# ICH-GCP E6 (R3) Glossary of terms (plain English)

Version 1.0

### Adverse Event (AE):

**Plain English:** Any unfavourable medical occurrence in a trial participant which does not necessarily have a causal relationship with the treatment

**ICH-GCP E6 (R3):** 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 Reaction (AR):* *Also referred to as: Adverse Drug Reaction (ADR)*

**Plain English** An Adverse Event which is considered related the medicinal product (in the opinion of an investigator)

**ICH-GCP E6 (R3)** 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.

### Amendments:

**Plain English:** Referred to modification in UK Regulations - See below

### Assent

**Plain English:** A clear, positive agreement from a child to take part in a clinical trial.

**ICH-GCP E6 (R3):** Affirmative agreement of a minor to participate in clinical trial. The absence of expression of agreement or disagreement should not be interpreted as assent.

### Audit

**Plain English:** An independent review of trial activities to confirm compliance with all requirements, which carried out either internally or by an external organisation.

**ICH-GCP E6 (R3):** 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).

### Certified Copy

**Plain English:** A copy of an original record, in any format, that has been checked and confirmed to be an exact match to the original. This includes metadata (where applicable). This confirmation may be shown by a dated signature or a validated process.

**ICH-GCP E6 (R3):** 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.

### Clinical Trial/Study Report (CSR)

**Plain English:** The formal report of a clinical trial which provides a complete description of the trial design, conduct, analysis, and result. Submitted as a webform on HRA website: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/ending-your-project/final-report-form/

**ICH-GCP E6 (R3):** 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).

### Chief Investigator

**Plain English:** The lead individual ultimately responsible for clinical trial conduct at all locations

**ICH-GCP E6 (R3):** An investigator assigned the responsibility for the coordination of investigators at different investigator sites participating in a multicentre trial.

### Computerised Systems Validation

**Plain English:** A risk-based process to confirm that a computerised system consistently works as intended throughout its lifecycle.

**ICH-GCP E6 (R3):** 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.

### Critical-to-Quality Factors (CtQ Factors)

- **Plain English:** the trial-specific activities that **matter most** for participant safety or data reliability and therefore require focused oversight.

Concept supported by ICH-GCP E6(R3)

### Data Governance

**Plain English:** The oversight controls that ensure trial data are accurate, reliable, secure, and fit for their intended use throughout the trial lifecycle.

Concept supported by ICH-GCP E6(R3)

### Decentralised Trial Elements

**Plain English:** Trial activities conducted outside traditional clinical trial locations, such as remote visits, home nursing, or use of digital technologies.

Concept supported by ICH-GCP E6(R3)

### Essential Records- Formerly Essential Documents

**Plain English:** Records and data, in any format, that demonstrate how a clinical trial was managed and whether it complied with GCP, regulatory requirements, and produced reliable results.

**ICH-GCP E6 (R3):** 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).

### Good Clinical Practice

**Plain English:** A quality standard for running and reporting clinical trials that protects participants and ensures trial data and results are reliable.

**ICH-GCP E6 (R3):** 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

### Impartial Witness

**Plain English:** An independent person who attends the consent process and documents the participants/legal representatives' willingness to voluntarily participate in the trial.

**ICH-GCP E6 (R3):** 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.

### Data Monitoring and Ethics Committee (DMEC)

**Plain English:** An independent committee, separate from the trial team, that reviews safety and data at planned intervals and advises the sponsor to continue, change, or stop the trial.

**ICH-GCP E6 (R3):** 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.

### Informed consent

**Plain English:** A process where a participant (or their legal representative) voluntarily agrees to take part in a trial after receiving and discussing the relevant information.

**ICH-GCP E6 (R3):** 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.

### Important Medical Event (IME)

**Plain English:** An adverse event which does not meet one of the 5 SAE criteria, but in your clinical judgement it should be treated as serious. If in doubt, report.

**KHP-CTO Training SOP 2: A**n 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 should generally be considered as serious.

### Inspection

**Plain English:** An official review by a regulatory authority (e.g., MHRA) of trial records, facilities, and systems to assess compliance with regulatory requirements

**ICH-GCP E6 (R3):** 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.

### Investigational Medicinal Product (IMP)

**Plain English:** A medicine under investigation, placebo, or reference used in a clinical trial. This includes authorised products used differently from their approved form, indication or when gaining further information.

**ICH-GCP E6 (R3):** 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.

### Investigator

**Plain English:** The person responsible for running the clinical trial and overseeing participants at a location. Often called the Principal Investigator (PI) when leading a trial team -OR- Chief Investigator (CI) when leading the entire trial.

**ICH-GCP E6 (R3):** 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."

**Investigator Site** *Referred to as Investigator location in UK legislation*

**Plain English:** The location(s) where the study is conducted.

**ICH-GCP E6 (R3):** The location(s) where trial-related activities are conducted and/or coordinated under the investigator's/institution's oversight.

**Legal Representative**

**Plain English:** A person or body legally authorised to give consent on behalf of a participant who cannot consent themselves

**ICH-GCP E6 (R3):** 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.

**Metadata**

**Plain English:** Information that provides context for a piece of data, helping explain what it is, how it was created, and how it should be used or interpreted.

**ICH-GCP E6 (R3):** 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.

**Modification (Minor)** *Referred to as Amendment in ICH-GCP E6 (R3)*

**UK Regulation:** Administrative and other minor changes that the MHRA and REC don't need to be aware of, examples included

- Changes in the processes associated with recording trial data
- Changes in the logistical arrangements for storing or transporting samples
- Internal changes to the sponsor's organisation

**Modification of Important details** *Referred to as Amendment in ICH-GCP E6 (R3)*

**UK Regulation:** Changes that do not significantly impact the safety or rights of the participants, but the authorities need to be aware of them for administrative or oversight purposes (e.g., changes to Sponsor contact details)

**Modification (substantial)** *Referred to as Amendment in ICH-GCP E6 (R3)*

**UK Regulation:** Categorised as Route A or Route B

- **Route A:** Likely to have a substantial impact on participant safety, rights, or data reliability. These require full MHRA and/or REC review.
- **Route B**: Changes that are less impactful on participant safety or data reliability but still significant enough to require notification to the MHRA (See MHRA definition in regulation 11B)

**Monitoring**

**Plain English:** Ongoing sponsor oversight of a clinical trial to ensure it is conducted in line with requirements. Often carried out by a Clinical Research Associate (CRA).

**ICH-GCP E6 (R3):** 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).

**Participants** *Formally subjects. Referred to as 'Trial participant' in ICH-GCP (R3)*

**Plain English:** An individual who takes part in a clinical trial.

**ICH-GCP E6 (R3):** 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

**Protocol**

**Plain English:** A document that explains how a clinical trial will be conducted, including its objectives, methods, and organisation. Amended if required.

**ICH-GCP E6 (R3):** 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.

**Quality by Design (QbD)**

**Plain English:** A systematic approach to designing a clinical trial that focuses on what is critical to participant safety and data reliability from the start.

Concept supported by ICH-GCP E6(R3)

## Reference Safety Information (RSI)

**Plain English:** The section of the Investigator's Brochure (IB) or SmPC used to determine expectedness for SUSAR reporting.

**ICH-GCP E6 (R3):** 'Contains a cumulative list of Adverse Drug Reactions 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.' This list should be used for determining the expectedness of a suspected serious adverse reaction and subsequently whether reporting needs to be expedited in accordance with applicable regulatory requirements

## Research Ethics Committee (REC)

**Plain English:** An independent committee that protects trial participants by reviewing and approving the trial protocol, investigators, facilities, and informed consent arrangements.

**ICH-GCP E6 (R3):** 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. Also Referred to as Institutional Review Board (IRB) and Independent Ethics Committee (IEC)

## Risk Proportionate Approach

**Plain English:** Applying oversight, controls, and documentation in proportion to the risks to participant safety and data reliability.

Concept supported by ICH-GCP E6(R3)

## Serious Adverse Event

**UK Regulation:** Any adverse even which meets one of the 5 criteria:

- results in death
- is life threatening (participant at immediate risk of death)
- requires hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability or incapacity
- consists of a congenital anomaly or birth defect

*Important medical events requiring intervention to prevent these outcomes should also be considered serious.*

### Serious Breach

**Plain English:** A deviation that significantly affects participant safety or the scientific value of the trial.

**UK Regulation:** A breach which is likely to effect to a significant degree: (a) the safety or physical or mental integrity of the subjects of the trial -OR- (b) the scientific value of the trial

### Service Provider *Formally Contract Research Organisation (CRO)*

**Plain English:** A person or organisation that provides services to support trial-related activities, acting on behalf of the sponsor or the investigator.

**ICH-GCP E6 (R3):** A person or organisation (commercial, academic or other) providing a service used by either the sponsor or the investigator to fulfil trial-related activities.

### Signature

**Plain English:** A handwritten or electronic mark used to show approval and confirm the identity of the signer.

**ICH-GCP E6 (R3):** 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.

### Source records *Formally source document*

**Plain English:** Original or certified copies of data recorded at the source, in any format, including medical records, participant-entered data, and data from laboratories or automated devices.

**ICH-GCP E6 (R3):** 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.

### Sponsor

**Plain English:** The organisation responsible for starting, managing, and funding a clinical trial.

**ICH-GCP E6 (R3):** A trial may have more than one sponsor (i.e., co-sponsor). 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.

### Sub investigator

**Plain English:** An individual member of the trial team who performs delegated trial-related tasks under the oversight of the investigator.

**ICH-GCP E6 (R3):** 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).

### Suspected Unexpected Serious Adverse Reaction (SUSAR)

**Plain English:** An adverse Event that is:

- Suspected: There is a reasonable possibility
- Unexpected: Not consistent with the reference safety information (RSI)
- Serious: meets at least one seriousness criterion (see above)
- Related: in the opinion of the investigator

**ICH-GCP E6 (R3):** 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.

### Trial location - referred to as 'trial site' in ICH-GCP (R3).

**Plain English:** The location(s) where trial activities are conducted or coordinated

**ICH-GCP E6 (R3):** The location(s) where trial-related activities are conducted and/or coordinated under the investigator's/institution's oversight.

## Trial Oversight

**Plain English:** Activities undertaken to ensure a trial is appropriately planned, conducted, and controlled, with a focus on participant safety and data reliability

Concept supported by ICH-GCP E6(R3)