Version 8

5 June 2025

Glossary of ICH terms and definitions

Compiled by CIOMS

from the International Council for Harmonization (ICH)'s

Quality Safety Efficacy Multidisciplinary

Guidelines

Council for International Organizations of Medical Sciences

CIOMS Glossary of ICH terms and definitions

Version 8, 5 June 2025

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 and listed in the Index of Guidelines on the ICH website (https://ich.org/page/search-index-ich-guidelines).

--- The Glossary includes all publicly available ICH guidelines and Q&A documents, including 'Step 2' (i.e., draft) and 'Step 4' (i.e., final) texts (see under 'ICH procedures' below for an explanation of the Steps). The documents included are listed at the end of the glossary, together with their status at the time of issuing this Glossary version. Documents that have been newly included since the previous Glossary version are marked with an asterisk (*), and a change history is given below. The Glossary includes only the definitions from the current ICH guidelines.

--- 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', 'mean[s]', for the 'purpose' of this guideline, 'denote[s], and 'refers'/'referred'. Where a definition occurs both in the main text and in the Glossary, only the latter was included.

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

--- The glossary was compiled in Excel format to enable filtering and sorting. Please note:

(1) Superscript and subscript font are not available in the database format. Instead, superscript characters are preceded by '^' (Example: 'cm^2'); subscript characters are preceded by '_' (Example: 'C_max').

(2) The PDF file was exported from Excel using automatic pagination. Page breaks will 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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--- **Disclaimer:** 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 in PDF format at: https://doi.org/10.56759/eftb6868

ICH procedures

The mission of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is to achieve greater harmonisation worldwide to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner. Harmonisation is achieved through the development of ICH Guidelines via a process of scientific consensus with regulatory and industry experts working side-by-side.
ICH harmonisation activities fall into 4 categories: Formal ICH Procedure, Q&A Procedure, Revision Procedure and Maintenance Procedure.

➔More: Process of Harmonisation

Harmonized guidelines on new topics are developed in five Steps:

Step 1 Consensus Building - Technical Document
Step 2 a. ICH Parties consensus on Technical Document /
b. Draft Guideline adoption by Regulators
Step 3 Regulatory Consultation and Discussion
Step 4 Adoption of an ICH Harmonised Guideline
Step 5 Implementation

➔More: Formal ICH procedure

If clarification is needed for an existing ICH guideline, additional guidance is developed. This is usually in the form of Questions and Answers, 'Q&As'. The five Steps outlined above are followed.

➔More: ICH Q&A Procedure

If the content of an existing ICH Guideline is out of date, no longer valid, or needs additional information, a revised guideline is developed. The revision is designated by 'R1' ('R2', 'R3', 'R4'…) after the Guideline title. Revisions follow the five Steps of the formal ICH procedure (see above).

➔More: ICH Revision Procedure

Certain guidelines are subject to a Maintenance procedure to keep their scientific content complete and current.

➔More: ICH Maintenance Procedure

Links to ICH Work Products

The ICH work products are found on the ICH website here:

Index of ICH Guidelines
Quality Guidelines
Safety Guidelines
Efficacy Guidelines
Multidisciplinary Guidelines

Version 1 of this glossary was published on 26 September 2022.

Change history

(A detailed list of ICH guidelines is found at the back of this glossary)

Version yy/mmm/dd	Updated with definitions from the following ICH guidelines:
Version 8: 5 Jun 2025	E6(R3) Step 4 (final), 6 January 2025
	E6(R3) Annex 2 Subgroup Step 2 (draft), 6 November 2024
	M11 Template Step 2 (draft), 13 March 2025
	M11 TS Step 2 (draft), 14 March 2025
	M13B EWG Step 2 (draft), 13 March 2025
	M15 EWG Step 2 (draft), 6 November 2024
	M4Q(R2) EWG Step 2 (draft), 14 May 2025
	Q1 EWG Step 2 (draft), 11 April 2025
	Q8/9/10 Q&As (R5) Step 4 (final), 30 October 2024
Version 7: 29 Oct 2024	E11A Step 4 (final), 21 August 2024
	M13A Step 4 (final), 23 July 2024
	M8 eCTD v4.0 Step 4 (final), 21 May 2024
	Q4B(R1) Final version, 5 June 2024
Version 6: 3 Jun 2024	E2D(R1) EWG Step 2 (draft), 5 February 2024
	M12 Step 4 (final), 21 May 2024
	M14 EWG Step 2 (draft), 21 May 2024
	Q3C(R9) Step 4 (final), 24 January 2024
Version 5: 7 Feb 2024	Q14 Step 4 (final), 1 November 2023
	Q2(R2) Step 4 (final), 1 November 2023
	Q5A(R2) Step 4 (final), 1 November 2023
Version 4: 20 Jul 2023	E6(R3) EWG Step 2 (draft), 19 May 2023
Version 3: 20 Apr 2023	E2B(R3) Q&As {version 2.4} Step 4 (final), 17 January 2023
	M2 Glossary. (Not subject to the formal ICH Step process), 11 June 2015
	M7(R2) Step 4 (final), 3 April 2023
	M7(R2) Addendum Step 4 (final), 3 April 2023
	M7(R2) Q&As Step 4 (final), 24 May 2022
	Q9(R1) Step 4 (final), 18 January 2023
	S12 Step 4 (final), 14 March 2023
Version 2: 17 Jan 2023	E19 Step 4 (final), 27 September 2022
	M11 EWG Step 2 (draft), 27 September 2022
	M13 EWG Step 2 (draft), 20 December 2022
	Q13 Step 4 (final), 16 November 2022
	Q5A(R2) EWG Step 2 (draft), 29 September 2022

Version 8

Terms and definitions

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A

Accelerated Studies

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Testing conducted on drug substance and drug product that have been stored under conditions intended to increase the rate of physical, chemical and/or biochemical change (temperature and when applicable humidity), over a defined time period. These data can be used to gain product knowledge and to support extrapolation, re-test period or shelf life determination and to evaluate the impact of excursions outside the label storage conditions.

Accelerated testing

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 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(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 10 March 1999 -- 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 -- Step 4 (final); 10 November 2000 -- Glossary

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

Acceptance criterion

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- Glossary

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

Accuracy

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 1 November 2023 -- 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 or set of values measured. (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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 or set of values measured. (ICH Q2)

Acknowledgement Message (ICSRACK)

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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 -- Step 4 (final); 10 March 1999 -- Glossary

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

Active Comparator

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A type of control, which has a demonstrated effect, administered as a comparator to participants in a clinical trial.
{See also: Dose Response {Control Type}, Placebo, Different Dose or Regimen {Control Type}, External {Control Type}, Sham Procedure}

Active pharmaceutical ingredient

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 10 November 2000 -- 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.

Active Process Controls

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- 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 process controls.

Actual impurities

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 5.1

Actual impurities include those observed in the drug substance above the ICH Q3A reporting thresholds.

ADC

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

antibody-drug conjugate

Additional production site

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- 4.2 Considerations for Multiple Production Sites in the Initial Regulatory Submission

An additional production site refers to any production site proposed in the initial regulatory submission other than the drug substance and drug product site where the original production scale batches are manufactured.

Additional Required Treatment {in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A medicinal product that must be administered along with the experimental treatment (e.g., drug studies wherein opioid blockers are administered to prevent overdose).

Adequate and Well-controlled Trial

E5(R1): Ethnic Factors in the Acceptability of Foreign Clinical Data -- Step 4 (final); 5 February 1998 -- 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

ADME

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

absorption, distribution, metabolism, and/or excretion

Administrative Claims Data

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Data that arise from a person's use of the healthcare system and reimbursement of healthcare providers for that care.
(FDA, United States. Guidance Pharmacoepidemiologic safety studies using electronic data) {Final guidance, May 2013. https://www.fda.gov/media/79922/download}

Advanced cancer

S9: Nonclinical Evaluation for Anticancer Pharmaceuticals -- Step 4 (final); 18 November 2009 -- 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(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Unintentionally introduced contaminant viruses.
See Virus.

Adverse Drug Reaction (ADR)

E2A: Clinical Safety Data Management: Definitions and Standards for Expedited Reporting -- Step 4 (final); 27 October 1994 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.1.2

Adverse drug reactions, as defined by local and regional requirements, 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 characterised by the fact that a causal relationship between the medicinal product 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 (see Section 5.1.1, AEs/ADRs).
{See also 'Adverse Event (AE)'}

E2D: Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting -- Step 4 (final); 12 November 2003 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

• In the pre-approval clinical experience with a new investigational product or its new usages (particularly as the therapeutic dose(s) may not be established): unfavourable and unintended responses, such as a sign (e.g., laboratory results), symptom or disease related to any dose of a medicinal product where a causal relationship between a medicinal product and an adverse event is a reasonable possibility. The level of certainty about the relatedness of the adverse drug reaction to an investigational product will vary. If the ADR is suspected to be medicinal product-related with a high level of certainty, it should be included in the reference safety information (RSI) and/or the Investigator’s Brochure (IB).
• For marketed medicinal products: a response to a drug that is noxious and unintended and that occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of diseases or for modification of physiological function. (See ICH E2A Clinical Safety Data Management: Definitions and Standards for Expedited Reporting.)

Adverse Event

E19: A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-approval or Post-Approval Clinical Trials -- Step 4 (final); 27 September 2022 -- 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 ICH E2A and ICH E6).

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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)]

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 9.2 Timing and Procedures for Collection and Reporting {of Adverse Events}

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

Adverse Event (AE)

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.1.1

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 the medicinal product. An adverse event can therefore be any unfavourable 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.
{'See also Adverse Drug Reaction (ADR)'}

E2D: Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting -- Step 4 (final); 12 November 2003 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Any unfavourable medical occurrence in a trial participant administered the investigational product. The adverse event does not necessarily have a causal relationship with the treatment.

Adverse Event (or Adverse Experience)

E2A: Clinical Safety Data Management: Definitions and Standards for Expedited Reporting -- Step 4 (final); 27 October 1994 -- 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

E19: A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-approval or Post-Approval Clinical Trials -- Step 4 (final); 27 September 2022 -- Glossary

An event (serious or non-serious) 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
(based on CIOMS VI; see ICH E2F).

E2F: Development Safety Update Report -- Step 4 (final); 17 August 2010 -- 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

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 9.2 Timing and Procedures for Collection and Reporting {of Adverse Events}

Reportable AESI {in a clinical trial}: An adverse event of special interest (serious or non-serious) is one of scientific and medical concern specific to the sponsor's product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor could be appropriate, and which is deemed to be reportable to the appropriate regulatory authority.
Not Reportable AESI {in a clinical trial}: An adverse event of special interest (serious or non-serious) is one of scientific and medical concern specific to the sponsor's product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor could be appropriate, and which is deemed to be not reportable to the appropriate regulatory authority.
{AESI=Adverse Event of Special Interest}

Agreement

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A document or set of documents describing the details of any arrangements on delegation or transfer, distribution and/or sharing of activities and, if appropriate, on financial matters between two or more parties. This could be in the form of a contract. The protocol may serve as the basis of an agreement.

Alkaline elution assay

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- Glossary

See DNA strand break assay.

Allometric and isometric growth

S11: Nonclinical Safety Testing in Support of Development of Paediatric Medicines -- Step 4 (final); 14 April 2020 -- 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.

Alpha Testing

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The first stage of testing is called Alpha testing and provides for the initial validation and testing of the technical components of the standard (e.g., DTD, schema, controlled vocabularies). Alpha testing is essentially a technical test of any DTDs or schemas to see if they are well formed and successfully validate against XML parsers. This phase of testing will also include a mapping of the ICH data points and concepts against the SDO technical solution to ensure that the message standard will meet all ICH and regional needs and that Beta testing can be initiated.
{DTD: Document Type Definition; SDO: Standards Development Organisation; XML: Extensible markup language; see also 'XML Schema'}

Alternative assay(s)

S5(R3): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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).

American National Standards Institute (ANSI)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations

The first organization for fostering development of technology standards in the United States. ANSI works with industry groups and is the U.S. member to the ISO.
{ISO: International Standards Organization}

American Standard Code for Information Interchange (ASCII)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations

A specification for representing text as computer-readable information.

Analysis

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

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

Analyte

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 27 October 1994 -- Note 1

The chemical entity assayed in biological samples.

Analytical procedure

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- 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.
{Reference} ICH Q2

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

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

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

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

Analytical procedure attribute

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- Glossary

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

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

Any analytical factor (including reagent quality) or analytical procedure operational condition 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 -- Step 4 (final); 1 November 2023 -- Glossary

An analytical procedure validation strategy describes the selection of analytical procedure performance characteristics for validation. In the strategy, data gathered during development studies and system suitability tests (SSTs) can be applied to validation and an appropriate set of validation tests can be predefined. (ICH Q14)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

An analytical procedure validation strategy describes the selection of analytical procedure performance characteristics for validation. In the strategy, data gathered during development studies and system suitability tests (SSTs) can be applied to validation and an appropriate set of validation tests can be predefined. (ICH Q14)

Analytical Run (also referred to as “Run”)

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 1 November 2023 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 1 November 2007 -- 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 -- Step 4 (final); 1 November 2007 -- 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 -- Step 4 (final); 17 August 2010 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 10 November 2000 -- 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): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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.

Applicability of the model(s)

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- 3. Model evaluation, and Appendix 3: Glossary

Applicability of the model(s) (also referred to as “fit-for-purpose”) characterizes the relevance and the adequacy of the data and model’s contribution in answering a Question of Interest.
{See also "Question of Interest"}

Applicable Regulatory Requirement(s)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

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

Applicant

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

The entity submitting the application for marketing authorisation to the relevant regulatory authority.

M7(R2) Q&As: Questions and Answers: Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 24 May 2022 -- Preface

“Applicant” is used throughout the {M7(R2)} Q&A document and should be interpreted broadly to refer to the marketing authorization holder, the filing applicant, the drug product manufacturer, and/or the drug substance manufacturer.

Appropriateness of Proposed MIDD

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

The rationale for why the proposed MIDD is suitable to answer the Question of Interest and cover the related key assumptions and required data.
{See also "Model-Informed Drug Development (MIDD)" and "Question of Interest"}

Architecture

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A general term for the design and construction of computer systems, including technical infrastructure, information (data), and applications.

Assay qualification (for regulatory use)

S5(R3): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- Glossary

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

Assent

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Affirmative agreement of a minor to participate in clinical trial. The absence of expression of agreement or disagreement should not be interpreted as assent.

Assessment

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- 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.

AUC

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary
Area under the concentration vs. time curve

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary
Area under the concentration vs. time curve

AUC_(0-72h)

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary
Area under the concentration vs. time curve from time 0 to 72 hours
{Characters preceded by "_" are in subscript font}

AUC_(0-inf)

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary
Area under the concentration vs. time curve extrapolated to infinity
{Characters preceded by "_" are in subscript font}

AUC_(0-t)

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary
Area under the concentration vs. time curve from time zero to the time of last quantifiable concentration
{Characters preceded by "_" are in subscript font}

AUC_(0-tauSS)

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary
Area under the concentration vs. time curve for one dosing interval at steady-state
{Characters preceded by "_" are in subscript font}

AUC_0- tau

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary
AUC for one dosing interval following multiple doses, generally at steady state
{AUC: Area under the curve; see also 'AUC'}

AUC_0-inf

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary
AUC extrapolated to infinity
{AUC: Area under the curve; see also 'AUC'}

AUC_0-t

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

AUC from time zero to time of last quantifiable observation (t)
{AUC: Area under the curve; see also 'AUC'}

AUCR

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

ratio of AUCs of the substrate (object) drug in the presence and absence of a precipitant drug
{AUC: Area under the curve; see also 'AUC'} {See also Object, Precipidant}

Audit

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A systematic and independent examination of trial-related activities and records performed by the sponsor, service provider (including contract research organisation (CRO)) or institution to determine whether the evaluated trial-related activities were conducted and the data were recorded, analysed and accurately reported according to the protocol, applicable standard operating procedures (SOPs), Good Clinical Practice (GCP) and the applicable regulatory requirement(s).

Audit Certificate

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

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

Audit Report

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A record describing the conduct and outcome of the audit.

Audit Trail

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Metadata records that allow the appropriate evaluation of the course of events by capturing details on actions (manual or automated) performed relating to information and data collection and, where applicable, to activities in computerised systems. The audit trail should show activities, initial entry and changes to data fields or records, by whom, when and, where applicable, why. In computerised systems, the audit trail should be secure, computer-generated and time stamped.

Authentication

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A security mechanism which verifies the identity of the sender of a message

Authorisation versus Approval

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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

Backbone

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

In eCTD usage the XML file which defines the overall structure of the electronic message and contains the links to the various individual files which carry the actual dossier content. The backbone is an equivalent of a Table of Contents and a definition of what comprises the actual dossier that is submitted. It contains not only information relating the individual files that make up an electronic message (the eCTD sequence) but also transactional information that relates versions of included files to versions previously submitted within the dossier.
{eCTD: electronic Common Technical Document; XML: Extensible markup language; see also 'XML Schema'}

Background Treatment {in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6.9.1 Background Trial Intervention

Medicinal products that are administered to each clinical trial participant, regardless of randomization group, a) to treat the indication which is the object of the study, or b) required in the protocol as part of standard care for a condition that is not the indication under investigation, and is relevant for the clinical trial design.
{The definition of "Background Trial Intervention" in the draft M11 Section 6.9.1 is the same as that of "Background Treatment" in Section 6.

Backward (or Downward) Compatibility

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The ability of the design to gracefully accept input created with older versions of itself. The concept can be applied to entire systems, data communications, protocols, file formats and computer programming languages. For example, if products designed for the new standard can receive, read, view or play older standards or formats, then the product is said to be Backward Compatible.

Base substitution

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- Glossary

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

Batch

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- 2.2

The ICH Q7 definition of a batch is applicable to all modes of CM, for both drug substances and drug products. Based on this definition, the size of a batch produced by CM can be defined in terms of one of the following:

- Quantity of output material
- Quantity of input material
- Run time at a defined mass flow rate

Other approaches to define batch size are possible, if scientifically justified based on the characteristics of the CM process and Good Manufacturing Practice.

A batch size can also be defined as a range. For example, a batch size range can be established by defining a minimum and maximum run time.

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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)

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- 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.

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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)

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- 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.

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 5 February 1998 -- 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.

BCRP

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

breast cancer resistance protein

Behavioral {intervention in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A technique used to change the behavior of a participant (e.g., psychotherapy, lifestyle counseling, or hypnosis).
{See also: Biologic, Vaccine, Combination Product, Device, Dietary Supplement, Drug, Genetic {intervention}, Surgery, Non-Surgical Procedure, Radiation {intervention}, Diagnostic Test}

Beta Testing

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The second stage of testing is called Beta testing. The purpose of Beta testing is to confirm the ICH business and technical requirements are fully met. Beta testing is intended to evaluate the usability of the new standard to create messages to support the technical and business scenarios represented by the Test Case Scenarios and as described in the ICH Implementation Guide (IG). In addition the ICH and Regional IGs will be examined to see if they are suitable for implementers or if they need to be amended.

Bias

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

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

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A systematic deviation in results from the truth.
(Proposed by CIOMS Working Group X. Bias (CIOMS X: Meta-analysis 2016 | Japanese) {https://doi.org/10.56759/lela7055, Japanese translation available}
{See also 'Immortal time bias'}

Bias (Statistical & Operational)

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

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

Bioanalytical Method

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

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

Biobatch strength(s)

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

The strength(s) of the drug product used in the in vivo BE study or studies.
{BE=bioequivalence}

Bioburden

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- 2

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).
{See also: 'Biodistribution (BD) study'; 'Nonclinical biodistribution (BD) assessment'}

Biodistribution (BD) study

S12: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- 4.1

Nonclinical studies for BD assessment can be conducted as stand-alone BD studies or in conjunction with nonclinical pharmacology and toxicology studies. Therefore, in this document the term “BD study” represents either scenario.
{See also: 'Biodistribution (BD) study'; 'Nonclinical biodistribution (BD) assessment'}

Bioinformatics

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Bioinformatics is an interdisciplinary field that combines biology, computer science, mathematics, and statistics to analyse and interpret biological data. It involves the use of computational tools and techniques to manage, process, and understand complex biological information, particularly large datasets generated by experiments such as DNA sequencing, protein structure analysis, and gene expression studies.

Biologic

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A product of biological origin applicable to the prevention, treatment, or cure of a disease or condition, for example: virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product.
{See also: Behavioral {intervention in a clinical trial}, Vaccine, Combination Product, Device, Dietary Supplement, Drug, Genetic {intervention}, Surgery, Non-Surgical Procedure, Radiation {intervention}, Diagnostic Test}

Biological Activity

Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products -- Step 4 (final); 10 March 1999 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

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

Biological Matrix

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

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

Biomaterials, human

M4E(R2): Revision of M4E Guideline on Enhancing the Format and Structure of Benefit-Risk Information in ICH: Efficacy -- Step 4 (final); 15 June 2016 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 16 July 1997 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 5 February 1998 -- 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 vs masking

M11 Template: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Template -- Step 2 (draft); 13 March 2025* -- Word Usage in Template

While "blinding" is the more commonly used term, masking is an alternative term which may be used in certain situations.
{While this is not a definition of "blinding" or "masking", it may serve to supplement definitions of either term included elsewhere in this glossary. Note: The M11 Template does not use the term "masking", nor does it explain in which situations it may be used.}

Blinding/Masking

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- 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 participant(s) being unaware, and double- blinding usually refers to the participant(s) and investigator(s) and, if appropriate, other investigator site staff or sponsor staff being unaware of the treatment assignment(s).

Bootstrapping

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

Bootstrapping is a resampling procedure that uses data from one sample to generate a sampling distribution by repeatedly taking random samples with replacement from the known sample.

Bracketing

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 7 February 2002 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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).

Bracketing approach

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

Is an approach of conducting BE studies on extreme strengths to support the demonstration of BE for all strengths. For demonstrating BE for all strengths, it is sufficient to conduct BE studies on the extreme strengths, i.e., a waiver of BE studies on the strengths in between can be applied.
{BE=bioequivalence}

Bridging Data Package

E5(R1): Ethnic Factors in the Acceptability of Foreign Clinical Data -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 5 February 1998 -- 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.

Bulk Material (Biologics)

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- 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.
{Reference} ICH Q6B

Bulk Product

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Bulk finished dosage form, that has completed all processing stages before immediate packaging
Note 1: This includes materials that may be held in potentially large quantities for an extended period of time under controlled and justified conditions (e.g. 10 000 tablets intended for blistering or 100L of solution for injection intended to fill vials)
Example: film-coated tablet or solution for injection before immediate packaging
{Reference} M4Q(R2) adapted from ICH Q6B/Bulk Material

Business case

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The reason for making an investment (in whatever form), performing a process or using a tool. It often includes economic or quality justification (costs/benefits), and is often combined with a larger description of what the process or tool should achieve. A business case often specifies RASCI (Who is Responsible, Accountable, Supporting, Consulted, Informed)

Business requirement

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The necessary components or activities to accomplish the desired task or process – 'what to do.' Business requirements are gathered from stakeholders. Business requirements are specific requirements rather than overall project objectives, and when connected to electronic messages or software, are used to develop the very specific functional requirements for a software tool.

C

C (Chemical) Development Studies

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Studies conducted to scale-up, optimise, and validate the manufacturing process for a new drug substance or a drug product.
{Reference} ICH Q3A/B
{The letter "C" before "(Chemical)" was added for sorting purposes}

C_avSS

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Average concentration observed during dosing interval at steady-state (AUC_0-tau / tau)
{Characters preceded by "_" are in subscript font}

C_max

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

maximum concentration of the drug after dosing

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Maximum concentration observed after dosing
{Characters preceded by "_" are in subscript font}

C_max,inlet,u

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

estimated unbound C_max of an inhibitor at liver inlet.
{See also 'C_max'}

C_max,u

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

unbound C_max
{See also 'C_max'}

C_maxSS

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Maximum concentration observed during dosing interval at steady-state
{Characters preceded by "_" are in subscript font}

C_min

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

minimum concentration during one dosing interval at steady state

C_minSS

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Minimum concentration observed during dosing interval at steady-state
{Characters preceded by "_" are in subscript font}

C_tau

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Concentration observed at end of dosing interval
{Characters preceded by "_" are in subscript font}

C_tauSS

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Concentration observed at end of dosing interval at steady-state
{Characters preceded by "_" are in subscript font}

Calibration

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 model

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

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

Calibration set

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Multivariate glossary

A set of data with matched known characteristics and measured analytical results. (ICH Q14)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Multivariate glossary

A set of data with matched known characteristics and measured analytical results. (ICH Q14)

Calibration Standard

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 4 June 2008 -- 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)

CAR

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

constitutive androstane receptor

Care Provider

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

The primary person in charge of the care of a patient, usually a family member or a designated health care professional.

Carry-over

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

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

Case

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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 Definition

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

The clinical, biological, psychological, and functional concepts of the condition, that reflect the medical and scientific understanding of the condition.
(FDA, United States. Guidance Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision Making for Drug and Biological Products) {Draft guidance, September 2021. https://www.fda.gov/media/152503/download}

Case Report Form (CRF)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A data acquisition tool designed to record protocol-required information to be reported by the investigator to the sponsor on each trial participant (see Data Acquisition Tool).

Cell bank

Q5D: Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products -- Step 4 (final); 16 July 1997 -- 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 -- Step 4 (final); 16 July 1997 -- 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 -- Step 4 (final); 9 November 2011 -- Glossary

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

Cell Substrate

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Cells used to manufacture product.

Centromere/kinetochore

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

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 as the original, including relevant metadata, where applicable.

Challenge Agent {in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A non-investigational medicinal product (NIMP) given to trial participants to produce a physiological response that is necessary before the pharmacological action of the investigational medicinal product can be assessed.
{see also "Non-investigational medical product (NIMP)"}

Change Management

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- Glossary

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

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- Glossary

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

Checksum

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A fixed length code value produced from a file (or message) which is a unique representation of the precise contents of the file, such that any character or byte which is changed in the file will change the code value.

Chemical Development Studies

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- Glossary

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

Chemical Drugs

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

Chemically synthesised drugs.

Chemical Transformation Step

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- 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.

Chewable Tablets

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

An oral dosage form designed to facilitate chewing and swallowing by the patient rather than swallowing a whole tablet. They must be chewed or crushed before swallowing.

Child assent

E11(R1): Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population -- Step 4 (final); 18 August 2017 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 13 November 2013 -- Glossary

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

Class

M8 eCTD v4.0: Electronic Common Technical Document (eCTD) v4.0. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 9 November 2011 -- Glossary

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

Climatic zone

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 17 August 2010 -- 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 -- Step 4 (final); 6 October 2021 -- 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: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 5.1

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

Clinical study

E8(R1): General Considerations for Clinical Studies -- Step 4 (final); 6 October 2021 -- 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

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Any interventional investigation in human participants 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.

Clinical Trial/Study Report (CSR)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A documented description of a trial of any investigational product conducted in human participants, in which the clinical and statistical description, presentations and analyses are fully integrated into a single report (see ICH E3 Structure and Content of Clinical Study Reports).

Clinical trials

M11 Template: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Template -- Step 2 (draft); 13 March 2025* -- Word Usage in Template

Because the scope of this protocol template is focused on interventional clinical trials, the term "clinical trials" is used rather than "clinical studies" when referring to interventional clinical trials.

Cloning efficiency

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 17 December 2012 -- Glossary

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

Code List (general definition)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A defined list of values and terms to be used for transmitting information on a topic in a specific field or element in a message. A code list will usually consist of a value (the code) and a label (the term being coded).

Code List, Technical

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A list of coded values that are used to structure the xml coding within a message. These values do not carry source data that is being transmitted by the message, i.e. they do not represent data contained in the content of a message, but instead are used to identify components of an xml file for parsing by an IT system receiving transmitted message. Usually they are not entered by an end user (for instance through a drop-down pick list such as used for coded elements), but are instead used by an implementing IT system to construct an xml message for export and transmission.
{XML: Extensible markup language; see also 'XML Schema'}

Cohort of concern {mutagens}

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 3

Some structural groups were identified to be of such high potency that intakes even below the Threshold of Toxicological Concern (TTC) would theoretically be associated with a potential for a significant carcinogenic risk. This group of high potency mutagenic carcinogens referred to as the "cohort of concern", comprises aflatoxin-like-, N-nitroso-, and alkyl-azoxy compounds.

Combination product

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A product composed of two or more different types of medical products (i.e., a combination of a drug, device, and/or biological product with one another and are referred to as "constituent parts" of the combination product).
{See also: Behavioral {intervention in a clinical trial}, Biologic, Vaccine, Device, Dietary Supplement, Drug, Genetic {intervention}, Surgery, Non-Surgical Procedure, Radiation {intervention}, Diagnostic Test}

Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 9 November 2011 -- Glossary

See DNA strand break assay.

Comité Consultatif International Télégraphique et Téléphonique (CCITT)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations

CCITT publishes the X.400 and the X.500 series of standards (now known as "Telecommunications Standards Sector of the ITU").
{ITU: International Telecommunication Union}

Commercially available chemical

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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.

Commitment stability studies

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Stability studies conducted under the accelerated, intermediate, or long-term storage conditions (as applicable) to establish or confirm the initial re-test period or shelf life in accordance with a commitment in the regulatory submission.

Common adverse events

M4E Q&As (R4): Questions & Answers: CTD on Efficacy -- Step 4 (final); 10 June 2004 -- Question 2

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.'}

Common Data Model

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A mechanism by which raw data are standardised to a common structure, format and terminology independently from any particular study in order to allow a combined analysis across several databases/datasets. Standardisation of structure and content allows the use of standardised applications, tools and methods across the data to answer a wide range of questions
(A Common Data Model for Europe? – Why? Which? How? – workshop report EMA/614680/2018)
{https://www.ema.europa.eu/en/events/common-data-model-europe-why-which-how}

Common Technical Document (CTD)

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

(See ICH M4Q)
{The ICH Q14 Glossary expands the abbreviation 'CTD', but does not further define it.}
{From the ICH M4(R4) guideline, page 1: 'Objective of the guideline: This guideline presents the agreed upon common format for the preparation of a well-structured Common Technical Document for applications that will be submitted to regulatory authorities.'}

Company

Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management -- Step 4 (final); 20 November 2019 -- Glossary

Manufacturing sites and Marketing Authorisation Holder (MAH) where relevant

Company Core Data Sheet (CCDS)

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 18 November 2004 -- 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 -- Step 4 (final); 18 November 2004 -- 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 -- Step 4 (final); 18 November 2004 -- 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

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

An investigational or authorised medicinal product (i.e., active control), placebo or standard of care used as a reference in a clinical trial.

Comparator Product

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

An investigational or marketed product, i.e., active control, or placebo, used as a reference in a clinical trial. In the context of this guideline, a comparator product is the drug product accepted by regulatory agencies that an applicant can use to compare against the test product in conducting a BE study.
{BE=bioequivalence}

Complete Clinical Data Package

E5(R1): Ethnic Factors in the Acceptability of Foreign Clinical Data -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 17 December 2012 -- Glossary

Clinical trial for which a final study report is available.
{Source:} ICH Guideline E2F

E2F: Development Safety Update Report -- Step 4 (final); 17 August 2010 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Adherence to the trial-related requirements, GCP requirements and the applicable regulatory requirements.

Compounds Insensitive to Ethnic Factors

E5(R1): Ethnic Factors in the Acceptability of Foreign Clinical Data -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 10 November 2000 -- Glossary

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

Computerised Systems Validation

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A process of establishing and documenting that the specified requirements of a computerised 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 trial participant protection and the reliability of trial results.

Computerized System

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- Glossary

A process or operation integrated with a computer system.

Conceptual Definition

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Explains a study construct (e.g., exposure, outcomes, covariates) or feature in general or qualitative terms.
(FDA, United States. Guidance Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products) {December 2023. https://www.fda.gov/media/154449/download}

Concomitant Therapy {in clinical trials}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6.10 Concomitant Therapy

Any pharmaceutical agent, other than the trial interventions, that is administered to or used by the subject prior to or during a specified time period.

Concomitant toxicokinetics

S3A: Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies -- Step 4 (final); 27 October 1994 -- Note 1

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

Confidentiality

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Prevention of disclosure to other than authorised individuals of a sponsor's proprietary information or of a participant's identity or their confidential information.

Confirmatory studies

Q1B: Stability Testing: Photostability Testing of New Drug Substances and Products -- Step 4 (final); 6 November 1996 -- 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 -- Step 4 (final); 10 March 1999 -- 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

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

{See "Specification"}

Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances -- Step 4 (final); 6 October 1999 -- 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.

Confounding

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Confounding results from the presence of an additional factor, known as a confounder or confounding factor, that is associated with both the exposure and the outcome, and is not in the causal pathway between exposure and the outcome. Confounding distorts the observed effect estimate for the outcome and the exposure under study.
(The European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Guide on Methodological Standards in Pharmacoepidemiology) {Revision 11, July 2023. https://encepp.europa.eu/encepp-toolkit/methodological-guide_en}

Conjugated Product

Q5C: Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products -- Step 4 (final); 30 November 1995 -- 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.

Consequence of Wrong Decision

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- 2.1. Key Assessment Elements, and Appendix 3: Glossary

The consequences (e.g., with respect to patient safety and/or efficacy) if a wrong decision is made, based on all available information.

Consistency of treatment effect

E17: General principles for planning and design of Multi-Regional Clinical Trials -- Step 4 (final); 16 November 2017 -- Glossary

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

Constitutive ingredients

S5(R3): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.6

{In individual case safety reports (ICSR)} Consumer is defined as a primary source who is not a healthcare professional. Examples include a patient, patient representative (including a legal representative), caregiver, friend, or relative of a patient.
{see also: 'Primary source'}

E2D: Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting -- Step 4 (final); 12 November 2003 -- 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

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

The sum of packaging components that together contain and protect the finished dosage form or any other material. This includes primary packaging components and secondary packaging components, if the latter are intended to provide additional protection to the drug product or packaged material.
{Reference} ICH M4Q(R2) adapted from ICH Q1A

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- 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 functional (e.g., combination of a drug product with a medical device) or intended to provide additional protection to the drug product. A packaging system is equivalent to a container closure system. For the drug substance the container closure system is the packaging proposed for storage and distribution. Commitment stability studies

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 26 April 2022 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 10 March 1999 -- 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

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

The undesired introduction of impurities of a chemical or microbiological nature, or of foreign matter, into or onto a raw material, intermediate, or drug substance during production, sampling, packaging or repackaging, storage or transport.
{Reference} ICH Q7

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 5 February 1998 -- 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. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- 2.1. Key Assessment Elements, and Appendix 3: Glossary

A description of the model(s) and its specific role and scope to answer the Question of Interest.
{See also "Question of Interest"}

Context of Use code and Keyword code combination

M8 eCTD v4.0: Electronic Common Technical Document (eCTD) v4.0. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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 -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 16 July 1997 -- Glossary

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

Continuous Manufacturing

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

CM: Continuous Manufacturing (ICH Q13)

{The ICH Q13 guideline provides clarification on CM concepts and describes scientific approaches and regulatory considerations specific to CM of drug substances and drug products. However, it does not define the term "Continuous manufacturing".}

Continuous Process Verification

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- Glossary

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

Q8(R2): Pharmaceutical Development -- Step 4 (final); 1 August 2009 -- Glossary (Part I)

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

Contract Manufacturer

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 Organisation (CRO)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

See Service Provider.

Control Cells

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Cells cultured in parallel with the production of the virus or viral vector without inoculation of the virus/viral vector seed. Control cells are maintained in conditions that are essentially equivalent to those used for the production cell cultures, including use of the same batches of media and media changes.

Control strategy

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- 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.
{Reference} ICH Q10

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 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 -- Step 4 (final); 4 June 2008 -- 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) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 26 April 2022 -- 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 -- Step 4 (final); 1 August 2009 -- 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 -- Step 4 (final); 26 April 2022 -- 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.

Control Type {in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A characterization or classification of the comparator against which the study intervention is evaluated. {See also: Active Comparator, Dose Response {Control Type}, Placebo, Different Dose or Regimen {Control Type}, External {Control Type}, Sham Procedure}

Controlled vocabulary

M8 eCTD v4.0: Electronic Common Technical Document (eCTD) v4.0. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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)

Controlled Vocabulary (CV)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A controlled vocabulary is an established list of standardized terminology for use in indexing and retrieval of information. CVs are established lists of preferred terms for cataloguing or indexing information (for example as descriptors in databases). CVs can address issues of synonyms or standardised headings. Sample CVs: MedDRA, ISO country codes, EDQM Routes of Administration, etc.) {EDQM: European Directorate for the Quality of Medicines & HealthCare; ISO: International Standards Organization; MedDRA: Medical Dictionary for Regulatory Activities}

Coordinating Investigator

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

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

Core formulation

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

Active and inactive ingredients that make up a drug product, not including tablet film coating or capsule shell.

Core weight deviation

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Annex II

Refers to the % deviation of the total core weight of the additional strength relative to the theoretical total core weight of the additional strength version assuming direct proportionality (see Annex I). {See also: Direct proportionality}

Corrective Action

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- 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)

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

CAPA: Corrective and Preventive Actions (ICH Q12)

Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management -- Step 4 (final); 20 November 2019 -- Glossary

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

Counterfeit Medicine

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 1 August 2009 -- 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)

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

CQA: Critical Quality Attributes (ICH Q8)

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 August 2009 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 10 November 2000 -- Glossary

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

Cross-over {intervention model in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

Participants receive one of two or more alternative intervention(s) during the initial epoch of the study and receive other intervention(s) during the subsequent epoch(s) of the trial.

{See also: Factorial, Parallel Group, Sequential, Single Group}

Culture confluency

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- Glossary

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

Cumulative intake

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- Glossary

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

CYP

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

cytochrome P450

Cytogenetic evaluation

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- Glossary

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

D

Daily Dose

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- Glossary

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

Data Accuracy

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 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).
(M10 EWG Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022)

Data Acquisition Tool (DAT)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A paper or electronic tool designed to collect data and associated metadata from a data originator in a clinical trial according to the protocol and to report the data to the sponsor. The data originator may be a human (e.g., the participant or trial staff), a machine (e.g., wearables and sensors) or a computer system from which the electronic transfer of data from one system to another has been undertaken (e.g., extraction of data from an electronic health record or laboratory system).
Examples of DATs include but are not limited to CRFs, interactive response technologies (IRTs), clinical outcome assessments (COAs), including patient-reported outcomes (PROs) and wearable devices, irrespective of the media used.

Data Completeness

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

The “presence of the necessary data” (National Institutes of Health 1263 Collaboratory 2014).
(FDA, United States. Guidance Real-World Data: Assessing Registries to Support Regulatory Decision Making for Drug and Biological Products) {December 2023.
https://www.fda.gov/media/154449/download}

Data Consistency

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Relevant uniformity in data across clinical sites, facilities, departments, units within a facility, providers, or other assessors.
(FDA, United States. Guidance Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products) {December 2023. https://www.fda.gov/media/154449/download}

Data Curation

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

The curation of the source data for the purpose of statistical analysis of specific clinical research questions. Data curation includes, but is not limited to, the following aspects: data extraction (including multiple data sources), data security processing (de-identification or anonymization, and protection from data corruption, leaking, theft, tampering, or unauthorized access), data cleaning (edit check and outliers processing, data completeness processing), data conversion (common data models, normalization, natural language processing, medical coding, derived variable calculation), data quality control, data transmission and storage.
(NMPA, China. Guideline on Using Real-World Data to Generate Real-World Evidence (Trial Version) English Translation) {April 2021. https://redica.com/wp-content/uploads/NMPA_-Attachment_-_Guiding-Principles-of-Real-World-Data-Used-to-Generate-Real-World-Evidence-Trial_.pdf}

Data Encryption Standard (DES)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

Data Encryption Standard based on a symmetric algorithm.

Data Governance

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 11.7 Data Governance

[A description of] the key processes to ensure data integrity, traceability and security, in order to enable accurate collection, reporting, monitoring, transfer, retention, access and publication.
{The words in square brackets {} are specific to the context of the draft M11 Technical Specification/Template.}

Data Holder

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A legal person, including public sector bodies and international organizations, or a natural person who is not a data subject with respect to the specific data in question, which, in accordance with applicable law, has the right to grant access to or to share certain personal data or non-personal data (Article 2(8) of the REGULATION (EU) 2022/868 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30 May 2022 on European data governance and amending Regulation (EU) 2018/1724 (Data Governance Act)) {https://eur-lex.europa.eu/eli/reg/2022/868/oj}

Data Integrity

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Data integrity includes the degree to which data fulfil key criteria of being attributable, legible, contemporaneous, original, accurate, complete, secure and reliable such that data are fit for purpose.

Data lock point

E2F: Development Safety Update Report -- Step 4 (final); 17 August 2010 -- 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

E2F: Development Safety Update Report -- Step 4 (final); 17 August 2010 -- Glossary

(Synonyms: Independent Data Monitoring Committee, Data and Safety Monitoring Board)
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 Protection

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 11.8 Data Protection

[A description of] the measures taken to protect the privacy and confidentiality of person information of trial participants in accordance with applicable regulatory requirements on personal data protection and any measures that should be taken in case of a data security breach.
{The words in square brackets {} are specific to the context of the draft M11 Technical Specification/Template.}

Data Provenance

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

An audit trail that “accounts for the origin of a piece of data (in a database, document or repository) together with an explanation of how and why it got to the present place.”
(FDA, United States. Guidance Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products) {December 2023. https://www.fda.gov/media/154449/download}

Data Relevance

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Data relevance includes the availability of key data elements (exposure, outcomes, covariates) and sufficient numbers of representative patients for the study.
(FDA, United States. Guidance Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision Making for Drug and Biological Products) {Draft guidance, September 2021. https://www.fda.gov/media/152503/download}

Data Reliability

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Data reliability includes data accuracy, completeness, provenance, and traceability.
(FDA, United States. Guidance Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision Making for Drug and Biological Products) {Draft guidance, September 2021. https://www.fda.gov/media/152503/download}

Data Traceability

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Permits an understanding of the relationships between the analysis results (tables, listings, and figures in the study report), analysis datasets, tabulation datasets, and source data.
(FDA, United States. technical specifications document Study Data Technical Conformance Guide (October 2019)) {Unchanged in the FDA Study data technical conformance guide dated 29 March 2024, https://www.fda.gov/media/153632/download}

Data transformation

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Multivariate glossary

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

Datatype

M8 eCTD v4.0: Electronic Common Technical Document (eCTD) v4.0. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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.

Date of production

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- 13.1.2 Start of Shelf Life for Synthetic Chemical Entity Drug Products

The start of shelf life should be the date of production, which is defined as the date of the first manufacturing step that combines drug substance with other ingredients. {NB: Section 13.1.2 goes on to describe other approaches to calculating the start of shelf life}.
{For biological drug products, "Date of manufacture" is described as follows in Section 13.1.3 of the guideline: "The start of shelf life for biological drug products begin on the date of manufacture e.g., date of filtration and/or filling for a liquid drug product. When the drug product filling operation takes place over more than one day, then the initial date of the filling operation is taken as the date of manufacture. Other approaches used to define the start of shelf life can be used if justified."}

DDI

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

drug-drug interaction

De facto standard

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A 'standard' which is in such widespread use that it is accepted as a standard but which has not been ratified by any official standards body, such as the International Standards Organization (ISO).

Decentralized elements in a clinical trial

E6(R3) Annex 2 Subgroup: Guideline for Good Clinical Practice (GCP). Annex 2. -- Step 2 (draft); 6 November 2024* -- 1. Introduction

For the purposes of Annex 2, decentralised elements in a clinical trial are those trial-related activities conducted outside the investigator's location (e.g., trial visit is conducted in the trial participant's home, local healthcare centre or mobile medical units or when data acquisition is performed remotely using digital health technologies (DHTs)).

Decision Maker(s)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

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

Degradation Product

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Molecular variants or impurities resulting from chemical or biochemical 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 container closure system and/or device component. Such changes may occur as a result of manufacture and/or storage (e.g., hydrolysis, deamidation, oxidation, aggregation, proteolysis). Degradation products may be either product-related substances or product-related impurities.

Q3B(R2): Impurities in New Drug Products -- Step 4 (final); 2 June 2006 -- 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 -- Step 4 (final); 30 November 1995 -- 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 -- Step 4 (final); 6 October 1999 -- 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 Product:.

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 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

Degradation Products

Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products -- Step 4 (final); 10 March 1999 -- 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 -- Step 4 (final); 2 June 2006 -- 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 -- Step 4 (final); 6 October 1999 -- Glossary

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

Dermal Drugs

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- Glossary

Products applied topically to the skin.

Design of Experiments (DoE)

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

{The ICH Q14 Glossary expands the abbreviation 'DoE', but does not further define it.}

Design Space

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- 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) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 1 August 2009 -- Part I, 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.

Q8(R2): Pharmaceutical Development -- Step 4 (final); 1 August 2009 -- Part II, 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).

Desired Product

Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products -- Step 4 (final); 10 March 1999 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

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

Detection limit (DL)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 17 August 2010 -- 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 -- Step 4 (final); 2 June 2006 -- Glossary

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

S5(R3): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- Glossary

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

Deviation

Q7 Q&As: Questions and Answers: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 June 2015 -- Question 20.1

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'}

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- Glossary

Departure from an approved instruction or established standard.

Device

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

Any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination for, one or more specific medical purpose(s).
{See also: Behavioral {intervention in a clinical trial}, Biologic, Vaccine, Combination Product, Dietary Supplement, Drug, Genetic {intervention}, Surgery, Non-Surgical Procedure, Radiation {intervention}, Diagnostic Test}

Diagnostic Test

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

Any procedure or test to diagnose a disease or disorder.
{See also: Behavioral {intervention in a clinical trial}, Biologic, Vaccine, Combination Product, Device, Dietary Supplement, Drug, Genetic {intervention}, Surgery, Non-Surgical Procedure, Radiation {intervention}}

Dietary Supplement

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

Preparations containing ingredient(s) intended to supplement the diet.
{See also: Behavioral {intervention in a clinical trial}, Biologic, Vaccine, Combination Product, Device, Drug, Genetic {intervention}, Surgery, Non-Surgical Procedure, Radiation {intervention}, Diagnostic Test}

Different Dose or Regimen {Control Type in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A type of control that comprises a different dose or dosage regimen in comparison to the investigational intervention dose or dosage regimen.
{See also: Active Comparator, Dose Response {Control Type}, Placebo, External {Control Type}, Sham Procedure}

Digital Health Technology (DHT)

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A system that uses computing platforms, connectivity, software, and/or sensors for health care and related uses. These technologies span a wide range of uses, from applications in general wellness to applications as a medical device. They include technologies intended for use as a medical product, in a medical product, or as an adjunct to other medical products (devices, drugs, and biologics). They may also be used to develop or study medical products.
(FDA, United States. Digital Health Technologies for Remote Data Acquisition in Clinical Investigations Guidance for Industry, Investigators, and Other Stakeholders) {December 2023. https://www.fda.gov/media/155022/download}

Digital Platform

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.7

{For individual case safety reports (ICSR)} A digital platform is the software and technology used to enable transmission of information between users (see Section 4.3, Digital Platforms).

Dilution Factor

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

The magnitude by which a sample is diluted.

Dilution Integrity

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

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

Dilution Linearity

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 16 July 1997 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Permission to examine, analyse and verify records that are important to the evaluation of a clinical trial and may be performed on-site or remotely. Any party (e.g., domestic and foreign regulatory authorities, sponsor's monitors and auditors) with direct access should take reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of participants' identities and their data and sponsor's proprietary information.

Direct Phototoxicity

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- Glossary

Phototoxicity induced by absorption of light by the drug or excipient

Direct proportionality

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Annex II

Each strength contains the same ingredients in the same proportion (see Section 2.2)

{See also: Annex I, EXAMPLES OF APPLICATION OF BIOWAIVER PRINCIPLES: Example 1: Direct proportionality of composition}

Dissolution similarity

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- 2.4 Assessment of Similarity

To demonstrate dissolution similarity, the lower bound of the 90% bootstrapped confidence interval (CI) for the similarity factor should be ≥46 and the point estimate (f_2) should be ≥50.
{See also: Bootstrapping; f_2 (Estimated similarity factor}

Disturbances

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- 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: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 9 November 2011 -- Glossary

Single or double strand scissions in the DNA.

DNA-reactive

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- Glossary

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

Document

M4(R4): Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use -- Step 4 (final); 15 June 2016 -- 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. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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 -- Step 4 (final); 1 November 2007 -- 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.

Document Type Definition (DTD)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A technical file that defines the components of an xml message, in particular the elements and attributes that may be used.
{XML: Extensible markup language; see also 'XML Schema'}

Dosage

E5(R1): Ethnic Factors in the Acceptability of Foreign Clinical Data -- Step 4 (final); 5 February 1998 -- Glossary

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

Dosage form

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

The type of physical manifestation (e.g., tablet, capsule, solution, cream, powder).
{Reference} ICH M4Q(R2). Adapted from ICH Q1A

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- Glossary

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

Dose Escalation Committee

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A type of safety monitoring committee that monitors dose escalation activities in first-in-human trials.
{See also: Independent Data Monitoring Committee, Endpoint Adjudication Committee}

Dose Regimen

E5(R1): Ethnic Factors in the Acceptability of Foreign Clinical Data -- Step 4 (final); 5 February 1998 -- Glossary

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

Dose Response {Control Type in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A type of control using different doses or regimens of the same treatment across the treatment arms.
{See also: Active Comparator, Placebo, Different Dose or Regimen {Control Type}, External {Control Type}, Sham Procedure}

Double Blind

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A study in which neither the participant nor the study personnel interacting with the participant or data during the study knows what intervention a participant is receiving.
{See also: Observer Blind, Open Label, Single Blind}

Double coded data and samples

E15: Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories -- Step 4 (final); 1 November 2007 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 5 February 1998 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- Glossary of Terms

(See Medicinal Product)

E2E: Pharmacovigilance Planning -- Step 4 (final); 18 November 2004 -- 1.1

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

E8(R1): General Considerations for Clinical Studies -- Step 4 (final); 6 October 2021 -- 1

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

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

An active natural, synthetic or semi-synthetic ingredient including endogenous body substance that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body, but does not include intermediates used in the synthesis of such ingredient
{See also: Behavioral {intervention in a clinical trial}, Biologic, Vaccine, Combination Product, Device, Dietary Supplement, Genetic {intervention}, Surgery, Non-Surgical Procedure, Radiation {intervention}, Diagnostic Test}

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- 1.2. Background (Footnote 3)

For the purpose of this guideline, the term “drug” is considered synonymous with investigational product, medicine, medicinal product, biological product, and pharmaceutical product; this includes “drugs” for which marketing authorization is sought.

Drug (Medicinal) Product

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- Glossary

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

Drug approval

E8(R1): General Considerations for Clinical Studies -- Step 4 (final); 6 October 2021 -- 1

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

Drug product

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

The Finished Dosage Form in the final immediate packaging intended for sale or supply.
Note: Some Drug Products do not necessarily include a Drug Substance (e.g. solvent for solution for injection in vial)
Note: Label is not included
Examples: film-coated tablet in blister or solution for injection in vial, solvent for solution for injection in vial
{Reference} ICH M4Q(R2)

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 10 March 1999 -- Glossary

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

Drug Release Profile

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Speed/rate at which a drug is released.

Drug substance

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Any substance or mixture of substances intended to be used in the manufacture of a finished dosage form and that, when so used, becomes an active ingredient of that finished 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.
{Reference} ICH M4Q(R2). Adapted from ICH Q7/ Active Substance/Active Ingredient

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 10 November 2000 -- Glossary
See Active Pharmaceutical Ingredient

Drug Substance (Bulk Material)

Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products -- Step 4 (final); 10 March 1999 -- 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 Substance Intermediate

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary
{See 'Substance Intermediate'}

Drug versus Pharmaceutical

E14/S7B: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- S7B Q&As, Question 1.1
Note that the word “drug(s)” in the Q&As is used interchangeably with {the} word “pharmaceutical(s)” in ICH S7B

Duplicate report

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 4.2. Lines 272-273
Individual Case Safety Reports (ICSRs) of the same case are reported by multiple MAHs (see Section 6.6, Duplicate Management)
{MAH=Marketing authorisation holder}

E

E_max

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary
maximum induction effect

Early Phase 1 {trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

Early Phase 1: First-in-human trials, in a small number of participants, that are conducted before Phase 1 trials and are intended to assess new candidate therapeutic and imaging agents. The study agent is administered at a low dose for a limited time, and there is no therapeutic or diagnostic intent.
{See also: Phase 1, Phase 1/Phase 2, Phase 1/Phase 2/Phase 3, Phase 1/Phase 3, Phase 2, Phase 2/Phase 3, Phase 2/Phase 3/Phase 4, Phase 3, Phase 3/Phase 4, Phase 4}

Early stage entities

M3(R2): Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals -- Step 4 (final); 11 June 2009 -- 17

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

EC_50

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

concentration causing half maximal effect

EDI Message

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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]

Effect Modification

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Effect modification occurs when the effect of a single exposure on an outcome depends on the values of another variable, i.e., the effect modifier, which does not necessarily need to be involved in the causal pathway. Interaction occurs when there is interest in the causal effect of two exposures on an outcome and how the effect of either exposure depends upon the value of the other exposure.
(ENCePP) {The European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Guide on Methodological Standards in Pharmacoepidemiology. Revision 11, July 2023. https://encepp.europa.eu/encepp-toolkit/methodological-guide_en}

Efficacy versus Effectiveness

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- Glossary of Terms

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

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations

A technology for exchanging structured information for the purpose of conducting business transactions

Electronic Health Record Data

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A collection of an individual patient records contained within an EHR system. A typical individual EHR may include a patient's medical history, diagnoses, treatment plans, immunization dates, allergies, radiology images, pharmacy records, and laboratory and test results.
(FDA, United States. Data Standards for Drug and Biological Product Submissions Containing Real-World Data) {CIOMS has verified the source of this definition: FDA Guidance. Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision Making for Drug and Biological Products (Draft)). September 2021, https://www.fda.gov/media/152503/download; citing the 2018 FDA Guidance on Use of Electronic Health Record Data in Clinical Investigations as the source (see https://www.fda.gov/media/97567/download, page 11 under "Electronic Health Record (EHR)").}

Emergency Consent Process

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 11.3 Informed Consent Process

A type of informed consent process that may occur during an emergency situation in which the participant or their legally authorized representative is not available to give consent.
{The term in the draft M11 Technical Specification/Template is "Description of Emergency Consent Process". The words "Description of" have been left out here, as they are specific to the context of the source document.}

Emergency Unblinding at the Site

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6.7.4 Emergency Unblinding at the Site

[A description of the methodology used for] unblinding of the trial treatment in the case of a sudden unforeseen crisis that requires immediate medical care of the participant.

Enabler

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- Glossary

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

Enantiomeric Impurity

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- 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

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Compounds with the same molecular formula that differ in the spatial arrangement of atoms within the molecule and are nonsuperimposable mirror images.

Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances -- Step 4 (final); 6 October 1999 -- 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.

End of Production Cells (EOPC)

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Cells harvested (under conditions comparable to those used in production) from the MCB or WCB cultured to a passage level or population doubling level comparable to or beyond the highest level reached in production. In certain situations, the chronological time in culture may be measured. The EOPC are also referred to as Extended Cell Banks (ECB) and these terms can be used interchangeably with LIVCA cells.
LIVCA: Limit of In Vitro Cell Age

Endogenous Compounds

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Compounds already present in the body either because the body produces them or because they are present in a normal diet.

Endogenous Virus

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Retrovirus whose genome is part of the germ line of the species of origin of the cell line and is stably integrated into the genome of the host species from which the parental cell line was derived. In this guideline, this also includes intentionally introduced, non-integrated viruses such as Epstein-Barr virus used to immortalise cell substrates or bovine papilloma virus.

Endpoint

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 3.1.1 Primary Objective

The variable to be obtained for each patient that is required to address the clinical question. The specification of the variable might include whether the patient experiences an intercurrent event.

Endpoint Adjudication Committee

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

An external committee whose purpose is to evaluate study data and decide whether a study endpoint or other criterion has been met.
{See also: Independent Data Monitoring Committee, Dose Escalation Committee}

Endpoint Subset

S11: Nonclinical Safety Testing in Support of Development of Paediatric Medicines -- Step 4 (final); 14 April 2020 -- 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) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 14 April 2020 -- 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 -- Step 4 (final); 5 February 1998 -- 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 Records

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Essential records are the documents and data (and relevant metadata), in any format, associated with a clinical trial that facilitate the ongoing management of the trial and collectively allow the evaluation of the methods used, the factors affecting a trial and the actions taken during the trial conduct to determine the reliability of the trial results produced and the verification that the trial was conducted in accordance with GCP and applicable regulatory requirements (see Appendix C).
{Note: Regarding the terms "Investigator site file (ISF)" and "Trial master file (TMF)", see Appendix C, Point C 2.3}: These essential records should be maintained in or referred to from repositories held by the sponsor and by the investigator/institution for their respective records. These repositories may be referred to as a trial master file (TMF). The repository held by the investigator/institution may also be referred to as the investigator site file (ISF).

Established Condition (EC)

Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 20 November 2019 -- 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.

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A precise description of the treatment effect reflecting the clinical question posed by the trial objective. It summarizes, at a population level, what the outcomes would be in the same patients under different treatment conditions being compared.
(ICH E9-R1 – Addendum: Statistical Principles for Clinical Trials, Glossary).

Estimate

E9(R1): Addendum: Statistical Principles for Clinical Trials -- Step 4 (final); 20 November 2019 -- Glossary

A numerical value computed by an estimator.

Estimator

E9(R1): Addendum: Statistical Principles for Clinical Trials -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 12 May 2005 -- 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.

Example instance

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A sample xml message containing dummy data to illustrate an actual example of a message. (Compare with Reference Instance)
{XML: Extensible markup language (see also 'XML Schema'). And see 'Reference Instance'}

Excipient

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

A substance or compound, other than the drug substance and packaging materials, that is intended or designated to be used in the manufacture of a finished dosage form.
Note: Excipients include e.g. fillers, disintegrants, lubricants, colouring matters, antioxidants, preservatives, adjuvants, stabilisers, thickeners, emulsifiers, solubilisers, permeation enhancers, flavouring and aromatic substances, processing aids etc., as well as the constituents of the outer covering of the finished dosage form, e.g. gelatine capsules.
{Reference} ICH M4Q(R2)

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- Glossary

Anything other than the drug substance in the dosage form.

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 10 March 1999 -- Glossary

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

Existing active pharmaceutical ingredient

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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.

Expedited Report

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.3

An expedited report is an individual case safety report that meets the requirements for reporting as soon as possible, but no later than 15 calendar days after day zero (see Section 5.2, Reporting Timeframes).

Experimental Intervention

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

The drug, device, therapy, procedure, or process under investigation in a clinical study that is believed to have an effect on outcomes of interest in a study (e.g., health-related quality of life, efficacy, safety, pharmacoeconomics).

Expert knowledge

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 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 -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 10 November 2000 -- 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

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

An exposure is the medicinal product or regimen of interest being evaluated in the proposed study (ICH M14 Expert Working Group).

M3(R2): Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals -- Step 4 (final); 11 June 2009 -- 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 -- Step 4 (final); 27 October 1994 -- 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 -- Step 4 (final); 15 June 2011 -- Section 2. Question 2

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 -- Step 4 (final); 15 June 2011 -- Section 1. Question 1

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 -- Step 4 (final); 30 November 1995 -- Glossary

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

Expression products

S12: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- Glossary

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

Extended Cell Bank (ECB)

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Cells cultured from the MCB or WCB and propagated to the proposed in vitro cell age used for production or beyond. May also referred to as EOPC.

EOPC: End of Production Cells

Extended Release

Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances -- Step 4 (final); 6 October 1999 -- Glossary

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

External {Control Type in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

The use of external control data as a control arm for those studies where ethical concerns and/or underserved disease indications may make it difficult to enroll participants.
{See also: Active Comparator, Dose Response {Control Type}, Placebo, Different Dose or Regimen {Control Type}, Sham Procedure}

Extraneous Contaminant

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 5 February 1998 -- 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.

Extreme strength(s)

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

The strength(s) of the drug product that represent the largest difference in composition. Often, but not always, these will be the highest and lowest strengths.

Extrinsic Ethnic Factors

E5(R1): Ethnic Factors in the Acceptability of Foreign Clinical Data -- Step 4 (final); 5 February 1998 -- 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

f_2 (Estimated similarity factor)

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

F_2, the similarity factor, is a model-independent measure for the comparison of two dissolution profiles.
{Note: The draft ICH M13B guideline shows the formula for the calculation of f_2 in mathematical notation. This glossary is derived from a database that cannot represent this format. The formula is therefore given here using Excel notation:
f_2 = 50*log(100/(SQRT(1+(1/P)*S)))
where
P is the number of time points,
R_j is the sample mean percent biobatch (reference) strength dissolved at jth time after initiation of the study,
T_j is the sample mean percent test strength dissolved at jth time after initiation of the study, and
S is the sum total of [(R_j - T_j)^2] at each time point from 1 to P.
Readers are encouraged to refer to the original draft ICH M13B guideline available at https://www.ich.org/page/multidisciplinary-guidelines#13-3, which is authoritative.}

f_u,p

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

unbound fraction in plasma

Factorial {intervention model in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

Two or more interventions, each alone or in combination, are evaluated in parallel against a control group. This study design allows for the comparison of active drug to placebo, presence of drug-drug interactions, and comparison of active drugs against each other.
{See also: Cross-over, Parallel Group, Sequential, Single Group}

Failure Mode Effects Analysis (FMEA)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Annex, I.3

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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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/preview/info_iec61025%7Bed2.0%7Den_d.pdf}

Federated Data Network

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A series of decentralized, interconnected nodes, which allows data to be queried or otherwise analyzed by other nodes in the network without the data leaving the node it is located at. Examples of FDNs include DARWIN EU, Sentinel, CNODES, OHDSI, and MID-NET.
(Hallock H, Marshall SE, 't Hoen PAC, Nygård JF, Hoorne B, Fox C, Alagaratnam S. Federated Networks for Distributed Analysis of Health Data. Front Public Health. 2021;9:712569.)
{https://doi.org/10.3389/fpubh.2021.712569}

Feedback / Feedforward

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- 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)

File Transfer Protocol (FTP)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations

A client-server protocol which allows a user of one computer to transfer files to and from another computer over a TCP/IP network.
{IP: Internet Protocol; TCP: Transmission Control Protocol}

Finished Dosage Form

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Final qualitative and quantitative composition containing one or more ingredients in the specific manufactured dosage form intended to be part of a drug product
Note: Some Finished Dosage Form do not necessarily include a Drug Substance (e.g. solvent for solution for injection)
Example: film coated tablet or solution for injection with specific qualitative and quantitative composition
{Reference} ICH M4Q(R2)/ Manufactured Item (ISO IDMP 11615) {ISO 11615:2017 Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information. https://www.iso.org/standard/70150.html}

Finished pharmaceutical product

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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.

Fitness for purpose of real-world data (RWD)

E6(R3) Annex 2 Subgroup: Guideline for Good Clinical Practice (GCP). Annex 2. -- Step 2 (draft); 6 November 2024* -- 3.5.1 Real-World Data Considerations

The sponsor should ensure the fitness for purpose of RWD, which can be described by their reliability and relevance.
{See also "Reliability {of real-world data}" and "Relevance {of real-world data}"

Fixed dose combination

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

A single dosage form that contains two or more drug substances.

Flanking Control Regions

Q5B: Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products -- Step 4 (final); 30 November 1995 -- 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.

Fluctuation

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Calculated as [(C_maxSS-C_minSS) / C_avSS]
{Characters preceded by "_" are in subscript font}

fm

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

fraction of systemic clearance of the substrate mediated by the CYP enzyme that is subject to inhibition/induction
{See also 'CYP', 'substrate'}

Forced degradation testing studies

Q1B: Stability Testing: Photostability Testing of New Drug Substances and Products -- Step 4 (final); 6 November 1996 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 1 August 2009 -- 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 {during inspections}

Q8/9/10 Q&As (R5): Questions and Answers (R5). Q8/Q9/Q10 - Implementation -- Step 4 (final); 30 October 2024* -- Section 5, Question 5

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

Formal stability studies

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Primary, commitment, ongoing or product lifecycle stability studies conducted under the accelerated, intermediate, or long-term storage conditions (as applicable) to establish or confirm a re-test period or a shelf life.

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The ability of the design to gracefully accept input intended for newer versions of itself. The concept can be applied to entire systems, data communications, protocols, file formats and computer programming languages. For example, if products designed for the older standard can receive, read, view or play the newer standard or format (excluding new functionality), then the product is said to be Forward Compatible.

M8 eCTD v4.0: Electronic Common Technical Document (eCTD) v4.0. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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 -- Step 4 (final); 14 April 2020 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 5 February 1998 -- 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 design stability protocol

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

A protocol which includes at least three batches of the drug substance or at least three batches of each strength or concentration of the drug product covering the container closure systems for every combination of all design factors and tested at all time points.
{See also Annex 1. Reduced stability protocol design': "A reduced stability protocol design is one in which samples for every factor combination are not all tested at all time points."}

Full Validation

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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): Questions and Answers (R3). ICH E14 Guideline: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs -- Step 4 (final); 10 December 2015 -- Question 1.2

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: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 1.2

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): Questions and Answers (R3). ICH E14 Guideline: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs -- Step 4 (final); 10 December 2015 -- Question 1.2

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: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 1.2

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.

Functional secondary packaging material

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Secondary packaging material considered critical to ensure the quality of the packaged substance/ product

Example: provides additional protection like for moisture sensitive products or serves to deliver the product

{Reference} ICH M4Q(R2) adapted from ICH

G

Gateway

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A device or program which accepts information into a network from an external source.

{XML: Extensible markup language; see also 'XML Schema'}

GD 0

S5(R3): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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 -- Step 4 (final); 9 November 2011 -- 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: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- 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: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- 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 -- Step 4 (final); 5 February 1998 -- 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.

genericode

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

An XML format for interchange, documentation and management of code lists (a.k.a. controlled vocabularies or coded value enumerations) in any processing context. Genericode is a project of OASIS (Organization for the Advancement of Structured Information Standards), a not-for-profit consortium that drives the development, convergence and adoption of open standards for the global information society. https://www.oasisopen.org/committees/codelist/faq.php
{XML: Extensible markup language; see also 'XML Schema'}

Genetic {intervention}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

Introduction of genetic material into cells in order to correct or treat an inherited or acquired disease. {See also: Behavioral {intervention in a clinical trial}, Biologic, Vaccine, Combination Product, Device, Dietary Supplement, Drug, Surgery, Non-Surgical Procedure, Radiation {intervention}, Diagnostic Test}

Genetic endpoint

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 1 November 2007 -- 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 -- Step 4 (final); 20 August 2010 -- 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 -- Step 4 (final); 6 September 2017 -- 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(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- Glossary

Carcinogens which produce cancer by affecting genes or chromosomes.

Genotoxicity

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- Glossary

A broad term that refers to any deleterious change in the genetic material regardless of the mechanism by which the change is induced.
{See also: 'Mutagenic potential'}

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 24 June 1993 -- 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 -- Step 4 (final); 5 February 1998 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A standard for the planning, initiating, performing, recording, oversight, evaluation, analysis and reporting of clinical trials that provides assurance that the data and reported results are reliable and that the rights, safety and well-being of trial participants are protected.

Group Title

M8 eCTD v4.0: Electronic Common Technical Document (eCTD) v4.0. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

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

Hazard

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

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

Hazard Analysis and Critical Control Points (HACCP)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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.

Header

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

Information placed in front of a message which ensures that the message is routed to its destination and that it can be opened and read by the receiving software.

Health Level 7 (HL7)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations

A set of standards used to facilitate the electronic interchange of data in a healthcare environment. {Website: http://www.hl7.org/about/index.cfm}

Healthcare Professional

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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 -- Step 4 (final); 12 November 2003 -- 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.

Healthcare Professional (HCP)

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.5

{In individual case safety reports (ICSR)} Healthcare professional is defined as a primary source who is medically-qualified such as a physician, dentist, pharmacist, nurse, coroner (if medically trained), or as otherwise specified by local or regional requirements.
{see also: 'Primary source'}

Helper Virus

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

A virus that provides helper functions allowing an otherwise replication-deficient coinfecting virus to replicate.
{See also 'Production Virus'}

Herbal Products

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 26 April 2022 -- 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: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 5.1

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 -- Step 4 (final); 10 June 2015 -- Question 4.1

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].

High potency drug product

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

A drug product where the %w/w of a given drug substance is ≤5% of the core weight in all strengths.
{w/w=weight/weight}

High variability

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- 2.4 Assessment of Similarity

High variability is defined as an SD >8% at any time point.
{SD=standard deviation}

Highest Non-Severely Toxic Dose (HNSTD)

S9: Nonclinical Evaluation for Anticancer Pharmaceuticals -- Step 4 (final); 18 November 2009 -- 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 -- Step 4 (final); 11 June 2009 -- 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 -- Step 4 (final); 6 October 1999 -- 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).

HLM

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary
human liver microsome

Hook Effect

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 16 July 1997 -- Glossary
See Parental cells.

Hypertext Mark-up Language (HTML)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations
Commonly used to format Web pages.

I

IC_50

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary
half-maximal inhibitory concentration

IC_50,u

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

unbound IC_50
{See also 'IC_50'}

ICH Regions

E5(R1): Ethnic Factors in the Acceptability of Foreign Clinical Data -- Step 4 (final); 5 February 1998 -- Glossary

European Union, Japan, The United States of America.

Identifiability

E2D: Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting -- Step 4 (final); 12 November 2003 -- 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 -- Step 4 (final); 25 October 2006 -- Glossary

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

Q3B(R2): Impurities in New Drug Products -- Step 4 (final); 2 June 2006 -- 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 -- Step 4 (final); 1 November 2007 -- 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 -- Step 4 (final); 2 June 2006 -- Glossary

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

Identified Impurity

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 6 October 1999 -- Glossary

An impurity for which a structural characterization has been achieved.

Identified risk

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 17 August 2010 -- 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 -- Step 4 (final); 6 November 1996 -- 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 -- Step 4 (final); 6 October 1999 -- Glossary

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

Immediate-Release

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

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

Immortal time bias

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 5.5.3

Immortal time bias refers to a period of cohort follow-up time during which an outcome of interest cannot occur.

Immunotoxicity

S8: Immunotoxicity Studies for Human Pharmaceuticals -- Step 4 (final); 15 September 2005 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- 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 participant or the participant's legally acceptable representative cannot read, and who reads the informed consent form and any other documented information supplied or read to the participant and/or their legally acceptable representative.

Impermeable Container

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

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

Impermeable containers

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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).

Implementation Guide (IG)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A guide for implementing a technical standard to meet ICH requirements. It provides instruction for how the pharmaceutical industry and regulatory authorities will use a standard to construct messages for exchanging regulated data between and among themselves in ICH regions and in other countries adopting ICH guidelines. Standards may be constrained from broader international SDOs (i.e. ICH may only implement a subset of a standard, for example in the case of E2B usage of the ISO ICSR standard), or ICH may define the content requirements for application of a standard (i.e. the acceptable content for using HL7 RPS2 for drugs in ICH regions). ICH IGs may also be intended to support the implementation of software tools for creating, editing, sending and receiving electronic messages.
{HL7: Health Level 7, see separate entry; ICSR: Individual Case Safety Report; IG: Implementation guide; ISO: International Standards Organization; SDOs: Standards Development Organisations}

Important identified risk, important potential risk

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 17 August 2010 -- 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 Medical Event

E19: A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-approval or Post-Approval Clinical Trials -- Step 4 (final); 27 September 2022 -- Glossary

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 serious outcomes; these events require medical and scientific judgement and fall under the expedited reporting rules (see ICH E2A).

Important missing information

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 6 July 2012 -- Question 7

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.)

Impurities Classification

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 6. Table 1

Class 1: Known mutagenic carcinogens
Class 2: Known mutagens with unknown carcinogenic potential (bacterial mutagenicity positive {Footnote}, no rodent carcinogenicity data)
{Footnote}: Or other relevant positive mutagenicity data indicative of DNA-reactivity related induction of gene mutations (e.g., positive findings in in vivo gene mutation studies)
Class 3: Alerting structure, unrelated to the structure of the drug substance; no mutagenicity data
Class 4: Alerting structure, same alert in drug substance or compounds related to the drug substance (e.g., process intermediates) which have been tested and are non- mutagenic
Class 5: No structural alerts, or alerting structure with sufficient data to demonstrate lack of mutagenicity or carcinogenicity

Impurity

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- 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.
(3) 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.
{Reference} ICH Q6A/B/ Degradation product

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- Glossary

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

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Any component of the drug substance or drug product which is not the synthetic chemical or biological entity defined as the active ingredient, excipient, or other additives to the drug product. The source of the impurity could be product or process related.

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- Glossary

See ICH Q3A, ICH Q6A and ICH Q6B.

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 2 June 2006 -- 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 -- Step 4 (final); 30 November 1995 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 10 March 1999 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 25 October 2006 -- Glossary

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

Q3B(R2): Impurities in New Drug Products -- Step 4 (final); 2 June 2006 -- Glossary

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

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- Glossary

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

In Vitro Cell Age

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

A measure of the period between thawing the MCB vial(s) and harvesting the production vessel that is measured by elapsed chronological time in culture, population doubling level of the cells, or passage level of the cells when sub cultivated by a defined procedure for dilution of the culture.
MCB: Master Cell Bank

Q5B: Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products -- Step 4 (final); 30 November 1995 -- 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 -- Step 4 (final); 16 July 1997 -- 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(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Reduction of virus infectivity caused by chemical or physical treatment.

Incurred Sample

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

A sample obtained from study subjects or animals.

Incurred Sample Reanalysis (ISR)

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 10 June 2015 -- Question 2.1

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

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A committee established by the sponsor to assess at intervals the progress of a clinical trial, safety data, and critical efficacy variables and recommend to the sponsor whether to continue, modify, or terminate the trial.
{See also: Dose Escalation Committee, Endpoint Adjudication Committee}

Independent Data Monitoring Committee (IDMC)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

An independent data monitoring committee (e.g., data safety monitoring board) that may be established by the sponsor to assess at intervals the progress of a clinical trial, the safety and relevant efficacy data, and to recommend to the sponsor whether to continue, modify or stop a trial.

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- Glossary

(Data and SafetyMonitoring Board, Monitoring Committee, Data Monitoring Committee)
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 sample

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- 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 precipitant

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

A drug recommended for use in a stand-alone clinical DDI study because it has a well-established potency and selectivity profile that causes a defined degree of inhibition or induction of a given elimination pathway when administered with a sensitive and specific substrate of that pathway.
{DDI = drug-drug interaction}

Index substrate

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

A drug recommended for use in a stand-alone clinical DDI study as substrate because it has a well-established sensitivity and specificity profile that demonstrates a defined degree of change in exposures when administered with a strong inhibitor or inducer for that specific elimination pathway.
{DDI = drug-drug interaction} {See also 'substrate'}

Indirect Phototoxicity

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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]
{Reference: ISO/HL7 27953-2:2011
Health informatics — Individual case safety reports (ICSRs) in pharmacovigilance — Part 2: Human pharmaceutical reporting requirements for ICSR. https://www.iso.org/standard/53825.html}

Individual Case Safety Report (ICSR)

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.2

An ICSR is a description of an AE/ADR or other observation in an individual patient at a specific point of time.
{ADR=Adverse drug reaction; AE=Adverse event}

Informed Consent

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A process by which a participant or their legally acceptable representative voluntarily confirms their willingness to participate in a trial after having been informed and been provided with the opportunity to discuss all aspects of the trial that are relevant to the participant's decision to participate. Varied approaches to the provision of information and the discussion about the trial can be used. This may include, for example, providing text in different formats, images and videos and using telephone or video conferencing with investigator site staff. Informed consent is documented by means of a written (paper or electronic), signed and dated informed consent form. Obtaining consent remotely may be considered when appropriate.

Inhalation Unit Risk

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- 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/m^3 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)
{Characters preceded by "^" are in superscript font}

In-house Primary Reference Material

Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products -- Step 4 (final); 10 March 1999 -- 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 -- Step 4 (final); 10 March 1999 -- 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 -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 6 October 1999 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- 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 accessed at the investigator site, at the sponsor's and/or service provider's (including CRO's) facilities, or at other establishments deemed appropriate by the regulatory authority(ies). Some aspects of the inspection may be conducted remotely.

Institution

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Any public or private entity or agency or medical or dental organisation in whose remit clinical trials are conducted.

Institutional Review Board (IRB)/Independent Ethics Committee (IEC)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- 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 participants 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), the facilities, and the methods and material to be used in obtaining and documenting informed consent of the trial participants. The legal status, composition, function, operations and regulatory requirements pertaining to IRBs/IECs may differ among countries but should allow the IRB/IEC to act in agreement with GCP as described in this guideline.

Integrated risk assessment

S7B: The Non-Clinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals -- Step 4 (final); 12 May 2005 -- 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 -- Step 4 (final); 30 November 1995 -- 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 -- Step 4 (final); 5 February 1998 -- 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.

Interacting medicinal product

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.2 Footnote 1

{In individual case safety reports (ICSR)} The term suspect medicinal product includes interacting medicinal products. “Interacting” medicinal products are products for which the reporter indicates a suspected interaction with other medicinal products. All interacting medicinal products are considered to be suspect medicinal products (See ICH E2B)

Interaction (Qualitative & Quantitative)

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- 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 FAQs: Frequently Asked Questions: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions -- --; 26 April 2012 -- 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.

Q4B(R1): Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions -- Final version; 5 June 2024 -- 3. Glossary

Where such status is indicated, any of the official texts from JP, Ph. Eur., USP or from the other pharmacopoeias referenced in the Q4B Annex can be substituted one for the other (appropriately referenced) in the ICH countries/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 pharmacopoeia referenced in the Q4B Annex is used.

Q4B: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions -- Step 4 (final); 1 November 2007 -- 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.

Intercurrent Events

E9(R1): Addendum: Statistical Principles for Clinical Trials -- Step 4 (final); 20 November 2019 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 5 February 1998 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

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

Intermediate

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

A material that is produced during a manufacturing process, which is not the final drug substance or the final drug product. Intermediates are identified by a manufacturer, who should establish and justify a control strategy to assure the intermediate's stability within conditions of the manufacturing process. Bulk drug products are considered drug product intermediates.

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- Glossary

See ICH Q7, ICH Q3A, and ICH Q5C.

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 30 November 1995 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 1 November 2023 -- Glossary

Intermediate precision expresses intra-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(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

Intermediate precision expresses intra-laboratory 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 -- Step 4 (final); 6 February 2003 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- 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. (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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. (ICH Q2)

International Birth Date (IBD)

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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

International Standards Organization (ISO)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations

Founded in 1946, it is the principal international standards-setting organization.
{Website: https://www.iso.org}

Interoperability

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The degree or extent to which diverse environments (hardware and software) are able to exchange information without loss of content, and in a manner transparent to the user.

Inter-Rater Reliability

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- Glossary

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

Interventional clinical trial

E2F: Development Safety Update Report -- Step 4 (final); 17 August 2010 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 5 February 1998 -- 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 conditions

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- 11.1 Purpose of In-Use Stability Testing

In-use conditions are defined as the conditions that mimic the intended use of the drug product after the primary container is first breached and, where applicable, through preparation, storage and administration as per the relevant instructions.

In-use period

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 17 August 2010 -- 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

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

A medicinal product or a drug under development that is investigated as to its potential to act as an affecting drug or an affected drug

Investigational medicinal product (IMP)

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A medicinal product which is being tested or used as a reference, including as a placebo, in a clinical trial.
{see also "Non-investigational medical product (NIMP)"}

Investigational Product

E19: A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-approval or Post-Approval Clinical Trials -- Step 4 (final); 27 September 2022 -- 1.2 Footnote 1

For the purpose of this Guideline, the term “investigational product” should be considered synonymous with “drug” and “medicinal product,” and includes both human drugs and biological products.

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- 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 authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use. Investigational products should be considered synonymous with drugs, medicines, medicinal products, vaccines and biological products.

Investigational products

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- I. Introduction (footnote 1) and Appendix A, A.1 Introduction (footnote 1)

For the purpose of this guideline, the term “investigational products” should be considered synonymous with drugs, medicines, medicinal products, vaccines and biological products.

Investigator

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A person responsible for the conduct of the clinical trial, including the trial participants for whom that person has responsibility during the conduct of the trial. If a trial is conducted by a team of individuals, the investigator is the responsible leader of the team and may be called the principal investigator. Where an investigator/institution is referenced in this guideline, it describes expectations that may be applicable to the investigator and/or the institution in some regions. Where required by the applicable regulatory requirements, the “investigator” should be read as “investigator and/or the institution.”

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

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 the trial site, the investigator is the responsible leader of the team and may be called the principal investigator.

Investigator Site

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

The location(s) where trial-related activities are conducted and/or coordinated under the investigator’s/institution’s oversight.

Investigator site file (ISF)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Appendix C, Point C 2.3

{See the note at the end of the definition of "Essential records"}

Investigator’s Brochure (IB)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A compilation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human participants (see Appendix A).

Irradiance

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- Glossary

The intensity of UV or visible light incident on a surface, measured in W/m^2 or mW/cm^2.
{Characters preceded by "^" are in superscript font}

Irradiation

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- Glossary

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

IVIVC

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

A predictive mathematical model describing the relationship between an in vitro property of a dosage form (usually the rate or extent of drug dissolution or release) and a relevant in vivo response, e.g., plasma drug concentration or amount of drug absorbed.
{IVIVC=in vitro-in vivo correlation}

J

Joint Initiative

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The Joint Initiative is a formal collaboration between several Standards Development Organisation{s} (SDOs) that operate in the Health Informatics sector. Its aim is collaborate in the development of single standards, recognised by each SDO. SDOs involved (as of 2013) include ISO, CEN, HL7, IHTSDO, GS-1 and CDISC. It is governed by the Joint Initiative Council (JIC). Further information is available at http://www.jointinitiativecouncil.org/
{CDISC: Clinical Data Interchange Standards Consortium; CEN:Comité Européen de Normalisation – European Committee for Standardization; IHTSDO: International Health Terminology Standards Development Organisation}

Juvenile Animal

S11: Nonclinical Safety Testing in Support of Development of Paediatric Medicines -- Step 4 (final); 14 April 2020 -- 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 -- Step 4 (final); 14 April 2020 -- 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

k_deg

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

apparent first-order degradation rate constant of the affected enzyme

k_el

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

The apparent terminal elimination rate constant
{Characters preceded by "_" are in subscript font}

K_i

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

inhibition constant causing half-maximal inactivation

K_i,u

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

unbound inhibition constant causing half-maximal inactivation

k_inact

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary
maximal inactivation rate constant

K_m

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary
Michaelis-Menton constant

K_obs

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary
apparent first-order inactivation rate constant of the affected enzyme

Knowledge management

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 1 November 2023 -- 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: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 4.1
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 -- Step 4 (final); 11 June 2009 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- Multivariate glossary

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

Legally Acceptable Representative

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

An individual or juridical or other body authorised under applicable law to consent, on behalf of a prospective participant, to the participant's participation in the clinical trial. When a legally acceptable representative provides consent on behalf of a prospective participant, activities related to the consenting process (and re-consent, if applicable) and, where relevant, activities associated with the withdrawal of consent described in this guideline are applicable to the participant's legally acceptable representative.

Lifecycle

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 1 August 2009 -- Part I, Glossary

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

Q8(R2): Pharmaceutical Development -- Step 4 (final); 1 August 2009 -- Part II, Glossary

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 -- Step 4 (final); 25 October 2006 -- Glossary

An agent with a strong affinity to a metal ion.

Ligand Binding Assay (LBA)

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 In Vitro Cell Age (LIVCA) Cells

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

LIVCA cells are derived from production cells at or beyond in vitro cell age by expansion of the MCB or WCB. LIVCA cells may be also referred to as EOPC or Extended Cell Bank (ECB) and these terms can be used interchangeably.
EOPC: End of Production Cells. MCB: Master Cell Bank. WCB: Working Cell Bank

Limit of Quantitation (LoQ)

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- 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)

Long term testing

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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.

Long-term Testing

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Stability studies under the recommended long-term storage condition for the re- test period or shelf life proposed (or approved) for labelling. Long-term testing results in real time data obtained at the long-term storage condition.

Lot

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

{See “Batch (for Reference Standards and Reagents)”}

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- Glossary

See Batch

Lot Number

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- Glossary

See Batch Number

Low solubility drug substances

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- 2.1.5, under "High risk products"

(as defined by the BCS low solubility criterion described in ICH M9)

Lower Limit of Quantification (LLOQ)

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- 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 -- Step 4 (final); 26 April 2022 -- 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 -- Step 4 (final); 26 April 2022 -- 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

M2 OID Registrar

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

An individual member of the M2 Expert Working Group (EWG) assigned the primary responsibility for maintenance of the ICH M2 Electronic Standards for the Transfer of Regulatory Information (ESTRI) OID system.

{OID: Object Identifier; see separate entry}

Maintenance Organization

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

An organization currently engaged in establishing, populating on an initial basis or maintaining controlled vocabularies (ISO). For example, EDQM, ICH, IHTSDO.
{EDQM: European Directorate for the Quality of Medicines & HealthCare; IHTSDO: International Health Terminology Standards Development Organisation; ISO: International Standards Organization}

Malformation

S5(R3): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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): Questions and Answers (R3). ICH E14 Guideline: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs -- Step 4 (final); 10 December 2015 -- Question 1.2

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.

E14/S7B: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 1.2

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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 18 November 2004 -- 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).
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 -- Step 4 (final); 18 November 2004 -- 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 -- Step 4 (final); 30 November 1995 -- Glossary

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

Market Research Program (MRP)

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.1

MRPs are ODCSs which are used for planned collections of healthcare professional and/or consumer insights by an MAH, on medicinal products and/or a disease area, for the purpose of marketing and business development.
{MAH=Marketing authorisation holder; ODCS=Organised Data Collection System}

Marketing Authorisation Holder

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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 -- Step 4 (final); 6 November 1996 -- Glossary

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

Mass balance

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

For synthetic chemical entities, 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.

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

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

Q5B: Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products -- Step 4 (final); 30 November 1995 -- 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 -- Step 4 (final); 16 July 1997 -- 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.

Master Virus Seed (MVS)

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

A MVS (stock, lot, or bank) is a preparation of a vector virus, a viral vector or production virus (i.e., helper virus or viral protein expression vector), from which all future production will be derived, either directly, or via a WVS. It is a live viral preparation of uniform composition (although not necessarily clonal) derived from a single culture process, aliquoted into appropriate storage containers, and stored under appropriate conditions.
wVS: Working Virus Seed

MATE

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

multidrug and toxin extrusion

Material

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

A general term used to denote raw materials, starting materials, substance intermediates, drug substances, excipients, reference standards, product intermediates, finished dosage forms, and packaging and labelling materials.
ICH M4Q(R2) //Adapted from ICH Q7

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- Glossary

The ability to track materials throughout the manufacturing process.

Matrix

S3A: Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies -- Step 4 (final); 27 October 1994 -- Note 1

Blood, plasma, urine, serum or other fluid or tissue selected for assay.

Matrix Effect

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 7 February 2002 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 11 March 2008 -- 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

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- 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 (28) can be used.

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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.
{Reference: Haynes JD. Worldwide virtual temperatures for product stability testing. J Pharm Sci. 1971;60(6):927-929. https://doi.org/10.1002/jps.2600600629}

Mean Photo Effect (MPE)

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- 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 Claims Data

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A compilation of information on medical claims submitted to insurance companies for reimbursement of medical expenses for treatments and other interventions. Medical claims data use standardized medical codes, such as the World Health Organization's International Classification of Diseases Coding (ICD-CM) diagnosis codes, to identify diagnoses and treatments.
(FDA, United States. Data Standards for Drug and Biological Product Submissions Containing Real-World Data) {CIOMS has verified the source of this definition: FDA Guidance. Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision Making for Drug and Biological Products (Draft)). September 2021, https://www.fda.gov/media/152503/download; citing the 2018 Framework for FDA's Real-World Evidence Program as the source (see https://www.fda.gov/media/120060/download?attachment, page 28, under "Medical claims data").}

Medical Dictionary for Regulatory Activities

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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]

M11 EWG: Clinical electronic Structured Harmonised Protocol (CeSHarP) -- Step 2 (draft); 27 September 2022 -- 1.3

The term “medicinal product” in this guideline, and the term “trial intervention” in the protocol Template refer to any therapeutic, prophylactic, or diagnostic agent including pharmaceuticals, biologics, vaccines, cell or gene therapy products (when applicable), as well as drug-device combination products when registered as a drug.

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Pharmaceutical product or combination of pharmaceutical products that can be administered to human beings or animals for treating or preventing disease, with the aim of making a medical diagnosis or to restore, correct or modify physiological functions
Note 1: A medicinal product may contain in the packaging one or more finished dosage form(s), and one or more pharmaceutical products.
Note 2: In certain regions, a medicinal product is defined as any substance or combination of substances that can be used to make a medical diagnosis.
{Reference} ISO IDMP 11615 {ISO 11615:2017 Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information. https://www.iso.org/standard/70150.html}

Medicine

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Any substance or combination of substances intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease.
(Section 201(g) of the Federal Food Drug and Cosmetic Act (FD&C Act).)
{https://uscode.house.gov/view.xhtml?req=granuleid:USC-prelim-title21-section321&num=0&edition=prelim}

Message

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A set of information that is exchanged for a specific reason. For ICH M2 the main examples are ICSRs containing safety information, regulatory submissions containing information related to the development, testing and manufacture of medicinal products, and drug dictionary information containing data to identify specific medicinal products. ICH M2 primarily deals with messages which are transmitted through electronic means (i.e. the eCTD and the E2B ICSR).
{eCTD: electronic Common Technical Document; ICSR: Individual Case Safety Report}

Message Standard

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A defined manner of packaging information for a message that has been agreed upon by multiple parties. Messaging standards define specific messages by a combination of content requirements (key data and structures for containing it) and transactional requirements (timing and specified content at stages). Messaging standards also define the means for coding such information in a manner that allows the exchange of this information between different systems.

Meta-Analysis

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- 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.

Metadata

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

The contextual information required to understand a given data element. Metadata is structured information that describes, explains or otherwise makes it easier to retrieve, use or manage data. For the purpose of this guideline, relevant metadata are those needed to allow the appropriate evaluation of the trial conduct.

Metazoan

Q5D: Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products -- Step 4 (final); 16 July 1997 -- Glossary

Organism of multicellular animal nature.

Method operable design region (modr)

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 16 November 2017 -- 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.

MIDD evidence

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

Model outcomes that have been determined by application of the MIDD evidence assessment framework, including Model Evaluation, to be appropriate to inform the answer to the Question of Interest.

{See also "Model-Informed Drug Development (MIDD)" and "Question of Interest"}

Migration

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The planned systematic transition from one application or system to another application or system.

Minimal Risk Level (MRL)

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- Glossary

An estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk. (ATSDR)

Minimum Criteria for Reporting

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.2

The minimum criteria for reporting ICSRs are:

- At least one AE/ADR – see Section 5.1.1, or other observation – see Section 5.1.3;
- At least one suspect or interacting medicinal product;
- An identifiable patient – see Section 6.1;
- At least one identifiable reporter – see Section 6.1.

{AE=Adverse event; ADR=Adverse drug reaction; ICSR=Individual case safety report; MAH=Marketing authorisation holder}

{See also: 'Interacting medicinal product'}

Minimum Exposure Time

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

The shortest period for which a treatment step will be maintained.

Minimum Required Dilution (MRD)

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 9 November 2011 -- Glossary

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

Model Evaluation

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

Model Evaluation refers to performing verification, validation, and applicability assessment of the model. For purposes of the assessment table, this should be presented as a brief discussion of the key results and conclusions of the technical evaluation of the model.

Model Impact

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

The contribution of the model outcomes in relation to current regulatory expectations or standards in answering the Question of Interest.
{See also "Question of Interest"}

Model Influence

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- 2.1. Key Assessment Elements, and Appendix 3: Glossary

The intended weight of the model outcomes in decision-making considering the contribution of other relevant information.

Model Maintenance

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- 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 -- Step 4 (final); 1 November 2023 -- Multivariate glossary

The process of ensuring continued model performance over the lifecycle of a multivariate model, which often includes outlier diagnostics and resulting actions for model redevelopment or change in the maintenance plans. (ICH Q14)

Model outcomes

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

Results derived from M&S (i.e., via model-based predictions or simulations) and associated conclusions that are typically aligned to a Question of Interest. These can be assessed as potential MIDD evidence using the associated framework.
{M&S=modeling and simulation. See also Footnote 2 on page 4: "While it is acknowledged that they are not always synonymous, the terms “model” or “modeling” are often used in this guideline to represent “M&S” to improve readability and reflect commonly used terminology."}

Model Risk

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

The contribution of the model outcomes to a possible wrong decision and subsequent potential undesirable consequences.

Model validation

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

The process of determining the suitability of a model by challenging it with independent test data and comparing the results against predetermined performance criteria.

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Multivariate glossary

The process of determining the suitability of a model by challenging it with independent test data and comparing the results against predetermined performance criteria. (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Multivariate glossary

The process of determining the suitability of a model by challenging it with independent test data and comparing the results against predetermined performance criteria. (ICH Q2)

Model verification

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

The process of ensuring the model is implemented as intended. For example, confirmation that the modelled data for the initially proposed shelf life or re-test period are comparable to confirmatory experimental data.

Model-Informed Drug Development (MIDD)

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- 1.2. Background, and Appendix 3: Glossary

For the purposes of this guideline, MIDD is defined as the strategic use of computational modeling and simulation (M&S) [footnote 2] methods that integrate nonclinical and clinical data, prior information, and knowledge (e.g., drug [footnote 3] and disease characteristics) to generate evidence.
[Footnote 2:] While it is acknowledged that they are not always synonymous, the terms "model" or "modeling" are often used in this guideline to represent "M&S" to improve readability and reflect commonly used terminology.
[Footnote 3:] For the purpose of this guideline, the term "drug" is considered synonymous with investigational product, medicine, medicinal product, biological product, and pharmaceutical product; this includes "drugs" for which marketing authorization is sought.

Modelling and Simulation (M&S)

E11(R1): Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population -- Step 4 (final); 18 August 2017 -- 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 -- Step 4 (final); 6 October 1999 -- 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(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- 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 -- Step 4 (final); 26 April 2022 -- 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 -- Step 4 (final); 13 November 2013 -- 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 -- Step 4 (final); 27 October 1994 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

The act of overseeing the progress of a clinical trial and of ensuring that the clinical trial is conducted, recorded and reported in accordance with the protocol, SOPs, GCP and the applicable regulatory requirement(s).

Monitoring Plan

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A document that describes the strategy, methods, responsibilities and requirements for monitoring the trial.

Monitoring Report

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A documented report following site and/or centralised monitoring activities.

Mother Liquor

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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.

MRP

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

multidrug resistance-associated protein

Multicentre

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

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

{See also: Single-Centre}

Multicentre Trial

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A clinical trial conducted according to a single protocol but at more than one investigator site.

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- 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.

Multiconstituent Product(s)

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Multiconstituent products consist of two or more constituents that are intended to be used together for a specific therapeutic, diagnostic or preventive purpose, and that are packaged in a container or in a unit as a marketing pack. Multiconstituent products may include one or more drug product constituents, or a combination of these with additional finished dosage forms and/or medical device(s).
Examples: a vial containing powder for solution for injection may be packaged with a vial containing the vehicle for preparation of solution for reconstitution, along with two syringes: one for preparation of the solution for injection and the other for administration of the solution for injection
{Reference} ICH M4Q(R2)

Multi-Regional Clinical Trial (MRCT)

E17: General principles for planning and design of Multi-Regional Clinical Trials -- Step 4 (final); 16 November 2017 -- Glossary

A clinical trial conducted in more than one region under a single protocol.

Multivariate analytical procedure

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Multivariate glossary

An analytical procedure where a result is determined through a multivariate calibration model utilising more than one input variable. (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Multivariate glossary

An analytical procedure where a result is determined through a multivariate calibration model utilising more than one input variable. (ICH Q2)

Multivariate Statistical Process Control

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- Glossary

The application of multivariate statistical techniques to analyse complex process data with potentially correlated variables. (Ph. Eur.)

Mutagenic impurity

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- Glossary

An impurity that has been demonstrated to be mutagenic in an appropriate mutagenicity test model, e.g., bacterial mutagenicity assay.

Mutagenic potential

M7(R2) Q&As: Questions and Answers: Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 24 May 2022 -- Question 1.1

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

NADPH

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

nicotinamide adenine dinucleotide phosphate (reduced form)

Namespace

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A technical identifier that allows the transmission of coded values for which there is no ICH accessible master list of values. Namespaces identify the source or domain of a coded value without providing the list of values to allow the code to be interpreted, i.e. namespaces identify the domain of an identifier.

Narrow therapeutic index

M9 Q&As: Questions and Answers: Biopharmaceutics Classification System-based Biowaivers -- Step 4 (final); 20 November 2019 -- Question 1.4

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 -- Step 4 (final); 12 May 2005 -- 2.2.2

{See "Thorough QT/QTc study"}

Neonates / Neonatal period

E11(R1): Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population -- Step 4 (final); 18 August 2017 -- 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 DDI study

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

A DDI investigation that is part of a clinical study (e.g., phase 2/3) in which the assessment of DDI is not the primary objective.
{DDI = drug-drug interaction}

Neurotoxicity

Q3C(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- Glossary

The ability of a substance to cause adverse effects on the nervous system.

New active pharmaceutical ingredient

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 6 November 1996 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 2 June 2006 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 5 February 1998 -- Glossary

The region where product registration is sought.

Newly identified signal

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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)

Next Generation Sequencing (NGS)

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Also referred to as high throughput sequencing or massive parallel sequencing or deep sequencing, multistep nucleic acid-based technology with broad capabilities for non-targeted (agnostic) detection of known and unknown adventitious viruses. In some cases, NGS can be used for targeted detection of known viruses by the sequencing strategy or by bioinformatic analysis.

No-effect boundaries

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

Interval within which a change in a systemic exposure measure is considered not significant enough to warrant clinical action (e.g., dose or schedule adjustment, additional therapeutic monitoring, avoid use)

Nominal Concentration

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

Theoretical or expected concentration.

Nonclinical biodistribution (BD) assessment

S12: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- 2

Nonclinical BD assessment entails 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.
{See also: 'Biodistribution (BD)'; 'Biodistribution (BD) study'}

Nonclinical safety assessment

M3(R2): Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals -- Step 4 (final); 11 June 2009 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Biomedical studies not performed on human participants.

Non-conformance

Q7 Q&As: Questions and Answers: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 June 2015 -- Question 20.1

'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-functional coating

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- Glossary

A coating that does not alter the dissolution/release characteristics of the dosage form. For the purpose of this guideline, coatings designed for functions such as appearance, stability, or strength differentiation are considered non-functional for bioequivalence decisions.

Non-Inferiority Trial

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 17 August 2010 -- 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-investigational medicinal product (NIMP) {in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A medicinal product that is related to the specific needs of the clinical trial as described in the protocol, but not as an investigational medicinal product.
{See also "Investigational medical product (IMP)"}

Non-proprietary Drug (generic) Name

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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).

Nonproprietary Name(s)

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

Drug name that is not protected by a trademark, usually descriptive of its chemical structure, and sometimes a public name. (ICH E2B)

Non-specific Model Virus

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- 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 downstream process).
{See also 'Virus'}

Non-Surgical Procedure

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A medical procedure that produces an effect, or that is intended to alter the course of a disease in a patient or population, which is not considered a surgical procedure.
{See also: Behavioral {intervention in a clinical trial}, Biologic, Vaccine, Combination Product, Device, Dietary Supplement, Drug, Genetic {intervention}, Surgery, Radiation {intervention}, Diagnostic Test}

No-Observed-Adverse-Effect Level (NOAEL)

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- 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(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- 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 -- Step 4 (final); 26 April 2022 -- 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 -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 27 October 1994 -- 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 -- Step 4 (final); 9 November 2011 -- 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

OCT

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

organic cation transporter

OAT

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

organic anion transporter

OATP

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

organic anion transporting polypeptide

Object

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

A substrate of enzyme or transporter

{Note, from Section 1.4}: Note that historically, some regions have used the term “victim” instead of “object” and the term “perpetrator” instead of “precipitant.”

Object Identifier (OID)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

An Object Identifier (OID) is a name used to identify an object. In the context of IT standards OIDs are globally unique identifiers. Most international standards, including ICH, use the ISO ASN.1 data type which consists of a sequence of one or more non-negative integers, often referred to as arcs, which define a hierarchy, or tree, of object identifier values. These are represented using a form that consists only of numbers and dots (e.g., "2.16.840.1.113883.3.989"). OIDs are paths in a tree structure, with the left-most number representing the root and the right-most number representing a leaf.
{ISO: International Standards Organization}

Observer Blind

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A study in which the study personnel who measure, record, or assess the participant do not know which intervention the participant is receiving or, in the context of observational studies, do not know the external factors to which a participant has been exposed.
{See also: Double Blind,Open Label, Single Blind}

Off-label Use

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 5.1.3.4

Intentional use of a product not in accordance with the terms of the marketing authorisation

OID Repository, OID Registry

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

Publicly accessible listings of Object Identifiers (OIDs) to allow identification and translation of the numeric strings, and to provide information on the owner and registrar for a particular OID.
{See also 'Object Identifier (OID)'}

Ongoing clinical trial

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 17 August 2010 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 17 December 2012 -- Glossary

A signal that remains under evaluation at the Data Lock Point (DLP).
{Source:} ICH Guideline E2C(R2)

Ongoing stability studies (also referred to as annual stability studies)

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Stability studies conducted under long-term storage conditions on an annual basis to ensure the consistency of stability related quality attributes at the approved storage conditions over the product lifecycle. These studies also allow for the monitoring of the stability characteristics and examine trends in the stability data to confirm the appropriate storage conditions relevant for the product and to confirm a re-test period or a shelf life.

Ongoing stability study

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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.

Open Dish Study

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

A study conducted without the protection of the immediate container, representing a worst-case scenario under controlled conditions.

Open Label

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A study in which participants and study personnel know which intervention each participant is receiving.
{See also: 'Double Blind', 'Observer Blind', 'Single Blind'}

Operational Definition

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

The data-specific operation or procedure a researcher followed to measure constructs in a particular study.
(FDA, United States. Guidance Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision Making for Drug and Biological Products (Draft)) {September 2021. https://www.fda.gov/media/152503/download}

Orally Disintegrating Tablet

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

A solid dosage form which is designed to disintegrate and dissolve rapidly on contact with saliva when placed on the tongue or in the oral cavity, thus eliminating the need to chew the tablet, swallow an intact tablet, or take the tablet with water.

Organised Data Collection System (ODCS)

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.8

{For individual case safety reports (ICSR)} An organised data collection system (ODCS) is an activity that gathers data in a planned manner, thereby enabling review to be performed. For the purposes of this Guideline, ODCS excludes the MAHs' standard procedures for the surveillance, receipt, evaluation, and reporting of spontaneous postmarketing AEs/ADRs and other postmarketing AEs/ADRs managed as spontaneous reports (i.e., the MAH's routine pharmacovigilance operations for spontaneous reports), see Section 4.
{ADR=Adverse drug reaction; AE=Adverse event; MAH=Marketing authorisation holder}

Other Observations

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.1.5

{In individual case safety reports (ICSR)} "Other observations" refers to certain occurrences associated with use of a medicinal product, including: use in pregnancy/lactation; lack of efficacy; overdose, abuse, misuse, medication error, occupational exposure; and off-label use. In some cases, "other observations" can occur without any associated AEs/ADRs, while in other cases "other observations" can occur with an associated AE/ADR.
{ADR=Adverse drug reaction; AE=Adverse event; ICSR=Individual case safety report; MAH=Marketing authorisation holder}

Other significant adverse events

E3: Structure and Content of Clinical Study Reports -- Step 4 (final); 30 November 1995 -- 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.

Outcome of the MIDD Evidence Assessment

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

A concise summary of the multidisciplinary assessment of the MIDD evidence to answer the Question of Interest. "Assessment" in this context does not refer to any regulatory review activities or processes.
{See also "Model-Informed Drug Development (MIDD)" and "Question of Interest"}

Outcomes Assessor {in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

The individual who evaluates the outcome(s) of interest.

Outlier diagnostic

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Multivariate glossary

Tests that can identify unusual or atypical data in a multivariate analytical procedure. (ICH Q14)

Outpatient Study

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- Glossary

A clinical study in which patients are not restricted to a clinical site.

Outsourced Activities

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- Glossary

Activities conducted by a contract acceptor under a written agreement with a contract giver. (ICH Q10)

P

Packaged Medicinal Product

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Medicinal Product in a container being part of a package, representing the entirety that has been packaged for sale or supply
Note: Packaged Medicinal Product may contain Multiconstituent Product
Examples: film-coated tablet in blister in carton box or solution for injection in vial in carton box or one vial with powder for solution for injection is packaged with one vial with the vehicle solution for reconstitution and with two syringes for preparation of the solution for injection and for administration of the solution for injection in a carton box
{Reference} ISO IDMP/ Marketing Pack {ISO 11615:2017 Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information. https://www.iso.org/standard/70150.html}

Packaging Material

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Any material intended to protect another material during storage and transport.
ICH M4Q(R2) adapted from ICH Q7

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 14 April 2020 -- 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 -- Step 4 (final); 14 April 2020 -- Glossary

Paediatric-only development describes development for treatment exclusively in paediatric ages (e.g., neonatal respiratory distress syndrome).

Parallel Group {intervention model in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

Participants are assigned to one of two or more treatment groups in parallel for the duration of the study.
{See also: 'Cross-over', 'Factorial', 'Sequential', 'Single Group'}

Parallelism

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 18 August 2017 -- 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 -- Step 4 (final); 16 July 1997 -- 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 -- Step 4 (final); 5 February 2001 -- Glossary

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

Partial Validation

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

Validation based on evaluation of selected validation parameters. Applicable to methods that were changed after full validation.

Participant

M11 Template: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Template -- Step 2 (draft); 13 March 2025* -- Word Usage in Template

"Participant" is used rather than "subject", "healthy volunteer", or "patient" when referring to an individual who has consented or was adequately/legally represented to participate in the clinical trial. "Patient" or "individual" is used to distinguish the population represented by the trial participants, when necessary.

Participant {in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A member of the clinical study population from whom data are being collected.

Patient Experience Data

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Data that are collected by any persons and are intended to provide information about patients' experiences with a disease or condition. Patient experience data can be interpreted as information that captures patients' experiences, perspectives, needs, and priorities related to (but not limited to): 1) the symptoms of their condition and its natural history; 2) the impact of the conditions on their functioning and quality of life; 3) their experience with treatments; 4) input on which outcomes are important to them; 5) patient preferences for outcomes and treatments; and 6) the relative importance of any issue as defined by patients.

(Title III, section 3001 of the 21st Century Cures Act, as amended by section 605 of the FDA Reauthorization Act of 2017 [FDARA])
https://uscode.house.gov/view.xhtml?req=(title:21%20section:360bbb-8c%20edition:prelim)}

Patient Identifiability

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 6.1

{In Individual Case Safety Reports (ICSR)} The term identifiable in this context refers to the verification of the existence of a patient and a reporter (i.e., a primary source; see Section 2.4, Primary Source). (...)
One or more of the following should automatically qualify a patient as identifiable: age (or age category, e.g., adolescent, adult, elderly), gestational age, gender, initials, date of birth, name, or patient identification number. (...)
In relation to cases from digital platforms, the identifiability of the reporter/patient refers to the existence of a real person (...). The presence of a digital platform username or identifier (i.e., "handle") in the absence of qualifying identifiers is insufficient to confirm that there is a real patient and/or reporter.
{See also: 'Reporter Identifiability'}

Patient perspective

M4E(R2): Revision of M4E Guideline on Enhancing the Format and Structure of Benefit-Risk Information in ICH: Efficacy -- Step 4 (final); 15 June 2016 -- 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.

Patient Support Program (PSP)

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.9

PSPs are ODCSs initiated by an MAH, in which patients enrol for the purpose of supporting their use of the MAH's medicinal product, or the management of their medical condition, and which include a mechanism for two-way communication between the MAH (or third party acting on the MAH's behalf) and patients or healthcare professionals. Examples of PSPs include adherence support, disease management, and certain reimbursement, and educational programs. See Section 4.4, Sources of ICSRs, PSPs, for further details.
Programs meet the definition of a PSP if 1) they solicit medical information about the patient's use of a medicinal product and/or 2) the design of the program is such that the MAH (or a third party acting on the MAH's behalf) would foreseeably receive medical information about the patient's use of a medicinal product (e.g., when a program involves HCP interaction with a patient to administer medication or provide medical advice).
MAH-initiated programs that do not meet the criteria above (e.g., delivery of a product to a patient's home, provision of vouchers or coupons) are not considered to be PSPs, as long as the MAH does not request medical information about the patient's use of a medicinal product. PSPs exclude: clinical trials; non-interventional studies, such as post-authorisation safety studies which have a scientific intent or are testing a hypothesis; all forms of compassionate use; and named patient supply.
{ICSR= individual case safety report; MAH=Marketing authorisation holder;ODCS=Organised Data Collection System}

pAUC

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

partial AUC. Area under the concentration vs. time curve between two specific time points
{AUC: Area under the curve; see also 'AUC'}

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Area under the concentration vs. time curve between two specific time points

Payload

M8 eCTD v4.0: Electronic Common Technical Document (eCTD) v4.0. Implementation Guide v1.6 -- Step 4 (final); 21 May 2024 -- 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'.

PBPK

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

physiologically-based pharmacokinetic

Pediatric extrapolation

E11(R1): Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population -- Step 4 (final); 18 August 2017 -- 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: Paediatric Extrapolation -- Step 4 (final); 21 August 2024 -- 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 and the expected response to a medicinal product would be sufficiently similar in the pediatric [target] and reference (adult or other pediatric) population."
{Note 1, from Section 1.2 of the ICH E11A guideline:} For the purposes of this document "disease" includes both "diseases" and "conditions". A condition may include a disease as well as being at risk for a disease.
{Note 2, from Section 1.4 of the ICH E11A guideline}: 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 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. (...) The use of extrapolation as discussed in this guideline reflects that a continuum of similarity/dissimilarity in disease, drug pharmacology, and response to treatment may exist between a reference and target population (Figure 1). The degree to which similarity is concluded will depend, in part, on a multidisciplinary assessment of the strength of the evidence, the confidence in the data reviewed, and the remaining gaps in knowledge.

Pediatric formulations

E11(R1): Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population -- Step 4 (final); 18 August 2017 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 1 November 2023 -- Glossary

A technology independent description of a characteristic that ensures the quality of the measured result. Typically, accuracy, precision, specificity/selectivity and range may be considered. Previous ICH Q2 versions referred this as 'Validation characteristic'. (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

A technology independent description of a characteristic that ensures the quality of the measured result. Typically, accuracy, precision, specificity/selectivity and range may be considered. Previous ICH Q2 versions referred to this as 'Validation characteristic'. (ICH Q2)

Performance criterion

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

An acceptance criterion describing a numerical range, limit or desired state to ensure the quality of the measured result for a given performance characteristic. (ICH Q14)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

An acceptance criterion describing a numerical range, limit or desired state to ensure the quality of the measured result for a given performance characteristic. (ICH Q14)

Performance Indicators

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- 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 Benefit-Risk Evaluation Report (PBRER)

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 1. Introduction

The Periodic Benefit-Risk Evaluation Report (PBRER) described in this Guideline is intended to be a common standard for periodic benefit-risk evaluation reporting on marketed products (including approved drugs that are under further study) among the ICH regions.

Periodic verification testing

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- Glossary

Also known as periodic or skip testing in ICH Q6A.

Permitted Daily Exposure (PDE)

Q3C(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- 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 -- Step 4 (final); 26 April 2022 -- Glossary

The maximum acceptable intake of elemental impurity in pharmaceutical products per day.

Persistence

S12: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- Glossary

The continued presence of transferred or modified genetic sequences in the host after acute exposure to a GT product, due either to integration of the genetic sequence into the host genome, deletion, insertion, or otherwise modified following genome editing, to latent infection with the viral vector bearing the transgene, or to the transferred genetic material in episomal form.
{GT: gene therapy}

P-gp

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

P-glycoprotein

Pharmaceutical

S5(R3): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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 Product

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Qualitative and quantitative composition of the product as administered to the patient in line with regulated product information.
Note 1: In many instances, the pharmaceutical product is equal to the finished dosage form. However, there are instances where the finished dosage form must undergo a transformation before being administered to the patient (as the pharmaceutical product) and the two are not equal.
Examples: film-coated tablet (taken without transformation) or reconstituted solution for injection using one vial with powder for solution for injection is packaged with one vial with the vehicle for preparation of solution for reconstitution
{Reference} ISO IDMP {ISO 11615:2017 Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information. https://www.iso.org/standard/70150.html}

Pharmaceutical Quality System (PQS)

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 1 November 2007 -- 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 -- Step 4 (final); 1 November 2007 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 1 November 2007 -- 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 -- Step 4 (final); 1 November 2007 -- Glossary

The pharmacopoeial monographs, general test chapters, and analytical methods emanating from the three regional pharmacopoeias.

Pharmacovigilance

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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;]
{Reference "WHO; 2002" not found in the PDF document. Reference from the CIOMS Cumulative Glossary, https://doi.org/10.56759/ocef1297 : The Importance of Pharmacovigilance: Safety Monitoring of Medicinal Products. Geneva, WHO, 2002. The publication is no longer available online, but the definition is reflected on the website of the WHO Regulation and Prequalification team at https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance, accessed 21 June 2022).}

E2E: Pharmacovigilance Planning -- Step 4 (final); 18 November 2004 -- 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.

Phase 1 {trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

The initial administration of an investigational medicinal product (IMP) into humans in order to examine clinical tolerability and therapeutic intent. Phase 1 trials are typically closely monitored and may be conducted in patients or healthy volunteer participants.
{See also: Early Phase 1 {trial}}

Phase 1/Phase 2 {trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

A clinical trial that combines elements characteristic of traditional Phase 1 and Phase 2 trials.

Phase 1/Phase 2/Phase 3 {trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

A clinical trial that begins as a Phase 1 trial and transitions into Phases 2 and 3 based upon successful completion of a milestone that enables transition.

Phase 1/Phase 3 {trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

A clinical trial that begins as a Phase 1 trial and transitions into a Phase 3 trial based upon successful completion of a milestone that enables transition.

Phase 2 {trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

Exploratory trials conducted to evaluate the safety and efficacy of the investigational intervention in patients with the disease or condition. Objectives can be clinical pharmacology, dose-ranging (dose-response, frequency of dosing), type of patients, or numerous other characteristics of safety and efficacy.

Phase 2/Phase 3 {trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

A class of clinical study that combines elements characteristic of traditional Phase 2 and Phase 3 trials.
A clinical trial that combines elements characteristic of traditional Phase 2 and Phase 3 trials.

Phase 2/Phase 3/Phase 4 {trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

A study that begins as a Phase 2 study and transitions into Phases 3 and 4 based upon successful completion of each previous portion.
A clinical trial that begins as a Phase 2 trial and transitions into Phases 3 and 4 based upon successful completion of a milestone that enables transition.

Phase 3 {trials}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

Confirmatory trials conducted to demonstrate safety, efficacy and tolerability of the intervention in patients with the disease or condition. Their objectives are to evaluate the overall benefit-risk relationship and to provide substantial evidence for regulatory approval and labeling.

Phase 3/Phase 4 {trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

A clinical trial that combines elements characteristic of traditional Phase 3 and Phase 4 trials.

Phase 4 {trials}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

Post-approval trials conducted to further understand the safety and efficacy of the drug in its approved indication. They are not considered necessary for approval but are often important for optimising the drug's use.

Phenotype / Phenotype Algorithm

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Observable and measurable information that is relevant to health or healthcare such as a disease (e.g., type 2 diabetes), a blood pressure measurement, a blood sugar value or an antibiotic prescription. It can be used to define any patient characteristics, from exposure to outcome. The translation of the case definition into an executable algorithm that involves querying clinical data elements from the EHRs is the Phenotyping algorithm. These algorithms identify and extract data from health records using clinical codes (for example ICD-10 or SNOMED). They can also be referred to as “electronic phenotype” or “computable phenotype”.
(www.ohdsi.github.io (The Book of OHDSI)) {E.g. See https://ohdsi.github.io/TheBookOfOhdsi/ClinicalValidity.html, under ‘16.2 Cohort validation’}

Photo Irritation Factor (PIF)

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- 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 -- Step 4 (final); 13 November 2013 -- 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 -- Step 4 (final); 13 November 2013 -- Glossary

New compounds/structures formed as a result of a photochemical reaction.

Photoreactivity

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- Glossary

The property of chemicals to react with another molecule as a consequence of absorption of photons.

Photosafety assessment

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- 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 the S10 guideline}

Photosensitization

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- 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 -- Step 4 (final); 13 November 2013 -- 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 -- Step 4 (final); 30 November 1995 -- 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

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- 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 synthetics chemical entities in solid dosage forms, a pilot scale is generally, at a minimum, one-tenth that of a full production scale or 100 000 units, whichever is the larger, unless otherwise adequately justified. For biologics, the steps of upstream and downstream processing should be identical except for the scale of production.
{See also Section 4.1, Table 2, Footnote 2: "In accordance with ICH Q13, the definition of a pilot batch for synthetics does not apply for continuous manufacturing."}

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 30 November 1995 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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.

Placebo

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 and 6

{Section 1.1.2:} An inactive, identical-appearing drug or treatment that does not contain the test product.

{Section 6:} A pharmaceutical preparation that does not contain the investigational agent and is generally prepared to be physically indistinguishable from the preparation containing the investigational product.

{See also: 'Active Comparator', 'Dose Response {Control Type}', 'Different Dose or Regimen {Control Type}', 'External {Control Type}', 'Sham Procedure'}

Plasmid

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- Glossary

Genetic element additional to the normal bacterial genome. A plasmid might be inserted into the host chromosome or form an extra-chromosomal element.

Plateau

M13B EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 2 (draft); 13 March 2025* -- 2.4 Assessment of Similarity

A plateau is defined by three successive time points differing by less than 5% in mean absolute dissolution.

Platform analytical procedure

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

An analytical procedure that is suitable to test quality attributes of different products without significant change to its operational conditions, system suitability and reporting structure. This type of analytical procedure can be used to analyse molecules that are sufficiently alike with respect to the attributes that the platform analytical procedure is intended to measure. (ICH Q2) PRECISION 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(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

An analytical procedure that is suitable to test quality attributes of different products without significant change to its operational conditions, system suitability and reporting structure. This type of analytical procedure can be used to analyse molecules that are sufficiently alike with respect to the attributes that the platform analytical procedure is intended to measure. (ICH Q2)

Platform Manufacturing

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- 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).

Platform Manufacturing (ICH Q11)

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- 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 mAbs using predefined host cell, cell culture, and purification processes for which considerable experience already exists).

Platform Validation

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Throughout this guideline, this term exclusively refers to validation of the process platform regarding viral clearance. In this context, platform validation is defined as the use of prior knowledge including in-house experience with viral reduction data from other products, to claim a reduction factor for a new similar product, according to current understanding.

Plausibility

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

The believability or truthfulness of data values.
(FDA, United States. Guidance Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision Making for Drug and Biological Products citing Kahn et al. 2016).
{FDA Draft guidance, September 2021. https://www.fda.gov/media/152503/download}

Point mutations

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 16 November 2017 -- 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 -- Step 4 (final); 16 November 2017 -- 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 -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 5 February 1998 -- Glossary

A population that includes the major racial groups within the new region.
{See"New region"}

Portable Document Format (PDF)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A document management format and current de-facto standard for the electronic transfer of documents. Although it began as a proprietary format from the Adobe corporation the current M2 recommendation is to use the public standard PDF described in ISO 320001:2008.
{ISO 32000-1:2008: Document management — Portable document format — Part 1: PDF 1.7. Available at: https://www.iso.org/standard/51502.html}

Positive study, positive control

E14: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs -- Step 4 (final); 12 May 2005 -- 2.2.2

{See "Thorough QT/QTc study"}

Possible causal relationship

E2B(R3) Q&As {version 2.4}: Questions and Answers: Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports -- Step 4 (final); 17 January 2023 -- Question 3.8 (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.
It is therefore not possible to provide a precise answer to this question. It is up to the company and receiver to define causality assessment method and classify the case-reports accordingly.

Post-Approval Change Management Protocol (PACMP)

Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management -- Step 4 (final); 20 November 2019 -- 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.

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

(See ICH Q12)

Post-approval CMC commitment

Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 11 June 2009 -- 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 -- Step 4 (final); 10 March 1999 -- 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 impurities

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 5.1

Potential impurities in the drug substance can include starting materials, reagents and intermediates in the route of synthesis from the starting material to the drug substance.

Potential Impurity

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 17 August 2010 -- 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.

Pragmatic elements in clinical trials

E6(R3) Annex 2 Subgroup: Guideline for Good Clinical Practice (GCP). Annex 2. -- Step 2 (draft); 6 November 2024* -- 1. Introduction

Pragmatic elements in clinical trials are those that integrate aspects of clinical practice into the design and conduct of the trial (e.g., simplified protocols with streamlined data collection).

Precipitant

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

A drug that can induce or inhibit an enzyme or a transporter.
{Note, from Section 1.4}: Note that historically, some regions have used the term “victim” instead of “object” and the term “perpetrator” instead of “precipitant.”

Precision

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 12 June 2011 -- 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): Questions and Answers (R3). ICH E14 Guideline: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs -- Step 4 (final); 10 December 2015 -- Question 4.2

{Baseline} taken shortly prior to dosing

E14/S7B: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 4.2

{Baseline} taken shortly prior to dosing

Preferred and Included Terms

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- 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): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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, 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 -- Step 4 (final); 4 June 2008 -- 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

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

A batch of a drug substance or drug product used in a primary stability study.

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 Data Collection

E6(R3) Annex 2 Subgroup: Guideline for Good Clinical Practice (GCP). Annex 2. -- Step 2 (draft); 6 November 2024* -- 1. Introduction

Data generated specifically for the trial

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Data collected specifically for the present study.
(Adapted from ICH E8)

Primary pack

Q1B: Stability Testing: Photostability Testing of New Drug Substances and Products -- Step 4 (final); 6 November 1996 -- Glossary

{See "Immediate (primary) pack"}

Primary pharmacodynamic studies

S7A: Safety Pharmacology Studies for Human Pharmaceuticals -- Step 4 (final); 8 November 2000 -- 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): The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Safety -- Step 4 (final); 20 December 2002 -- 2.6.2.2

See ICH Guideline S7, Safety Pharmacology Studies for Human Pharmaceuticals, Note 2. p. 8, for definitions

Primary Source

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.4

A primary source(s) is a person who provides facts about a case. Primary sources, often referred to as "reporters", include healthcare professionals and consumers who provide facts about a case to the MAH or regulatory authority. Primary sources should be distinguished from senders who gather information on a case from primary sources and transmit it (e.g., MAH to regulatory authority). Several sources, such as healthcare professionals and/or consumers, may provide information on the same case. The 'primary source for regulatory purposes is the person who first provided facts on the case (see ICH E2B). In the case of a literature article, the author(s) is/are a primary source.
{MAH=Marketing authorisation holder}

Primary Stability Studies

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Stability studies conducted under the accelerated and long term (and, where applicable, intermediate) storage conditions undertaken on primary stability batches to establish a re- test period or a shelf life. Where appropriate, the primary stability studies may be conducted on non- production scale batches.

Principal Stratification

E9(R1): Addendum: Statistical Principles for Clinical Trials -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 20 November 2019 -- Glossary

Change to an approved established condition that requires regulatory review and approval prior to implementation

Prior Knowledge

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Prior knowledge refers to existing knowledge and includes internal knowledge (e.g., development and manufacturing experience), external knowledge (e.g., scientific and technical publications, including vendors' data, literature and peer-reviewed publications), or the application of established scientific principles (e.g., chemistry, physics and engineering principles).

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Prior knowledge refers to existing knowledge and includes internal knowledge (e.g., development and manufacturing experience), external knowledge (e.g., scientific and technical publications, including vendors' data, literature, and peer-reviewed publications), or the application of established scientific principles (e.g., chemistry, physics, and engineering principles).

Probe substrate

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

A drug used in in vitro studies that measure individuals enzyme inhibition or induction properties of an investigational drug. The probe substrate should be selective, or the formation of a specific metabolite should be selective for the evaluated enzyme.
{See also 'Substrate'}

Procedure

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 1 August 2009 -- 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(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 10 November 2000 -- Glossary

See In-Process Control.

Process Dynamics

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- Glossary

The response of a manufacturing process to changing inputs or conditions or transient events.

Process Evaluation Studies of Viral Clearance

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- 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) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 1 August 2009 -- Glossary (Part I)

Ability of a process to tolerate variability of materials and changes of the process and equipment without negative impact on quality.

Process Robustness of Viral Clearance

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

The term robustness is used to describe one or both of the different characteristics. One characteristic is the ability of a process or process step to tolerate variability of materials and changes of the process without negative effect on clearing a virus. The other characteristic is the ability to clear a wide range of specific and non-specific “model” viruses.

Processed Sample

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 10 March 1999 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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 -- Step 4 (final); 18 November 2004 -- 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 complaints {in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 9.1.3 Definitions of Product Complaints

Trial Intervention Complaint: Any concern about the safety and/or quality of any trial-related interventions.

Medical Device Product Complaint: Any concern about the safety, quality, and/or performance of a trial-related drug-device combination.

Product Intermediate

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

A material that is produced as part of the drug product manufacturing process after the defined drug substance(s) and subject to further processing before the finished dosage form.

Note 1: Generally, a product intermediate will have established specifications to determine the successful completion of its manufacture before the continuation of the drug product manufacturing process.

Note 2: This includes materials that may be held for an extended period of time under controlled and justified conditions or tested against the established specification immediately prior to further processing.

Note 3: A product intermediate may be produced by the final drug product manufacturer or manufactured or sourced via an independent manufacturing process by a different manufacturer

Note 4: A product intermediate may not contain the drug substance such as excipient mixtures, granulated excipients, tablet core without drug substance, placebo intermediates.

{Reference} ICH M4Q(R2). Adapted from ICH Q5C/ Pharmaceutical intermediate

Product Lifecycle

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- Glossary

All phases in the life of the product from the initial development through marketing until the product's discontinuation. (ICH Q9)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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 -- Step 4 (final); 20 November 2019 -- 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 lifecycle stability studies

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Stability studies conducted under the accelerated, intermediate, or long-term storage conditions (as applicable) to support product lifecycle changes by assessing whether the change has an impact on any stability related quality attributes of the commercial drug substance or product under the labelled storage, handling and use conditions.

Product Quality Review (PQR)

Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management -- Step 4 (final); 20 November 2019 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 10 November 2000 -- 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

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

A batch of a drug substance or drug product manufactured at production scale using production equipment and process in the commercial production site as specified in the regulatory submission.

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Cell substrate used to manufacture product.

Production Virus

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

A production virus is a process related virus and may include a helper virus or a viral vector for protein expression.
{See also 'Helper Virus' and 'Viral Vector for Protein Expression'}

Product-Related Impurities

Q6B: Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products -- Step 4 (final); 10 March 1999 -- 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 -- Step 4 (final); 10 March 1999 -- 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.

Products

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 1.2

This guideline applies to analytical procedures used for release and stability testing of commercial drug substances and products, hereafter referred to as ‘products’

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 1.2
This guideline applies to analytical procedures used for release and stability testing of commercial drug substances and products, hereafter referred to as 'products'.

Profile

S3A: Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies -- Step 4 (final); 27 October 1994 -- 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).

Proprietary Name(s)

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page
A commercial name granted by an authority for use in marketing/registering a product.

Protocol

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary
A document that describes the objective(s), design, methodology, statistical considerations and organisation 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.

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

A document that describes the objective(s), design, methodology, statistical considerations, and organisation of a study. The protocol usually also gives the background and rationale for the study, but these could be provided in other protocol referenced documents. Throughout ICH E6, Good Clinical Practice, the term protocol refers to protocol and protocol amendments.

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions
A set of rules to which all IT companies and software products have to adhere; the language spoken between computers to help them exchange information.

Protocol Amendment

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary
A documented description of a change(s) to a protocol.

Protocol deviation

E3 Q&As (R1): Questions & Answers: Structure and Content of Clinical Study Reports -- Step 4 (final); 6 July 2012 -- Question 7
A protocol deviation is any change, divergence, or departure from the study design or procedures defined in the protocol.
{See also 'Important protocol deviations'}

Prototyping

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The creation of a model and the simulation of all aspects of a product.

Proven Acceptable Range

Q8(R2): Pharmaceutical Development -- Step 4 (final); 1 August 2009 -- 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 -- Step 4 (final); 1 November 2023 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

{See “Hook Effect”}

Purge factor

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- 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.

Purified Bulk

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

The term purified bulk refers to material at the end of the purification process. While in most cases this represents drug substance, the purified material without excipients may be used instead in order to avoid interference with testing assays.

PXR

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

pregnane X receptor

Q

Q -(Q)SAR and SAR

M7(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- Glossary

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 letter "Q" before the term "(Q)SAR and SAR" was added for sorting purposes.}

Q4B Outcome

Q4B(R1): Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions -- Final version; 5 June 2024 -- 3. Glossary

Produced by the Q4B evaluation; 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.

Q4B: Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions -- Step 4 (final); 1 November 2007 -- 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: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 5.1

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 -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 2 June 2006 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 25 October 2006 -- Glossary

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

Q3B(R2): Impurities in New Drug Products -- Step 4 (final); 2 June 2006 -- Glossary

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

Quality

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

The suitability of either a drug substance or a drug product for its intended use. This term includes such attributes as identity, strength, and purity. The degree to which a set of inherent properties of a product, system or process fulfils requirements.
ICH Q6A //ICH Q9

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 26 April 2022 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 1 August 2009 -- Part I, 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 (from ICH Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances).

Q8(R2): Pharmaceutical Development -- Step 4 (final); 1 August 2009 -- Part II, Glossary

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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- 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 GCP and the applicable regulatory requirement(s).

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

All those planned and systematic actions that are established to ensure that the study is performed and the data are generated, documented (recorded), and reported to an appropriate quality standard and applicable regulatory requirements.
(Adapted from E6(R2) Good Clinical Practice (GCP) - Step 4 (final); 9 November 2016 – Glossary)

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 18 November 2004 -- 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 -- Step 4 (final); 1 August 2009 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

The operational techniques and activities undertaken to verify that the requirements for quality of the trial-related activities have been fulfilled.

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the study-related activities have been fulfilled.
(Adapted from E6(R2) Good Clinical Practice (GCP) -- Step 4 (final); 9 November 2016 – Glossary)

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- Glossary

Checking or testing that specifications are met.

Quality Control Sample (QC)

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 4 June 2008 -- Glossary

Document specifying the quality management system of an organisation. (ISO 9000:2005)

Quality Objectives

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- Glossary

A means to translate the quality policy and strategies into measurable activities. (ICH Q10)

Quality Planning

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 26 April 2022 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 26 April 2022 -- Glossary

The sum of all aspects of a system that implements quality policy and ensures that quality objectives are met. (ICH Q10)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 1 August 2009 -- 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 -- Step 4 (final); 10 November 2000 -- 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 (QL)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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 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)

Quantitative Bias Analysis

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Quantitative bias analysis is an overarching term applied to methods that estimate quantitatively the direction, magnitude, and uncertainty associated with systematic errors that influence measures of associations.
(Lash TL, Fox MP, Cooney D, Lu Y, Forshee RA. Quantitative Bias Analysis in Regulatory Settings. Am J Public Health. 2016;106(7):1227-30.) {https://doi.org/10.2105/ajph.2016.303199}

Quarantine

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- Glossary

The status of materials isolated physically or by other effective means pending a decision on their subsequent approval or rejection.

Question of Interest

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- 2.1. Key Assessment Elements, and Appendix 3: Glossary

The question that MIDD is intended to answer.
{See also "Model-Informed Drug Development (MIDD)"}

R

Racemate

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

A composite (solid, liquid, gaseous, or in solution) of equimolar quantities of two enantiomeric species. It is devoid of optical activity.

Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances -- Step 4 (final); 6 October 1999 -- Glossary

A composite (solid, liquid, gaseous, or in solution) of equimolar quantities of two enantiomeric species. It is devoid of optical activity.

Radiation {intervention}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

Use of targeted or whole body radiation to treat a disease.
{See also: 'Behavioral {intervention in a clinical trial}', 'Biologic', 'Vaccine', 'Combination Product', 'Device', 'Dietary Supplement', 'Drug', 'Genetic {intervention}', 'Surgery', 'Non-Surgical Procedure', 'Diagnostic Test'}

Randomisation

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

The process of deliberately including an element of chance when assigning participants to groups that receive different treatments in order to reduce bias.

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

The process of assigning trial participants to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.
{See also: 'Stratification', 'Stratified Randomisation'}

Range

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

The range of an analytical procedure is the interval between the lowest and the highest 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 -- Step 4 (final); 6 October 1999 -- 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.

Rapporteur

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

The Rapporteur is the primary responsible person for a given ICH project or topic. Each Expert Working Group (EWG) and Implementation Working Group (IWG) has a Rapporteur (or occasionally two co-Rapporteurs).

Raw Material

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

A general term used to denote reagents, solvents and processing aids intended for use in the production of substance intermediate(s) or drug substance(s) and not being the defined starting material(s).
Adapted from ICH Q7

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 13 November 2013 -- Glossary

Reactive Oxygen Species, including superoxide anion and singlet oxygen.

Reagent

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 1 August 2009 -- 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) -- Step 4 (final); 1 May 2012 -- 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 -- Step 4 (final); 1 November 2023 -- 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)

Real-World Data (RWD)

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources. Examples of RWD include data derived from electronic health records (EHRs); medical claims and billing data; data from product and disease registries; patient-generated data, including from mobile devices and wearables; and data gathered from other sources that can inform on health status (e.g., genetic and other biomolecular phenotyping data collected in specific health systems).
(Adapted from
FDA, United States. Guidance Real-World Data: Assessing Registries To Support Regulatory Decision-Making for Drug and Biological Products DECEMBER 2023
{https://www.fda.gov/media/154449/download} and
FDA, United States. Draft Guidance Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision Making for Drug and Biological Products) {September 2021. https://www.fda.gov/media/152503/download}

Real-world data (RWD) incorporated in clinical trials

E6(R3) Annex 2 Subgroup: Guideline for Good Clinical Practice (GCP). Annex 2. -- Step 2 (draft); 6 November 2024* -- 1. Introduction

RWD incorporated in clinical trials include the use of data relating to patient health status collected from a variety of sources outside of clinical trials (e.g., electronic health records (EHRs), registries, claims data).

Real-World Evidence

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

The clinical evidence about the usage and potential benefits or risks of a medicinal product derived from analysis of real-world data (RWD).
(FDA, United States. Guidance Real-World Data: Assessing Registries To Support Regulatory Decision-Making for Drug and Biological Products DECEMBER 2023)
{https://www.fda.gov/media/154449/download}

Reanalysis

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 27 October 1994 -- 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 -- Step 4 (final); 5 February 2001 -- Glossary
The intended recipient of the transmission.

Recombination

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- Glossary
Breakage and balanced or unbalanced rejoining of DNA.

Recovery

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 analytical procedure

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- 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 Information Model (RIM)

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- Glossary of Terms

The HL7 information model from which all other information models, e.g. RMIMS, and messages are derived.

Reference instance

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A version of an xml message designed to provide a reference to how a message should be constructed. A reference instance may not actually be valid since it may contain multiple examples of message components that are actually mutually exclusive. It also may contain data that is explanatory (such as ICH IG element numbers) for understanding the structure of the message but not actually valid content per the schema.)
{IG: Implementation Guide; XML: Extensible markup language; see also 'XML Schema'}

Reference material

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

A suitably characterised material, sufficiently homogeneous and stable with regard to one or more defined attributes, which has been established to be fit for the intended purpose. Reference materials may include national/international reference standards, pharmacopoeial reference standards, or in-house primary/secondary reference materials. (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

A suitably characterised material, sufficiently homogeneous and stable with regard to one or more defined attributes, which has been established to be fit for the intended purpose. Reference materials may include national/international reference standards, pharmacopoeial reference standards, or in-house primary/secondary reference materials. (ICH Q2)

Reference Safety Information (RSI)

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Contains a cumulative list of ADRs that are expected for the investigational product being administered to participants in a clinical trial. The RSI is included in the Investigator's Brochure or alternative documents according to applicable regulatory requirements. Refer to ICH E2F Development Safety Update Report for more information about RSI.

Reference sample

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

A well-characterised substance of known purity and identity used to prepare calibration and quality control samples.

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Primary: 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.
Secondary: 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, Primary RS) ICH Q7/ Reference Standard/ In-house Primary Reference Material/ Reference standards and-or material/ Specified substance
(Reference, Secondary RS) ICH Q7/ Reference Standard/ In-house Working Reference Material/ Secondary Reference Standard Specified Substance

Reference Standard, Primary

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 10 March 1999 -- Glossary

Refer to international or national standards.

Refined Message Information Model (RMIM)

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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 -- Step 4 (final); 16 November 2017 -- Glossary

A geographical region, country or regulatory region

Regional Pharmacovigilance Centre

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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.

Registration Authority

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

From HL7: Each Object Identifier (OID) is created by a Registration Authority. Each of these authorities may, in turn, delegate assignment of new OIDs under it to other registration authorities that work under its auspices, and so on down the line. Eventually, one of these authorities assigns a unique (to it) number that corresponds to a leaf node on the tree. The leaf may represent a registration authority (in which case the OID identifies the authority), or an instance of an object. A registration authority owns the namespace consisting of its sub-tree. ICH M2 ESTRI is a Registration Authority under the arc of HL7 with responsibility to assign its own OIDs.
{HL7: Health Level 7, see separate entry; see also 'Object Identifier (OID)'}

Registry

E2E: Pharmacovigilance Planning -- Step 4 (final); 18 November 2004 -- 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 -- Step 4 (final); 17 August 2010 -- 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

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A registry is an organized system that collects prespecified uniform data from a population defined by a specific disease, condition, or exposure.
(Adapted from:
FDA Real-World Data: Assessing Registries To Support Regulatory DecisionMaking for Drug and Biological Products DECEMBER 2023 {https://www.fda.gov/media/154449/download} and
EMA Guideline on registry-based studies 24 September 2020)
{https://www.ema.europa.eu/en/guideline-registry-based-studies-scientific-guideline}

Regulatory Agency or Regulatory Authorities

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Bodies having the power to regulate, including those that review submitted protocols and clinical data and those that conduct inspections. These bodies are sometimes referred to as competent authorities.

Regulatory Region

E17: General principles for planning and design of Multi-Regional Clinical Trials -- Step 4 (final); 16 November 2017 -- Glossary

A region comprised of countries for which a common set of regulatory requirements applies for drug approval (e.g., EU).

Reintegration

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 9 November 2011 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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.

Relevance

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 5.2

For the purposes of this guidance, the term relevance includes the availability of key data elements (patient characteristics, exposures, outcomes) and a sufficient number of representative patients for the study (target population)

Relevance {of real-world data}

E6(R3) Annex 2 Subgroup: Guideline for Good Clinical Practice (GCP). Annex 2. -- Step 2 (draft); 6 November 2024* -- 3.5.1 Real-World Data Considerations

The term relevance includes the availability of key data elements (e.g., exposure, outcomes, covariates) to answer the specific trial question with the specific method.
{See also "Fitness for purpose of real-world data (RWD)" and "Reliability {of real-world data}"

Relevant Genotypic and Phenotypic Markers

Q5B: Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products -- Step 4 (final); 30 November 1995 -- 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(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Virus used in the process evaluation studies that 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'}

Reliability

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 5.2

For the purposes of this guidance, […] the term reliability includes data accuracy, completeness, provenance, and traceability.
{See also 'Data accuracy', 'Data completeness', 'Data provenance', 'Data traceability'}

Reliability {of real-world data}

E6(R3) Annex 2 Subgroup: Guideline for Good Clinical Practice (GCP). Annex 2. -- Step 2 (draft); 6 November 2024* -- 3.5.1 Real-World Data Considerations

The term reliability includes accuracy, completeness and traceability.
{See also "Fitness for purpose of real-world data (RWD)" and "Relevance {of real-world data}"

Repeat Analysis

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

{See “Reanalysis”}

Repeatability

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

One of several determinations or measurements of a sample, calibration standards or quality control sample (QC).

Replication Competent Virus (RCV)

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Recombination of the viral vector with trans-complementing viral sequences generating a replication competent virus.
{See also 'Virus'}

Reportable range

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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 acceptance criterion. (ICH Q2)
See also: 'Range', 'Working range'

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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 acceptance criterion. (ICH Q2)
See also: 'Range', 'Working range'

Reportable result

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 5 February 2001 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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)]

Reporter Identifiability

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 6.1

{in Individual Case Safety Reports (ICSR)} The term identifiable in this context refers to the verification of the existence of a patient and a reporter (i.e., a primary source; see Section 2.4, Primary Source). (...) Examples of characteristics that qualify a reporter as identifiable include but are not limited to: name, initials, or address (e.g., reporter's organisation, department, street, city, state or province, postcode, country, email, phone number), qualification (e.g., healthcare professional, lawyer, consumer or other non-healthcare professional). For cases where the reporter wishes to remain anonymous, the ICSR should still be reported, as long as the existence of an individual as the reporter is known. (...)
In relation to cases from digital platforms, the identifiability of the reporter/patient refers to the existence of a real person (...). The presence of a digital platform username or identifier (i.e., "handle") in the absence of qualifying identifiers is insufficient to confirm that there is a real patient and/or reporter.
{See also: 'Patient Identifiability'}

Reporting

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.1.6

{Of AE(s)/ADR(s) in ICSR} Throughout this guideline, the term "reporting", unless specifically indicated otherwise, refers to MAHs submitting ICSRs to a regulatory authority (i.e., regulatory reporting), as opposed to MAHs receiving or collecting information about a case from a primary source. For the purpose of reporting, requirements in some regions refer only to ADRs, whereas other regions refer to AEs. For simplicity, the term AE(s)/ADR(s) is used throughout this guideline. (…)The term "AE(s)/ADR(s)" includes AE(s)/ADR(s) or other observations, unless specifically stated otherwise.
{ADR=Adverse drug reaction; AE=Adverse event; ICSR=Individual case safety report; MAH=Marketing authorisation holder}

Reporting Threshold

Q3A(R2): Impurities in New Drug Substances -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 2 June 2006 -- Glossary

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

Reprocessing

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

The extent to which consistent results are obtained when an experiment is repeated.

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

Reproducibility expresses the precision between laboratories (e.g., inter-laboratory studies, usually applied to standardisation of methodology). (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

Reproducibility expresses the precision between laboratories (e.g., inter-laboratory studies, usually applied to standardisation of methodology). (ICH Q2)

Requirements

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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.

Rescue Medicine {in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

Medicinal products identified in the protocol as those that may be administered to participants when the efficacy of the investigational medicinal product (IMP) is not satisfactory, the effect of the IMP is too great and is likely to cause a hazard to the patient, or to manage an emergency situation.

Rescue Therapy {in clinical trials}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6.9.2 Rescue Therapy

Any rescue medications, treatments, and/or procedures identified in the protocol as those that may be administered to participants when the efficacy of the investigational intervention is not satisfactory, its effect is too great and is likely to cause a hazard to the patient, or to manage an emergency situation. {See also 'Rescue Medicine'}

Researcher

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 2 General principles

In this guideline we refer to “researcher” as those responsible for designing and executing the study; this may be a regulatory agency, sponsor, contract research organization, academic group, or others.

Residence Time Distribution (RTD)

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- Glossary

A measure of the range of residence times experienced by material passing through a specific process environment/vessel/unit operation.

Residual solvents

Q3C(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- 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 -- Step 4 (final); 1 November 2023 -- 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) or activity of analyte in the sample by some known mathematical function. (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- 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) or activity of analyte in the sample by some known mathematical function. (ICH Q2)

Response Function

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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.

Retest date

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 10 November 2000 -- Glossary

The date when a material should be re-examined to ensure that it is still suitable for use.

Re-test date

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- 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.

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

The re-test period is a period of time during which the drug substance is expected to remain within its specification and, therefore, can be used in manufacture of a given drug product, provided the drug substance has been stored under the defined conditions. After this period, a batch of drug substance can be re-tested for compliance with its specification and then used immediately for manufacture of drug product. A re-test period is normally applicable to synthetic drug substances and may be applicable to certain well-characterised biological drug substances.

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 1 November 2023 -- Glossary

Demonstration that an analytical procedure is still fit for the 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 -- Step 4 (final); 1 November 2023 -- Glossary

Demonstration that an analytical procedure is still fit for the 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(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 6 October 2021 -- 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 -- Step 4 (final); 26 April 2022 -- Glossary

The combination of the probability of occurrence of harm and the severity of that harm. (ISO/IEC Guide51, ICH Q9)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

The combination of the probability of occurrence of harm and the severity of that harm (ISO/IEC Guide 51:2014).
{Reference: ISO/IEC Guide 51:2014 - Safety Aspects - Guideline for their inclusion in standards.}

Risk Acceptance

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- Glossary

The decision to accept risk. (ISO Guide 73)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

An informed decision to take a particular risk. (ISO Guide 73:2009).
{Reference: ISO Guide 73:2009. Risk management — Vocabulary}

Risk Analysis

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- Glossary

The estimation of the risk associated with the identified hazards. (ICH Q9)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

The estimation of the risk associated with the identified hazards.

Risk Assessment

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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 -- Step 4 (final); 26 April 2022 -- Glossary

Actions implementing risk management decisions. (ISO Guide 73)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

Actions implementing risk management decisions (ISO Guide 73:2009).
{Reference: ISO Guide 73:2009. Risk management — Vocabulary}

Risk Evaluation

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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 -- Step 4 (final); 26 April 2022 -- Glossary

The systematic use of information to identify potential sources of harm (hazards) referring to the risk question or problem description. (ICH Q9)

Risk Management

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- Glossary

The systematic application of quality management policies, procedures, and practices to the tasks of assessing, controlling, communicating, and reviewing risk. (ICH Q9)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- 13.1

Risk reduction is defined in ICH Q9 as actions taken to lessen the probability of occurrence of harm and the severity of that harm.

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions
Actions taken to lessen the probability of occurrence of harm and the severity of that harm.

Risk Review

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions
An approach to, or a process of, making decisions that considers knowledge about risks relevant to the decision and whether risks are at an acceptable level.

Robustness

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary
The robustness of an analytical procedure is a measure of its capacity to meet the expected performance criteria during normal use. Robustness is tested by deliberate variations of analytical procedure parameters. (ICH Q14)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary
The robustness of an analytical procedure is a measure of its capacity to meet the expected performance criteria during normal use. Robustness is tested by deliberate variations of analytical procedure parameters. (ICH Q14)

Room temperature

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- 7.2 and 13.2.5

{From Section 7.2–Considerations for Products Intended to be Stored at Room Temperature:} The recommended storage conditions that are applicable to each climatic zone are outlined in the table below {i.e. Table 3: Storage Condition Recommendations for Each Climatic Zone.}
{From Section 13.2.5–Extrapolation for Synthetic Chemical Entities:} The term “room temperature” refers to the general customary environment and should not be inferred to be the storage statement for labelling (refer to Section 14 –Labelling).

Q1E: Evaluation of Stability Data -- Step 4 (final); 6 February 2003 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary
{See “Analytical Run”}

Run Summary Table

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- Glossary

The time interval used to produce a quantity of output material.

S

Safety

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 26 April 2022 -- 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 -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 26 April 2022 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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): The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Safety -- Step 4 (final); 20 December 2002 -- 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 -- Step 4 (final); 8 November 2000 -- 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 -- Step 4 (final); 1 November 2023 -- 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. (ICH Q14)

Satellite groups

S3A: Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies -- Step 4 (final); 27 October 1994 -- 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 data use

E6(R3) Annex 2 Subgroup: Guideline for Good Clinical Practice (GCP). Annex 2. -- Step 2 (draft); 6 November 2024* -- 1. Introduction

Data obtained from sources external to the trial that are collected for other purposes

Secondary pack

Q1B: Stability Testing: Photostability Testing of New Drug Substances and Products -- Step 4 (final); 6 November 1996 -- Glossary

{See "Marketing pack"}

Secondary pharmacodynamic studies

S7A: Safety Pharmacology Studies for Human Pharmaceuticals -- Step 4 (final); 8 November 2000 -- 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).

Secondary Use of Data

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Use of existing data for a different purpose than the one for which they were originally collected. (EMA Guideline on registry-based studies) {https://www.ema.europa.eu/en/guideline-registry-based-studies-scientific-guideline}

Section

M4 Q&As (R3): Questions & Answers: Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use -- Step 4 (final); 10 June 2004 -- Question 15

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'}

Selective safety data collection

E19: A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-approval or Post-Approval Clinical Trials -- Step 4 (final); 27 September 2022 -- 1.1; 2.1

{1.1} Selective safety data collection refers to the reduced collection of certain types of data in a clinical trial after thorough consideration of factors that would justify such an approach.
{2.1} The selective safety data collection approach described in this Guideline refers to the recording of certain data (see Section 2.5) by investigators in case report forms, as well as to their reporting to sponsors for subsequent evaluation and submission to regulatory authorities.
Importantly, this approach does not affect the responsibilities of investigators, as health care professionals, to monitor trial participants and ensure they are treated according to prevailing standards of care. Specifically, selective safety data collection does not affect the monitoring and clinical care of individual trial participants or documentation of their adverse events in medical records. Moreover, selective safety data collection does not obviate other reporting obligations of health care professionals, such as safety reporting in accordance with local/regional requirements.

Selectivity

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Containers that allow the passage of solvent or gas, while preventing solute loss. Examples of semi-permeable containers include plastic bags and semi-rigid, low-density polyethylene (LDPE) pouches for large volume parenteral (LVPs), and LDPE ampoules, bottles and vials.

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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.

Semi-synthetic drug substance

M7(R2) Q&As: Questions and Answers: Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 24 May 2022 -- Question 2.1

The following compounds used in the manufacturing process of semi-synthetic drug substances and drug products should be considered within the scope of the application of ICH M7:
• chemically-synthesized intermediates and actual impurities therein
• reagents
If a semi-synthetic drug substance, as defined in ICH Q11, is manufactured using steps that could introduce mutagenic impurities or degradation products (e.g., post-modification of a fermentation product or late-stage introduction of a linker) a risk assessment is warranted.

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- 5.1.2

For purposes of this guideline, a semi-synthetic drug substance is one in which the structural constituents have been introduced by a combination of chemical synthesis and elements of biological origin (e.g., obtained from fermentation or by extraction from botanical material).

Sender

E2B(R2): Maintenance of the ICH guideline on clinical safety data management: Data elements for transmission of individual case safety reports -- Step 4 (final); 5 February 2001 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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 -- Step 4 (final); 4 June 2008 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 20 November 2019 -- 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.

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 10.4.1.4 Sensitivity Analysis

A [description of the] series of analyses conducted to explore the robustness of inferences from the main estimator to deviations from its underlying modeling assumptions and limitations in the data. {The words in square brackets {} are specific to the context of the draft M11 Technical Specification/Template.}

Sequential {intervention model in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

Groups of participants are assigned to receive interventions based on prior milestones being reached in the study.
{See also: 'Cross-over', 'Factorial', 'Parallel Group', 'Single Group'}

Serious Adverse Event

E19: A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-approval or Post-Approval Clinical Trials -- Step 4 (final); 27 September 2022 -- Glossary

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

(see ICH E2A and ICH E6).

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 9.2 Timing and Procedures for Collection and Reporting {of Adverse Events}

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.

Serious Adverse event (AE)/Adverse Drug Reaction (ADR)

E2D: Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting -- Step 4 (final); 12 November 2003 -- 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 (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)
- 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 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 -- Step 4 (final); 27 October 1994 -- 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)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Any unfavourable medical occurrence that is considered serious at any dose if it:
• 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.
(see ICH E2A).
An important medical event that may not be immediately life-threatening or result in death or hospitalisation, that may jeopardise the participant or that may require intervention to prevent serious outcomes (see ICH E2A and E19) should generally be considered as serious.

Serious Adverse Reaction or Serious Adverse Drug Reaction

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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)]

Serious AE/ADR

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.1.3

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 (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);
• 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 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 which may occur following the use of a medicinal product 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 dependency or substance use disorder.

Service Provider

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A person or organisation (commercial, academic or other) providing a service used by either the sponsor or the investigator to fulfil trial-related activities.

Severe versus Serious

E2A: Clinical Safety Data Management: Definitions and Standards for Expedited Reporting -- Step 4 (final); 27 October 1994 -- 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 -- Step 4 (final); 26 April 2022 -- Glossary

A measure of the possible consequences of a hazard. (ICH Q9)

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

A measure of the possible consequences of a hazard.

Sham Procedure

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A type of negative control in which a procedure is performed that mimics the procedure under study but does not include investigational processes or components.
{See also: 'Active Comparator', 'Dose Response {Control Type}', 'Placebo', 'Different Dose or Regimen {Control Type}', 'External {Control Type'}'}

Shedding

S12: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- 1.3

The release of a GT product outside the body via excreta and secreta (faeces, urine, saliva, nasopharyngeal fluids, etc.), or through the skin (pustules, sores, wounds) is termed “shedding”.

Shelf life

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

The time period during which a drug substance or drug product is expected to remain within the approved shelf life specification, provided that it is stored under the conditions defined on the label.
{See also "Date of production", as defined in Section 13.1.2 Start of Shelf Life for Synthetic Chemical Entity Drug Products}

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 17 August 2010 -- 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

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

A unique mark, symbol or entry executed, adopted or authorised by an individual, in accordance with applicable regulatory requirements and/or practice to show expression of will and allow authentication of the signatory (i.e., establish a high degree of certainty that a record was signed by the claimed signatory). A signature may be physical or electronic.

Signature (signed)

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- Glossary

See definition for signed

Signed (signature)

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 6 February 2003 -- 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.
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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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 Change for Synthetics

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

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 (e.g., for antibiotics); (2) Any degradation product exceeding its acceptance criterion; (3) Failure to meet the acceptance criteria for appearance, physical attributes and functionality test (e.g., colour, phase separation, re-suspendability, 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; (5) Failure to meet the specification for dissolution testing; or, (6) A 5% loss in water from its initial value for products stored in semi-permeable containers.

Significant increase in clinical dose {that can warrant a reevaluation of the mutagenic impurity limits}

M7(R2) Q&As: Questions and Answers: Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 24 May 2022 -- Question 4.1

Any increase in dose of the active pharmaceutical ingredient (API) that would increase any mutagenic impurity to levels above the acceptable limits is considered significant (see Tables 2 and 3 and the addendum of ICH M7).

In such cases a re-evaluation of the mutagenic impurity limits is recommended.

Significant structural fragment

Q11 Q&As: Questions & Answers: Selection and Justification of Starting Materials for the Manufacture of Drug Substances -- Step 4 (final); 23 August 2017 -- Question 5.5

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 Blind

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A study in which one party, either the participant or study personnel, does not know which intervention is administered to the participant.

{See also: 'Double Blind', 'Observer Blind', 'Open Label'}

Single Cell Gel Electrophoresis assay

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 1 November 2007 -- 2.3.2.1

Single coded data and samples are usually labelled with a single specific code and do not carry any personal identifiers.

Single Group {intervention model in a clinical trial}

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

All trial participants are assigned to a single treatment group for the duration of the study.
{See also: 'Cross-over', 'Factorial', 'Parallel Group', ' Sequential'}

Single-Centre

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

A clinical study that is conducted at a single study site.
{See also: 'Multicentre'}

Soft Sensors

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- 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 Report

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 3.2

{Type of ICSR} Solicited reports are those derived from ODCSs (see Section 2.8, ODCS). For the purposes of reporting, solicited ICSRs should be classified as “report from study” in ICH E2B format and should have a causality assessment (see Section 5.1.1, AEs/ADRs).
{ADR=Adverse drug reaction; AE=Adverse event; ICSR=Individual Case Safety Reports MAH=Marketing authorisation holder; ODCS=Organised Data Collection System}

Solicited reports

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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 -- Step 4 (final); 12 November 2003 -- 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 -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 10 November 2000 -- 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 Records

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Original documents or data (which includes relevant metadata) or certified copies of the original documents or data, irrespective of the media used. This may include trial participants' medical/health records/notes/charts; data provided/entered by trial participants (e.g., electronic patient-reported outcomes (ePROs)); healthcare professionals' records from pharmacies, laboratories and other facilities involved in the clinical trial; and data from automated instruments, such as wearables and sensors.

Spare Subject

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

A study subject that is included in the drug administration and sample collection regimens of a study but, as per study protocol, whose data will only be included in the PK and statistical analyses if the number of subjects with evaluable data for primary statistical analysis drops below a pre-specified number due to subject dropouts and/or withdrawals (use of spare subjects is not acceptable). {PK=pharmacokinetic}

Special Safety Situations

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 9.4 Special Safety Situations

[A characterization or classification of] those trial specific situations that are associated with the trial intervention(s) and require regulatory reporting, but that do not qualify as an adverse event or serious adverse event for the given trial.
{The words in square brackets {} are specific to the context of the draft M11 Technical Specification/Template.}

Speciation

Q3D(R2): Guideline for Elemental Impurities -- Step 4 (final); 26 April 2022 -- 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(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 6 October 1999 -- 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

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- 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.
ICH Q6A/B

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- Glossary

See Q6A and Q6B.

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 10 March 1999 -- 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 -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 6 February 2003 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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).

Specificity/selectivity

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

Specificity and selectivity are both terms to describe the extent to which other substances interfere with the determination of an analyte according to a given analytical procedure. Specificity is typically used to describe the ultimate state, measuring unequivocally a desired analyte. Selectivity is a relative term to describe the extent to which 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 -- Step 4 (final); 1 November 2023 -- Glossary

Specificity and selectivity are both terms to describe the extent to which other substances interfere with the determination of an analyte according to a given analytical procedure. Specificity is typically used to describe the ultimate state, measuring unequivocally a desired analyte. Selectivity is a relative term to describe the extent to which particular analytes in mixtures or matrices can be measured without interferences from other components with similar behaviour. (ICH Q2)

Specified Degradation Product

Q3B(R2): Impurities in New Drug Products -- Step 4 (final); 2 June 2006 -- 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 -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 6 October 1999 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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 -- Step 4 (final); 17 August 2010 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

An individual, company, institution or organisation that takes responsibility for the initiation, management and arrangement of the financing of a clinical trial. A clinical trial may have one or several sponsors where permitted under regulatory requirements. All sponsors have the responsibilities of a sponsor set out in this guideline. In accordance with applicable regulatory requirements, sponsors may decide in a documented agreement setting out their respective responsibilities. Where the documented agreement does not specify to which sponsor a given responsibility is attributed, that responsibility lies with all sponsors.

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical study.

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

An individual, company, institution, or organisation which takes responsibility for the initiation, management, and/or financing of a clinical trial.

Sponsor Confidentiality Statement

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

A written message within the study protocol that asserts a statement of non-disclosure, such that information contained within the protocol document may only be shared with authorized parties.

Sponsor- investigator

E2F: Development Safety Update Report -- Step 4 (final); 17 August 2010 -- 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(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- 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 participant. The term does not include any person other than an individual (e.g., the term 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

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 3.1

{Type of ICSR} A spontaneous report is a direct communication by an HCP or consumer to an MAH, regulatory authority or other organisation (e.g., World Health Organisation Uppsala Monitoring Center, Regional Pharmacovigilance Center) that describes one or more AEs/ADRs in a patient who was exposed to one or more medicinal products and that was not gathered as part of an ODCS.
In certain situations, public communication about an AE/ADR (e.g., a "Dear Healthcare Professional" communication, litigation, or publication or reporting in the media) results in stimulated reporting (i.e., increased reporting by primary sources regarding the AE/ADR). Stimulated reports should be considered spontaneous reports.
Local or regional requirements may require HCPs to report AEs/ADRs not gathered as part of an ODCS to regulatory authorities; these reports should also be managed as spontaneous reports.
{ADR=Adverse drug reaction; AE=Adverse event; ICSR=Individual Case Safety Report; MAH=Marketing authorisation holder; ODCS=Organised Data Collection System}

Spontaneous report or spontaneous notification

E2C(R2): Periodic Benefit-Risk Evaluation Report -- Step 4 (final); 17 December 2012 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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 -- Step 4 (final); 12 November 2003 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 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 DDI studies

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

A clinical DDI study with the primary objective of determining the presence or absence of a clinical DDI and the magnitude of the DDI.
{DDI = drug-drug interaction}

Standard

E2B(R3) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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.

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A technical specification which addresses a business requirement, has been implemented in viable commercial products, and, to the extent practical, complies with recognized standards organizations such as ISO.
{ISO: International Standards Organization}

Standard Curve

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 calibration Curve.

Standard of Care

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

Treatment that is accepted by medical experts as a proper treatment for a certain type of disease or condition and that is widely used by healthcare professionals. Also called best practice, standard medical care, or standard therapy.
(National Cancer Institute Dictionary) {https://www.cancer.gov/publications/dictionaries/cancer-terms/def/standard-of-care}

Standard Operating Procedure (SOP)

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

Detailed written instructions to achieve uniformity of the performance of a specific function and/or process(es).

Standard Operating Procedures (SOPs)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Detailed, documented instructions to achieve uniformity of the performance of a specific activity.

Standardized Generalized Markup Language (SGML)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations

An ISO standard for describing structured information in a platform independent manner.
{ISO: International Standards Organization}

Standards Development Organisation (SDO)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

An organisation that is specifically created and organised to develop, maintain, define or govern standards (sets of mutually agreed requirements, specifications, guidelines or characteristics). SDOs may be national or international in scope, and may be focused on a specific functional area, industrial sector, or type of activity. SDOs may have defined memberships or may be open to the public. In general SDOs have a specified set of criteria governing what types of standards may be developed or governed, who the required stakeholders are for approval, and what the process for reaching agreement is.

Starting Material

Q11 Q&As: Questions & Answers: Selection and Justification of Starting Materials for the Manufacture of Drug Substances -- Step 4 (final); 23 August 2017 -- Question 5.2

{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 -- Step 4 (final); 25 October 2006 -- 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.

Starting/Source Material

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

A material from which the drug substance is extracted or used in the production of a drug substance and ultimately incorporated as an element into the structure of the drug substance (directly or via one of its substance intermediate).
Note 1: Starting material can be commercially available, produced in-house by the final drug substance manufacturer or externally by one or more different manufacturers under contract or commercial agreement.
Note 2: Starting materials are normally of defined chemical properties and structure.
{Reference} ICH M4Q(R2) //Adapted from ICH Q3A(R2)

State of Control

Q10: Pharmaceutical Quality System -- Step 4 (final); 4 June 2008 -- 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 -- Step 4 (final); 5 February 1998 -- 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.

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 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.
(E9 Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 – Glossary)

Steady State

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- Glossary

A stable condition that does not change over time.

Stock Solution

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

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

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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.

Storyboard

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A particular approach to explaining Use Cases in the context of the definition of requirements. Storyboards stem from old advertising/movie practice of drawing rough pictures of what final piece will look like (after filming or art). In technical implementations a graphic illustration of the steps that make up the Use Case.
{See also 'Use case'}

Stratification

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

Grouping defined by important prognostic factors measured at baseline.
{See also: 'Randomisation', 'Stratified Randomisation'}

Stratified Randomisation

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.1.2 Overall Design

The process of grouping trial participants into strata according to important prognostic factors and then assigning participants within each stratum to different treatment or control groups using an element of chance and in order to reduce bias.
{See also: 'Randomisation', 'Stratification'}

Stress Studies

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Studies undertaken to assess the effect of stress conditions on the drug substance and/or drug product which can be divided into two categories:
1) Studies conducted under stress conditions that are more severe than the accelerated conditions, but not necessarily intended to deliberately degrade the sample, which may be useful in gaining product knowledge and evaluating the effect of excursions outside the label storage conditions.
2) Studies conducted under forced degradation conditions that are intended to deliberately degrade the sample (such as elevated temperature, humidity, pH, oxidation, agitation and light) and may be used to: investigate the potential degradation pathways; gain product knowledge; understand the intrinsic stability of drug substance; and used to develop and confirm stability-indicating nature of the analytical procedure.

Stress testing (drug product)

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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 -- Step 4 (final); 6 February 2003 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- 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(R2): Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk -- Step 4 (final); 3 April 2023 -- Glossary

In the context of this guideline, a chemical grouping or molecular (sub) structure which is associated with mutagenicity.

Studies of lesser quality {carcinogenicity studies}

M7(R2) Addendum: Application of the principles of the ICH M7 guideline to calculation of compound-specific acceptable intakes. Addendum to M7(R2) -- Step 4 (final); 3 April 2023 -- Methods; 1.2 Selection of studies

For the purposes of this Addendum additional criteria were applied when studies were of lesser quality. Studies of lesser quality are defined here as those where one or more of the following scenarios were encountered:

< 50 animals per dose per sex;

< 3 dose levels;

Lack of concurrent controls;

Intermittent dosing (< 5 days per week);

Dosing for less than lifetime.

Studies with index precipitants and index substrates

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

Clinical DDI studies conducted with index precipitants or index substrates that aim to investigate the greatest magnitude of interaction with the investigational drug for the studied pathway and which results usually can be extrapolated to other drug combinations.
{DDI = drug-drug interaction} {See also 'Precipitant'}

Study samples

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

Samples from animals or subjects enrolled in nonclinical or clinical studies.

Style Sheet

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

A style sheet is a file that describes in machine-readable format how to display an XML document.
{XML: Extensible markup language, see also 'XML Schema'}

Subcontracting

Q7 Q&As: Questions and Answers: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 June 2015 -- Question 16.3

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].

Sub-Investigator

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

Any individual member of the clinical trial team designated and under the oversight of the investigator to perform significant trial-related procedures and/or to make important trial- related decisions (e.g., associates, residents, research fellows).

Submission

Q12: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management -- Step 4 (final); 20 November 2019 -- Glossary

Communication to a regulatory authority regarding a change to an established condition that could be prior approval or notification.

Substance

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Matter of defined composition that has discrete existence, whose origin may be biological, mineral or chemical.
{Reference} ISO IDMP {ISO 11615:2017 Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information. https://www.iso.org/standard/70150.html}

Substance Intermediate

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

defined starting material(s) and subject to further processing before the drug substance.
Note 1: Substance intermediates may or may not be isolated.
Note 2: Generally, a substance intermediate will have established specifications or in-process controls to determine the successful completion of its manufacture before the continuation of the drug substance manufacturing process.
Note 3: This includes materials that may be held for an extended period of time under controlled and justified conditions or tested against the established specification immediately prior to further processing
Note 4: A substance intermediate can be produced in-house by the main drug substance manufacturer or manufactured or sourced via a separate manufacturing process or by a different manufacturer
Note 5: In some cases, the active substance might be considered as a substance intermediate of the final drug substance (e.g. diclofenac free base is a substance intermediate of the diclofenac sodium drug substance)
Note 6: For very complex end to end biologic drug substance manufacturing processes or cases where the sub-part of the end-to-end drug substance manufacturing process up to a specific substance intermediate is performed by a different manufacturer, the applicant may segregate the manufacture of specific substance intermediates (e.g. viral vectors, ADC linker etc.) from the main drug substance manufacturing process.
Note 7: The level of quality information expected for a substance intermediate will depend on its complexity and on the potential impact of the quality of this material to the quality of the final drug substance; with higher level risk materials (e.g. viral vectors, ADC linkers, etc.) requiring a level of information close to a drug substance.
Examples: an isolated or non-isolated substance intermediate manufactured as part of the main drug substance manufacturing process, or a chemical or a biological substance manufactured outside of the main drug substance manufacturing process (a linker used in ADC manufacture, a viral vector used in cell and gene therapy manufacture etc.).
Further processing examples: further chemical transformation, further molecular change/modification,

Substrate

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 1.4

Because objects of DDIs are substrates of enzymes and/or transporters, the term “substrate” in this guideline refers to drugs that may be objects of DDIs.
{See also: Object, Precipitant}

Superiority Trial

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 20 November 2019 -- 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.

Supplementary Test Method

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

A test method used to provide additional data to support the conventional testing.

Support

S3A: Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies -- Step 4 (final); 27 October 1994 -- 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

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- 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.

Q1A(R2): Stability Testing of New Drug Substances and Products -- Step 4 (final); 6 February 2003 -- 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.

Supportive stability studies

Q1 EWG: Stability testing of drug substances and drug products -- Step 2 (draft); 11 April 2025* -- Glossary

Ancillary stability studies that are conducted (as applicable) to support the practical use of the product (including label claims) or a re-test period or a shelf life (e.g., photostability, in-use, short-term studies and studies to support excursions or modelling). Data to support short-term storage conditions, where relevant, may be provided as part of the primary stability studies.

Supratherapeutic dose

E14/S7B: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 5.1

Dose that provides exposures (mean Cmax) exceeding the high clinical scenario
{see also 'High clinical exposure' as defined in Q5.1 of this document}

Surgery

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A diagnostic or treatment procedure performed by manual and/or instrumental means, often involving an incision and the removal or replacement of a diseased organ or tissue; of or relating to or involving or used in surgery or requiring or amenable to treatment by surgery.
{See also: 'Behavioral {intervention in a clinical trial}', 'Biologic', 'Vaccine', 'Combination Product', 'Device', 'Dietary Supplement', 'Drug', 'Genetic {intervention}', 'Non-Surgical Procedure', 'Radiation {intervention}', 'Diagnostic Test'}

Surrogate Matrix

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 9 November 2011 -- Glossary

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

Suspected Unexpected Serious Adverse Reaction (SUSAR)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

An adverse reaction that meets three criteria: suspected, unexpected and serious.
• Suspected: There is a reasonable possibility that the drug caused the adverse drug reaction.
• Unexpected: An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure or alternative documents according to applicable regulatory requirements; see RSI).
• Serious: See above for SAE.

Swing

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Calculated as [(C_maxSS – C_minSS) / C_minSS]
{Characters preceded by "_" are in subscript font}

System

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- Glossary

A manufacturing architecture that, in the context of continuous manufacturing (CM), consists of individual pieces of equipment, their connections to one another, monitoring and control systems, and spatial layout.

System Suitability

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 1 November 2023 -- Glossary

System suitability tests are developed and used to verify that the measurement system and the analytical operations associated with the analytical procedure are fit for the intended purpose and increase the detectability of unacceptable performance. (ICH Q14)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

System suitability tests are developed and used to verify that the measurement system and the analytical operations associated with the analytical procedure are fit for the intended purpose and increase the detectability of unacceptable performance. (ICH Q14)

Systemic drugs

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- Glossary

Products administered by a route that is intended to produce systemic exposure.

T

t_1/2

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

elimination half-life

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

The apparent terminal elimination half-life
{Characters preceded by "_" are in subscript font}

t_max

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

time to C_max
{See also ‘C_max’}

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Time to maximum observed concentration
{Characters preceded by "_" are in subscript font}
{See also "C_max"}

Tag Image File Format (TIFF)

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Abbreviations

A CCITT standard for electronically storing images.
{CCITT: Comité Consultatif International Télégraphique et Téléphonique; see separate entry}

Target Trial

M14 EWG: General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines -- Step 2 (draft); 21 May 2024 -- 12 Glossary

A hypothetical randomized trial that would answer the question of interest if it were feasible.
(Adapted from: National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Care Services; Committee on Developing a Protocol to Evaluate the Concomitant Prescribing of Opioids and Benzodiazepine Medications and Veteran Deaths and Suicides. An Approach to Evaluate the Effects of Concomitant Prescribing of Opioids and Benzodiazepines on Veteran Deaths and Suicides. Washington (DC): National Academies Press (US); 2019 Sep 24. 2, Specifying the Target Trial.) {https://nap.nationalacademies.org/catalog/25532/an-approach-to-evaluate-the-effects-of-concomitant-prescribing-of-opioids-and-benzodiazepines-on-veteran-deaths-and-suicides}

Tau

M13A: Bioequivalence for Immediate-Release Solid Oral Dosage Forms -- Step 4 (final); 23 July 2024 -- Glossary

Dosing Interval

TDI

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

time-dependent inhibition

Technical Criteria

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

A summary and rationale of the key criteria for Model Evaluation and model outcomes to establish the acceptability of the model (e.g., using an acceptance standard such as bioequivalence acceptance limits).
{See also "Model Evaluation"}

Teratogenicity

Q3C(R9): Guideline for Residual Solvents -- Step 4 (final); 24 January 2024 -- Glossary

The occurrence of structural malformations in a developing fetus when a substance is administered during pregnancy.

Therapeutic context

M4E(R2): Revision of M4E Guideline on Enhancing the Format and Structure of Benefit-Risk Information in ICH: Efficacy -- Step 4 (final); 15 June 2016 -- 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: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 5.1

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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 12 May 2005 -- 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 -- Step 4 (final); 26 April 2022 -- 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 -- Step 4 (final); 26 April 2022 -- 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): Questions and Answers (R3). ICH E14 Guideline: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs -- Step 4 (final); 10 December 2015 -- Question 4.2

{Baseline} taken at exactly the same time-points on the day prior to the beginning of treatment as on the treatment day

E14/S7B: First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential -- Step 4 (final); 21 February 2022 -- E14 Q&As, Question 4.2

{Baseline} taken at exactly the same time-points on the day prior to the beginning of treatment as on the treatment day

Tissue tropism

S12: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- Glossary

For GT products, the propensity of a given vector to transduce or transfect a distinct group of tissues (or cells).

{GT: gene therapy}

Total Error

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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 -- Step 4 (final); 27 October 1994 -- 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 -- Step 4 (final); 27 October 1994 -- 5., Note 1

Assessment of Systemic Exposure
{See also 'Exposure'}

Traditional approach

Q11: Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities) -- Step 4 (final); 1 May 2012 -- 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. "}

Transformation

M4Q(R2) EWG: The Common Technical Document for the registration of pharmaceuticals for human use: Quality -- Step 2 (draft); 14 May 2025* -- Glossary

Procedure that is carried out in order to convert a finished dosage form that requires such a modification into a pharmaceutical product, i.e. from its manufactured dosage form to its administrable dosage form
Note 1: A transformation is not required when the drug product dosage form is equal to the pharmaceutical product.
Note 2: In certain circumstances, the transformation may be used, alone or in combination with one or more other pharmaceutical dosage form attributes, to describe a medicinal product where a pharmaceutical dosage form term cannot be used, for example as part of an adverse event report in which the precise pharmaceutical dosage form is unknown, but the transformation is known.
Note 3: The transformation should be applied within context of product quality and M4Q (R2) guideline and should not be interpreted in a biological sense, such as genetic cellular alterations or change from normal to malignant cells etc.
Examples: Dilution, dissolution, dispersion, suspension, reconstitution.
{Reference} ICH M4Q(R2). Adapted from ISO IDMP 11615 {ISO 11615:2017 Health informatics — Identification of medicinal products — Data elements and structures for the unique identification and exchange of regulated medicinal product information. https://www.iso.org/standard/70150.html}

Transgene

S12: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- Glossary

Transcriptionally or translationally active genetic material transferred by a vector intended to confer biological activity following expression in cells.

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- Glossary

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

Transient Events

Q13: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- 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 -- Step 4 (final); 5 February 1998 -- 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 -- Step 4 (final); 5 February 1998 -- Glossary

An event that emerges during treatment having been absent pre-treatment, or worsens relative to the pre-treatment state.

Trend

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- Definitions

A statistical term referring to the direction or rate of change of a variable(s).

Trial Acronym

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page

Acronym or abbreviation used publicly to identify the clinical trial.

Trial conduct

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- I. Introduction

The term “trial conduct” in this document includes processes from planning to reporting, including planning, initiating, performing, recording, oversight, evaluation, analysis and reporting activities as appropriate.

Trial intervention

M11 EWG: Clinical electronic Structured Harmonised Protocol (CeSHarP) -- Step 2 (draft); 27 September 2022 -- 1.3

The term “medicinal product” in this guideline, and the term “trial intervention” in the protocol Template refer to any therapeutic, prophylactic, or diagnostic agent including pharmaceuticals, biologics, vaccines, cell or gene therapy products (when applicable), as well as drug-device combination products when registered as a drug.

M11 Template: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Template -- Step 2 (draft); 13 March 2025* -- Word Usage in Template

"Trial intervention" refers to any therapeutic, prophylactic, or diagnostic agent including pharmaceuticals, biologics, vaccines, cell or gene therapy products, and drug-device combination products when registered as a drug. Trial interventions are all pre-specified investigational and noninvestigational medicinal products, medical devices or other interventions intended for the participants during the trial. Procedures conducted to manage participants or to collect data are excluded from the usage of this term.

Trial master file (TMF)

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Appendix C, Point C 2.3
{See the note at the end of the definition of "Essential records"}

Trial Oversight

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 11.2 Trial Oversight
[A description of] the [planned] processes and procedures to govern and conduct a clinical trial in order to protect the rights, safety and welfare of the trial participants.
{The words in square brackets {} are specific to the context of the draft M11 Technical Specification/Template.}

Trial Participant

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

An individual who participates in a clinical trial who is expected to receive the investigational product(s) or as a control. In this guideline, trial participant and participant are used interchangeably.

Trial Participant Identification Code

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- Glossary

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

Trial Phase

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- {unnumbered section} Title page
A stage in the clinical research and development of a therapy from first-in-human to post-approval clinical trials.
{See also: Early Phase 1, Phase 1, Phase 1/Phase 2, Phase 1/Phase 2/Phase 3, Phase 1/Phase 3, Phase 2, Phase 2/Phase 3, Phase 2/Phase 3/Phase 4, Phase 3, Phase 3/Phase 4, Phase 4}

Trial Schema

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 1.2 Trial Schema
A diagram that outlines the decision points (e.g. randomisation, response evaluation) that define the different paths a participant could take through the trial.

Trial Statistician

E9: Statistical Principles for Clinical Trials -- Step 4 (final); 5 February 1998 -- 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.

Trial Stopping Rules

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 4.3 Trial Stopping Rules

A criterion that, when met by the accumulating data, indicates that the trial can or should be stopped early to avoid putting participants at risk unnecessarily or because the intervention effect is so great that further data collection is unnecessary.

U

UGT

M12: Drug Interaction Studies -- Step 4 (final); 21 May 2024 -- 7.1 Glossary

uridine diphosphate (UDP)-glucuronosyl transferase

Ultraviolet light A (UVA)

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- Glossary

Wavelengths between 320 and 400 nm

Ultraviolet light B (UVB)

S10: Photosafety Evaluation of Pharmaceuticals -- Step 4 (final); 13 November 2013 -- Glossary

Wavelengths between 280 and 320 nm; as a part of sunlight wavelengths between 290 and 320 nm.

Uncertainty

Q9(R1): Quality Risk Management -- Step 4 (final); 18 January 2023 -- 5.1

The term “uncertainty” in quality risk management means lack of knowledge about hazards, harms and, consequently, their associated risks.

Unexpected ADR

E2D: Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting -- Step 4 (final); 12 November 2003 -- 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 -- Step 4 (final); 27 October 1994 -- 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.)

Unexpected AE/ADR

E2D(R1) EWG: Post Approval Safety Data Management: Definition and Standards for Expedited Reporting -- Step 2 (draft); 5 February 2024 -- 2.1.4

MAHs should treat AEs/ADRs in ICSRs as unexpected if the reported AE/ADR is not included in any section of the local/regional product labelling (e.g., Prescribing Information or Summary of Product Characteristics). In addition, an AE/ADR in an ICSR whose nature, severity, or specificity is not consistent with the term or description used in the local/regional product labelling should be considered unexpected.

NOTE: In contrast to the term “unexpected”, the term “unlisted” is not applicable to individual case safety reporting but is used to characterise the ADR according to the Company Core Safety Information (refer to the ICH E2C guideline for definitions).

{ADR=Adverse drug reaction; AE=Adverse event; ICSR=Individual case safety report; MAH=Marketing authorisation holder}

Unidentified Degradation Product

Q3B(R2): Impurities in New Drug Products -- Step 4 (final); 2 June 2006 -- 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 -- Step 4 (final); 25 October 2006 -- 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 -- Step 4 (final); 6 October 1999 -- 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 -- Step 4 (final); 6 October 1999 -- 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: Continuous Manufacturing of Drug Substances and Drug Products -- Step 4 (final); 16 November 2022 -- Glossary

A basic step in a process. Unit operations involve a physical, chemical or biological transformation such as: reaction, crystallisation, filtration, blending, granulation, tableting, cell culture, purification or virus inactivation.

Universal test

Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances -- Step 4 (final); 6 October 1999 -- 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(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- 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 bioreactor.

Unscheduled DNA synthesis (UDS)

S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use -- Step 4 (final); 9 November 2011 -- 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 -- Step 4 (final); 2 June 2006 -- 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 -- Step 4 (final); 25 October 2006 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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) EWG/IWG: Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification -- Version 5.02; 10 November 2016 -- 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]

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

In software engineering and system engineering, a use case is a technique for capturing functional requirements of systems. Use cases tend to focus on how an end-user would operate software in order to conduct their activities. High level: A specific example of a process or tool Low level: A use case is an interaction between a user and a system (or part of a system) to define a discrete goal that a user wants to achieve with system, without revealing the system's internal structure. It sets out the situation before execution of the activities, and how that situation is changed by such activities. Multiple Use Cases can make up a 'Business Use Case.'

User requirement

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

Roughly comparable to business requirements but more – 'how to do'. User requirements are more commonly found in technical development and may reflect specific elements or operations needed to perform the process. These are gathered from end-user participants and stakeholders.

Utilization period

Q1F: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- Glossary

See in-use period.

V

Vaccine

M11 TS: Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS) -- Step 2 (draft); 14 March 2025* -- 6 Trial Intervention and Concomitant Therapy

A medicinal product inducing immunity against disease, most often to prevent occurrence of a disease, (e.g., a preventative vaccine against infectious disease), but also to treat a disease, (e.g., a therapeutic vaccine against cancer).
{See also: 'Behavioral {intervention in a clinical trial}', 'Biologic', 'Combination Product', 'Device', 'Dietary Supplement', 'Drug', 'Genetic {intervention}', 'Surgery', 'Non-Surgical Procedure', 'Radiation {intervention}', 'Diagnostic Test'}

S5(R3): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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 -- Step 4 (final); 27 October 1994 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

Demonstration that a bioanalytical method is suitable for its intended purpose.

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

A process that aims to assess the adequacy of the model robustness and performance.

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 activities

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- 3. Model evaluation

Validation activities aim to assess the adequacy of the model robustness and performance.128 Validation activities include assessing the relevance and appropriateness of the following: the data, the model's conceptual form (i.e., overall structure and complexity), the model assumptions, the approach to model development, and the graphical and numerical approaches to model performance and external validation. An important underlying principle is the comparison of the model versus data, prior information, and knowledge.

Validation Protocol

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 1 November 2023 -- Multivariate glossary

A set of data used to give an independent assessment of the performance of the calibration model. (ICH Q2

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Multivariate glossary

A set of data used to give an independent assessment of the performance of the calibration model. (ICH Q2)

Validation study

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

An evaluation of prior knowledge, data or deliberate experiments (i.e., validation tests) to determine the suitability of an analytical procedure for the intended purpose. (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

An evaluation of prior knowledge, data or deliberate experiments (i.e., validation tests) to determine the suitability of an analytical procedure for the intended purpose. (ICH Q2)

Validation test

Q14: Analytical Procedure Development -- Step 4 (final); 1 November 2023 -- Glossary

Validation tests are deliberate experiments designed to authenticate the suitability of an analytical procedure for the intended purpose. (ICH Q2)

Q2(R2): Validation of Analytical Procedures -- Step 4 (final); 1 November 2023 -- Glossary

Validation tests are deliberate experiments designed to authenticate the suitability of an analytical procedure for the intended purpose. (ICH Q2)

Variation

S5(R3): Detection of Toxicity to Reproduction for Human Pharmaceuticals -- Step 4 (final); 18 February 2020 -- 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: Stability Data Package for Registration Applications in Climatic Zones III and IV -- Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10 -- 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: Nonclinical Biodistribution Considerations for Gene Therapy Products -- Step 4 (final); 14 March 2023 -- Glossary

Gene therapy delivery vehicles or carriers, containing transcriptionally/translationally active therapeutic genetic material or genetic material to alter the host genome that is manufactured to transfer the genetic material into the 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.

Verification

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- Appendix 3: Glossary

A process that aims to ensure user-generated codes (i.e., instructions written by the user of a programming language or software) for processing the data and conducting the analysis are error-free, equations reflecting the model assumptions and their representation in the programming language or software are correct, and calculations are accurate.

Verification activities

M15 EWG: General Principles for Model-Informed Drug Development -- Step 2 (draft); 6 November 2024* -- 3. Model evaluation

Verification activities aim to ensure user-generated codes (i.e., instructions written by the user of a programming language or software) for processing the data and conducting the analysis are error-free, equations reflecting the model assumptions and their representation in the programming language or software are correct, and calculations are accurate.

Viral Clearance

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Removal of viral particles or inactivation of viral infectivity.

Viral Vector

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

A recombinant virus that may be applied in vivo as a medicinal product or applied ex vivo for other advanced therapeutic applications.

Viral Vector Derived Product

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

A product encoded and expressed by a viral vector, where the recombinant virus is referred to as a viral vector for production, such as a baculovirus.

Viral Vector for Protein Expression

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

A recombinant virus, such as baculovirus, that can be used to express a recombinant protein or a virus like particle, or to produce a viral vector.

Virus

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Intracellularly replicating infectious agents that are potentially pathogenic, that possess only a single type of nucleic acid (either RNA or DNA), that are unable to grow and undergo binary fission, and that multiply in the form of their genetic material.
See also 'Non-Specific Model Virus', 'Relevant Virus', 'Replication Competent Virus (RCV)' and 'Specific Model Virus'.
{From Section 1 (Introduction) of the guideline:} In this document, the term virus excludes nonconventional transmissible agents like
those associated with mammalian prions (e.g., bovine spongiform encephalopathy, scrapie).

Virus reduction factor

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Annex 3

The virus reduction factor of an individual removal or inactivation step is defined as the log10 of the ratio of the virus load in the pre-processed material and the virus load in the post-processed material that is ready for use in the next step of the process.

Virus-like Particles

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

Structures which morphologically appear to be related to known viruses. May or may not contain the viral genome.

Vulnerable Participants

E6(R3): Guideline for Good Clinical Practice -- Step 4 (final); 6 January 2025* -- 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 participants may include 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 -- Step 4 (final); 14 April 2020 -- 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.

Working Cell Bank (WCB)

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

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

Q5B: Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products -- Step 4 (final); 30 November 1995 -- 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 -- Step 4 (final); 16 July 1997 -- 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 -- Step 4 (final); 1 November 2023 -- 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 -- Step 4 (final); 1 November 2023 -- Glossary

A working range corresponds to the lowest and the highest level of the quality attribute to be measured (e.g., content or purity) as presented to the analytical instrument and for which the analytical procedure provides reliable results. (ICH Q2)
See also: 'Range', 'Reportable range'

Working Solution

M10: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- 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).

Working Virus Seed (WVS)

Q5A(R2): Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin -- Step 4 (final); 1 November 2023 -- Glossary

A WVS (stock, lot, or bank) is produced from the MVS.
MVS: Master Virus Seed

Worst-case scenario

E14: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs -- Step 4 (final); 12 May 2005 -- 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)

X

XML Schema

M2: Electronic Standards for the Transfer of Regulatory Information -- Glossary. (Not subject to the formal ICH Step process); 11 June 2015 -- Definitions

XML Schemas express shared vocabularies and allow machines to carry out rules made by people. They provide the means for defining the structure, content, and semantics of XML documents. (W3C)
{XML: Extensible markup language, see https://www.w3.org/XML/; W3C: World Wide Web Consortium}

Y

Yield, Expected

Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients -- Step 4 (final); 10 November 2000 -- 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 -- Step 4 (final); 10 November 2000 -- 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: Bioanalytical Method Validation and Study Sample Analysis -- Step 4 (final); 24 May 2022 -- Glossary

A blank sample spiked with an Internal Standard (IS).

Version 8

ICH guidelines referenced

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
Efficacy guidelines	
E1 **The Extent of Population Exposure to Assess Clinical Safety for Drugs Intended for Long-Term Treatment of Non-Life Threatening Conditions** Step 4 (final); 27 October 1994 https://database.ich.org/sites/default/files/E1_Guideline.pdf	0
E10 **Choice of Control Group and Related Issues in Clinical Trials** Step 4 (final); 20 July 2000 https://database.ich.org/sites/default/files/E10_Guideline.pdf	0
E11(R1) **Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population** Step 4 (final); 18 August 2017 https://database.ich.org/sites/default/files/E11_R1_Addendum.pdf	6
E11A **Paediatric Extrapolation** Step 4 (final); 21 August 2024 https://database.ich.org/sites/default/files/ICH_E11A_Guideline_Step4_2024_0821.pdf	1
E12 **Principles for Clinical Evaluation of New Antihypertensive Drugs** Principle document; 2 March 2000 https://database.ich.org/sites/default/files/E12_Guideline.pdf	0
E14 **The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs** Step 4 (final); 12 May 2005 https://database.ich.org/sites/default/files/E14_Guideline.pdf	4
E14 Q&As (R3) **Questions and Answers (R3). ICH E14 Guideline: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs** Step 4 (final); 10 December 2015 https://database.ich.org/sites/default/files/E14_Q%26As_R3_Q%26As.pdf	5
E14/S7B **First Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential** Step 4 (final); 21 February 2022 https://database.ich.org/sites/default/files/E14-S7B_QAs_Step4_2022_0221.pdf	12
E14/S7B IWG **Second Round Questions & Answers: Clinical and Nonclinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential** -- * [Work in progress]	0

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
E15 **Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories** Step 4 (final); 1 November 2007 https://database.ich.org/sites/default/files/E15_Guideline.pdf	8
E16 **Biomarkers Related to Drug or Biotechnology Product Development: Context, Structure and Format of Qualification Submissions** Step 4 (final); 20 August 2010 https://database.ich.org/sites/default/files/E16_Guideline.pdf	1
E17 **General principles for planning and design of Multi-Regional Clinical Trials** Step 4 (final); 16 November 2017 https://database.ich.org/sites/default/files/E17EWG_Step4_2017_1116.pdf	6
E18 **Genomic Sampling and Management of Genomic Data** Step 4 (final); 6 September 2017 https://database.ich.org/sites/default/files/E18_Guideline.pdf	1
E19 **A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-approval or Post-Approval Clinical Trials** Step 4 (final); 27 September 2022 https://database.ich.org/sites/default/files/ICH_E19_Guideline_Step4_2022_0826_0.pdf	6
E20 EWG **Adaptive Clinical Trials** Step 1 [Work in progress]	0
E21 EWG **Inclusion of Pregnant and Breastfeeding Individuals in Clinical Trials** Step 1; 15 May 2025* https://database.ich.org/sites/default/files/ICH_E21EWG_Step2_Draft_Guideline_2025_0514.docx	0
E2A **Clinical Safety Data Management: Definitions and Standards for Expedited Reporting** Step 4 (final); 27 October 1994 https://database.ich.org/sites/default/files/E2A_Guideline.pdf	6
E2B(R2) **Maintenance of the ICH guideline on clinical safety data management: Data elements for transmission of individual case safety reports** Step 4 (final); 5 February 2001 https://admin.ich.org/sites/default/files/inline-files/E2B_R2_Guideline.pdf	4
E2B(R3) EWG/IWG **Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs). Data Elements and Message Specification** Version 5.02; 10 November 2016 [See link to Step 4 ICH IG package at https://ich.org/page/e2br3-individual-case-safety-report-icsr-specification-and-related-files]	28

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
E2B(R3) Q&As {version 2.4} **Questions and Answers: Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports** Step 4 (final); 17 January 2023 https://database.ich.org/sites/default/files/ICH_E2B-R3_QA_v2_4_Step4_2022_1202.pdf	1
E2C(R2) **Periodic Benefit-Risk Evaluation Report** Step 4 (final); 17 December 2012 https://database.ich.org/sites/default/files/E2C_R2_Guideline.pdf	21
E2C(R2) Q&As **Questions & Answers: Periodic Benefit-Risk Evaluation Report** Step 4 (final); 31 March 2014 https://database.ich.org/sites/default/files/E2CR2_Q%26As_Q%26As.pdf	0
E2D **Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting** Step 4 (final); 12 November 2003 https://database.ich.org/sites/default/files/E2D_Guideline.pdf	9
E2D(R1) EWG **Post Approval Safety Data Management: Definition and Standards for Expedited Reporting** Step 2 (draft); 5 February 2024 https://database.ich.org/sites/default/files/ICH_E2D%28R1%29_Step3_Draft%20Guideline_2024_0205.pdf	23
E2E **Pharmacovigilance Planning** Step 4 (final); 18 November 2004 https://database.ich.org/sites/default/files/E2E_Guideline.pdf	3
E2F **Development Safety Update Report** Step 4 (final); 17 August 2010 https://database.ich.org/sites/default/files/E2F_Guideline.pdf	18
E3 **Structure and Content of Clinical Study Reports** Step 4 (final); 30 November 1995 https://database.ich.org/sites/default/files/E3_Guideline.pdf	1
E3 Q&As (R1) **Questions & Answers: Structure and Content of Clinical Study Reports** Step 4 (final); 6 July 2012 https://database.ich.org/sites/default/files/E3_Q%26As_R1_Q%26As.pdf	2
E4 **Dose-Response Information to Support Drug Registration** Step 4 (final); 10 March 1994 https://database.ich.org/sites/default/files/E4_Guideline.pdf	0
E5 Q&As (R1) **Questions & Answers: Ethnic Factors in the Acceptability of Foreign Clinical Data** Step 4 (final); 2 June 2006 https://database.ich.org/sites/default/files/E5_Q%26As__R1_Q%26As.pdf	0

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
E5(R1) **Ethnic Factors in the Acceptability of Foreign Clinical Data** Step 4 (final); 5 February 1998 https://database.ich.org/sites/default/files/E5_R1__Guideline.pdf	20
E6(R3) **Guideline for Good Clinical Practice** Step 4 (final); 6 January 2025* https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf	66
E6(R3) Annex 2 Subgroup **Guideline for Good Clinical Practice (GCP). Annex 2.** Step 2 (draft); 6 November 2024* https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Annex%202_Step2_DraftGuideline_2024_1024.pdf	8
E7 **Studies in Support of Special Populations: Geriatrics** Step 4 (final); 24 June 1993 https://database.ich.org/sites/default/files/E7_Guideline.pdf	1
E7 Q&As **Questions & Answers: Studies in Support of Special Populations: Geriatrics** Step 4 (final); 16 July 2010 https://database.ich.org/sites/default/files/E7_Q%26As_Q%26As.pdf	0
E8(R1) **General Considerations for Clinical Studies** Step 4 (final); 6 October 2021 https://database.ich.org/sites/default/files/ICH_E8-R1_Guideline_Step4_2021_1006.pdf	5
E9 **Statistical Principles for Clinical Trials** Step 4 (final); 5 February 1998 https://database.ich.org/sites/default/files/E9_Guideline.pdf	29
E9(R1) **Addendum: Statistical Principles for Clinical Trials** Step 4 (final); 20 November 2019 https://database.ich.org/sites/default/files/E9-R1_Step4_Guideline_2019_1203.pdf	8
Multidisciplinary guidelines	
M1 **MedDRA - Medical Dictionary for Regulatory Activities** Step 4 (final); 1 January 1999 [MedDRA not considered in this glossary]	0
M1 PtC WG **MedDRA Points to Consider** -- [MedDRA not considered in this glossary]	0
M10 **Bioanalytical Method Validation and Study Sample Analysis** Step 4 (final); 24 May 2022 https://database.ich.org/sites/default/files/M10_Guideline_Step4_2022_0524.pdf	66

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
M10 Q&As **Questions and Answers: Bioanalytical Method Validation and Study Sample Analysis** Step 4 (final); 16 November 2022 https://database.ich.org/sites/default/files/ICH_M10_QAs_2022_1111.pdf	0
M11 EWG **Clinical electronic Structured Harmonised Protocol (CeSHarP)** Step 2 (draft); 27 September 2022 https://database.ich.org/sites/default/files/ICH_M11_draft_Guideline_Step2_2022_0904.pdf	2
M11 Template **Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Template** Step 2 (draft); 13 March 2025* https://database.ich.org/sites/default/files/ICH_M11_Template_Updated%20Step%202_ForReferenceOnly_2025_0203.pdf	4
M11 TS **Clinical electronic Structured Harmonised Protocol (CeSHarP): M11 Technical Specification (TS). {This glossary includes selected definitions of the controlled terminology}** Step 2 (draft); 14 March 2025* https://database.ich.org/sites/default/files/ICH_M11_Technical%20Specification_Updated%20Step%202_2025_0203.pdf	80
M12 **Drug Interaction Studies** Step 4 (final); 21 May 2024 https://database.ich.org/sites/default/files/ICH_M12_Step4_Guideline_2024_0521_0.pdf	53
M12 Q&As **Questions and Answers: Drug Interaction Studies** Step 4 (final); 21 May 2024 https://database.ich.org/sites/default/files/ICH_M12_Step4_Q%26As_2023_0521.pdf	0
M13A **Bioequivalence for Immediate-Release Solid Oral Dosage Forms** Step 4 (final); 23 July 2024 https://database.ich.org/sites/default/files/ICH_M13A_Step4_Final_Guideline_2024_0723.pdf	32
M13A Q&As **Questions and Answers: Bioequivalence for Immediate-Release Solid Oral Dosage Forms** Step 4 (final); 23 July 2024 https://database.ich.org/sites/default/files/ICH_M13A_Step4_QAs_2024_0723.pdf	0
M13B EWG **Bioequivalence for Immediate-Release Solid Oral Dosage Forms** Step 2 (draft); 13 March 2025* https://database.ich.org/sites/default/files/M13B_Draft%20Guideline_Step2_2025_0212_0.pdf	15
M13C EWG **Bioequivalence for Immediate-Release Solid Oral Dosage Forms** -- * [Work in progress]	0

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
M14 EWG **General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines** Step 2 (draft); 21 May 2024 https://database.ich.org/sites/default/files/ICH_M14_Step3_DraftGuideline_2024_0521.pdf	42
M15 EWG **General Principles for Model-Informed Drug Development** Step 2 (draft); 6 November 2024* https://database.ich.org/sites/default/files/ICH_M15_EWG_Step2_DraftGuideline_2024_1031.pdf	19
M2 **Electronic Standards for the Transfer of Regulatory Information** Glossary. (Not subject to the formal ICH Step process); 11 June 2015 https://admin.ich.org/sites/default/files/inline-files/M2_Glossary_v2%200%20_11%20June%202015.pdf	54
M2 EWG **Electronic Standards for the Transfer of Regulatory Information** -- * [Work in progress]	0
M3(R2) **Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals** Step 4 (final); 11 June 2009 https://database.ich.org/sites/default/files/M3_R2__Guideline.pdf	6
M3(R2) Q&As (R2) **Questions & Answers: Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals** Step 4 (final); 15 June 2011 https://database.ich.org/sites/default/files/M3_R2_Q%26As_R2_Q%26As_0.pdf	2
M4 Q&As (R3) **Questions & Answers: Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use** Step 4 (final); 10 June 2004 https://database.ich.org/sites/default/files/M4_Q%26As_R3_Q%26As.pdf	1
M4(R4) **Organisation of the Common Technical Document for the Registration of Pharmaceuticals for Human Use** Step 4 (final); 15 June 2016 https://database.ich.org/sites/default/files/M4_R4__Guideline.pdf	1
M4E Q&As (R4) **Questions & Answers: CTD on Efficacy** Step 4 (final); 10 June 2004 https://database.ich.org/sites/default/files/The_M4_Efficacy_Questions___Answers__R4_.pdf	1
M4E(R2) **Revision of M4E Guideline on Enhancing the Format and Structure of Benefit-Risk Information in ICH: Efficacy** Step 4 (final); 15 June 2016 https://database.ich.org/sites/default/files/M4E_R2__Guideline.pdf	3

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
M4Q Q&As (R1) **Questions & Answers: CTD on Quality** Step 4 (final); 1 June 2003 https://database.ich.org/sites/default/files/M4Q_Q%26As_R1_Q%26As.pdf	0
M4Q(R1) **The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Quality** Step 4 (final); 12 September 2002 https://database.ich.org/sites/default/files/M4Q_R1_Guideline.pdf	0
M4Q(R2) EWG **The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Quality** Step 2 (draft); 14 May 2025* https://database.ich.org/sites/default/files/ICH%20M4Q%28R2%29_Draft_Guideline_2025_0514.docx	33
M4S Q&As (R2) **Questions & Answers: CTD on Safety** Step 4 (final); 11 November 2003 https://database.ich.org/sites/default/files/M4S_Q%26As_R2_Q%26As.pdf	0
M4S(R2) **The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Safety** Step 4 (final); 20 December 2002 https://database.ich.org/sites/default/files/M4S_R2_Guideline.pdf	2
M5 **Data Elements and Standards for Drug Dictionaries** -- [No guideline, refers to E2B(R3)]	0
M6 **Virus and Gene Therapy Vector Shedding and Transmission** -- [Topic ceased in April 2011]	0
M7 Subgroup **Risk assessment and control of nitrosamine impurities** Step 1 [Work in progress]	0
M7(R2) **Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk** Step 4 (final); 3 April 2023 https://database.ich.org/sites/default/files/ICH_M7%28R2%29_Guideline_Step4_2023_0216_0.pdf	19
M7(R2) Addendum **Application of the principles of the ICH M7 guideline to calculation of compound-specific acceptable intakes. Addendum to M7(R2)** Step 4 (final); 3 April 2023 https://database.ich.org/sites/default/files/ICH_M7%28R2%29_Addendum_Step4_2023_0216.pdf	1

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
M7(R2) Q&As **Questions and Answers: Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk** Step 4 (final); 24 May 2022 https://database.ich.org/sites/default/files/M7R2_QAs_Step3_2022_0517-Error%20Corrected.pdf	4
M7(R3) Maintenance EWG/IWG **Assessment and Control of DNA Reactive (Mutagenic) Impuities in Pharmaceuticals to Limit Potential Carcinogenic Risk** -- [To respond to any proposals for revisions of the M7 guideline]	0
M8 eCTD v3.2.2 **Electronic Common Technical Document (eCTD) v3.2.2** Step 4 (final); 1 July 2008 https://admin.ich.org/sites/default/files/inline-files/eCTD_Specification_v3_2_2_0.pdf	0
M8 eCTD v4.0 **Electronic Common Technical Document (eCTD) v4.0. Implementation Guide v1.6** Step 4 (final); 21 May 2024 https://admin.ich.org/sites/default/files/inline-files/eCTD_v4.0_Implementation_Guide_0.zip -- filename: ICH_eCTDv4_0_ImplementationGuide_v1_6_2024_0522.pdf	11
M8 EWG/IWG **Electronic Common Technical Document (eCTD)** Step 4 (final); 6 August 2018 [See https://ich.org/page/electronic-standards-estri; eCTD version documentation not considered in this glossary]	0
M9 **Biopharmaceutics Classification System-based Biowaivers** Step 4 (final); 20 November 2019 https://database.ich.org/sites/default/files/M9_Guideline_Step4_2019_1116.pdf	0
M9 Q&As **Questions and Answers: Biopharmaceutics Classification System-based Biowaivers** Step 4 (final); 20 November 2019 https://database.ich.org/sites/default/files/M9_QAs_Step4_2021_0106.pdf	1
MIDD DG **Model-Informed Drug Development** Discussion group [See https://ich.org/page/reflection-papers under "Discussion Groups"]	0
Quality guidelines	
Q1 EWG **Stability testing of drug substances and drug products** Step 2 (draft); 11 April 2025* https://database.ich.org/sites/default/files/ICH_Q1EWG_Step2_Draft_Guideline_2025_0411.pdf	38
Q10 **Pharmaceutical Quality System** Step 4 (final); 4 June 2008	

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
https://database.ich.org/sites/default/files/Q10%20Guideline.pdf	23

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
Q11 **Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities)** Step 4 (final); 1 May 2012 https://database.ich.org/sites/default/files/Q11%20Guideline.pdf	18
Q11 Q&As **Questions & Answers: Selection and Justification of Starting Materials for the Manufacture of Drug Substances** Step 4 (final); 23 August 2017 https://database.ich.org/sites/default/files/Q11_Q%26As_Q%26As.pdf	2
Q12 **Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management** Step 4 (final); 20 November 2019 https://database.ich.org/sites/default/files/Q12_Guideline_Step4_2019_1119.pdf	13
Q13 **Continuous Manufacturing of Drug Substances and Drug Products** Step 4 (final); 16 November 2022 https://database.ich.org/sites/default/files/ICH_Q13_Step4_Guideline_2022_1116.pdf	15
Q14 **Analytical Procedure Development** Step 4 (final); 1 November 2023 https://database.ich.org/sites/default/files/ICH_Q14_Guideline_2023_1116.pdf	54
Q1A(R2) **Stability Testing of New Drug Substances and Products** Step 4 (final); 6 February 2003 https://database.ich.org/sites/default/files/Q1A%28R2%29%20Guideline.pdf	33
Q1B **Stability Testing: Photostability Testing of New Drug Substances and Products** Step 4 (final); 6 November 1996 https://database.ich.org/sites/default/files/Q1B%20Guideline.pdf	6
Q1C **Stability Testing for New Dosage Forms** Step 4 (final); 6 November 1996 https://database.ich.org/sites/default/files/Q1C%20Guideline.pdf	1
Q1D **Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products** Step 4 (final); 7 February 2002 https://database.ich.org/sites/default/files/Q1D%20Guideline.pdf	2
Q1E **Evaluation of Stability Data** Step 4 (final); 6 February 2003 https://database.ich.org/sites/default/files/Q1E%20Guideline.pdf	1
Q1F **Stability Data Package for Registration Applications in Climatic Zones III and IV** Withdrawn, definitions included here are from: WHO TRS 1010 2018, Annex 10	

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
https://database.ich.org/sites/default/files/Q1F_Stability_Guideline_WHO_2018.pdf	36
Q2(R2) **Validation of Analytical Procedures** Step 4 (final); 1 November 2023 https://database.ich.org/sites/default/files/ICH_Q2%28R2%29_Guideline_2023_1130.pdf	38
Q2(R2)/Q14 IWG **Analytical Procedure Development and Revision of Q2 (R1) Analytical Validation** Step 4 (final); 1 November 2023 [See Q2(R2) and Q14]	0
Q3A(R2) **Impurities in New Drug Substances** Step 4 (final); 25 October 2006 https://database.ich.org/sites/default/files/Q3A%28R2%29%20Guideline.pdf	22
Q3B(R2) **Impurities in New Drug Products** Step 4 (final); 2 June 2006 https://database.ich.org/sites/default/files/Q3B%28R2%29%20Guideline.pdf	14
Q3C(R10) Maintenance EWG **Maintenance of the Guideline for Residual Solvents** Step 1 [To respond to any proposals for revisions of the Q3D guideline]	0
Q3C(R9) **Guideline for Residual Solvents** Step 4 (final); 24 January 2024 https://database.ich.org/sites/default/files/ICH_Q3C%28R9%29_Guideline_MinorRevision_2024_2024_Approved.pdf	10
Q3D(R2) **Guideline for Elemental Impurities** Step 4 (final); 26 April 2022 https://database.ich.org/sites/default/files/Q3D-R2_Guideline_Step4_2022_0308.pdf	33
Q3D(R3) Maintenance EWG **Maintenance of the Guideline for Elemental Impurities** -- [To respond to any proposals for revisions of the Q3C guideline]	0
Q3E EWG **Impurity: Assessment and Control of Extractables and Leachables for Pharmaceuticals and Biologics** Step 1 [Work in progress]	0
Q4A **Pharmacopoeial Harmonisation** -- [Harmonisation through the Pharmacopoeial Discussion Group (PDG); see Q4B and Annexes]	0
Q4B **Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions** Step 4 (final); 1 November 2007 https://database.ich.org/sites/default/files/Q4B%20Guideline.pdf	5

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
Q4B Annex 1(R1) **Residue on Ignition/Sulphated Ash General Chapter** Step 4 (final); 27 September 2010 https://database.ich.org/sites/default/files/Q4B%20Annex%201%28R1%29%20Guideline.pdf	0
Q4B Annex 10(R1) **Polyacrylamide Gel Electrophoresis General Chapter** Step 4 (final); 27 September 2010 https://database.ich.org/sites/default/files/Q4B%20Annex%2010%28R1%29%20Guideline.pdf	0
Q4B Annex 11 **Capillary Electrophoresis General Chapter** Step 4 (final); 9 June 2010 https://database.ich.org/sites/default/files/Q4B%20Annex%2011%20Guideline.pdf	0
Q4B Annex 12 **Analytical Sieving General Chapter** Step 4 (final); 9 June 2010 https://database.ich.org/sites/default/files/Q4B%20Annex%2012%20Guideline.pdf	0
Q4B Annex 13 **Bulk Density and Tapped Density of Powders General Chapter** Step 4 (final); 7 June 2012 https://database.ich.org/sites/default/files/Q4B%20Annex%2013%20Guideline.pdf	0
Q4B Annex 14 **Bacterial Endotoxins Test General Chapter** Step 4 (final); 18 October 2012 https://database.ich.org/sites/default/files/Q4B%20Annex%2014%20Guideline.pdf	0
Q4B Annex 2(R1) **Test for Extractable Volume of Parenteral Preparations General Chapter** Step 4 (final); 27 September 2010 https://database.ich.org/sites/default/files/Q4B%20Annex%202%28R1%29%20Guideline.pdf	0
Q4B Annex 3(R1) **Test for Particulate Contamination: Sub-Visible Particles General Chapter** Step 4 (final); 27 September 2010 https://database.ich.org/sites/default/files/Q4B%20Annex%203%28R1%29%20Guideline.pdf	0
Q4B Annex 4A(R1) **Microbiological Examination of Non-Sterile Products: Microbial Enumeration Tests General Chapter** Step 4 (final); 27 September 2010 https://database.ich.org/sites/default/files/Q4B%20Annex4A%28R1%29%20Guideline.pdf	0
Q4B Annex 4B(R1) **Microbiological Examination of Non-Sterile Products: Tests for Specified Micro-Organisms General Chapter** Step 4 (final); 27 September 2010 https://database.ich.org/sites/default/files/Q4B%20Annex4B%28R1%29%20Guideline.pdf	0
Q4B Annex 4C(R1) **Microbiological Examination of Non-Sterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use General Chapter** Step 4 (final); 27 September 2010 https://database.ich.org/sites/default/files/Q4B%20Annex4C%28R1%29%20Guideline.pdf	0

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
Q4B Annex 5(R1) **Disintegration Test General Chapter** Step 4 (final); 27 September 2010 https://database.ich.org/sites/default/files/Q4B%20Annex%205%28R1%29%20Guideline.pdf	0
Q4B Annex 6 **Uniformity of Dosage Units General Chapter** Step 4 (final); 13 November 2013 https://database.ich.org/sites/default/files/Q4B%20Annex%206%20Guideline.pdf	0
Q4B Annex 7(R2) **Dissolution Test General Chapter** Step 4 (final); 11 November 2010 https://database.ich.org/sites/default/files/Q4B%20Annex%207%20%28R2%29%20Guideline.pdf	0
Q4B Annex 8(R1) **Sterility Test General Chapter** Step 4 (final); 27 September 2010 https://database.ich.org/sites/default/files/Q4B%20Annex%208%28R1%29%20Guideline.pdf	0
Q4B Annex 9(R1) **Tablet Friability General Chapter** Step 4 (final); 27 September 2010 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** --; 26 April 2012 https://database.ich.org/sites/default/files/Q4B_FAQs_FAQs.pdf	1
Q4B(R1) **Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions** Final version; 5 June 2024 https://database.ich.org/sites/default/files/ICH_Q4B%28R1%29_Guideline_2024_0605.pdf	2
Q5A(R2) **Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin** Step 4 (final); 1 November 2023 https://database.ich.org/sites/default/files/Q5A%28R1%29%20Guideline_0.pdf	38
Q5B **Analysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products** Step 4 (final); 30 November 1995 https://database.ich.org/sites/default/files/Q5B%20Guideline.pdf	8
Q5C **Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products** Step 4 (final); 30 November 1995 https://database.ich.org/sites/default/files/Q5C%20Guideline.pdf	6

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
Q5D **Derivation and Characterisation of Cell Substrates Used for Production of Biotechnological/Biological Products** Step 4 (final); 16 July 1997 https://database.ich.org/sites/default/files/Q5D%20Guideline.pdf	11
Q5E **Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process** Step 4 (final); 18 November 2004 https://database.ich.org/sites/default/files/Q5E%20Guideline.pdf	7
Q6(R1) EWG **Revision of the Specifications Guidelines** -- [Work in progress]	0
Q6A **Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances** Step 4 (final); 6 October 1999 https://database.ich.org/sites/default/files/Q6A%20Guideline.pdf	28
Q6B **Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products** Step 4 (final); 10 March 1999 https://database.ich.org/sites/default/files/Q6B%20Guideline.pdf	19
Q7 **Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients** Step 4 (final); 10 November 2000 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** Step 4 (final); 10 June 2015 https://database.ich.org/sites/default/files/Q7%20Q%26As%20Questions%20%26%20Answers.pdf	5
Q8(R2) **Pharmaceutical Development** Step 4 (final); 1 August 2009 https://database.ich.org/sites/default/files/Q8%28R2%29%20Guideline.pdf	17
Q8/9/10 Q&As (R5) **Questions and Answers (R5). Q8/Q9/Q10 - Implementation** Step 4 (final); 30 October 2024* https://database.ich.org/sites/default/files/ICH_Q9%28R1%29_Annex_1_Q8Q9Q10_QAs%28R5%29_1030.pdf	1
Q9(R1) **Quality Risk Management** Step 4 (final); 18 January 2023 https://database.ich.org/sites/default/files/ICH_Q9%28R1%29_Guideline_Step4_2025_0115.pdf	32

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
Safety guidelines	
S10 **Photosafety Evaluation of Pharmaceuticals** Step 4 (final); 13 November 2013 https://database.ich.org/sites/default/files/S10_Guideline.pdf	21
S11 **Nonclinical Safety Testing in Support of Development of Paediatric Medicines** Step 4 (final); 14 April 2020 https://database.ich.org/sites/default/files/S11_Step4_FinalGuideline_2020_0310.pdf	9
S12 **Nonclinical Biodistribution Considerations for Gene Therapy Products** Step 4 (final); 14 March 2023 https://database.ich.org/sites/default/files/ICH_S12_Step4_Guideline_2023_0314_WithCorrection_0.pdf	11
S13 EWG **Nonclinical Safety Studies for Oligonucleotide-Based Therapeutic** -- * [Work in progress]	0
S1A **Need for Carcinogenicity Studies of Pharmaceuticals** Step 4 (final); 29 November 1995 https://database.ich.org/sites/default/files/S1A%20Guideline.pdf	0
S1B(R1) **Testing for Carcinogenicity of Pharmaceuticals** Step 4 (final); 4 August 2022 https://database.ich.org/sites/default/files/S1B-R1_FinalGuideline_2022_0719.pdf	0
S1C(R2) **Dose Selection for Carcinogenicity Studies of Pharmaceuticals** Step 4 (final); 11 March 2008 https://database.ich.org/sites/default/files/S1C%28R2%29%20Guideline.pdf	1
S2(R1) **Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use** Step 4 (final); 9 November 2011 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** Step 4 (final); 27 October 1994 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** Step 4 (final); 16 November 2017 https://database.ich.org/sites/default/files/S3A_Q%26As_Q%26As.pdf	1

*ICH guideline (sorted alphabetically, e.g. E10 before E2). *=New entry*	*# definitions found*
S3B **Pharmacokinetics: Guidance for Repeated Dose Tissue Distribution Studies** Step 4 (final); 27 October 1994 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)** Step 4 (final); 2 September 1998 https://database.ich.org/sites/default/files/S4_Guideline.pdf	0
S5(R3) **Detection of Toxicity to Reproduction for Human Pharmaceuticals** Step 4 (final); 18 February 2020 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** [To respond to any proposals for revisions of annexes to the S5 guideline]	0
S6(R1) **Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals** Step 4 (final); 12 June 2011 https://database.ich.org/sites/default/files/S6_R1_Guideline_0.pdf	1
S7A **Safety Pharmacology Studies for Human Pharmaceuticals** Step 4 (final); 8 November 2000 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** Step 4 (final); 12 May 2005 https://database.ich.org/sites/default/files/S7B_Guideline.pdf	2
S8 **Immunotoxicity Studies for Human Pharmaceuticals** Step 4 (final); 15 September 2005 https://database.ich.org/sites/default/files/S8_Guideline_0.pdf	1
S9 **Nonclinical Evaluation for Anticancer Pharmaceuticals** Step 4 (final); 18 November 2009 https://database.ich.org/sites/default/files/S9_Guideline.pdf	2
S9 Q&As **Questions and Answers: Nonclinical Evaluation for Anticancer Pharmaceuticals** Step 4 (final); 27 April 2018 https://database.ich.org/sites/default/files/S9_Q%26As_Q%26As.pdf	0