

University of California, San Diego  
Human Research Protections Program  
Institutional Review Board  
Standard Operating Policies and Procedures

Section 8.2  
Definitions

**Act:** The Federal Food, Drug, and Cosmetic Act, as amended (21 CFR)

**Adverse Drug Reaction (ADR):** In the pre-approval clinical experience with an experimental, investigational (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 the medicinal product and an adverse event is at least a reasonable possibility (for example, 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. (ICH 1.1)

**Adverse Event (AE):** Any untoward medical occurrence in a patient or research subject administered a pharmaceutical product or other research intervention and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product or research procedure, whether or not related to the medicinal (investigational) product or procedure. (ICH 1.2)

**Approval Date:** The IRB Approval Date is the date that the IRB approval memo for a project is signed as approved by the IRB Chair or his/her designee.

**Approved Off-Site Location:** A research site outside of the UCSD facilities.

**Associated with the use of the drug:** There is a reasonable possibility that the experience may have been caused by the drug (21 CFR 312.32).

**Audit:** A systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's standard operating procedures (SOPs), good clinical practice (GCP), and the applicable regulatory requirement(s) (ICH 1.6).

**Clinical Trial:** Any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to

the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of 21 CFR 58, regarding nonclinical laboratory studies. The terms clinical study, clinical trial, and clinical investigation are deemed to be synonymous for purposes of this Manual.

**Coded Sample:** A coded sample is one that is associated with a code that could permit an agent of the repository to link it with the subject. Even though the investigator may not be able to directly link the sample with a subject, research using such samples is subject to IRB review.

**Confidentiality:** Prevention of disclosure, to other than authorized individuals, of a sponsor's proprietary information or of a subject's identity. (ICH 1.16)

**Conflict of Interest:** A convergence of an investigator's private interests with his or her research interests, such that an independent observer might reasonably question whether the investigator's professional actions or decisions are improperly influenced by considerations of personal financial gain.

**Continuing Review Deadline:** The Continuing Review Deadline is exactly 365 days after the date of the most recent review of the study at a convened IRB meeting, or shorter if required by the IRB. Beyond this date, study approval expires and a study cannot continue.

**Department or Agency Head:** The head of any Federal Department or Agency and any other officer or employee of any Department or Agency to whom authority has been delegated. (45 CFR 46).

**Direct Access:** Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical trial. Any party (e.g., domestic and foreign regulatory authorities, sponsors, monitors, and auditors) with direct access should take all reasonable precautions within the constraints of the applicable regulatory requirement(s) to maintain the confidentiality of subjects' identities and sponsor's proprietary information (ICH1.21).

**Disability:** A substantial disruption of a person's ability to conduct normal life functions (21 CFR 312.32).

**Documentation:** All records, in any form (including, but not limited to, written, electronic, magnetic, and optical records; and scans, x-rays, and electrocardiograms) that describe or record the methods, conduct, and/or results of a trial, the factors affecting a trial, and the actions taken. (ICH 1.22)

**Emergency use:** The use of a test article on a human subject in a life-threatening situation, in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

**Enrolled:** An eligible, appropriately informed individual agreeing to participate in a study. For instance, when an individual signs an informed consent document, that individual is considered enrolled in the study. (<https://irb.ucsd.edu/enrollment-definition.shtml>)

**Exculpatory:** To clear from a charge of fraud or guilt.

**Fabrication:** The making up of data or results and recording or reporting them.

**Falsification:** Manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record.

**Family member:** Any one of the following legally competent persons: spouse; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship. (21 CFR)

**Generalizable Knowledge:** Knowledge obtained from activities designed (with intent) to collect information about some individuals to draw general conclusions about other individuals that are predictive of future events and that can be widely applied as expressed in theories, principles, and statements and that enhance scientific or academic understanding.

**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 1.24)

**Human Biological Material:** Any material derived from human subjects, such as blood, urine, tissues, organs, hair, nail clippings, genetic material, or any other cells or fluids, whether collected for research purposes or as residual specimens from diagnostic, therapeutic or surgical procedures.

**Human Research Protection Program:** The systematic and comprehensive approach by an organization to ensure human subject protection in all research. The implementation of any part of the program may be delegated to specific committees, individuals or entities.

**Human subject:** As defined by DHHS regulations means a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. [45 CFR 46.102(f)]. As defined by FDA regulations, “human subject” means an individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. [21 CFR 50.3(g), 21 CFR 56.102(e)] A human subject includes an individual on whose specimen a medical device is used. [21 CFR 812.3(p)]

**Human subjects research:** Research involving one or more human subject, as they are defined here. This definition includes all clinical trials, as defined above, as well as all other types of research involving human subjects.

**Identified information:** As defined by DHHS, means information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

**Impartial witness:** A person, who is independent of the trial, who cannot be unfairly influenced by people involved with the trial, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent form and any other written information supplied to the subject. (ICH 1.26)

**Informed Consent:** A process by which a subject or their legally authorized representative voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form (ICH 1.28).

**Institutional Review Board (IRB):** Any board, committee, or other group formally designated by an institution to review biomedical research involving human subjects, to approve the initiation of, and to conduct continuing review of such research (21 CFR 50, 45 CFR 46). An independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects (ICH 1.31).

**Interaction:** As defined by DHHS regulations, means communication or interpersonal contact between investigator and subject. [45 CFR 46.102(f)]

**Intervention:** As defined by DHHS regulations, means both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. [45 CFR 46.102(f)]

**IRB approval:** The determination of the IRB that the human subjects research has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and by other institutional and Federal requirements.

**Investigational Product:** A pharmaceutical form of an active ingredient, device 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 1.33)

**Investigator:** An individual who actually conducts human subjects research, i.e., under whose immediate direction the test article or research procedure is administered or performed upon, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team (21 CFR).

**Investigator's Brochure (IB):** A compilation of the clinical and nonclinical data on the investigational product(s), which is relevant to the study of the investigational product(s) in human subjects. (ICH 1.36). This document is also known as an Investigational Drug Brochure.

**Legally Authorized Representative:** An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject's participation in the procedure(s) involved in the research (21 CFR 50, 45 CFR 46). In the State of California, "legally authorized representative" includes only persons appointed as healthcare agents under Durable Powers of Attorney for Health Care (DPHAC) and court appointed conservators of the person.

**Life-threatening adverse drug experience:** Any adverse drug experience that places the patient, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death (21 CFR 312.32)

**Linked sample:** A sample associated with a personal identifier or a code that allows it to be linked with a subject, even if the investigator may not be able to directly link the sample with a subject. Research using such samples is subject to IRB review.

**Minimal risk:** The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (21 CFR 56.102, 45 CFR 46.102(i))

**Plagiarism:** The appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

**Private Information:** As defined by DHHS regulations, means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record) [45 CFR 46.102(f)]. Private information must be individually identifiable (i.e., the identity of the of the subject is or may be readily ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects (45 CFR 46).

**Protocol:** A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents (ICH 1.44)

**Protocol Amendment:** A written description of a change(s) to or formal clarification of a protocol (ICH 1.45).

**Randomization:** The process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias (ICH 1.48).

**Regulatory Noncompliance:** Failure to adhere to institutional policies and procedures, state laws, federal laws or other regulations governing the conduct of human subjects research. This includes such acts as failure to obtain or maintain approval for research or to adhere to an approved protocol, failure to obtain informed consent when required, coercion of human subjects, performance of an unapproved procedure, performance of research at an unapproved site, or failure to file protocol modifications, applications for study reapproval, and adverse event reports.

**Research:** As defined by DHHS regulations means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. [45 CFR 46.102(d)]. As defined by FDA regulations means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the Federal Food, Drug, and Cosmetic Act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the Federal Food, Drug, and Cosmetic Act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The terms research, clinical research, clinical study, study, and clinical investigation are synonymous for purposes of FDA regulations [21 CFR 50.3(c), 21 CFR 56.102(c)].

Research includes the following:

1. Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) of the Federal Food, Drug, and Cosmetic Act” means any use of a drug other than the use of an approved drug in the course of medical practice. [21 CFR 312.3(b)]
2. Experiments that must meet the requirements for prior submission to the Food and Drug Administration under section 520(g) of the Federal Food, Drug, and Cosmetic Act” means any activity that evaluates the safety or effectiveness of a medical device. [21 CFR 812.2(a)]
3. Any activity in which results are being submitted to or held for inspection by FDA as part of an application for a research or marketing permit is considered to be FDA-regulated research. [21 CFR 50.3(c), 21 CFR 56.102(c)]

**Scientific Misconduct:** Serious deviation from accepted practice in carrying out research or in reporting the results of research, or material failure to comply with Federal requirements affecting specific aspects of the conduct of research, such as the protection of human subjects. This may include plagiarism, misrepresentation of authorship, fabrication falsification or destruction of data, or other serious deviations from accepted scientific practices, such as obstruction of another’s research, violation of confidentiality, intentional deception, omission, research dishonesty, or repeated incidents of regulatory noncompliance. (VHA Handbook 1200.05)

**Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR):** An AE or ADR occurring in a patient or subject enrolled in a research study is serious if it results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or is a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization, may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalizations, or the development of drug dependency or drug abuse (21 CFR 312. 32).

**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 and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medical or technical departments involved in the clinical trial)(ICH 1.52)

**Sponsor:** A person or other entity that initiates human subjects research, but that does not actually conduct the investigation, i.e., the test article is administered or dispensed to, or used involving, a subject under the immediate direction of another individual. A corporation or agency that uses one or more of its own employees to conduct an investigation that it has initiated is considered to be a sponsor (not a sponsor-investigator), and the employees are considered to be investigators (21 CFR)

**Sponsor-investigator:** An individual who both initiates and actually conducts, alone or with others, human subjects research, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject. The term does not include a corporation or agency. The obligations of a sponsor-investigator under FDA regulations include both those of a sponsor and those of an investigator. (21 CFR)

**Standard Operating Policy and Procedures (SOPPs):** Detailed, written instructions to achieve uniformity of the performance of a specific function (ICH 1.55).

**Subinvestigator:** Any individual member of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows) (ICH 1.56).

**Systematic Investigation:** Activities that attempt to answer a research question or questions that is methodology driven in that it collects data or information in an organized and consistent way, and the data or information is analyzed in some way, be it quantitative or qualitative data and conclusion or conclusions are drawn from the results.

**Test article:** Any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Act or under sections 351 and 354-360F of the Public Health Service Act (21 CFR)

**Unanticipated adverse drug experience:** Any adverse experience the specificity or severity of which is not consistent with the current Investigator Brochure, or if an Investigator Brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure only listed cerebral vascular accidents. "Unanticipated" as used in this definition, refers to an adverse drug experience that has not been previously observed (e.g., included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product (21 CFR 312.32).

**Unanticipated Problems Involving Risks to Participants:** An "unanticipated problem involving risks to participants or others" are events that: negatively affect the risk and benefit ratio of the research, were unanticipated by the investigator at the time the research was approved, and are more likely than not related to the research study.

**Unidentified Sample:** An anonymous or unidentified sample is one supplied to the researcher from a repository that has a collection of unidentified human specimens. There is no possibility of linking such samples to the individual. This differs from samples that have been "anonymized" or unlinked by removal of identifiers (see Unlinked Sample).

**Unlinked Sample:** A biological sample that lacks any identifier or code that may link the sample to an individual. An investigator must differentiate between an unlinked sample that is provided to him by a third party and a sample under the investigator's control from which the investigator proposes to remove any identifying material ("anonymized") for the purposes of research.

**Vulnerable subjects:** Individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. Examples are members of a group with a hierarchical structure, such as medical, pharmacy, dental, and nursing students, subordinate hospital and laboratory personnel, employees of the pharmaceutical industry, members of the armed forces, and persons kept in detention. Other vulnerable subjects include patients with incurable diseases, persons in nursing homes, unemployed or impoverished persons, patients in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, minors, and those incapable of giving consent. (ICH 1.61) Mentally disabled individuals are a vulnerable population.

**Well-being (of the trial subjects):** The physical and mental integrity of the subjects participating in a clinical trial (ICH 1.62).