

GLOSSARY

Adverse Drug Reaction (or Experience)	(ADR or ADE) In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established, all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions. The phrase "responses to a medicinal product" means that a causal relationship between a medicinal product and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out. Regarding marketed medicinal products, an ADR is a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function (see the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).
Adverse Event	(AE) Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product 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, whether or not related to the medicinal (investigational) product.
Amendment (to the Protocol)	See Protocol Amendment.
Applicable Regulatory Requirement(s)	Any law(s) and regulation(s) addressing the conduct of clinical studies of investigational products.
Applicant	The party who submits a marketing application to FDA for approval of a drug, biologic or medical device. The applicant is responsible for submitting the appropriate financial certification or disclosure statements (Forms FDA 3454 or FDA 3455) to FDA.
Approval (in Relation to Institutional Review Boards)	The affirmative decision of the institutional review board (IRB) that the clinical 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.
Archive File	A file in which the original and all subsequent revised versions of a standard operating procedure (SOP) or other document (including those marked as "Obsolete") are maintained, so that the origination and revision history for an SOP or other document is available for review.
Assent	A child's affirmative agreement to participate in research. Failure to object should not be construed as assent.
Associated with the Use of a Gene Transfer Product	For Office of Biotechnology Activities (OBA) safety reporting purposes, there is a reasonable possibility that the event may have been caused by the use of that gene transfer product.
Associated with the Use of the Drug	For FDA safety reporting purposes, there is a reasonable possibility that the AE may have been caused by the drug. Determination of causality could include the following definitions: Definitely – The AE <ul style="list-style-type: none"> · follows a reasonable temporal sequence from drug administration, · abates upon discontinuation of the drug, · is confirmed by reappearance of the reaction on repeat exposure (re-challenge). Probably – The AE <ul style="list-style-type: none"> · follows a reasonable temporal sequence from drug administration, · abates upon discontinuation of the drug, · cannot be reasonably explained by the known characteristics of the patient's clinical state. Possibly – The AE <ul style="list-style-type: none"> · follows a reasonable temporal sequence from drug administration,

	<ul style="list-style-type: none"> · could have been produced by the patient's clinical state or by other modes of therapy administered to the patient. <p>Unrelated – The AE</p> <ul style="list-style-type: none"> · is definitely produced by the patient's clinical state or by other modes of therapy administered to the patients.
Audit	A systematic and independent examination of study-related activities and documents to determine whether the evaluated study-related activities were conducted, and that the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's SOPs, GCP, and the applicable regulatory requirements.
Audit Certificate	A written statement, signed by an institutional official or an auditor, which documents that an audit was performed.
Audit Report	A written evaluation by the auditor of the results of the audit.
Audit Trail	The documentation ("paper trail") that allows reconstruction of the course of events. When referring to electronic systems, it means a secure, computer generated, time-stamped electronic record that allows reconstruction of the course of events relating to the creation, modification, and deletion of an electronic record.
Auditor	A person qualified by training and experience to conduct an audit.
Authorization	A detailed document that gives covered entities permission to use protected health information for specified purposes, which are generally other than treatment, payment, or health care operations, or to disclose protected health information to a third party specified by the individual. ¹ (HIPAA)
Biologic Product	Any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, applicable to the prevention, treatment or cure of diseases or injuries to humans. Biologic products include, but are not limited to, bacterial and viral vaccines, human blood and plasma and their derivatives, and certain products produced by biotechnology, such as interferons and erythropoietins. In contrast to most drugs, which are chemically synthesized and whose structure is known, biologics are derived from living sources, such as humans, animals, plants and microorganisms. With respect to clinical investigations to assess safety and effectiveness, investigational biologics are treated as investigational new drugs.
Biometrics	A method of verifying an individual's identity based on measurement of the individual's physical feature(s) or repeatable action(s) where those features and/or actions are both unique to that individual and measurable.
Blinding/Masking	A procedure in which one or more parties to the study are kept unaware of the treatment assignment(s). Single-blinding usually refers to the subject(s) being unaware, and double-blinding usually refers to the subject(s), investigator(s), monitor, and, in some cases, data analyst(s) being unaware of the treatment assignment(s).
Case Report Form	(CRF) A printed, optical, or electronic document designed to record protocol-required data for each study subject and sent to the sponsor for purposes of statistical analysis.
Certified Copy	A copy of original information that has been verified, as indicated by dated signature, as an exact copy having all of the same attributes and information as the original.
Clinical Investigator	For the purpose of financial disclosure, only a listed or identified investigator or co-investigator or sub-investigator who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the clinical investigator.
Clinical Research	As defined by the National Institutes of Health (NIH), research performed on human subjects or on material or information obtained from human subjects as part of human experimentation.
Clinical Study	Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational drug,

	and/or to identify any adverse reactions to an investigational drug, and/or to study absorption, distribution, metabolism, and excretion of an investigational drug with the object of ascertaining its safety and/or efficacy. The terms clinical trial and clinical investigation are synonymous.
Clinical Study 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 analyses are fully integrated into a single report.
Clinical Trial	See Clinical Study
Closeout Visit	A final site visit by a monitor that must be conducted after a study has been completed, suspended or terminated for any reason.
Cohort	A group of subjects who share a common exposure or research experience. Examples are the treatment and control cohorts.
Co-investigator	Two or more investigators who have equivalent authority and responsibility in the conduct of a clinical study. They may be considered co-investigators or co-principal investigators. See also Investigator.
Common Rule	The colloquial name for 45 CFR 46, Subpart A, the basic Department of Health and Human Services (HHS) policy for protection of human research subjects. This regulation consolidates requirements for IRB review and informed consent to participate in human subject research. It applies to any HHS-funded research conducted on human subjects. FDA regulations (21 CFR Parts 50 and 56) closely mirror the Common Rule. Both sets of regulations apply when research is FDA-regulated and federally funded (wholly or partially).
Comparator	An investigational or marketed product (i.e., active control), or placebo, used as a reference in a clinical study.
Compensation Affected by the Outcome of Clinical Studies	Compensation that could be higher for a favorable outcome than for an unfavorable outcome, such as compensation that is explicitly greater for a favorable result or compensation to the investigator in the form of an equity interest in a sponsor of a covered study or in the form of compensation tied to sales of the product, such as a royalty interest.
Complaint	Any concern communicated by a person questioning any act or failure to act relating to an individual's rights to access to his/her protected health information (PHI), to maintain the privacy of his/her health information, to request restrictions on uses or disclosures of his/her PHI, to request confidential communications regarding his/her PHI, to request amendment of his/her PHI, or to receive an accounting of disclosures of his/her PHI. (HIPAA)
Compliance	Adherence to all study-related requirements, GCP requirements, and the applicable regulatory requirements.
Computerized System	Computer hardware, software, and associated documents (e.g., user manual) that create, modify, maintain, archive, retrieve, or transmit in digital form, information related to the conduct of a clinical study.
Confidentiality	The prevention of disclosure, to other than authorized individuals, of a sponsor's proprietary information or of a subject's identity or other medical information.
Contract	A written, dated, and signed agreement between two or more involved parties that sets out any arrangements on delegation and distribution of tasks and obligations and, if appropriate, on financial matters.
Contract Research Organization	(CRO) A person or an organization (commercial, academic, or other) contracted by a sponsor to perform one or more of that sponsor's clinical study-related duties and functions.
Controlled Document	A document whose initial version and each subsequent modification must undergo review and approval by the research management team (as defined by the sponsor, before the document can be implemented. Examples of controlled documents may include: regulatory submissions, protocols, protocol amendments, CRF, the Investigator's Brochure (IB), and templates.
Controlled Substance	A drug or other substance, or immediate precursor, included in schedule I, II, III, IV, or V of part B of Title 21 of the United States Code, Food and Drugs, Chapter

	13, Drug Abuse Prevention and Control, Subchapter i, Control and Enforcement, also cited as the "Controlled Substances Act."
Covered Clinical Study	For financial disclosure purposes, any study of a drug/ biologic/medical device in humans submitted in a marketing application or reclassification petition subject to FDA regulations that the applicant or FDA relies on to establish that the product is effective (including studies that show equivalence to an effective product) or any study in which a single investigator makes a significant contribution to the demonstration of safety. This would, in general, not include Phase 1 tolerance studies or pharmacokinetic studies, most clinical pharmacology studies (unless they are critical to an efficacy determination), large open safety studies conducted at multiple sites, treatment protocols, and parallel track protocols.
Data Safety Monitoring Board	(DSMB) See Data Monitoring Committee.
Data Monitoring Committee	(DMC) An independent data monitoring committee (DMC) that may be established by a sponsor to assess at intervals the progress of a clinical study, the safety data, and the critical efficacy endpoints, and to recommend to the sponsor whether to continue, modify, or stop a study. The terms "data safety monitoring board" and "independent data monitoring board" are synonymous with data monitoring committee.
Deviation (from the Protocol)	Any change to a process, procedure, test or other requirement stated in an approved protocol. See also Protocol Violation.
Digital Signature	An electronic signature based upon cryptographic methods of originator authentication, computed by using a set of rules and a set of parameters such that the identity of the signer and the integrity of the data can be verified.
Direct Access	Permission to examine, analyze, verify, and reproduce any records and reports that are important to evaluation of a clinical study. 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.
Direct Entry	Recording data where an electronic record is the original capture of the data. Examples are the keying by an individual of original observations into the system, or automatic recording by the system of the output of a balance that measures subject's body weight. In these cases, the electronic document is the source document.
Disability	For FDA safety reporting purposes, a substantial disruption of a person's ability to conduct normal life functions.
Disclosure	The external release, transfer, provision of access to, or divulging in any other manner, of PHI by a CE. (HIPAA)
Documentation	All records, in any forms (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 study, the factors affecting a study, and the actions taken.
Effective Date	The date on which an SOP or other document becomes available for use by personnel, after documented training.
Electronic Case Report Form	(e-CRF) An auditable electronic record that is used in place of or in conjunction with the paper CRF defined above.
Electronic Media	The mode of electronic transmission. It includes the Internet (wide-open), Extranet (using Internet technology to link a business with information only accessible to collaborating parties), leased lines, dial-up lines, private networks, and those transmissions that are physically moved from one location to another using magnetic tape, disk, or compact disk media.
Electronic Patient Diary	An electronic record into which a subject participating in a clinical study directly enters observations or directly responds to an evaluation checklist.
Electronic Record	Any combination of text, graphics, data, audio, pictorial, or other information representation in digital form that is created, modified, maintained, archived,

	retrieved, or distributed by a computer system.
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.
Eligibility	The determination that a potential subject satisfies or meets the enrollment criteria for inclusion into a clinical study. Subjects not meeting the criteria are ineligible to participate in the study.
Enrollment	The point at which a potential subject, who has met the enrollment criteria and any other study screening processes, has completed the informed consent process, and is ready to actively participate in a study.
Enrollment Criteria	A set of specific criteria (demographic, physical, laboratory) that determine whether or not a potential subject can be enrolled into a clinical study. They may also be referred to as inclusion and exclusion criteria.
Essential Documents	All the documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.
FDA-Regulated Human Subject Research	Any research conducted on human subjects using investigational drugs, biologics and medical devices that is intended to support an application to the agency.
Form	A tool used to facilitate the implementation of SOPs, e.g., to record data and information required by an SOP.
Good Clinical Practice	(GCP) A standard established by the International Conference on Harmonisation (ICH) for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical studies that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of study subjects are protected.
Good Laboratory Practice	(GLP) Refers to the FDA regulation 21 CFR 58, Good Laboratory Practice for Non-clinical Laboratory Studies. No clinical laboratory study means in vivo or in vitro experiments in which investigational products are studied prospectively in test systems under laboratory conditions to determine their safety. The term does not include studies utilizing human subjects or clinical studies or field trials in animals. The term does not include basic exploratory studies carried out to determine whether an investigational product has any potential utility or to determine physical or chemical characteristics of the investigational product.
Health Oversight Agency	An agency or authority of the United States, or State that is authorized by law to oversee the health care system (whether public or private) or government programs in which health information is necessary to determine eligibility or compliance, or to enforce civil rights laws for which health information is relevant.
Impartial Witness	A person who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the subject or the subject's legally authorized representative cannot read, and who reads the informed consent form and any other written information supplied to the subject.
IND Amendment	Refers to the submission to FDA of a change or an addition to an IND that is currently in effect.
Independent Data Monitoring Committee	(IDMC) See Data Monitoring Committee.
Individually Identifiable Health Information	Information that is a subset of health information, including demographic information collected from an individual, and- <ul style="list-style-type: none"> · Is created or received by a health care provider, health plan, employer, or health care clearinghouse; and · Relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and · That identifies the individual; or · With respect to which there is a reasonable basis to believe the information can be used to identify the individual. (HIPAA)

Informed Consent	The process by which a subject voluntarily confirms his or her willingness to participate in a particular study, after having been informed of all aspects of the study 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 (ICF).
Informed Consent Form	(ICF) The form on which the process of conducting and achieving informed consent from potential study subjects is documented.
Initiation Visit	A meeting between the sponsor representative(s) and investigator(s) (and other key personnel), at which the objectives and the methodology of the clinical study are defined, regulatory requirements are reviewed, and appropriate training of the site's key personnel is conducted.
Inspection	The act by a regulatory authority of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority to be related to the clinical study and that may be located at the site of the study, at a sponsor's and/or CRO's facilities, or at other establishments deemed appropriate by the regulatory authority.
Institutional Biosafety Committee	(IBC) A committee that reviews, approves, and oversees clinical research studies in accordance with the responsibilities defined in the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines).
Institutional Review Board	(IRB) 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 research study by, among other things, reviewing, approving, and providing continuing review of studies, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the study subjects.
Interim Study Report	A report of intermediate results and their evaluation based on analyses performed during the course of a study.
International Conference on Harmonisation	(ICH) A tripartite group comprised of representatives from industry and regulatory agencies from the European Union, Japan and the United States, that seeks to harmonize regulatory requirements for pharmaceutical products.
Investigational Drug Product	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical study, 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.
Investigational New Drug	(IND) Refers to the regulations in 21 CFR 312. An IND that is in effect means that a 30 day has elapsed from the date that a complete IND application was submitted to FDA and an appropriate IRB has reviewed and approved the sponsor's clinical study, all the requirements under 21 CFR 312 are met, and an investigational product can be distributed to investigators.
Investigator	A person who participates in the conduct of the clinical study at a study site. If a team of individuals at a site conducts a study, the investigator who is the responsible leader of the team may be called the principal investigator (PI).
Investigator's Brochure	(IB) A document that is provided by a clinical study sponsor to investigators participating in that study. It is a compilation of the clinical and non-clinical data on the investigational product(s), which is relevant to the study of the investigational product(s) in human subjects.
Key Personnel	As defined by NIH, all individuals responsible for the design and conduct of a research study.
Label	According to FDA, a display of written, printed, or graphic matter upon the immediate container of any article.
Labeling	According to FDA, all labels and other written, printed, or graphic matter upon any article or any of its containers or wrappers, or accompanying such article.
Lead Monitor	See Monitor (noun).
Legally Authorized	An individual, judicial or other body authorized under applicable law to consent, on

Representative	behalf of a prospective subject, to the subject's participation in the procedures(s) involved in the research. The term is synonymous with Legally Acceptable Representative.
Life-threatening Adverse Drug Experience	For FDA safety reporting purposes, any adverse drug experience that places the subject, 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.
Minor Protocol Changes	Editorial changes and the correcting of typographical errors, which do not affect a study design. Changes to study design are not considered minor changes, e.g., changing enrollment criteria or capturing additional data not specified in the original protocol.
Monitor (noun)	The person who periodically oversees the progress of a clinical study, and ensures that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory requirement(s). The Lead monitor is the monitor who assumes a supervisory role when more than one monitor participates in the monitoring of a clinical study.
Monitor or Monitoring (verb)	The act of overseeing the progress of a clinical study, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory requirement(s).
Monitoring Report	A written report from the monitor to the sponsor after each monitoring visit and/or other study-related communication according to the sponsor's SOPs.
Multicenter Study	A clinical study conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.
New Drug Application	(NDA) An FDA submission for marketing approval of new drugs.
No clinical Laboratory Study	In vivo or in vitro experiments in which investigational products are studied prospectively in test systems under laboratory conditions to determine their safety. The term does not include studies utilizing human subjects or clinical studies or field trials in animals. The term does not include basic exploratory studies carried out to determine whether an investigational product has any potential utility or to determine physical or chemical characteristics of the investigational product. See also GLP.
Noncontrolled Document	A working form or other tool (e.g., checklist, log) that once developed, may be modified as necessary, provided a list of modifications is maintained.
Objective Evidence	Verifiable qualitative or quantitative information, records or factual statements pertaining to an item or process, and used by an auditor to support an observation made during an audit.
Observation	A statement of fact made during an audit and substantiated with objective evidence.
Participant	See Subject.
Phase 1 Study	The initial introduction of an investigational new drug/biologic into humans, Phase 1 studies are primarily designed to evaluate safety and are usually include healthy subjects (depending on a number of factors, including expected toxicity and side effects, may be conducted using subjects with the disease or condition under study). Data from Phase 1 studies are used to determine the metabolism and pharmacologic actions of the drug/biologic in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
Phase 2 Study	Conducted subsequent to Phase 1, Phase 2 studies are designed to evaluate the effectiveness of the drug/biologic for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks associated with the drug/biologic. Phase 2 studies are typically well-controlled, closely monitored, and conducted in a relatively small number of patients, usually involving no more than several hundred subjects.
Phase 3 Study	Phase 3 studies are performed after preliminary evidence suggesting effectiveness of the drug/biologic has been obtained. and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug/biologic and to provide an adequate basis for

	physician labeling. Phase 3 studies are expanded controlled and uncontrolled studies that usually include from several hundred to several thousand subjects. .
Phase 4 Study	Phase 4 are conducted after marketing approval has been granted. Also known as post-marketing studies, they may be conducted as a condition of marketing approval or at a sponsor's initiative. Since many more patients receive the drug/biologic once it is approved for use than received it during the formal clinical investigation phases, less common toxicities may be recognized. Populations not specifically targeted in the earlier phases of investigation may be included in Phase 4 studies.
Principal Investigator	(PI) See Investigator.
Proprietary Interest (in the Product)	Property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement.
Protected Health Information	(PHI) Individually identifiable health information that is- <ul style="list-style-type: none"> • Transmitted by electronic media; • Maintained in any medium described in the definition of <i>electronic media</i> • Transmitted or maintained in any other form or medium. (HIPAA)
Protocol	A document that describes the objective(s), design, methodology, statistical considerations, and organization 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.
Protocol Amendment	Any revision to a previously approved protocol for an investigation of an unapproved drug, biologic or medical device, or any change of investigator or subinvestigator that must be reported to regulatory authorities. Minor editorial or typographical changes or corrections are not considered a protocol amendment.
Protocol Violation	Any deviation from an approved protocol, except if intended to eliminate a hazard to subjects or to protect the life or well-being of subjects in an emergency.
Protocol Waiver	An authorization to deviate from an approved protocol.
Protocol-Related Procedures	Any examination, interview or test that is performed for the sole purpose of determining a subject's eligibility to participate in a clinical study (screening), or once enrolled, performed on the subject as part of the study protocol. Protocol-related procedures may not be conducted until the potential subject has given informed consent. However, if in the course of routine medical care certain examinations, procedures or tests are being or have been performed, these may be used to assess eligibility if allowed by protocol, even if they were not obtained as a direct result of screening for a specific protocol.
Public Health Authority	An agency or authority of the United States, or a State that is responsible for public health matters as part of its official mandate, or a person or entity acting under a grant of authority from such public agency. (EUD equivalent – Competent Authority)
Quality Assurance	(QA) 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 in compliance with GCP and the applicable regulatory requirement(s).
Quality Control	(QC) 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.
Randomization	The process of assigning study subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.
Record	Any item, collection, or grouping of information that includes protected health information and is maintained, collected, used, or disseminated by or for a CE. (HIPAA)
Regulatory Authorities	Bodies having the power to regulate. In the ICH GCP Guidelines the expression regulatory authorities includes the authorities that review submitted clinical data and those that conduct inspections, such as FDA. In the European Union, these bodies are sometimes referred to as competent authorities.

Regulatory Master File	(RMF) The term used in this template to designate a file, which is maintained by the sponsor, that contains the documentation verifying that a clinical trial has been conducted in accordance with regulatory requirements.
Research	A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.
Screening	A planned examination and/or interview process of a potential subject to assess his/her eligibility for enrollment in a clinical study.
Screening Failure	When a potential subject does not meet one or more criteria for inclusion in a clinical study.
Serious Adverse Drug Reaction (or Experience)	<p>For FDA safety reporting purposes, any adverse drug experience occurring at any dose that results in any of the following outcomes:</p> <ul style="list-style-type: none"> • Death, • A life-threatening adverse drug experience, • Inpatient hospitalization or prolongation of existing hospitalization, • A persistent or significant disability/incapacity, or • A congenital anomaly/birth defect. <p>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 hospitalization, or the development of drug dependency or drug abuse.</p> <p>The term "serious adverse event" (serious AE) is used consistently in this template in place of serious adverse drug reaction or experience.</p>
Serious Adverse Event	<p>For OBA safety reporting purposes, any event occurring at any dose that results in any of the following outcomes</p> <ul style="list-style-type: none"> • Death, • A life-threatening event, • Inpatient hospitalization or prolongation of existing hospitalization, • A persistent or significant disability/incapacity, • A congenital anomaly/birth defect. <p>An important medical event that may not result in death, be life-threatening, or require hospitalization may be considered a serious AE when, upon the basis of appropriate medical judgment, the event may jeopardize the human gene transfer research subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.</p>
Severity Definitions	<p>The severity of adverse changes in physical signs or symptoms may be classified as follows:</p> <ul style="list-style-type: none"> • Mild – Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required. • Moderate – Mild to moderate limitation in activity, some assistance may be needed; no or minimal medical intervention/therapy required. • Severe – Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalizations possible. • Life threatening – Extreme limitation in activity, significant assistance required; significant medical intervention/therapy required, hospitalization or hospice care probable.
Significant Equity Interest	Any ownership interest, stock options, or other financial interest whose value

(in a sponsor of a covered study)	cannot be readily determined through reference to public prices (generally, interests in a non-publicly traded corporation), or any equity interest in a publicly traded corporation that exceeds \$50,000 during the time the investigator is carrying out the study and for one year following completion of the study.
Significant Payments (of Other Sorts)	Payments made by a sponsor of a covered study to the clinical investigator or the institution to support activities of the clinical investigator that have a monetary value of more than \$25,000, exclusive of the costs of conducting the clinical study or other clinical studies, (e.g., a grant to fund ongoing research, compensation in the form of equipment or retainers for ongoing consultation or honoraria) during the time the clinical investigator is carrying out the study and for one year following the completion of the study.
Source Data	All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical study/trial necessary for the reconstruction and evaluation of the study. Source data are contained in source documents (original records or certified copies).
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 medico-technical departments involved in the clinical study).
Sponsor	An individual, company, institution or organization that takes responsibility for the initiation, management, and/or financing of a clinical study.
Sponsor-Investigator	An individual who both initiates and conducts, alone or with others, a clinical study, 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.
Standard Operating Procedure	(SOP) A document that specifies all the operational steps, acceptance criteria, personnel responsibilities, and materials required to accomplish a task.
Subinvestigator	Any individual member of the clinical study team designated and supervised by the investigator at a study site to perform critical study-related procedures and/or to make important study-related decisions (e.g., associates, residents, research fellows).
Subject	An individual who participates in a clinical study, either as a recipient of the investigational drug or medical device, or as a control. The terms subject and participant are used synonymously.
Subject Identification Code	A unique identifier assigned by the investigator to each study subject to protect the subject's identity and used in lieu of the subject's name when the investigator reports AEs and/or other study-related data.
Template	A document that contains all the required elements and format for another final, controlled document, e.g., the SOP Template.
Test Article	For AE reporting, a product given to a study subject, including the investigational product, a comparator or a placebo.
Treatment (in the context of clinical research)	The period of use of any investigational product, including comparators and placebo, administered during the course of the study and during a period extending to four weeks after the last dose, or longer if necessitated by the half-life of the test drug. It does not include placebo run-in periods or non-drug periods prior to randomization, unless defined otherwise in the protocol or other study-specific document.
Treatment (in the context of the Privacy Rule)	The provision, coordination, or management of health care and related services by one or more health care providers, including: <ul style="list-style-type: none"> • Coordination or management of health care by a health care provider with a third party

	<ul style="list-style-type: none"> • Consultation between health care providers relating to a patient; or • Referral of a patient for health care from one health care provider to another. (HIPAA)
Treatment-Emergent AEs	AEs that occur after the start of dosing in a clinical study or are present prior to the start of dosing but are reported at an increase in severity after the start of dosing. These AEs are considered treatment emergent. An example could be mild headache that was present prior to dosing. After dosing is initiated, the patient reports a severe headache. This change in severity allows this AE to be defined as treatment-emergent.
Treatment Use	Any use of an investigational drug/biologic/medical device in a patient who is not otherwise enrolled as a subject in a clinical study of that investigational product, but who has a serious or life-threatening disease or condition that qualifies him/her for that treatment use.
Unexpected	An adverse drug experience that has not been previously observed and included in the Investigator's Brochure (IB). If the adverse drug experience has been previously observed but not included in an updated IB, then it continues to be reported as unexpected.
Unexpected Adverse Drug Experience (Reaction)	For FDA safety reporting purposes, any adverse drug experience, the specificity or severity of which is not consistent with the current IB; or, if an IB 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 IB only referred to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the IB only listed cerebral vascular accidents.
Unexpected Serious Adverse Event	For OBA safety reporting purposes, any serious AE for which the specificity or severity is not consistent with the risk information currently available in the protocol.
Violation (of the Protocol)	See Protocol Violation.
Vulnerable Subject	An individual whose willingness to volunteer in a clinical study 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 company; 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.
Waiver	See Protocol Waiver.
Waiver of Authorization	An alteration to or waiver, in whole or in part, of the individual authorization required by §164.508 for use or disclosure of protected health information in accordance with 45 CFR 164.512 (i) (HIPAA)
Well-being (of the Subjects)	The physical and mental integrity of the subjects participating in a clinical study.

Note: Most definitions are adapted from the International Conference on Harmonisation; Good Clinical Practice: Consolidated Guideline (E6) Glossary, as published in the *Federal Register*, Volume 62, No. 90, May 9, 1997, from Title 21 of the Code of Federal Regulations, FDA or from 45 CFR 46, HHS. Terms and definition that are applicable to the HIPAA Privacy Rule are from 45 CFR 164 (HHS).

1. The definition of Authorization is from the Office for Civil Rights, Privacy Rule Guidance, Questions and Answers, URL <www.hhs.gov/ocr/hipaa/privacy.html> (answer ID 264).