

## Clinical Trials Glossary

**ADME:** an acronym for absorption, distribution, metabolism and elimination. ADME studies determine how a drug is absorbed by the body, the chemical changes that it may undergo and how it is eliminated from the body.

**Adverse event (AE):** a bothersome event that occurs in a study participant. AEs may be related to the treatment being tested or may be due another cause (e.g., another treatment, another medical condition, an accident, or a surgery).

**Arm:** a specific type of treatment to which a group of clinical trial participants is assigned. Some clinical trials have one arm and some have two arms, while others have three or more arms. For example, a clinical trial comparing two different doses of an investigational drug versus a placebo would have three arms: participants receiving a higher dose of the investigational drug, participants receiving a lower dose of the investigational drug, and participants receiving the placebo.

**Baseline:** a point in time at the beginning of a clinical trial before the study participants receive any treatment. At the baseline, participants usually have certain types of tests. During and after treatment, the same tests may be performed and the results compared with the baseline results to see if the drug has caused changes.

**Bias:** a factor – such as a preconceived idea about the effects of the benefits and risks of a treatment or a lack of balance in selection of patients for a study – that reduces the likelihood that the study results are true. Methods such as blinding and randomization are used to limit the potential for bias.

**Bioavailability:** the portion of the dose of a drug that reaches the bloodstream. For example, if the drug is administered intravenously, its bioavailability is 100 percent; however, if the drug is administered in any other way, such as orally, topically, or through intramuscular injection, its bioavailability will decrease due to incomplete absorption.

**Bioequivalence study:** a test performed to compare the portion of a drug in the bloodstream when administered in different dosage forms.

**Biologic product:** any substance that can be used in prevention, treatment or cure of disease. Some examples include vaccines, blood, virus, toxin, antitoxin, and therapeutic serum.

**Biopsy:** the removal of cells or tissue from a patient for examination, which is usually done under a microscope. A tissue sample might be taken for genetic studies. Sometimes there is a difference between the blood genotype and the skin or other tissue genotype. This term can also refer to the tissue sample that has been obtained by such a procedure.

**Blinding:** a process used to prevent the participants, the researchers or both from knowing what specific treatment is being given to participants in a clinical trial. The process of blinding helps to reduce bias because study participants and researchers are less likely to be unconsciously influenced by the knowledge of what the study participant is actually receiving. If only the participants are blinded, the study is called a single-blind study. If both participants and researchers are blinded, the study is called a double-blind study.

**Carcinogenicity studies:** long-term studies conducted in animal models to determine a drug's likelihood of causing cancer.

**Clinical efficacy:** a compound's ability to produce the desired effect.

**Clinical pharmacology:** a science that studies properties of drugs in relation to their therapeutic value in humans.

**Clinical study or Clinical trial:** a medical experiment in human beings that helps to determine how a disease, drug, or medical device affects study participants. Clinical studies are necessary to answer specific questions about how to better diagnose, prevent, or treat a disease or condition.

**Cohort:** a group of study participants who have certain characteristics in common, such as female sex, a defined age range, or particular severity of disease. Dividing study participants into cohorts is often done as part of the analyses of study data.

**Contraindication:** a factor that makes the use of a particular drug inadvisable. For example, a person who has had an allergic reaction to penicillin in the past is considered to have a contraindication to using penicillin in the future.

**Control group:** a group of participants not receiving the investigational drug, but instead receiving a standard treatment for their disease or receiving a placebo. The results observed in the group of patients receiving the investigational drug are compared with the results observed in the control group.

**Crossover study:** a study design with two or more arms, where participants receive one treatment for a period of time and then switch over to a second treatment for a period of time. Such a study design allows the effects of the two treatments to be compared in the same patient.

**Data Monitoring Committee (DMC) or Data Safety and Monitoring Board (DSMB):** A committee of experts that periodically reviews the accumulating data from an ongoing multicenter clinical trial. Members of a DMC/DSMB must be independent, ie, they cannot be participating as investigators in the clinical trial. Based on their review, the DMC/DSMB experts advise the sponsor regarding whether it is safe and acceptable to continue with the study or whether the data suggest that the study should be modified or stopped. A DMC/DSMB may recommend that a trial be stopped if there are safety concerns or if the trial objectives have been achieved.

**Dose-ranging study:** a clinical trial in which two or more doses of an investigational drug are tested to determine which dose is likely to offer the best combination of safety and efficacy in later clinical trials or in medical care.

**Efficacy or effectiveness:** the ability of a drug to prevent, cure, or slow a disease process or to alleviate the symptoms of a disease or condition.

**Eligibility:** a determination made during the screening period for a clinical study of whether a person's participation in the trial is likely to be safe and can contribute data that will help achieve the study goals.

**Endpoint:** occurrence of a disease, symptom, sign or test result that constitutes one of the target outcomes of a clinical trial.

**Inclusion/exclusion criteria:** the factors defined in the protocol of a study that determine whether a person's participation in a clinical trial is likely to be safe and can contribute data that will help achieve the study goals. Study candidates undergo evaluation during the study screening period to determine if they meet all of the inclusion criteria and do not meet any of the exclusion criteria as defined in the protocol. These criteria usually consider such factors as age, sex, type of disease, stage of disease, previous treatment history, and other medical conditions in determining eligibility for the study.

**Informed consent (assent):** a process by which medical researchers provide necessary information to a person about a clinical study and the person voluntarily confirms his or her willingness to participate in the study. Children who are considered old enough to have a basic understanding of the study may need to provide assent to be involved in the study; a parent or legal guardian must also give informed consent for such a child to participate.

**Informed consent (assent) form:** a document that describes a clinical study to the participants (or their parents/guardians). The informed consent (assent) form includes information about the goals of the study, the study design and duration, the types of tests to be performed, the potential risks and inconveniences, the potential benefits, the possible costs or payments associated with study participation, the available alternative therapies, the rights and responsibilities of the participant, and the people to contact if the participant has questions. The informed consent (assent) form must be reviewed and signed before the participant has any study tests or treatment, including the tests performed during the screening period at the beginning of the study. Participants are given a copy of the informed consent (assent) form to take home.

**Institutional Review Board (IRB) or Independent Ethics Committee (IEC):** a board of physicians, statisticians, researchers, community advocates, and others who are responsible for ensuring the protection of the rights, safety and well-being of participants in a clinical trial at a study center. This board is called an IRB in the United States and is often called an IEC in other countries. IRB/IECs review and approve important study documents (eg, protocols, informed consent forms, study advertisements, and patient

brochures) before the start of the study, and periodically review the progress of the study while it is ongoing.

**Investigational Drug:** a drug that is being tested as a potential treatment for a disease or condition but has not yet been proven safe and effective for that use.

**Investigator:** a physician or other health care worker who carries out a clinical trial by enrolling, treating, and monitoring participants and recording the results.

**In vitro testing:** testing conducted in test tubes or other artificial environments.

**In vivo testing:** testing conducted in living animals or humans.

**Longitudinal study:** a clinical study that involves observations of the same items over long periods, often many decades. Because longitudinal studies track the same people, they are often used to study trends across the life span, to uncover predictors of certain diseases, or to track the effects of a particular treatment on a patient's condition over time.

**Multicenter study:** a study conducted at more than one location. Multicenter clinical studies are generally performed when each individual clinical trial site does not have enough study candidates to complete a large trial.

**Natural history study:** a study of the natural development of a disease or condition over a period of time. Natural history studies are usually longitudinal studies.

**New Drug Application (NDA):** the registration document through which a pharmaceutical company formally proposes that the FDA approve a new drug for manufacturing and sale. The application includes detailed reports of pharmacology, toxicology, manufacturing and chemistry as well as data from clinical trials.

**Open-label study:** a study in which the participants and the investigators know which treatment is being given. In an open-label study, there is no blinding and none of the participants receives a placebo.

**Orphan disease:** a disease or condition that affects a relatively small number of people. In the US, this defined as fewer than 200,000 people. In Europe, this is defined as fewer than five in 110,000 people.

**Orphan drug:** a drug intended to treat an orphan disease.

**Participant or subject:** a patient or healthy volunteer who participates in a clinical trial.

**Phase 1:** the initial phase of testing of an investigational drug in humans. Usually a Phase 1 clinical study is conducted in a small number of healthy volunteers or patients with a disease for which the drug may be useful. Generally, the study is designed to determine the side effects of the drug and its pharmacokinetics. Some information

regarding drug efficacy may be collected if patients with a disease participate. A phase frequently encompasses more than one clinical trial. Phase 1 sometimes is sub-divided into Phases 1a and 1b, for example when the first set of Phase 1 trials (Phase 1a) is performed in healthy volunteers and a second set of Phase 1 trials (Phase 1b) is performed in patients with a disease.

**Phase 2:** the intermediate phase of testing of an investigational drug in humans. Usually a Phase 2 clinical study conducted in patients with a disease for which the drug may be useful. Generally, the study is designed to evaluate dosing, to obtain preliminary data on the effectiveness of the drug, and to acquire more safety information. Phase 2 sometimes is sub-divided into Phases 2a and 2b. Phase 2a studies typically are smaller and shorter in duration and evaluate different drug doses to see how they affect certain tests that can indicate whether the drug is working as expected. Phase 2b studies typically enroll more patients, are of longer duration and evaluate whether the drug is offering clinical benefits to patients. Phase 2b studies sometimes are considered pivotal or registration-directed.

**Phase 3:** the final phase of testing an investigational drug in humans before regulatory approval. Phase 3 studies are usually conducted in a large population of patients and are generally designed to confirm the effectiveness of the drug and to evaluate the overall risk-benefit ratio. Phase 3 studies usually test the investigational drug in comparison with a standard treatment for the disease or a placebo.

**Phase 4:** testing of a drug in humans after it has already been approved by regulatory authorities and can be used in medical practice. Phase 4 studies may be conducted to compare the drug to a similar type of drug, to explore whether it may help patients with other diseases, to further study the long-term safety of the drug, or for other reasons.

**Pivotal study:** a study that is designed to generate the data required by regulatory authorities to decide whether to approve an investigational drug. A pivotal study is usually a large, randomized Phase 2b or Phase 3 study, and often is blinded and uses a placebo as a control. Sometimes a pivotal study is described as a registration-directed study.

**Placebo:** an inactive version of an investigational drug. A placebo has a similar appearance to the investigational drug but is expected to have no therapeutic value. A placebo is used as a comparison treatment to reduce bias in randomized studies.

**Preapproval access program:** an umbrella term for programs that allow seriously ill patients to receive an investigational drug when they are unable to participate in clinical trials and there is no alternative treatment. This is sometimes referred to as compassionate use. Types of pre-approval access programs include expanded access, parallel-track, named patient program, single-patient exemption, and treatment IND. The timing for starting an expanded access program usually depends upon what is known about the risk-benefit of the drug and whether the drug can be provided in a manner that is fair to patients with the disease.

**Preclinical (nonclinical) testing:** testing of a drug in test tubes or in animals. A drug undergoes preclinical testing before being tested in humans to make sure that it shows evidence of desired effects and is sufficiently safe for study in people. Preclinical testing sometimes also helps to determine the doses of the drug that should be evaluated in humans. Preclinical testing is sometimes called nonclinical testing.

**Protocol:** a document describing what types of people may participate in a clinical study and the objectives, treatments, measurements, statistical methods, timing, and organization of a clinical trial. The protocol must be prepared in advance of the study and must be reviewed and approved by review committees and regulatory authorities before the study is started. Investigators must follow the protocol to carry out the study.

**Randomization:** assignment of participants to treatment arms based on chance. This is usually done by a computer program in a way that does not allow either the participants or the investigators to choose who is assigned to which arm. Randomization is used to reduce bias in clinical trials.

**Risk-benefit ratio:** the balance of the risk of side effects expected with use of a drug versus the potential for benefit with the use of that drug. A drug with a good risk-benefit ratio has few side effects and is very effective.

**Serious adverse event (SAE):** an adverse event that is life-threatening, requires inpatient hospitalization or lengthens a hospital stay, leads to substantial disability, leads to a birth defect, or results in death.

**Side effect:** any effect of a drug other than the desired effect. Side effects are often unwanted and may be bothersome. Other names for a bothersome side effect are adverse drug reaction (ADR) or drug toxicity.

**Screening period:** a period at the beginning of a clinical trial when candidates for the study are evaluated to determine if their participation is likely to be safe and can contribute data that will help achieve the study goals.

**Significant or statistically significant:** an outcome in a clinical trial is likely to result from a real difference (eg, due to an effect of a treatment) and is unlikely to be due to chance alone. The level of statistical significance is often expressed in terms of a p-value, which indicates the probability that a difference is not due to chance alone. Usually, a p-value smaller 0.05 is considered statistically significant.

**Sponsor:** the organization responsible for financing and coordinating a clinical trial. Most often, this is a pharmaceutical or biotechnology company.

**Standard treatment:** a treatment currently in wide use, often approved by regulatory agencies, and generally considered effective in the treatment of a specific disease or condition.

**Toxicity:** a side effect produced by a drug that is bothersome to the person taking the drug.

**Toxicology:** the study of the adverse effects of chemicals conducted in animal models to predict potential adverse effects in humans. Some studies are conducted during clinical development to evaluate dosing regimens.