NIDCR Glossary of Clinical Research Terms

| **Term** | **Definition** |
| --- | --- |
| **Adverse drug reaction** | In the preapproval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established, all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase "responses to a medicinal product" means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.  Regarding marketed medicinal products: A response to a drug that is noxious and unintended and that occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function (see the ICH guidance for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting). [ICH E6 Glossary] |
| **Adverse event (AE)** | An unfavorable change in the health of a participant, including abnormal laboratory findings, that happens during a clinical study or within a certain time period after the study is over. This may or may not be caused by the intervention being studied. [ClinicalTrials.gov 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 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. [modified from ICH E2A] NOTE: For further information, see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. *Synonyms: side effect, adverse experience. See also serious adverse event*.  For studies that do not involve a pharmaceutical intervention, see definition of unanticipated problem. |
| **Approval**  **(in relation to institutional review boards)** | The affirmative decision of the IRB that the clinical trial or study has been reviewed and may be conducted at the institution site within the constraints set forth by the IRB, the institution, good clinical practice (GCP), and the applicable regulatory requirements. [modified from ICH E6 Glossary] |
| **Audit** | A systematic and independent examination of trial- or study-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s). [modified from ICH E6 Glossary] |
| **Case report form (CRF)** | 1. A printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor for each trial subject. 2. A record of clinical study observations and other information that a study protocol designates must be completed for each subject. NOTE: In common usage, CRF can refer to either a CRF page, which denotes a group of one or more data items linked together for collection and display, or a casebook, which includes the entire group of CRF pages on which a set of clinical study observations and other information can be or have been collected, or the information actually collected by completion of such CRF pages for a subject in a clinical study. [1. ICH E6 Glossary] *Synonyms: case book, data collection form.* |
| **Causality assessment** | An evaluation performed by a medical professional concerning the likelihood that a therapy or product under study caused or contributed to an adverse event. |
| **Clean database** | A set of reviewed data in which errors have been resolved to meet quality assurance (QA) requirements for error rate and in which measurements and other values are provided in acceptable units; database that is ready to be locked. *See also database lock.* |
| **Clinical development plan** | A document that describes the collection of clinical studies that are to be performed in sequence, or in parallel, with a particular active substance, device, procedure, or treatment strategy, typically with the intention of submitting them as part of an application for a marketing authorization. NOTE: the plan should have appropriate decision points and allow modification as knowledge accumulates. [from ICH E9] |
| **Clinical research** | Patient-oriented research, including epidemiologic and behavioral studies, outcomes research, and health services research. Patient-oriented research is research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) in which a researcher directly interacts with human subjects. It includes research on mechanisms of human disease, therapeutic interventions, clinical trials, and development of new technologies, but does not include in vitro studies using human tissues not linked to a living individual. Studies falling under [45 CFR 46.101(b) (4)](http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#46.101) are not considered clinical research for purposes of this definition. [from NIH Glossary] |
| **Clinical significance** | Change in a subject's clinical condition regarded as important whether or not due to the test intervention. NOTE: Some statistically significant changes (in blood tests, for example) have no clinical significance. The criterion or criteria for clinical significance should be stated in the protocol. The term "clinical significance" is not advisable unless operationally defined. |
| **Clinical site** | Location where study is performed, subjects or participants come for a visit, or where study staff conduct study procedures on a subject. If participant visits occur at a home or at a location that varies within the study (church basement, store-front, etc.), the clinical site will be the office location of the research staff. *Synonyms: performance site, clinic, study site.* |
| **Clinical study (trial) report** | A written description of a study of any therapeutic, prophylactic, or diagnostic agent conducted in human subjects, in which the clinical and statistical description, presentations, and analysis are fully integrated into a single report. NOTE: A clinical study report is generally done for FDA-regulated studies. For further information, see the ICH Guideline for Structure and Content of Clinical Study Reports. [ICH E6 Glossary] |
| **Clinical trial** | A research investigation involving human subjects that is designed to answer specific questions about the safety and efficacy of a biomedical intervention (drug, treatment, device) or new ways of using a known drug, treatment, or device. [modified from ICH E6 Glossary, Directive 2001/20/EC]  Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. [from World Health Organization (WHO)]  Clinical trials are used to determine whether biomedical or behavioral interventions are safe, feasible, acceptable, efficacious, and effective. Clinical research involving an intervention to modify individual, family or group behavior (e.g., oral hygiene, nutrition, drug use or abuse, family functioning, stress and coping, chronic disease management), or care provider behavior (e.g., provider-patient communication, provider referral patterns) fits this definition of a clinical trial. [from the R34 Funding Opportunity Announcement (FOA)] *Synonym: clinical investigation or study*. |
| **Consent document / consent form** | Document signed by a subject to indicate his/her understanding of, and willingness to participate in a study.  Document used during the informed consent process that is the basis for explaining to potential subjects the risks and potential benefits of a study and the rights and responsibilities of the parties involved. NOTE: The consent document provides a summary of a clinical trial or study (including its purpose, the treatment procedures or data/specimen collection procedures and schedule, potential risks and benefits, alternatives to participation, etc.) and explains an individual's rights as a subject. It is designed to begin the informed consent process, which consists of conversations between the subject and the research team. If the individual then decides to enter the trial or study, s/he gives her/his official consent by signing the document. This document must be IRB approved prior to implementation. [modified from First Clinical Research Glossary] *Synonym: informed consent form (ICF)* |
| **Control** | Comparator against which the study treatment is evaluated (e.g., concurrent [placebo, no treatment, dose-response, active], and external [historical, published literature]). NOTE: The protocol incorporates scientific rationale for selection of comparator and describes how the comparator serves as a reference point for the evaluation. [after ICH E10] |
| **Control(s) – Computer system** | Processes or operations intended to ensure authenticity, integrity, and confidentiality of electronic records. [after 21 CFR Part 11; CSUCT] |
| **Data integrity** | A dimension of data contributing to its trustworthiness and pertaining to the systems and processes for data capture, correction, maintenance, transmission, and retention. Key elements of data integrity include security, privacy, access controls, a continuous pedigree from capture to archive, stability (of values, of attribution), protection against loss or destruction, ease of review by users responsible for data quality, proper operation and validation of systems, training of users. NOTE: For regulated clinical research, the FDA requires that data relied on to determine safety and efficacy of therapeutic interventions be trustworthy and establishes guidance and regulations concerning practices and system requirements needed to promote an acceptable level of data integrity. [FDA, CSUICI, IEEE]. |
| **Data monitoring** | Process by which clinical data are examined for completeness, consistency, and accuracy. |
| **Data validation** | 1. Checking data for correctness and/or compliance with applicable standards, rules, and conventions. 2. Process used to determine if data are inaccurate, incomplete, or unreasonable. The process may include format checks, completeness checks, check key tests, reasonableness checks, and limit checks. [1. FDA; 2. ISO] |
| **Database lock** | Action taken to prevent further changes to a clinical trial database. NOTE: Locking of a database is done after review, query resolution, and a determination has been made that the database is ready for analysis. |
| **Declaration of Helsinki** | A set of recommendations or basic principles that guide medical doctors in the conduct of biomedical research involving human subjects. It was originally adopted by the 18th World Medical Assembly (Helsinki, Finland, 1964) and recently revised (52nd WMA General Assembly, Edinburgh, Scotland, October 2000). |
| **Documentation** | All records, in any form (including, but not limited to: written, electronic, magnetic, and optical records; x-rays; electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken. [modified from ICH E6 Glossary] |
| **Effectiveness** | The capacity of a drug or treatment (study intervention) to produce beneficial effects on the course or duration of a disease at the dose tested and against the illness (and patient population) for which it is designed.  Effectiveness measures how well a study intervention works under real life conditions, and takes into account tolerability of a drug, acceptability of a behavioral intervention, ease of use, etc. |
| **Efficacy** | The measure of a study intervention's desired influence on a disease or condition as demonstrated by substantial evidence from adequate and well-controlled investigations.  Efficacy measures how well a study intervention works in an ideal, controlled setting. |
| **Electronic signature** | A computer data compilation of any symbol or series of symbols, executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual's handwritten signature. [CSUCT Glossary; 21 CFR Part 11.3(7)] |
| **Endpoint** | Variable that pertains to the efficacy or safety evaluations of a trial. NOTE: Not all endpoints are themselves assessments since certain endpoints might apply to populations or emerge from analysis of results. That is, endpoints might be facts about assessments (e.g., prolongation of survival). *See also variable*. |
| **Enrollment criteria** | The combination of all inclusion and exclusion criteria that define requirements for participation in a clinical study. *See also inclusion criteria and exclusion criteria.* |
| **Equipoise** | A state in which an investigator is uncertain about which arm of a clinical trial would be therapeutically superior for a patient. NOTE: An investigator who has a treatment preference or finds out that one arm of a comparative trial offers a clinically therapeutic advantage should disclose this information to subjects participating in the trial. |
| **Equivalence trial** | A trial with the primary objective of showing that the response to two or more treatments differs by an amount that is clinically unimportant. NOTE: This is usually demonstrated by showing that the true treatment difference is likely to lie between a lower and an upper equivalence margin of clinically acceptable differences. |
| **Essential documents** | Documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced. [ICH E6 Glossary] |
| **Evaluable** | Pertains to data or subjects that meet pre-established criteria for inclusion in Efficacy and/or Safety populations.  Data or subjects in non-interventional studies can also be classified as evaluable or not-evaluable depending on the completeness of data or condition of biospecimens. |
| **Exclusion criteria** | List of characteristics in a protocol, any one of which may exclude a potential subject from participation in a study. *See also inclusion criteria.* |
| **Generalizability** | 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. [ICH E9] |
| **Good clinical practice (GCP)** | A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected. [ICH E6 Glossary] NOTE: For Guidance on Good Clinical Practice see COMP/ICH/135/95; Declaration of Helsinki; 21 CFR 50, 21 CFR 54, 21 CFR 56, and 21 CFR 312. |
| **Good laboratory practice (GLP)** | Principles intended to promote the quality and validity of test data. It is a managerial concept covering the organizational process and the conditions under which laboratory studies are planned, performed, monitored, recorded and reported. [from WHO and OECD GLP Guideline] |
| **Human subject** | Individual who is or becomes a participant in research. A subject may be either a healthy human or a patient. *Synonyms: subject, trial subject, participant, volunteer*.  A living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention, interaction, or observation with the individual or obtains identifiable private information. Regulations governing the use of human subjects in research extend to use of human organs, tissues, and body fluids from identifiable individuals as human subjects and to graphic, written, or recorded information derived from such individuals. (See section 4.1.14 Human Subjects Protections in the NIHGPS and the OER Research Involving Human Subjects Webpage.) [[NIH Glossary](http://grants.nih.gov/grants/glossary.htm#H)] |
| **Inclusion criteria** | The criteria in a protocol that prospective subjects must meet to be eligible for participation in a study. NOTE: Exclusion and inclusion criteria define the study population. *See also exclusion criteria*. |
| **Indication** | A health problem or disease that is identified as likely to be benefited by a therapy being studied in clinical trials. NOTE: Where such a benefit has been established and approved by regulatory authorities, the therapy is said to be approved for such an indication. |
| **Informed consent** | An ongoing process that provides the subject with explanations that will help in making educated decisions about whether to begin or continue participating in a trial or study. Informed consent is an ongoing, interactive process, rather than a one-time information session. NOTE: Under 21 CFR 50.20, no informed consent form may include any "language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence." [ICH] *See also consent document / consent form*.  Person's voluntary agreement, based upon adequate knowledge and understanding, to participate in human subjects research or undergo a medical procedure.  In giving informed consent, people may not waive legal rights or release or appear to release an investigator or sponsor from liability for negligence. Go to 21 CFR 50.20 and 50.25 [NIH Glossary] |
| **Institutional review board (IRB)** | An independent body constituted of medical, scientific, and non-scientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial or study by, among other things, reviewing, approving, and providing continuing review of trial/study protocol and of the methods and material to be used in obtaining and documenting informed consent of the trial/study subjects. [modified from ICH E6 Glossary]  *Synonyms: independent review board, independent ethics committee, committee for the protection of human subjects*. |
| **Intention-to-treat** | A strategy for analyzing data in which all participants are included in the group to which they were assigned, whether or not they completed the intervention given to the group.  Intention-to-treat analysis prevents bias caused by the loss of participants, which may disrupt the baseline equivalence established by random assignment and which may reflect non-adherence to the protocol. [CONSORT] *Synonym: intent-to-treat.* |
| **Intermediate Visit** | Any visit following the baseline visit and prior to the final study visit. For interventional studies, often these are visits during the interventional period. |
| **Intervention** | The drug, device, therapy, or process under investigation in a clinical trial which has an effect on outcome of interest in a study: e.g., health-related quality of life, efficacy, safety, pharmacoeconomics. *Synonyms: therapeutic intervention, behavioral intervention, medical product. See also investigational product*. |
| **Investigational New Drug (IND)** | A new drug or biological drug that is used in a clinical investigation.  IND application: Under regulation 21 CFR 312, application filed by a drug sponsor with FDA on Form FDA 1571 to conduct clinical trials, including detailed descriptions of all phases, protocols, IRB members, and investigators. Once clinical evaluation is completed, a new drug application must be submitted to FDA to obtain approval to market the drug. [NIH Glossary] |
| **Investigational product** | A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use. [ICH E6 Glossary] NOTE: CDISC includes test articles in its definition of investigational products.  *Synonyms: study drug, test article, drug product, medicinal product.* |
| **Investigator** | 1. A person responsible for the conduct of the clinical trial or study at a clinical site. If a trial/study is conducted by a team of individuals at a clinical site, the investigator is the responsible leader of the team and may be called the principal investigator. 2. The individual "under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team." [1. modified from ICH E6 1.35; 2. from 21 CFR 50.3] |
| **Investigator Site File (ISF)** | The collection of essential documents maintained at each clinical site which represents the regulatory history of the study. These documents include, but are not limited to: the protocol and amendments, IRB-approved consent document templates, IRB approvals and communication, study personnel CVs and licenses, AE/SAE/UP reporting documentation, and records of Investigational Product use. *Synonyms: Regulatory Binder, Regulatory File, Investigator Site Documents* |
| **Label** | Description of a drug product/device that includes: the indication, who should use it, adverse events, instructions for use, and safety information. NOTE: Labels must be approved by regulatory authorities. [FDA; SPL] *Synonyms: package insert, patient package leaflet*. |
| **Legally acceptable representative** | An individual or juridical or other body authorized under applicable law to consent, on behalf of a prospective subject, to the subject's participation in the clinical trial. [ICH E6 Glossary] |
| **Masking** | A procedure in which one or more parties to the trial are kept unaware of the treatment assignment(s). Single-masked usually refers to the subject(s) being unaware, and double-masked usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s). [ICH E6] *Synonym: blinding.* |
| **Medical monitor** | A sponsor representative who has medical authority for the evaluation of the safety aspects of a clinical trial. |
| **Monitor** | Person employed by the sponsor or contract research organization (CRO) who is responsible for verifying that the rights and well-being of subjects are protected, that the trial or study data are accurate, complete, and verifiable from source documents, and that the conduct of the trial or study is in compliance with the currently approved protocol, with GCP and with applicable regulatory requirements. [modified from ICH E6, 5.18] *Synonym: clinical research associate*. |
| **Monitoring** | The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s). [ICH E6 Glossary] |
| **New Drug Application (NDA)** | An application to FDA for a license to market a new drug in the United States. |
| **Objective** | The reason for performing a trial or study in terms of the scientific questions to be answered by the analysis of data collected during the trial or study. NOTE: The primary objective is the main question to be answered and drives any statistical planning for the trial or study (e.g., calculation of the sample size to provide the appropriate power for statistical testing). The study should have one primary objective. Secondary objectives are goals of a trial or study that will provide further information on the use of the treatment in a trial, or on the risk factors, natural history, variations in disease progression or disease treatment in an observational study. |
| **Outcome measure** | A planned measurement described in the protocol that is used to determine the effect of interventions on participants in a clinical trial. For observational studies, a measurement or observation that is used to describe patterns of diseases or traits, or associations with exposures, risk factors, or treatment. Types of outcome measures include Primary Outcome Measure and Secondary Outcome Measure. NOTE: The primary and secondary outcome measures should be aligned with the primary and secondary study objectives. [ClinicalTrials.gov Glossary] |
| **Pharmacogenomics** | Science that examines inherited variations in genes that dictate drug response and explores the ways such variations can be used to predict whether a person will respond favorably, adversely, or not at all to an investigational product. |
| **Pharmacokinetics** | Study of the processes of bodily absorption, distribution, metabolism, and excretion (ADME) of medicinal products. |
| **Pharmacovigilance** | All scientific and data gathering activities relating to the detection, assessment, and understanding of adverse events. [FDA Guidance on Pharmacovigilance] |
| **Preclinical studies** | Animal studies that support Phase 1 (first-in-humans) safety and tolerance studies and must comply with good laboratory practice (GLP). NOTE: Data about a drug's activities and effects in animals help establish boundaries for safe use of the drug in subsequent human testing (clinical studies or trials). |
| **Protocol** | A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial or study. 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. NOTE: Present usage can refer to any of three distinct entities: 1) the plan (i.e., content) of a protocol, 2) the protocol document, and 3) a series of tests or treatments (as in oncology). [ICH E6 Glossary] |
| **Protocol amendment** | A written description of a change(s) to or formal clarification of a protocol. NOTE: Any amendment to a protocol must receive IRB approval before it is implemented. [ICH E6 Glossary] |
| **Protocol deviation** | A variation from processes or procedures defined in a protocol. Deviations usually do not preclude the overall evaluability of subject data for either efficacy or safety (or other outcomes in a non-interventional study), and are often acknowledged and accepted in advance by the sponsor. NOTE: Good clinical practice recommends that deviations be summarized by site and by category as part of the report of study results so that the possible importance of the deviations to the findings of the study can be assessed. [see ICH E6] |
| **Quality assurance (QA)** | All those planned and systematic actions that are established to ensure that the trial or study is performed and the data are generated, documented (recorded), and reported in compliance with good clinical practice (GCP) and the applicable regulatory requirement(s). [modified from ICH E6 Glossary] |
| **Quality control (QC)** | The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial or study related activities have been fulfilled. [modified from ICH E6 Glossary] |
| **Query** | A request for clarification on a data item collected for a clinical trial or study; specifically a request from a sponsor, sponsor's representative, or data coordinating center to an investigator to resolve an error or inconsistency discovered during data review. |
| **Recruitment (subjects)** | Process used by investigators to find and enroll appropriate subjects (those selected on the basis of the protocol's inclusion and exclusion criteria) into a clinical study. |
| **Research hypothesis** | The proposition that a study sets out to support (or disprove); for example, "blood pressure will be lowered by [specific endpoint] in subjects who receive the test product." The null hypothesis is the converse to what the researcher expects to happen in reference to the target outcome. Inferential statistical analyses are designed around accepting or rejecting the null hypothesis. |
| **Responsible party** | The entity or individual who is responsible for registering a clinical investigation and submitting Clinical Trial Information to the Clinical Trial Registry Data Bank. [Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (PL 110-85). [More Info](http://grants.nih.gov/clinicaltrials_fdaaa/Responsible_Party.htm)] |
| **Safety** | Relative freedom from harm. In clinical trials, this refers to an absence of harmful side effects resulting from use of the product and may be assessed by laboratory testing of biological samples, special tests and procedures, psychiatric evaluation, and/or physical examination of subjects. |
| **Serious adverse event (SAE) /**  **Serious adverse drug reaction (Serious ADR)** | An adverse event or adverse drug reaction is defined as serious if it:   * 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.   [modified from ICH E6 Glossary] *See also adverse event, adverse drug reaction*. *Synonym: serious adverse experience.* |
| **Source data** | All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial or study necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies). [modified from ICH E6; CSUCT] |
| **Source documents** | Original documents, data, and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medicotechnical departments involved in the clinical trial).[modified from ICH; CSUICI] |
| **Sponsor** | 1. An individual, company, institution, or organization that takes responsibility for the initiation, management, and/or financing of a clinical trial. 2. A corporation or agency whose employees conduct the investigation is considered a sponsor and the employees are considered investigators. [1. ICH; 2. 21 CFR 50.3] |
| **Trial Master File** | The collection of essential documents maintained by the sponsor which represents the regulatory history of the study. The file includes documents for each site and the study overall. Examples include: the protocol and all protocol amendments, IRB-approved consent document templates, IRB approvals and communication, study personnel CVs and licenses, AE/SAE/UP reporting documentation, and records of Investigational Product use. |
| **Unanticipated Problem** | Any incident, experience, or outcome that meets **all** of the following criteria:  (1)  unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;  (2)  related or possibly related to participation in the research (in this guidance document, *possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and  (3)  suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.  [45 CFR part 46] |
| **Variable** | An element or factor that the research is designed to study, either as an experimental intervention or a possible outcome (or factor affecting the outcome) of that intervention. [IRB Guidebook; Glossary of Terms] |
| **Window**  **(Visit Window)** | Range of days in which a subject visit can occur according to the study protocol, typically around a date determined by the number of days since the initial visit. [First Clinical Research Glossary] |