeatability is also termed intra-assay precision. (ICH Q2)

Replicate

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

One of several determinations or measurements of a sample, calibration standards or quality control sample (QC).

Reportable range

Q14 Analytical Procedure Development, Glossary

The reportable range of an analytical procedure includes all values from the lowest to the highest reportable result for which there is a suitable level of precision and accuracy. Typically, the reportable range is given in the same unit as the specification. (ICH Q2)

{See also “Range”, “Working Range”}

Q2(R2) Validation of Analytical Procedures, Glossary

The reportable range of an analytical procedure includes all values from the lowest to the highest reportable result for which there is a suitable level of precision and accuracy. Typically, the reportable range is given in the same unit as the specification. (ICH Q2)

{See also “Range”, "Working range"}

Reportable result

Q14 Analytical Procedure Development, Glossary

The result as generated by the analytical procedure after calculation or processing and applying the described sample replication. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

The result as generated by the analytical procedure after calculation or processing and applying the described sample replication. (ICH Q2)

Reporter

E2B(R2) Maintenance of the ICH guideline on clinical safety data management : Data elements for transmission of individual case safety reports , Glossary

Reporter is the primary source of the information, (i.e., a person who initially reports the facts). This should be distinguished from the sender of the message, though the reporter could also be a sender.

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

The primary source of the information, e.g. a person who initially reports the facts provided in the ICSR. This should be distinguished from the sender of the message, though the reporter could also be a sender.[ICH E2B(R2)]

Reporting Threshold

Q3A(R2) Impurities in New Drug Substances, Glossary

A limit above (>) which an impurity should be reported. Reporting threshold is the same as reporting level in Q2B.

Q3B(R2) Impurities in New Drug Products, Glossary

A limit above (>) which a degradation product should be reported.

Reprocessing

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Introducing an intermediate or Active Pharmaceutical Ingredient (API), including one that does not conform to standards or specifications, back into the process and repeating a crystallization step or other appropriate chemical or physical manipulation steps (e.g., distillation, filtration, chromatography, milling) that are part of the established manufacturing process. Continuation of a process step after an in-process control test has shown that the step is incomplete is considered to be part of the normal process, and not reprocessing.

Reproducibility

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The extent to which consistent results are obtained when an experiment is repeated.

Q14 Analytical Procedure Development, Glossary

Reproducibility expresses the precision between laboratories (e.g., inter-laboratory studies, usually applied to standardization of methodology). (ICH Q2)

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

Reproducibility expresses the precision between laboratories (collaborative studies, usually applied to standardization of methodology).

Q2(R2) Validation of Analytical Procedures, Glossary

Reproducibility expresses the precision between laboratories (e.g., inter-laboratory studies, usually applied to standardization of methodology). (ICH Q2)

Requirements

Q9 Quality Risk Management, Definitions

The explicit or implicit needs or expectations of the patients or their surrogates (e.g., health care professionals, regulators and legislators). In this document, “requirements” refers not only to statutory, legislative, or regulatory requirements, but also to such needs and expectations.

Q9(R1) EWG Quality Risk Management, Definitions

The explicit or implicit needs or expectations of the patients or their surrogates (e.g., health care professionals, regulators and legislators). In this document, “requirements” refers not only to statutory, legislative, or regulatory requirements, but also to such needs and expectations.

Residence Time Distribution (RTD)

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

A measure of the range of residence times experienced by material passing through a specific process environment/vessel/unit operation. (ASTM E2968-14. Standard Guide for Application of Continuous Processing in the Pharmaceutical Industry)

Residual solvents

Q3C(R8) Guideline for Residual Solvents, 1

Residual solvents in pharmaceuticals are defined here as organic volatile chemicals that are used or produced in the manufacture of drug substances or excipients, or in the preparation of drug products.

Response

Q14 Analytical Procedure Development, Glossary

The response of an analytical procedure is its ability (within a given range) to obtain a signal which is effectively related to the concentration (amount) of analyte in the sample by some known mathematical function. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

The response of an analytical procedure is its ability (within a given range) to obtain a signal which is effectively related to the concentration (amount) of analyte in the sample by some known mathematical function. (ICH Q2)

Response Function

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A mathematical expression which adequately describes the relationship between instrument response (e.g., peak area or height ratio or signal) and the concentration (amount) of analyte in the calibration standards. Response function is defined within a given range. See also Calibration Curve.

Results

E6(R3) EWG Good Clinical Practice (GCP) - Draft principles, Draft principles; Footnote 1

{For the purposes of this guideline} The “results” are a composition of organized and fit-for-purpose information.
{See also "Information" and "Data"}

Retest date

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The date after which an active pharmaceutical ingredient should be re-examined to ensure that the material is still in compliance with the specification and thus is still suitable for use in the manufacture of a finished pharmaceutical product.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The date when a material should be re-examined to ensure that it is still suitable for use.

Re-test date

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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.

Retest period

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The period of time during which the active pharmaceutical ingredient (API) is expected to remain within its specification and, therefore, can be used in the manufacture of a given finished pharmaceutical product (FPP), provided that the API has been stored under the defined conditions. After this period, a batch of API destined for use in the manufacture of an FPP should be retested for compliance with the specification and then used immediately. A batch of API can be retested multiple times and a different portion of the batch used after each retest, as long as it continues to comply with the specification. For most substances known to be labile, it is more appropriate to establish a shelf life than a retest period. The same may be true for certain antibiotics.

Re-test period

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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.

Revalidation

Q14 Analytical Procedure Development, Glossary

Demonstration that an analytical procedure is still fit for its intended purpose after a change to the product, process or the analytical procedure itself. Revalidation can involve all (full revalidation) or a subset (partial revalidation) of performance characteristics. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

Demonstration that an analytical procedure is still fit for its intended purpose after a change to the product, process or the analytical procedure itself. Revalidation can involve all (full revalidation) or a subset (partial revalidation) of performance characteristics. (ICH Q2)

Reversible Toxicity

Q3C(R8) Guideline for Residual Solvents, Glossary

The occurrence of harmful effects that are caused by a substance and which disappear after exposure to the substance ends.

Reworking

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

Subjecting an intermediate or Active Pharmaceutical Ingredient (API) that does not conform to standards or specifications to one or more processing steps that are different from the established manufacturing process to obtain acceptable quality intermediate or API (e.g., recrystallizing with a different solvent).

Risk

E8(R1) General Considerations for Clinical Studies, 3.2

The term risk is used here in the context of general risk management methodology applicable to all factors of a study.

Q3D(R2) Guideline for Elemental Impurities, Glossary

The combination of the probability of occurrence of harm and the severity of that harm. (ISO/IEC Guide51, ICH Q9)

Q9 Quality Risk Management, Definitions

The combination of the probability of occurrence of harm and the severity of that harm (ISO/IEC Guide 51).
{Reference: ISO/IEC Guide 51:1999 - Safety Aspects - Guideline for their inclusion in standards.}

Q9(R1) EWG Quality Risk Management, Definitions

The combination of the probability of occurrence of harm and the severity of that harm (ISO/IEC Guide 51).
{Reference: ISO/IEC Guide 51:2014 - Safety Aspects - Guideline for their inclusion in standards.}

Risk Acceptance

Q3D(R2) Guideline for Elemental Impurities, Glossary

The decision to accept risk. (ISO Guide 73)

Q9 Quality Risk Management, Definitions

The decision to accept risk (ISO Guide 73).
{Reference: ISO/IEC Guide 73:2002 - Risk Management - Vocabulary - Guidelines for use in Standards.}

Q9(R1) EWG Quality Risk Management, Definitions

The decision to accept risk (ISO Guide 73).
{Reference: ISO/IEC Guide 73:2002 - Risk Management - Vocabulary - Guidelines for use in Standards.}

Risk Analysis

Q3D(R2) Guideline for Elemental Impurities, Glossary

The estimation of the risk associated with the identified hazards. (ICH Q9)

Q9 Quality Risk Management, Definitions

The estimation of the risk associated with the identified hazards.

Q9(R1) EWG Quality Risk Management, Definitions

The estimation of the risk associated with the identified hazards.

Risk Assessment

Q3D(R2) Guideline for Elemental Impurities, Glossary

A systematic process of organizing information to support a risk decision to be made within a risk management process. It consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards. (ICH Q9)

Q9 Quality Risk Management, Definitions

A systematic process of organizing information to support a risk decision to be made within a risk management process. It consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.

Q9(R1) EWG Quality Risk Management, Definitions

A systematic process of organizing information to support a risk decision to be made within a risk management process. It consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards.

Risk Communication

Q9 Quality Risk Management, Definitions

The sharing of information about risk and risk management between the decision maker and other stakeholders.

Q9(R1) EWG Quality Risk Management, Definitions

The sharing of information about risk and risk management between the decision maker and other stakeholders.

Risk Control

Q3D(R2) Guideline for Elemental Impurities, Glossary

Actions implementing risk management decisions. (ISO Guide 73)

Q9 Quality Risk Management, Definitions

Actions implementing risk management decisions (ISO Guide 73).
{Reference: ISO/IEC Guide 73:2002 - Risk Management - Vocabulary - Guidelines for use in Standards.}

Q9(R1) EWG Quality Risk Management, Definitions

Actions implementing risk management decisions (ISO Guide 73).
{Reference: ISO/IEC Guide 73:2002 - Risk Management - Vocabulary - Guidelines for use in Standards.}

Risk Evaluation

Q9 Quality Risk Management, Definitions

The comparison of the estimated risk to given risk criteria using a quantitative or qualitative scale to determine the significance of the risk.

Q9(R1) EWG Quality Risk Management, Definitions

The comparison of the estimated risk to given risk criteria using a quantitative or qualitative scale to determine the significance of the risk.

Risk Identification

Q3D(R2) Guideline for Elemental Impurities, Glossary

The systematic use of information to identify potential sources of harm (hazards) referring to the risk question or problem description. (ICH Q9)

Q9 Quality Risk Management, Definitions

The systematic use of information to identify potential sources of harm (hazards) referring to the risk question or problem description.

Risk Management

Q3D(R2) Guideline for Elemental Impurities, Glossary

The systematic application of quality management policies, procedures, and practices to the tasks of assessing, controlling, communicating, and reviewing risk. (ICH Q9)

Q9 Quality Risk Management, Definitions

The systematic application of quality management policies, procedures, and practices to the tasks of assessing, controlling, communicating and reviewing risk.

Risk Ranking and Filtering

Q9 Quality Risk Management, Annex I.8

Risk ranking and filtering is a tool for comparing and ranking risks. Risk ranking of complex systems typically requires evaluation of multiple diverse quantitative and qualitative factors for each risk. The tool involves breaking down a basic risk question into as many components as needed to capture factors involved in the risk. These factors are combined into a single relative risk score that can then be used for ranking risks. “Filters,” in the form of weighting factors or cut-offs for risk scores, can be used to scale or fit the risk ranking to management or policy objectives.

Q9(R1) EWG Quality Risk Management, Annex I.8

Risk ranking and filtering is a tool for comparing and ranking risks. Risk ranking of complex systems typically requires evaluation of multiple diverse quantitative and qualitative factors for each risk. The tool involves breaking down a basic risk question into as many components as needed to capture factors involved in the risk. These factors are combined into a single relative risk score that can then be used for ranking risks. “Filters,” in the form of weighting factors or cut-offs for risk scores, can be used to scale or fit the risk ranking to management or policy objectives.

Risk Reduction

Q9 Quality Risk Management, Definitions

Actions taken to lessen the probability of occurrence of harm and the severity of that harm.

Risk Review

Q9 Quality Risk Management, Definitions

Review or monitoring of output/results of the risk management process considering (if appropriate) new knowledge and experience about the risk.

Risk-based Decision Making

Q9(R1) EWG Quality Risk Management, Definitions

An approach or process that considers knowledge about risks relevant to the decision and whether risks are at an acceptable level.

Robustness

Q14 Analytical Procedure Development, Glossary

The robustness of an analytical procedure is a measure of its capacity to meet the expected performance requirements during normal use. Robustness is tested by deliberate variations of analytical procedure parameters. (ICH Q14)

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

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.

Q2(R2) Validation of Analytical Procedures, Glossary

The robustness of an analytical procedure is a measure of its capacity to meet the expected performance requirements during normal use. Robustness is tested by deliberate variations of analytical procedure parameters. (ICH Q14)

Room temperature

Q1E Evaluation of Stability Data, 1.3

The term “room temperature” refers to the general customary environment and should not be inferred to be the storage statement for labeling.

Run

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

{See “Analytical Run”}

Run Summary Table

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Tabular output of all data from individual samples, quality control samples (QCs) and calibration standards within the analytical run (e.g., for chromatography retention times, analyte and Internal Standard (IS) responses, concentrations, and dilution factors if any; for ligand binding assays analyte responses concentrations, dilution factors).

Run Time

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

The time interval used to produce a quantity of output material.

S

Safety

Q3D(R2) Guideline for Elemental Impurities, Glossary

Practical certainty that adverse effects will not result from exposure to an agent under defined circumstances. (Ref. 2)

{Ref 2: IPCS. Principles and methods for the risk assessment of chemicals in food, chapter 5:dose-response assessment and derivation of health based guidance values.Environmental Health Criteria 240. International Programme on Chemical Safety.World Health Organization, Geneva. 2009;Table 5.5} https://www.who.int/publications/i/item/9789241572408}

Safety & Tolerability

E9 Statistical Principles for Clinical Trials, Glossary

The safety of a medical product concerns the medical risk to the subject, usually assessed in a clinical trial by laboratory tests (including clinical chemistry and haematology), vital signs, clinical adverse events (diseases, signs and symptoms), and other special safety tests (e.g. ECGs, ophthalmology). The tolerability of the medical product represents the degree to which overt adverse effects can be tolerated by the subject.

Safety Assessment

Q3D(R2) Guideline for Elemental Impurities, Glossary

An approach that focuses on the scientific understanding and measurement of chemical hazards as well as chemical exposures, and ultimately the risks associated with them. This term is often (and in this guideline) used synonymously with risk assessment. (Ref. 2)
{Ref. 2: IPCS. Principles and methods for the risk assessment of chemicals in food, chapter 5:dose-response assessment and derivation of health based guidance values.Environmental Health Criteria 240. International Programme on Chemical Safety.World Health Organization, Geneva. 2009;Table 5.5} https://www.who.int/publications/i/item/9789241572408}

Safety concern

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

An important identified risk, important potential risk, or important missing information.
{Source:} ICH Guideline E2C(R2)

Safety Factor

Q3D(R2) Guideline for Elemental Impurities, Glossary

A composite (reductive) factor applied by the risk assessment experts to the NOAEL or other reference point, such as the benchmark dose or benchmark dose lower confidence limit, to derive a reference dose that is considered safe or without appreciable risk, such as an acceptable daily intake or tolerable daily intake (the NOAEL or other reference point is divided by the safety factor to calculate the reference dose). The value of the safety factor depends on the nature of the toxic effect, the size and type of population to be protected, and the quality of the toxicological information available. See related terms: Assessment factor, Uncertainty factor. (Ref. 2)
{Ref. 2: IPCS. Principles and methods for the risk assessment of chemicals in food, chapter 5:dose-response assessment and derivation of health based guidance values.Environmental Health Criteria 240. International Programme on Chemical Safety.World Health Organization, Geneva. 2009;Table 5.5} https://www.who.int/publications/i/item/9789241572408}

Safety Message

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

A safety message is an EDI message including the information provided for one/more Individual Case Safety Reports contained in one safety file exchanged between one sender and one receiver in one message transaction.[EMA]

Safety pharmacology studies

M4S(R2) CTD on Safety , 2.6.2.4

See ICH Guideline S7, Safety Pharmacology Studies for Human Pharmaceuticals, Note 2. p. 8, for definitions

S7A Safety Pharmacology Studies for Human Pharmaceuticals, 1.5

For the purpose of this document, safety pharmacology studies are defined as those studies that investigate the potential undesirable pharmacodynamic effects of a substance on physiological functions in relation to exposure in the therapeutic range and above.
{See also: "Primary pharmacodynamic studies", "Secondary pharmacodynamic studies"; and "Nonclinical safety assessment"}

Sample suitability assessment

Q14 Analytical Procedure Development, Glossary

A sample or sample preparation is considered suitable if the measurement response on the sample satisfies pre-defined acceptance criteria for the analytical procedure attributes that have been developed for the validated analytical procedure. Sample suitability is a pre-requisite for the validity of the result along with a satisfactory outcome of the system suitability test. Sample suitability assessment generally consists of the assessment of the similarity of the response between a standard and the test sample and may include a requirement of no interfering signals arising from the sample matrix. (ICH Q14)

Sample suitability assessment

Q2(R2) Validation of Analytical Procedures, Glossary

sample or sample preparation is considered suitable if the measurement response on the sample satisfies pre-defined acceptance criteria for the analytical procedure attributes that have been developed for the validated analytical procedure. Sample suitability is a pre-requisite for the validity of the result along with a satisfactory outcome of the system suitability test. Sample suitability generally consists of the assessment of the similarity of the response between a standard and the test sample and may include a requirement of no interfering signals arising from the sample matrix. (ICH Q14)

Satellite groups

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

Groups of animals included in the design and conduct of a toxicity study, treated and housed under conditions identical to those of the main study animals, but used primarily for toxicokinetics.

Secondary pack

Q1B Stability Testing : Photostability Testing of New Drug Substances and Products, Glossary

{See "Marketing pack"}

Secondary pharmacodynamic studies

S7A Safety Pharmacology Studies for Human Pharmaceuticals, 3. Note 2

Studies on the mode of action and/or effects of a substance not related to its desired therapeutic target are secondary pharmacodynamic studies (these have sometimes been referred to as part of general pharmacology studies).

Section

M4 Q&As (R3) Questions & Answers: Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use, Q15

Each section in the CTD is identified by a number and a heading. Please refer to the Granularity Document Annex for a description documents to be provided in each section.

{See also "Document"}

Selectivity

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Ability of an analytical method to differentiate and measure the analyte in the presence of interfering substances in the biological matrix (non-specific interference).

Semi-permeable containers

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

Containers that allow the passage of solvent, usually water, while preventing solute loss. The mechanism for solvent transport occurs by absorption into 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.

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

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 and LDPE and high-density polyethylene (HDPE) ampoules, bottles and vials.

Sender

E2B(R2) Maintenance of the ICH guideline on clinical safety data management : Data elements for transmission of individual case safety reports , Glossary

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.

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

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.[ICH E2B(R2)]

Senior Management

Q10 Pharmaceutical Quality System, Glossary

Person(s) who direct and control a company or site at the highest levels with the authority and responsibility to mobilise resources within the company or site. (ICH Q10 based in part on ISO 9000:2005)

Sensitivity

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The lowest analyte concentration that can be measured with acceptable accuracy and precision (i.e. Lower Limit of Quantification, LLOQ).

Sensitivity Analysis

E9(R1) Addendum: Statistical Principles for Clinical Trials, Glossary

A series of analyses conducted with the intent to explore the robustness of inferences from the main estimator to deviations from its underlying modelling assumptions and limitations in the data.

Serious Adverse event (AE)/Adverse Drug Reaction (ADR)

E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting, 2.3

In accordance with the ICH E2A guideline, a serious adverse event or reaction is any untoward medical occurrence that at any dose:
* results in death,
* is life-threatening {see NOTE below}
* requires inpatient hospitalisation or results in prolongation of existing hospitalisation,
* results in persistent or significant disability/incapacity,
* is a congenital anomaly/birth defect,
* is a medically important event or reaction.

(NOTE: The term “life-threatening” in the definition of “serious” refers to an event/reaction in which the patient was at risk of death at the time of the event/reaction; it does not refer to an event/ reaction which hypothetically might have caused death if it were more severe)

{Note following the definition:} Medical and scientific judgment should be exercised in deciding whether other situations should be considered serious such as important medical events that might not be immediately life-threatening or result in death or hospitalisation but might jeopardise the patient or might require intervention to prevent one of the other outcomes listed in the definition above. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

Serious adverse event (experience) or reaction

E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting, II.B

A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose:
* results in death,
* is life-threatening, {see NOTE}
* requires inpatient hospitalisation or prolongation of existing hospitalisation,
* results in persistent or significant disability/incapacity, or
* is a congenital anomaly/birth defect.

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe. -- Medical and scientific judgement should be exercised in deciding whether expedited reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed in the definition above. These should also usually be considered serious. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalisation; or development of drug dependency or drug abuse.

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR)

E6(R2) Good Clinical Practice (GCP), Glossary

Any untoward medical occurrence that at any dose:
* results in death,
* is life-threatening,
* requires inpatient hospitalization or prolongation of existing hospitalization,
* results in persistent or significant disability/incapacity, or
* is a congenital anomaly/birth defect

(see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

Serious Adverse Reaction or Serious Adverse Drug Reaction

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

Any untoward medical occurrence that at any dose:
- results in death,
- is life-threatening,
- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity, or -
is a congenital anomaly/birth defect
(see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).[ICH E6(R1)]

Severe versus Serious

E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting, II.B

The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a patient's life or functioning. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

Severity

Q3D(R2) Guideline for Elemental Impurities, Glossary

A measure of the possible consequences of a hazard. (ICH Q9)

Q9 Quality Risk Management, Definitions

A measure of the possible consequences of a hazard.

Shedding

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, 1.3

The release of a GT product outside the body via excreta (feces), secreta (urine, saliva, nasopharyngeal fluids, etc.), or through the skin (pustules, sores, wounds) is termed ‘shedding’.

Shelf life

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The period of time during which an active pharmaceutical ingredient (API) or finished pharmaceutical product (FPP), if stored under the conditions in which stability was established, is expected to comply with the specification as determined by stability studies on a number of batches of the API or FPP. The shelf life is used to establish the expiry date of each batch.

Shelf life (also referred to as expiration dating period)

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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 conditions defined on the container label.

Shelf-life specification

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

The combination of physical, chemical, biological and microbiological tests and acceptance criteria that an active pharmaceutical ingredient or finished pharmaceutical product should meet throughout its retest period or shelf life.

Signal

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

Information that arises from one or multiple sources (including observations and experiments), that suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify further action to verify. For the purpose of Section 16.2 of the Periodic Benefit-Risk Evaluation Report (PBRER) , signals relate to adverse effects.
{Source:} ICH Guideline E2C(R2)

E2F Development Safety Update Report, Glossary

A report or reports of an event with an unknown causal relationship to treatment that is recognised as worthy of further exploration and continued surveillance.
{Source: } CIOMS VI

Signature (signed)

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

See definition for signed

Signed (signature)

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The record of the individual who performed a particular action or review. This record can be initials, full handwritten signature, personal seal, or authenticated and secure electronic signature.

Significant change

Q1A(R2) Stability Testing of New Drug Substances and Products, 2.1.7 and 2.2.1.7

{In this guideline} “Significant change” for a drug substance is defined as failure to meet its specification. -- In general, “significant change” for a drug product is defined as: 1. A 5% change in assay from its initial value; or failure to meet the acceptance criteria for potency when using biological or immunological procedures; 2. Any degradation product’s exceeding its acceptance criterion; 3. Failure to meet the acceptance criteria for appearance, physical attributes, and functionality test (e.g., color, phase separation, resuspendibility, caking, hardness, dose delivery per actuation); however, some changes in physical attributes (e.g., softening of suppositories, melting of creams) may be expected under accelerated conditions; and, as appropriate for the dosage form: 4. Failure to meet the acceptance criterion for pH; or 5. Failure to meet the acceptance criteria for dissolution for 12 dosage units.

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

(See sections 2.1.7 and 2.2.7.) “Significant change” for an active pharmaceutical ingredient (API) is defined as failure to meet its specification. In general “significant change” for a finished pharmaceutical product is defined as: a 5% or more change in assay from its initial content of API(s), or failure to meet the acceptance criteria for potency when using biological or immunological procedures. -- Any degradation product exceeding its acceptance criterion. 1. Failure to meet the acceptance criteria for appearance, physical attributes and functionality test (e.g. colour, phase separation, resuspendability, caking, hardness, dose delivery per actuation). However, some changes in physical attributes (e.g. softening of suppositories, melting of creams or partial loss of adhesion for transdermal products) may be expected under accelerated conditions. Also, as appropriate for the dosage form: 2. failure to meet the acceptance criterion for pH; or 3. failure to meet the acceptance criteria for dissolution for 12 dosage units.

Significant structural fragment

Q11 Q&As Questions & Answers: Selection and Justification of Starting Materials for the Manufacture of Drug Substances, Q5.5

The selection principle about “significant structural fragment” has frequently been misinterpreted as meaning that the proposed starting material should be structurally similar to the drug substance. However, as stated in ICH Q11, this general principle is intended to help distinguish starting materials from reagents, catalysts, solvents, or other raw materials.

Single Cell Gel Electrophoresis assay

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

Comet assay. See DNA strand break assay.

Single coded data and samples

E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories, 2.3.2.1

Single coded data and samples are usually labelled with a single specific code and do not carry any personal identifiers.

Soft Sensors

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

A model that is used in lieu of physical measurement to estimate a variable or attribute (e.g., a quality attribute of material) based on measured data (e.g., process data). The model development, including selection of such data variables, is driven by comprehensive product and process understanding.

Solicited reports

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

Solicited reports are those derived from organized data collection systems, which include clinical trials, registries, post-approval named patient use programs, other patient support and disease management programs, surveys of patients or healthcare providers, or information gathering on efficacy or patient compliance.

{Source:} ICH Guideline E2D

Solicited Sources

E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting, 3.2

Solicited reports are those derived from organized data collection systems, which include clinical trials, registries, post-approval named patient use programs, other patient support and disease management programs, surveys of patients or healthcare providers, or information gathering on efficacy or patient compliance. Adverse event reports obtained from any of these should not be considered spontaneous. One or more of the following should automatically qualify a patient as identifiable: age (or age category, e.g., adolescent, adult, elderly), gender, initials, date of birth, name, or patient identification number. In addition, in the event of second-hand reports, every reasonable effort should be made to verify the existence of an identifiable patient and reporter.

Solvent

Q3A(R2) Impurities in New Drug Substances, Glossary

An inorganic or an organic liquid used as a vehicle for the preparation of solutions or suspensions in the synthesis of a new drug substance.

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

An inorganic or an organic liquid used as a vehicle for the preparation of solutions or suspensions in the synthesis of a new drug substance or the manufacture of a new drug product.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

An inorganic or organic liquid used as a vehicle for the preparation of solutions or suspensions in the manufacture of an intermediate or Active Pharmaceutical Ingredient (API).

Source Data

E6(R2) Good Clinical Practice (GCP), Glossary

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

E6(R2) Good Clinical Practice (GCP), Glossary

Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, 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).

Speciation

Q3D(R2) Guideline for Elemental Impurities, 8

Speciation is defined as the distribution of elements among chemical species including isotopic composition, electronic or oxidation state, and/or complex or molecular structure.

When the toxicities of different species of the same element are known, the PDE has been established using the toxicity information on the species expected to be in the drug product.

Specific Model Virus

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Virus which is closely related to the known or suspected virus (same genus or family), having similar physical and chemical properties to those of the observed or suspected virus.
{See also “Virus”}

Specific test

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

A test which is considered to be applicable to particular new drug substances or particular new drug products depending on their specific properties and/or intended use.

Specification

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

See Q6A and Q6B.

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

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 an active pharmaceutical ingredient or finished pharmaceutical product should conform to be considered acceptable for its intended use. See Release specification and Shelf-life specification.

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

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 or drug product should conform to be considered acceptable for its intended use. "Conformance to specifications" means that the drug substance and / or drug product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are critical quality standards that are proposed and justified by the manufacturer and approved by regulatory authorities.

Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Glossary

A specification is defined as 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 materials 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.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A list of tests, references to analytical procedures, and appropriate acceptance criteria that are numerical limits, ranges, or other criteria for the test described. It establishes the set of criteria to which a material should conform to be considered acceptable for its intended use. “Conformance to specification” means that the material, when tested according to the listed analytical procedures, will meet the listed acceptance criteria.

Specification – Release

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

The combination of physical, chemical, biological, and microbiological tests and acceptance criteria that determine the suitability of a drug product at the time of its release.

Specification - Shelf life

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

The combination of physical, chemical, biological, and microbiological tests and acceptance criteria 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

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Ability of an analytical method to detect and differentiate the analyte from other substances, including its related substances (e.g., substances that are structurally similar to the analyte, metabolites, isomers, impurities or concomitant medications).

Q2(R1) Validation of Analytical Procedures: Text and Methodology, Glossary

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 implications: Identification: to ensure the identity of an analyte. 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.

Specificity/selectivity

Q14 Analytical Procedure Development, Glossary

Specificity and selectivity are both terms to describe the extent to which other substances interfere with the determination of a substance according to a given analytical procedure. Such other substances might include impurities, degradation products, related substances, matrix or other components present in the operating environment. Specificity is typically used to describe the ultimate state, measuring unequivocally a desired analyte. Selectivity is a relative term to describe to which extent particular analytes in mixtures or matrices can be measured without interferences from other components with similar behaviour. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

Specificity and selectivity are both terms to describe the extent to which other substances interfere with the determination of a substance according to a given analytical procedure. Such other substances might include impurities, degradation products, related substances, matrix or other components present in the operating environment. Specificity is typically used to describe the ultimate state, measuring unequivocally a desired analyte. Selectivity is a relative term to describe to which extent particular analytes in mixtures or matrices can be measured without interferences from other components of similar behaviour. (ICH Q2)

Specified Degradation Product

Q3B(R2) Impurities in New Drug Products, Glossary

A degradation product that is individually listed and limited with a specific acceptance criterion in the new drug product specification. A specified degradation product can be either identified or unidentified.

Specified Impurity

Q3A(R2) Impurities in New Drug Substances, Glossary

An impurity that is individually listed and limited with a specific acceptance criterion in the new drug substance specification. A specified impurity can be either identified or unidentified.

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

An identified or unidentified impurity that is selected for inclusion in the new drug substance or new drug product specification and is individually listed and limited in order to assure the quality of the new drug substance or new drug product.

Sponsor

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial. [ICH E6(R1) & E2F]

E2F Development Safety Update Report, Glossary

An individual, company, institution, or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.
{Source: } ICH E6 (R1)

E6(R2) Good Clinical Practice (GCP), Glossary

An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Sponsor- investigator

E2F Development Safety Update Report, Glossary

An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.
{Source: } ICH E6

Sponsor-Investigator

E6(R2) Good Clinical Practice (GCP), Glossary

An individual who both initiates and conducts, alone or with others, a clinical trial, and under whose immediate direction the investigational product is administered to, dispensed to, or used by a subject. The term does not include any person other than an individual (e.g., it does not include a corporation or an agency). The obligations of a sponsor-investigator include both those of a sponsor and those of an investigator.

Spontaneous report or spontaneous notification

E2C(R2) Periodic Benefit-Risk Evaluation Report, Glossary

An unsolicited communication to a company, regulatory authority, or other organization that describes an Adverse Drug Reaction (ADR) in a patient given one or more medicinal products and which does not derive from a study or any organized data collection scheme.

{Source:} ICH Guideline E2D

Spontaneous Reporting

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

An unsolicited communication to a company, regulatory authority or other organisation that describes an adverse drug reaction in a patient given one or more medicinal products and which does not derive from a study or any organized data collection scheme.[ICH E2C(R1)]

Spontaneous Reports

E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting, 3.1.1

A spontaneous report is an unsolicited communication by a healthcare professional or consumer to a company, regulatory authority or other organization (e.g. WHO, Regional Center, Poison Control Center) that describes one or more adverse drug reactions in a patient who was given one or more medicinal products and that does not derive from a study or any organized data collection scheme.

Stability

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Measure of the intactness of an analyte (lack of degradation) in a given matrix under specific storage and use conditions relative to the starting material for given time intervals.

Stability studies (stability testing)

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

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 retest period (or shelf life) of an active pharmaceutical ingredient or the shelf life of a finished pharmaceutical product.

Stability-indicating methods

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

Validated analytical procedures that can detect the changes with time in the chemical, physical or microbiological properties of the active pharmaceutical ingredient (API) or finished pharmaceutical product, and that are specific so that the content of the API, degradation products and other components of interest can be accurately measured without interference.

Stakeholder

Q9 Quality Risk Management, Definitions

Any individual, group or organization that can affect, be affected by, or perceive itself to be affected by a risk. Decision makers might also be stakeholders. For the purposes of this guideline, the primary stakeholders are the patient, healthcare professional, regulatory authority, and industry.

Stand-alone drug-drug interaction (DDI) study

M12 EWG Drug Interaction Studies , 3.1.1

A stand-alone drug-drug interaction (DDI) study is a clinical study with the primary objective of determining the presence or absence of a clinical DDI and the magnitude of the DDI.

Standard

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

A technical specification which addresses a business requirement, has been implemented in viable commercial products, and, to the extent practical, complies with recognised standards organisations such as ISO.

Standard Curve

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

{See “Calibration curve”}

The relationship between the instrument response (e.g., peak area, height or signal) and the concentration (amount) of analyte in the calibration standards within a given range. Also referred to as calibration Curve.

Standard Operating Procedure (SOP)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Detailed written instructions to achieve uniformity of the performance of a specific function and/or process(es).

Standard Operating Procedures (SOPs)

E6(R2) Good Clinical Practice (GCP), Glossary

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

Starting Material

Q11 Q&As Questions & Answers: Selection and Justification of Starting Materials for the Manufacture of Drug Substances, Q5.2

{See the definition of "API starting material" in ICH Q7}
ICH Q11 states that the GMP provisions described in ICH Q7 apply to each branch of the drug substance manufacturing process beginning with the first use of a “starting material”. ICH Q7 states that appropriate GMP (as defined in that guideline) should be applied to the manufacturing steps immediately after “API starting materials” are entered into the process (see ICH Q7 Q&A 1.1). Because ICH Q11 sets the applicability of ICH Q7 as beginning with the “starting material”, and ICH Q7 sets the applicability of ICH Q7 as beginning with the “API starting material”, these two terms are intended to refer to the same material. ICH Q7 states that an “API starting material” is a raw material, intermediate, or an API that is used in the production of an API. ICH Q7 provides guidance regarding good manufacturing practices for the drug substance, but does not provide specific guidance on the selection and justification of starting materials. When a chemical, including one that is also an API, is proposed to be a starting material, all ICH Q11 general principles still need to be considered.

Q3A(R2) Impurities in New Drug Substances, Glossary

A material used in the synthesis of a new drug substance that is incorporated as an element into the structure of an intermediate and/or of the new drug substance. Starting materials are normally commercially available and of defined chemical and physical properties and structure.

State of Control

Q10 Pharmaceutical Quality System, Glossary

A condition in which the set of controls consistently provides assurance of continued process performance and product quality. (ICH Q10)

Statistical Analysis Plan

E9 Statistical Principles for Clinical Trials, Glossary

A statistical analysis plan is a document that contains a more technical and detailed elaboration of the principal features of the analysis described in the protocol, and includes detailed procedures for executing the statistical analysis of the primary and secondary variables and other data.

Steady State

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

A stable condition that does not change over time.

Stock Solution

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

An analyte in a solvent or mixture of solvents at a known concentration, which is used to prepare calibration standards or quality control samples (QCs).

Storage condition tolerances

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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 this guideline. 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 effect assessed.

Stress testing (drug product)

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

Studies undertaken to assess the effect of severe conditions on the drug product. Such studies include photostability testing (see ICH Q1B) and specific testing on certain products, (e.g., metered dose inhalers, creams, emulsions, refrigerated aqueous liquid products).

Stress testing (drug substance)

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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.

Stress testing (of the active pharmaceutical ingredient (API))

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

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

Stress testing (of the finished pharmaceutical product (FPP))

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

Studies undertaken to assess the effect of severe conditions on the FPP. Such studies include photostability testing and specific testing on certain products (e.g. metered-dose inhalers, creams, emulsions, refrigerated aqueous liquid products). supporting stability data. Supplementary data, such as stability data on small-scale batches, related formulations, and products presented in containers not necessarily the same as those proposed for marketing, and scientific rationales that support the analytical procedures, the proposed retest period or the shelf life and storage conditions.

Strongly Suspected Human Carcinogen

Q3C(R8) Guideline for Residual Solvents, Glossary

A substance for which there is no epidemiological evidence of carcinogenesis but there are positive genotoxicity data and clear evidence of carcinogenesis in rodents.

Structural alert

M7(R1) Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk, Glossary

In the context of this guideline, a chemical grouping or molecular (sub) structure which is associated with mutagenicity.

Study samples

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Samples from animals or subjects enrolled in nonclinical or clinical studies.

Subcontracting

Q7 Q&As Questions and Answers: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Q16.3

Subcontracting as used in [ICH Q7, Section 16.14] refers to the contract acceptor further contracting out a specific activity to another party (third party).

This should only be done when the written and approved contract, as described in [ICH Q7, Section 16.12], specifically allows for such subcontracting. Even when subcontracting is allowed, the original contract giver should approve specific subcontracting before it occurs as stated in [ICH Q7, Section 16.14].

Subinvestigator

E6(R2) Good Clinical Practice (GCP), Glossary

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.

Subject Identification Code

E6(R2) Good Clinical Practice (GCP), Glossary

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.

Subject/Trial Subject

E6(R2) Good Clinical Practice (GCP), Glossary

An individual who participates in a clinical trial, either as a recipient of the investigational product(s) or as a control.

Submission

Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management, Glossary

Communication to a regulatory authority regarding a change to an established condition that could be prior approval or notification.

Sufficiently similar

E11A EWG Paediatric Extrapolation, 1.4

In the ICH E11(R1) definition of pediatric extrapolation, “sufficiently similar” might suggest a threshold that must be exceeded for pediatric extrapolation to be acceptable for regulatory consideration. However, whether the course of disease and expected response to treatment can be considered sufficiently similar between a target and reference population is not simply a “yes or no” question. Therefore, this guidance does not use discrete categories (e.g., full, partial or none) to describe the different approaches to pediatric extrapolation, in favour of identifying the clinical trial designs which can address the remaining uncertainties based on an assessment of the existing data. The use of extrapolation as discussed in this guideline reflects that a continuum of dissimilarity/similarity may exist. There may be uncertainties associated with the data supporting extrapolation to the target pediatric population. The extrapolation approach should address these uncertainties, utilizing clinical judgement to establish the tolerable level of uncertainty that will be acceptable (see Figure 1). Options for trial designs will depend on the level of uncertainty that needs to be resolved.

Superiority Trial

E9 Statistical Principles for Clinical Trials, Glossary

A trial with the primary objective of showing that the response to the investigational product is superior to a comparative agent (active or placebo control).

Supplementary Analysis

E9(R1) Addendum: Statistical Principles for Clinical Trials, Glossary

A general description for analyses that are conducted in addition to the main and sensitivity analysis with the intent to provide additional insights into the understanding of the treatment effect.

Support

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

In the context of a toxicity study - to ratify or confirm the design of a toxicity study with respect to pharmacokinetic and metabolic principles. This process may include 2 separate steps: a) confirmation using toxicokinetic principles that the animals on a study were exposed to appropriate systemic levels of the administered compound (see 3.4) and/or its metabolite(s). b) confirmation that the metabolic profile in the species used was acceptable; data to support this will normally be derived from metabolism studies in animals and in humans.

Supporting data

Q1A(R2) Stability Testing of New Drug Substances and Products, Glossary

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.

Supratherapeutic dose

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q5.1

Dose that provides exposures (mean Cmax) exceeding the high clinical scenario
{see also 'High clinical exposure' as defined in Q5.1 of this document}

Surrogate Matrix

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

An alternative to a study matrix of limited availability (e.g., tissue, cerebrospinal fluid, bile) or where the study matrix contains an interfering endogenous counterpart.

Surrogate molecule

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

A molecule showing similar pharmacologic activity in the test species as that shown by the human pharmaceutical in the human.

Surrogate Variable

E9 Statistical Principles for Clinical Trials, Glossary

A variable that provides an indirect measurement of effect in situations where direct measurement of clinical effect is not feasible or practical.

Survival (in the context of mutagenicity testing)

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

System

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

A manufacturing architecture that, in the context of continuous manufacturing (CM), consists of individual pieces of equipment, their connections to one another and monitoring and control systems, and spatial layout.

System Suitability

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Determination of instrument performance (e.g., signal-to-noise ratio, peak shape, retention time) by analysis of a prepared, spiked sample conducted prior to the analytical run and is not a part of the sample analysis.

System suitability test (SST)

Q14 Analytical Procedure Development, Glossary

These tests are developed and used to verify that the measurement system and the analytical operations associated with the analytical procedure are adequate for the intended analysis and increase the detectability of potential failures (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

These tests are developed and used to verify that the measurement system and the analytical operations associated with the analytical procedure are adequate for the intended analysis and increase the detectability of potential failures (ICH Q14)

Systemic drugs

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

Products administered by a route that is intended to produce systemic exposure.

T

Teratogenicity

Q3C(R8) Guideline for Residual Solvents, Glossary

The occurrence of structural malformations in a developing fetus when a substance is administered during pregnancy.

Therapeutic context

M4E(R2) CTD on Efficacy, 2.5.6.1

The term 'therapeutic context' describes the disease or condition to be treated, the population intended to be treated, and the benefits and risks of current therapies.2

{Footnote 2} For purposes of Section 2.5.6, the term "therapy" encompasses both pharmacologic and non-pharmacologic interventions,

as well as preventive measures and diagnostics. In addition, the terms "therapy" and "treatment" are used interchangeably.

Therapeutic dose

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q5.1

Dose evaluated in Phase 3 trial or recommended in product labeling

Therapeutic Dose Range

E5(R1) Ethnic Factors in the Acceptability of Foreign Clinical Data, Glossary

The difference between the lowest effective dose and the highest dose that gives further benefit.

Thorough QT/QTc Study: positive control; negative study, positive study

E14 The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs, 2.2.2

Interpretation of the 'Thorough QT/QTc Study' -- It is difficult to determine whether there is an effect on the mean QT/QTc interval that is so small as to be of no consequence. However, drugs that prolong the mean QT/QTc interval by around 5 ms or less do not appear to cause Torsade de Pointes (TdP). On that basis, the positive control (whether pharmacological or non-pharmacological) should be well-characterized and consistently produce an effect on the QT/QTc interval that is around the threshold of regulatory concern (5 ms, section 2.2). --Based on similar considerations, a negative 'thorough QT/QTc study' is one in which the upper bound of the 95% one-sided confidence interval for the largest time-matched mean effect of the drug on the QTc interval excludes 10 ms. This definition is chosen to provide reasonable assurance that the mean effect of the study drug on the QT/QTc interval is not greater than around 5 ms. When the largest time-matched difference exceeds the threshold, the study is termed 'positive'. A positive study influences the evaluations carried out during later stages of drug development, but does not imply that the drug is pro-arrhythmic. -- As with other data, the presence of outliers (see section 3.2.2) should also be explored.

Threshold Limit Value (TLV)

Q3D(R2) Guideline for Elemental Impurities, Glossary

The concentration in air to which it is believed that most workers can be exposed daily without an adverse effect (i.e., effectively, the threshold between safe and dangerous concentrations). The values were established (and are revised annually) by the American Conference of Governmental Industrial Hygienists (ACGIH) and are time- weighted concentrations (TWA) for a 7- or 8-hour workday and 40-hour workweek, and thus related to chronic effects. (International Programme for Chemical Safety, IUPAC）

Time Weighted Average (TWA)

Q3D(R2) Guideline for Elemental Impurities, Glossary

As defined by the American Conference of Governmental Industrial Hygienists (ACGIH), time-weighted average concentration for a conventional 8-hour workday and a 40-hour workweek. (International Programme for Chemical Safety, IUPAC)

Time-matched baseline

E14 Q&As (R3) The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs, Q4.2

{Baseline} taken at exactly the same time-points on the day prior to the beginning of treatment as on the treatment day

E14/S7B Q&As IWG Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential, E14 Q&As, Q4.2

{Baseline} taken at exactly the same time-points on the day prior to the beginning of treatment as on the treatment day

Total analytical error

Q14 Analytical Procedure Development, Glossary

Total analytical error (TAE) represents the overall error in a test result that is attributed to imprecision and inaccuracy. TAE is the combination of both systematic error of the procedure and random measurement error. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Glossary

Total analytical error (TAE) represents the overall error in a test result that is attributed to imprecision and inaccuracy. TAE is the combination of both, systematic error of the procedure and random measurement error. (ICH Q14)

Total Error

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The sum of the absolute value of the errors in accuracy (%) and precision (%). Total error is reported as percent (%) error.

Toxicokinetics

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, 1

In this context, toxicokinetics is defined as the generation of pharmacokinetic data, either as an integral component in the conduct of non-clinical toxicity studies or in specially designed supportive studies, in order to assess systemic exposure. These data may be used in the interpretation of toxicology findings and their relevance to clinical safety issues.

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

Assessment of Systemic Exposure
{See also "Exposure"}

Traditional approach

Q11 Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities), 1

In a traditional approach {to developing a drug substance}, set points and operating ranges for process parameters are defined and the drug substance control strategy is typically based on demonstration of process reproducibility and testing to meet established acceptance criteria.
Traditional and enhanced approaches are not mutually exclusive. A company can use either a traditional approach or an enhanced approach to drug substance development, or a combination of both. {And see 3.1.3: "These concepts apply equally to the development of the drug substance manufacturing process. "}

Transgene

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, Glossary

Transcriptionally or translationally active genetic material intended to be delivered into cells with therapeutic purpose. It does not include vector or chemically synthesised oligonucleotides.

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

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

Transient Events

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

A temporary condition in which a process goes through a dynamic change. This change may be due to a disturbance or an intentional alteration in the selected operating conditions (e.g., start-up, shutdown, changes from one operating condition to another).

Treatment Effect

E9 Statistical Principles for Clinical Trials, Glossary

An effect attributed to a treatment in a clinical trial. In most clinical trials the treatment effect of interest is a comparison (or contrast) of two or more treatments.

Treatment Emergent

E9 Statistical Principles for Clinical Trials, Glossary

An event that emerges during treatment having been absent pre-treatment, or worsens relative to the pre-treatment state.

Trend

Q9 Quality Risk Management, Definitions

A statistical term referring to the direction or rate of change of a variable(s).

Trial Site

E6(R2) Good Clinical Practice (GCP), Glossary

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

Trial Statistician

E9 Statistical Principles for Clinical Trials, Glossary

A statistician who has a combination of education/training and experience sufficient to implement the principles in this guidance and who is responsible for the statistical aspects of the trial.

U

Ultraviolet light A (UVA)

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

Wavelengths between 320 and 400 nm

Ultraviolet light B (UVB)

S10 Photosafety Evaluation of Pharmaceuticals, Glossary

Wavelengths between 280 and 320 nm; as a part of sunlight wavelengths between 290 and 320 nm.

Unexpected ADR

E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting, 2.4

An ADR whose nature, severity, specificity, or outcome is not consistent with the term or description used in the local/regional product labeling (e.g. Package Insert or Summary of Product Characteristics) should be considered unexpected. When a Marketing Authorisation Holder (MAH) is uncertain whether an ADR is expected or unexpected, the ADR should be treated as unexpected.

{Clarifications} An expected ADR with a fatal outcome should be considered unexpected unless the local/regional product labeling specifically states that the ADR might be associated with a fatal outcome. "Class ADRs" should not automatically be considered to be expected for the subject drug. {Additional clarifications follow in the guideline}

NOTE: The term "listedness" is not applicable to expedited reporting but should be used to characterize the ADR according to the Company Core Safety Information (refer to ICH E2C guideline for definitions).

Unexpected Adverse Drug Reaction

E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting, II.A.3

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 medicinal product). (See section III.C.)

E6(R2) Good Clinical Practice (GCP), Glossary

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 Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

Unidentified Degradation Product

Q3B(R2) Impurities in New Drug Products, Glossary

A degradation product for which a structural characterisation has not been achieved and that is defined solely by qualitative analytical properties (e.g., chromatographic retention time).

Unidentified Impurity

Q3A(R2) Impurities in New Drug Substances, Glossary

An impurity for which a structural characterisation has not been achieved and that is defined solely by qualitative analytical properties (e.g., chromatographic retention time).

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

An impurity which is defined solely by qualitative analytical properties, (e.g., chromatographic retention time).

Uniformity of dosage unit

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, 3.3.2.1, 3.3.2.2, 3.3.2.3

This term includes both the mass of the dosage form and the content of the active substance in the dosage form; a pharmacopoeial procedure should be used {as a test for uniformity of dosage unit}.

Unit Operation

Q13 EWG Continuous Manufacturing of Drug Substances and Drug Products, Glossary

A basic step in a process. Unit operations involve a physical or chemical transformation such as a reaction, crystallisation, blending, purification, granulation, filtration, and virus inactivation.

Universal test

Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, Glossary

A test which is considered to be potentially applicable to all new drug substances, or all new drug products; e.g., appearance, identification, assay, and impurity tests.

Unprocessed Bulk

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

One or multiple pooled harvests of cells and culture media. When cells are not readily accessible, the unprocessed bulk would constitute fluid harvested from the fermenter.

Unscheduled DNA synthesis (UDS)

S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use, Glossary

DNA synthesis that occurs at some stage in the cell cycle other than S-phase in response to DNA damage. It is usually associated with DNA excision repair.

Unspecified Degradation Product

Q3B(R2) Impurities in New Drug Products, Glossary

A degradation product that is limited by a general acceptance criterion, but not individually listed with its own specific acceptance criterion, in the new drug product specification.

Unspecified impurity

Q3A(R2) Impurities in New Drug Substances, Glossary

An impurity that is limited by a general acceptance criterion, but not individually listed with its own specific acceptance criterion, in the new drug substance specification.

Upper Limit of Quantification (ULOQ)

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

The highest amount of an analyte in a sample that can be quantitatively determined with pre- defined precision and accuracy.

Use Case

E2B(R3) Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification, Glossary of Terms

A description of a system's behaviour as it responds to a request that originates from outside of that system.[Objectory AB]

Utilization period

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

See in-use period.

V

Vaccine

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

For the purpose of this guideline, this term refers to preventative or therapeutic vaccines for infectious diseases. Vaccine (inclusive of the term vaccine product) is defined as the complete formulation and includes antigen(s) (or immunogen(s)) and any additives such as adjuvants, excipients or preservatives. The vaccine is intended to stimulate the immune system and result in an immune response to the vaccine antigen(s). The primary pharmacological effect of the vaccine is the prevention and/or treatment of an infection or infectious disease.

Validate

S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies, Note 1

In the context of an analytical method - to establish the accuracy, precision, reproducibility, response function and the specificity of the analytical method with reference to the biological matrix to be examined and the analyte to be quantified.

Validation

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

Demonstration that a bioanalytical method is suitable for its intended purpose.

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

A documented program that provides a high degree of assurance that a specific process, method, or system will consistently produce a result meeting pre-determined acceptance criteria.

Validation of Computerized Systems

E6(R2) Good Clinical Practice (GCP), Glossary (Addendum)

A process of establishing and documenting that the specified requirements of a computerized system can be consistently fulfilled from design until decommissioning of the system or transition to a new system. The approach to validation should be based on a risk assessment that takes into consideration the intended use of the system and the potential of the system to affect human subject protection and reliability of trial results.

Validation Protocol

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

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

Q14 Analytical Procedure Development, Multivariate glossary

A set of data used to give an independent assessment of the performance of the calibration model, ideally over a similar operating range. (ICH Q14)

Q2(R2) Validation of Analytical Procedures, Multivariate glossary

A set of data used to give an independent assessment of the performance of the calibration model, ideally over a similar operating range. (ICH Q14)

Validation study

Q14 Analytical Procedure Development, Glossary

An evaluation of prior knowledge, data or deliberate experiments to determine the suitability of an analytical procedure for its intended purpose. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

An evaluation of prior knowledge, data or deliberate experiments to determine the suitability of an analytical procedure for its intended purpose. (ICH Q2)

Validation test

Q14 Analytical Procedure Development, Glossary

Validation tests are deliberate experiments designed to determine the suitability of an analytical procedure for its intended purpose. (ICH Q2)

Q2(R2) Validation of Analytical Procedures, Glossary

Validation tests are deliberate experiments designed to authenticate the suitability of an analytical procedure for its intended purpose. (ICH Q2)

Variation

S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals, Glossary

Structural change that does not impact viability, development, or function (e.g., delays in ossification) which can be reversible, and are found in the normal population under investigation.

Variations

Q1F (WHO) Stability Data Package for Registration Applications in Climatic Zones III and IV, Glossary

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

Vectors

S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products, Glossary

Gene therapy delivery vehicles, or carriers, containing transcriptionally/ translationally active therapeutic genetic material or genetic material to alter the host genome for delivery to cells. They include both genetically modified viruses such as adenovirus or adeno-associated virus, and non-viral vectors such as plasmids and gene modified microorganisms, and can include targeted nanoparticles which have the capability to transfer genetic materials or gene editing components to the cells.

Viral Clearance

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

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

Virus

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Intracellularly replicating infectious agents that are potentially pathogenic, possessing only a single type of nucleic acid (either RNA or DNA), are unable to grow and undergo binary fission, and multiply in the form of their genetic material.

{From Section 1 of the guideline:} For the purposes of this document the term virus excludes nonconventional transmissible agents like those associated
with Bovine Spongiform Encephalopathy (BSE) and scrapie.

Virus Removal

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

Physical separation of virus particles from the intended product.

Virus-like Particles

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

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

Vulnerable Subjects

E6(R2) Good Clinical Practice (GCP), Glossary

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 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.

W

Weight of Evidence

S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines, Glossary

An approach that evaluates information from several sources to decide if there is sufficient evidence to support the development of pharmaceuticals for paediatric use or whether additional nonclinical testing is warranted to address potential safety concerns. The weight given to the available evidence depends on factors such as the quality of the data, consistency of results, nature and severity of effects, and relevance of the information. The weight of evidence approach requires use of scientific judgment and, therefore, should consider the robustness and reliability of the different data sources.

Well-being (of the trial subjects)

E6(R2) Good Clinical Practice (GCP), Glossary

The physical and mental integrity of the subjects participating in a clinical trial.

Working Cell Bank (WCB)

Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Glossary

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

Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products, Glossary

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

Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products, Glossary

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

Working range

Q14 Analytical Procedure Development, Glossary

The working range of an analytical procedure is the lowest and the highest concentration that the analytical procedure provides meaningful results. Working ranges may be different before sample preparation (sample working range) and when presented to the analytical instrument (instrument working range). (ICH Q2)

{See also “Range”, "Reportable range"}

Q2(R2) Validation of Analytical Procedures, Glossary

The working range of an analytical procedure is the lowest and the highest concentration that the analytical procedure provides meaningful results. Working ranges may be different before sample preparation (sample working range) and when presented to the analytical instrument (instrument working range). (ICH Q2)

{See also “Range”, "Reportable range"}

Working Solution

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A non-matrix solution prepared by diluting the stock solution in an appropriate solvent. It is mainly added to matrix to prepare calibration standards and quality control samples (QCs).

Worst-case scenario

E14 The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs, 5.1

In any case, it is important to identify the “worst case scenario” for drugs that have demonstrated effects on QT/QTc interval as a part of risk assessment (i.e., the QT/QTc interval measured in the target patient population at the time of peak effect and under conditions of the highest blood levels that can be attained during therapy)

Y

Yield, Expected

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The quantity of material or the percentage of theoretical yield anticipated at any appropriate phase of production based on previous laboratory, pilot scale, or manufacturing data.

Yield, Theoretical

Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients, Glossary

The quantity that would be produced at any appropriate phase of production, based upon the quantity of material to be used, in the absence of any loss or error in actual production.

Z

Zero Sample

M10 EWG Bioanalytical Method Validation and Study Sample Analysis, Glossary

A blank sample spiked with an Internal Standard (IS).

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26 September 2022

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Q4B Annex 5(R1) Disintegration Test General Chapter https://database.ich.org/sites/default/files/Q4B%20Annex%205%28R1%29%20Guideline.pdf	0
Q4B Annex 6 Uniformity of Dosage Units General Chapter https://database.ich.org/sites/default/files/Q4B%20Annex%206%20Guideline.pdf	0

ICH guideline (sorted alphabetically, e.g. E10 before E2)	*# definitions found*
Q4B Annex 7(R2) Dissolution Test General Chapter https://database.ich.org/sites/default/files/Q4B%20Annex%207%20%28R2%29%20Guideline.pdf	0
Q4B Annex 8(R1) Sterility Test General Chapter https://database.ich.org/sites/default/files/Q4B%20Annex%208%28R1%29%20Guideline.pdf	0
Q4B Annex 9(R1) Tablet Friability General Chapter https://database.ich.org/sites/default/files/Q4B%20Annex%209%28R1%29%20Guideline.pdf	0
Q4B FAQs Frequently Asked Questions: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions https://database.ich.org/sites/default/files/Q4B_Frequently%20Asked%20Questions_26.April__7.pdf	1
Q5A(R1) Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin https://database.ich.org/sites/default/files/Q5A%28R1%29%20Guideline_0.pdf	20
Q5A(R2) EWG Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin No guideline	0
Q5B Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products https://database.ich.org/sites/default/files/Q5B%20Guideline.pdf	8
Q5C Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products https://database.ich.org/sites/default/files/Q5C%20Guideline.pdf	6
Q5D Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products https://database.ich.org/sites/default/files/Q5D%20Guideline.pdf	11
Q5E Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process https://database.ich.org/sites/default/files/Q5E%20Guideline.pdf	7
Q6A Specifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances https://database.ich.org/sites/default/files/Q6A%20Guideline.pdf	28
Q6B Specifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products https://database.ich.org/sites/default/files/Q6B%20Guideline.pdf	19

ICH guideline (sorted alphabetically, e.g. E10 before E2)	*# definitions found*
Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients https://database.ich.org/sites/default/files/Q7%20Guideline.pdf	55
Q7 Q&As Questions and Answers: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients https://database.ich.org/sites/default/files/Q7%20Q%26As%20Questions%20%26%20Answers.pdf	5
Q8(R2) Pharmaceutical Development https://database.ich.org/sites/default/files/Q8%28R2%29%20Guideline.pdf	17
Q8/9/10 Q&As (R4) Q8/Q9/Q10 - Implementation https://database.ich.org/sites/default/files/Q8_Q9_Q10_Q%26As_R4_Q%26As_0.pdf	1
Q9 Quality Risk Management https://database.ich.org/sites/default/files/Q9%20Guideline.pdf	30
Q9(R1) EWG Quality Risk Management https://database.ich.org/sites/default/files/ICH_Q9-R1_Document_Step2_Guideline_2021_1118.pdf	25
S10 Photosafety Evaluation of Pharmaceuticals https://database.ich.org/sites/default/files/S10_Guideline.pdf	21
S11 Nonclinical Safety Testing in Support of Development of Paediatric Medicines https://database.ich.org/sites/default/files/S11_Step4_FinalGuideline_2020_0310.pdf	9
S12 EWG Non-clinical Biodistribution Considerations for Gene Therapy Products https://database.ich.org/sites/default/files/ICH_S12_Step2_DraftGuideline_2021_0603.pdf	10
S1A Need for Carcinogenicity Studies of Pharmaceuticals https://database.ich.org/sites/default/files/S1A%20Guideline.pdf	0
S1B Testing for Carcinogenicity of Pharmaceuticals https://database.ich.org/sites/default/files/S1B%20Guideline.pdf	0
S1B(R1) EWG Rodent Carcinogenicity Studies for Human Pharmaceuticals https://database.ich.org/sites/default/files/ICH_S1BR1_Step2_DraftGuideline_2021_0510.pdf	0
S1C(R2) Dose Selection for Carcinogenicity Studies of Pharmaceuticals https://database.ich.org/sites/default/files/S1C%28R2%29%20Guideline.pdf	1

ICH guideline (sorted alphabetically, e.g. E10 before E2)	*# definitions found*
S2(R1) Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use https://database.ich.org/sites/default/files/S2%28R1%29%20Guideline.pdf	33
S3A Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies https://database.ich.org/sites/default/files/S3A_Guideline.pdf	12
S3A Q&As Questions and Answers: Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure - Focus on Microsampling https://database.ich.org/sites/default/files/S3A_Q%26As_Q%26As.pdf	1
S3B Pharmacokinetics: Guidance for Repeated Dose Tissue Distribution Studies https://database.ich.org/sites/default/files/S3B_Guideline.pdf	0
S4 Duration of Chronic Toxicity Testing in Animals (Rodent and Non Rodent Toxicity Testing) https://database.ich.org/sites/default/files/S4_Guideline.pdf	0
S5(R3) Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals https://database.ich.org/sites/default/files/S5-R3_Step4_Guideline_2020_0218_1.pdf	12
S5(R4) Maintenance EWG Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals No guideline; concerns updates to annexes of S5(R3)	0
S6(R1) Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals https://database.ich.org/sites/default/files/S6_R1_Guideline_0.pdf	1
S7A Safety Pharmacology Studies for Human Pharmaceuticals https://database.ich.org/sites/default/files/S7A_Guideline.pdf	3
S7B The Non-Clinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals https://database.ich.org/sites/default/files/S7B_Guideline.pdf	2
S8 Immunotoxicity Studies for Human Pharmaceuticals https://database.ich.org/sites/default/files/S8_Guideline_0.pdf	1
S9 Nonclinical Evaluation for Anticancer Pharmaceuticals https://database.ich.org/sites/default/files/S9_Guideline.pdf	2
S9 Q&As Questions and Answers: Nonclinical Evaluation for Anticancer Pharmaceuticals https://database.ich.org/sites/default/files/S9_Q%26As_Q%26As.pdf	0