



ACE. Adverse Clinical Event

ADME. Absorption, distribution, metabolism, and excretion. *See pharmacokinetics.*

Adverse drug reaction (ADR). In the pre-approval clinical experience with a new medicinal product or its new usage, 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.

Adverse event, adverse experience (AE). 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 unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product. See the ICH Guideline for Clinical Safety Data Management: Definitions and Standards for Expedited Reporting).

Adverse reaction. Unwanted physical and/or psychological symptoms and signs resulting from treatment. *Synonyms: adverse drug reaction, ADR.*

Area under the curve (AUC). A statistical method for determining percentiles. In drug development, used to plot the concentration of drug against time. The area under the curve provides a means of comparing bioavailability profiles.

Audit (of a clinical trial). A comparison of raw data and associated records with the interim or final report in order to determine whether the raw data have been accurately reported, to determine whether testing was carried out in accordance with the protocol and standard operating procedures (SOP), to obtain additional information not provided in the final report, and to establish whether practices were employed in

the development of data that would impair their validity.

Audit trail. The documentation of events at each step of a clinical trial process and used by auditors to trace the source and determine the authenticity of clinical trial data.

Bioavailability. Rate and extent to which a drug is absorbed or is otherwise available to the treatment site in the body.

Bioequivalence. Scientific basis on which generic and brandname drugs are compared. To be considered bioequivalent, the bioavailability of two products must not differ significantly when the two products are given in studies at the same dosage under similar conditions.

Blind study. (or masked study) One in which the patient or the investigator (or both) is unaware of what trial product a patient is taking.

Case Report Form (CRF). Standard record of data and other information about each subject in a trial. Records may be on paper or magnetic or optical media, such as floppy disks or CD-WORM.

CBER. FDA Center for Biologics Evaluation and Research.

CCRA. Certified clinical research associate. A study coordinator or data manager who has achieved certification by either Associates of Clinical Research Professionals (ACRP) or Society for Clinical Research Associates (SOCRA) by passing certification examinations and maintaining continuing education units.

CCRC. Certified clinical research coordinator. A study coordinator who has achieved certification by either Associates of Clinical Research Professionals (ACRP) or Society for Clinical Research Associates (SOCRA) based on years of clinical research experience, by passing certification examinations and maintaining continuing education units.

CDER. FDA Center for Drug Evaluation and Research.

CFR. Code of Federal Regulations (usually cited by part and chapter, as 21 CFR 211).



CLIA. Clinical Laboratory Improvement Act of 1988 (USA).

Clinical investigation. Systematic study of a test article (treatment, drug, or device) in one or more human subjects. *Synonym: clinical trial.* (CFR 50.3)

Clinical research coordinator (CRC). Person who handles most of the administrative responsibilities of a clinical trial; acts as liaison between investigative site and sponsor; reviews all data and records before monitor's visits. *Synonyms: trial coordinator, study coordinator, research coordinator, clinical coordinator.*

Clinical significance. Change in a subject's clinical condition regarded as important whether or not due to the test article. Some statistically significant changes (in blood tests, for example) have no clinical significance. Criteria for clinical significance should be stated in the protocol. *See also statistical significance.*

Clinical trial/study. Any investigation in human subjects intended to discover or verify the clinical, pharmacological, and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and/or to study absorption, distribution, metabolism, and excretion of an investigational product(s) with the object of ascertaining its safety and/or efficacy. The terms "clinical trial" and "clinical study" are synonymous.

C_{max}. Maximum concentration of drug.

Comparator drug. The product (usually a standard treatment or placebo) against which an investigational product is compared in a comparative study.

Contract research organization (CRO). Company or institution that contracts to conduct research tasks and assume research responsibilities for a sponsor.

Controlled study. A study in which a test article is compared with a treatment that has known effects. The control group may receive no treatment, or placebo.

CPMP. Committee for Proprietary Medicinal Products.

CRA. Clinical research associate.

CRC. Clinical research coordinator. *See also CCRC.*

CRO. Contract research organization.

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 adopted by the 18th World Medical Assembly (Helsinki, Finland, 1964) and revised by the 29th (Tokyo, 1975), 35th (Venice, Italy, 1983), and 41st (Hong Kong, 1989) World Medical Assemblies. The full text is in 21 CFR 312.120, in an appendix to the Nordic Council on Medicines Guidelines for Good Clinical Practice, and in other reference materials.

DHHS. Department of Health and Human Services

Dosage regimen. (a) The number of doses per given time period; (b) the time that elapses between doses (for example, every six hours) or the time that the doses are to be given (for example, at 8 a.m. and 4 p.m. daily); or (c) the amount of a medicine (the number of capsules, for example) to be given at each specific time of dosing.

Double-blind study. A study in which neither the subject nor the investigators know what treatment a subject is receiving.

Drug brochure. *See investigator's brochure.*

DSMB. Data and Safety Monitoring Board. (sometimes called SMC – Safety Monitoring Committee or DMC – Data Monitoring Committee.)

Effectiveness. The desired measure of a drug's influence on a disease condition. Effectiveness must be proven by substantial evidence consisting of adequate and well-controlled investigations, including human studies by qualified experts, that prove the drug will have the effect claimed on its labeling.



Efficacy. A product’s ability to produce beneficial effects on the course or duration of a disease.

Endpoint. An indicator measured in a subject or biological sample to assess safety, efficacy, or another trial objective. Some endpoints are derived from primary endpoints (for example, cardiac output is derived from stroke volume and heart rate). *See also Surrogate marker.*

Exclusion criteria. A list of requirements and characteristics, any one of which excludes a potential subject from participation in a study.

EU. European Union.

FDA. Food and Drug Administration

First-in-human study. The first Phase 1 study in which the test product is administered to human beings.

GCP. Good Clinical Practices.

GCRC. General Clinical Research Centers

GLP. Good Laboratory Practices.

GMP. Good Manufacturing Practices.

Healthy volunteer. A healthy person who agrees to participate in a clinical trial for reasons other than medical and who receives no direct health benefit from participating.

HHS. U.S. Department of Health and Human Services.

Human subject. An “individual who is or becomes a participant 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). *Synonym: subject.*

ICH. International Conference on Harmonization.

IDE. Investigational device exemption.

Inclusion criteria. Requirements that prospective subjects must meet to be eligible for participation in a study.

IND. Investigational new drug application that sponsor companies must submit to FDA before beginning tests of a new drug in humans.

Independent ethic committee (IEC). *See institutional review board.*

Informed consent. Investigators must obtain legally effective informed consent from each subject or subject’s legally authorized representative. Requests for consent must take place under circumstances that minimize the possibility of undue influence and that provide prospective subjects and representatives sufficient opportunity to consider potential risks and benefits explained in language they can understand. No informed consent 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” (21 CFR 50.20).

Institutional review board (IRB). An IRB is a board, committee, or other group formally designated by an institution to review biomedical research involving human subjects. It reviews the protocol, approves initiation of and periodically reviews the conduct of such research. It must include at least five people, both men and women, and represent more than one profession. At least one member must have a nonscientific background, and at least one member must be independent of, and familiarly unrelated to the institution. No IRB member may participate in any review in which they may have a conflict of interest. *Synonym: independent ethics committee.*

International Air and Transport Association (IATA) The governing body that creates the regulations for international air transport

Investigational device exemption (IDE). CDRH equivalent of an IND.

Investigational new drug application (IND). The application CBER or CDER must approve before a sponsor can begin studies of new drugs or biologics.

Investigator. The individual under whose immediate direction a test product is



administered, or dispensed to, or used involving a subject or the responsible leader (principal investigator) of a team of investigators. (CFR 50.3)

Investigator’s brochure (IB). Document provided to investigators by the sponsor of a clinical trial. It contains information about a drug’s formulation and, often, its structural formula. It summarizes pharmacokinetic and pharmacodynamic data from animal studies and any earlier trials in human subjects, safety and effectiveness data, and, on the basis of prior studies, describes potential risks and side effects. It also recommends precautions or special monitoring appropriate to the investigational use of the product under study. When new data emerge during the course of the trial, information in the brochure is updated.

Legally authorized representative. *See representative.*

Manual of Operating Procedures (MOP) Text *providing an expansion of the protocol – proving additional information on how to conduct the study. Often monitored as closely as the protocol.*

Medical report. A complete and comprehensive description of the trial after its completion including a description of experimental (including statistical) methods and materials, a presentation and evaluation of the results, statistical analyses, and critical statistical appraisal.

Meta-analysis. A statistical process for pooling data from many clinical trials to glean a clear answer.

Monitor. Person (usually employed by sponsor) responsible for determining that a trial is being conducted according to the protocol.

MOU. Memorandum of understanding (between FDA and a regulatory agency in another country) that allows mutual recognition of inspections.

Multicenter study. A trial conducted under a single protocol but at more than one investigational site and by more than one investigator. Special issues in multicenter trials

include a need to balance treatments at each center and to ensure consistency in assessment methods and measurements across all centers.

NCRR. National Center for Research Resources

New drug application (NDA). An application to FDA for a license to market a new drug in the United States for human use in interstate commerce. The application must contain, among other things, data from clinical studies needed for FDA review from specific technical viewpoints, including chemistry, pharmacology, medical, biopharmaceutics, statistics, and--for anti-infectives—microbiology.

NHLBI. National Heart, Lung, and Blood Institute

NHSC. National Health Service Corps

NIA. National Institute of Aging

NIAAA. National Institute of Alcohol and Alcohol Abuse

NIAID. National Institute of Allergies and Infectious Diseases (an NIH institute).

NIAMS. National Institute of Arthritis, Musculoskeletal and Skin Diseases

NICHHD. National Institute of Child and Human Development

NIDA. National Institute of Drug Abuse

NIDCD. National Institute of Deafness and Communicative Disorders

NIDDK. National Institute of Diabetes, Digestive and Kidney Diseases

NIDR. National Institute for Dental Research

NIDRR. National Institute on Disability and Rehabilitation Research

NIGMS. National Institute of General Medical Sciences

NIH. National Institutes of Health, an agency of the U.S. Department of Health and Human Services with several institutes and centers for



specific areas of research. NIH awards grants for biomedical and behavioral research projects and issues guidelines for research conduct.

NIMH. National Institute of Mental Health

NINDS. National Institute of Neurological Diseases and Stroke

NSF. National Science Foundation

p value. (statistics) The lowest level of significance at which a given null hypotheses can be rejected; that is, the necessary criterion for determining that the result probably did not happen by chance. *See statistical significance.*

Parallel trial. Volunteers are randomized to one of two differing treatment groups (usually medicine and placebo) and usually receive the assigned treatment during the entire trial. *Also called parallel group trial, parallel design trial.*

Patient. Person under a physician's care for a particular disease or condition. *See also healthy volunteer.*

Patient file. A file contains demographic and medical information about a patient or subject. It may be paper-based or a mixture of computer and paper records.

Pharmacodynamics (PD). The branch of pharmacology that studies reactions between drugs and living structures, including the processes of bodily responses to pharmacological, biochemical, physiological, and therapeutic effects.

Pharmacoeconomics. Branch of economics that applies cost-benefit, cost-effectiveness, cost-minimization, and cost-utility analyses to compare the economics of different pharmaceutical products or to compare drug therapy to other treatments. *Sometimes referred to as outcomes research.*

Pharmacogenetics. The study of the way drugs interact with genetic makeup or the genetic response to a drug.

Pharmacokinetics (PK). The study of the processes of bodily absorption, distribution,

metabolism, and excretion (ADME) of compounds and medicines.

Pharmacovigilance. A European term similar to adverse event monitoring and reporting, increasingly used in the United States because of international harmonization efforts.

Phase 1 unit. A facility designed specifically for conducting studies involving normal, healthy volunteers. It may be operated by a sponsor company, a contract research organization (CRO), or a special unit of a hospital.

Phase IIa. Pilot clinical trials to evaluate efficacy and safety in selected populations of approximately 100 to 300 patients with the disease or condition to be treated, diagnosed, or prevented. Objectives may focus on dose-response, type of patient, frequency of dosing, or numerous other characteristics of safety and efficacy.

Phase IIb. Well-controlled trials to evaluate safety and efficacy in patients with the disease or condition to be treated, diagnosed, or prevented. These trials usually represent the most rigorous demonstration of a medicine's efficacy. *Synonym: pivotal trials.*

Phase IIIa. These are conducted in populations of approximately 1000 to 3000 patients for whom the drug is eventually intended. Phase III trials generate additional safety and efficacy data in relatively large numbers of patients in both controlled and uncontrolled designs. Trials are also conducted in special groups of patients or under special conditions dictated by the nature of the medicine and disease. These trials often provide much of the information needed for the package insert and labeling of the medicine.

Phase IIIb. These trials are conducted after submission of the new drug application (NDA), but prior to the product's approval and market launch. These trials may supplement earlier trials, complete earlier trials, or may be directed toward new types of trials (for example, quality of life or marketing) or Phase IV evaluations. This is the period between submission for approval of a regulatory dossier for marketing authorization.



Phase IV. After a medicine is marketed, Phase IV trials provide additional details about the product's safety and efficacy. Formulations, dosages, durations of treatment, medicine interactions, and other factors may be evaluated, and patients from various demographic groups can be studied. An important part of many Phase IV studies is detecting and defining previously unknown or inadequately quantified adverse reactions and related risk factors. To distinguish them from well-controlled Phase IV trials and marketing studies, Phase IV studies that are primarily observational or non-experimental are frequently referred to as post-marketing surveillance.

Phases of a clinical trial. Four phases of clinical trials and medicine development exist. An Investigational medicine or product is often evaluated in two or more phases simultaneously in different trials. Also, some clinical trials may overlap two different phases.

Pivotal trials. Well-controlled trials to evaluate safety and efficacy in patients that have the disease or condition to be treated, diagnosed, or prevented. *Often referred to as Phase III trials.*

Placebo. A pharmaceutical preparation that contains no active agent. In blinded studies, it is generally made to look just like the active product.

Post-marketing surveillance. Ongoing safety monitoring of marketed drugs.

Preclinical studies. Animal studies that support Phase 1 safety and tolerance studies and must comply with good laboratory practice (GLP). 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). Because many animals have much shorter life spans than humans, preclinical studies can provide valuable information about a drug's possible toxic effects over an animal's life cycle and on its offspring.

Protocol. A document that states the rationale, objectives, statistical design, and methodology of the trial with the conditions under which it is to be performed and managed. *Synonym: Study protocol.*

Random allocation. Assignment of subjects to treatment (or control) groups in an unpredictable way. Assignment sequences are concealed, but available for disclosure in the event a subject has an adverse experience.

Randomization. A process that aims to prevent bias by secretly and arbitrarily assigning subjects to treatment or control groups.

RCT. Randomized clinical trial

Representative. Person or body (such as judicial) authorized under applicable law to consent on behalf of a prospective subject to that subject's participation in the procedure(s) involved in the research.

R&D. Research and development

Risk. In clinical trials, the probability of harm or discomfort for subjects. Acceptable risk differs depending on the condition for which a product is being tested. A product for sore throat, for example, will be expected to have a low incidence of side effects. However, unpleasant side effects may be an acceptable risk when testing a promising treatment for a life-threatening illness.

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 experience. An AE that is fatal, life-threatening, or disabling or that results in hospitalization or (in the case of an already-hospitalized patient) prolonging of hospitalization; also congenital anomalies and the occurrence of malignancies. The Nordic Guidelines for Good Clinical Trial Practice further define a serious AE as "Any experience that suggests a significant hazard, contraindication, side effect or precaution."

Source documents. Original documents, date, 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 the medico-technical departments involved in the clinical trial).

Sponsor. An individual or organization that takes responsibility for initiating, managing, and/or financing a clinical trial. When an investigator independently initiates and takes full responsibility for a trial that may subsequently become part of a marketing authorization, the investigator assumes the role of the sponsor and is often referred to as a sponsor-investigator.

Sponsor-investigator. An individual who both initiates and actually conducts—alone or with others—a clinical investigation. Under 21 CFR 50.3, the term is used only for an individual person; it does not apply to corporations or agencies.

Standard operating procedure (SOP). Standard, detailed instructions for managing a clinical trial. SOP documents provide a general framework to provide the means of efficient implementation and performance of all the functions and activities for the trial described in the SOP

Statistical significance. Level at which an investigator can conclude that observed differences are not due to chance alone; for example, a p value of .05 (also called significance at the .05 level) indicates that there is about 1 chance in 20 that the differences observed occurred by chance alone.

Study coordinator. *See clinical research coordinator.*

Study protocol. *See protocol.*

Subject. *See human subject.*

SURF. Summer Undergraduate Research Fellowships

t_{max} . Time of occurrence for maximum (peak) drug concentration.

Trial coordinator. *See clinical research coordinator.*

Volunteer. *See healthy volunteer.*

WHO. World Health Organization.