

## Glossary of Clinical Trials Terms

**ADJUVANT THERAPY:** Therapy given after primary therapy to kill cancer cells that may have begun to spread. Adjuvant therapy may be radiation, chemotherapy, or hormone therapy and is often used when the primary therapy is surgery to remove the cancer.

**ARM:** Any of the treatment groups in a randomised trial. Most randomised trials have two "arms," but some have three or even more (See **Randomised Trial**). A clinical trial comparing two doses of a new medication with a placebo would have three arms (dose 1, dose 2, and placebo).

**BASELINE:** 1. Information gathered at the beginning of a study against which variations found in the study are measured. 2. A known value or quantity with which an unknown is compared when measured or assessed. 3. The initial time point in a clinical trial, just before a participant starts to receive the experimental treatment being tested. At this reference point, measurable values such as blood counts are recorded. Safety and efficacy of a drug are often determined by monitoring changes from the baseline values.

**BIAS:** When a point of view or the conditions of a study prevents impartial judgment on issues relating to the subject of that point of view. For example, bias may occur when a study is not "blinded" or it may derive from a sampling error, e.g., when the population enrolled in the study is not representative of the overall population with the disease. In clinical studies, bias is controlled by such measures as blinding and randomisation (See **Blind** and **Randomisation**).

**BIOPSY:** The removal of a tissue sample for examination under the microscope. The tissue sample can be called a biopsy.

**BLIND OR BLINDING:** When the researchers, the participants, or both, do not know which people are getting which potential treatment being studied in a clinical trial. The process of blinding improves the reliability of a study's results because no one is unconsciously influenced by the knowledge. If only researchers or only participants are blinded, the study is often called single blind. If both researchers and participants are blinded, the study is double blind. Because the terms "single blind" and "double blind" are imprecise, many researchers prefer to specify who is blinded—investigators, participants, outcome assessors, or statisticians.

**CANCER:** A malignant growth, usually caused by a combination of genetic and environmental factors. In cancer, abnormal cells usually proliferate without responding to the normal signals that stop growth, and thus spread to tissues and organs beyond the original site.

**CELL PROLIFERATION:** An increase in the number of cells through cell growth and division and/or lack of cell death.

**CHEMOTHERAPY:** Use of cytostatic drugs (drugs that prevent cell division), or cytotoxic drugs (those that cause cell death) to treat disease, such as cancer.

**CLINICAL:** Pertaining to or founded on observation and treatment of human participants, as distinguished from theoretical or basic science.

**CLINICAL INVESTIGATOR:** A medical researcher in charge of and/or carrying out a clinical trial's protocol.

**CLINICAL TRIAL:** A clinical trial is a research study in healthy volunteers or patients that helps to determine whether a new drug or device is safe and effective. Each study is designed to answer scientific questions and tries to find better ways to screen, diagnose, prevent, or treat a disease or condition. Carefully conducted clinical trials (also called medical research and research studies) are the fastest and safest way to find treatments that work in people. (See **Phase I, II, III, and IV Trials**).

**COHORT:** In epidemiology, a group of individuals with some characteristics in common, such as age or sex.

**COMMUNITY-BASED CLINICAL TRIAL (CBCT):** A clinical trial conducted primarily through primary-care physicians or community-based oncologists rather than at academic research facilities.

**CONTRAINDICATION:** A specific circumstance under which the use of certain treatments could be harmful.

**CONTRACT RESEARCH ORGANISATION (CRO):** A company contracted by the trial's sponsor to manage specific parts of a clinical trial.

**CONTROL GROUP:** The standard by which experimental observations are evaluated. In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is given either a standard treatment for the illness or a placebo (See **Placebo** and **Standard Treatment**).

**CROSSOVER TRIAL:** A study design with two or more groups, where participants in one group receive one intervention for a period of time, then switch over to the second intervention (and vice versa—participants in the other group start with the second intervention and switch back to the first).

**DATA SAFETY AND MONITORING BOARD (DSMB):** An independent committee composed of community representatives and clinical research experts that reviews data while a clinical trial is in progress to ensure that participants are

not exposed to undue risk. A DSMB may recommend that a trial be stopped if there are safety concerns or if the trial objectives have been achieved.

**DIAGNOSTIC TRIALS:** Trials that are conducted to find better tests or procedures for diagnosing a particular disease or condition. Diagnostic trials usually include people who have signs or symptoms of the disease or condition being studied.

**DISEASE FREE SURVIVAL (DFS):** The length of time a patient survives without any detectable cancer. This may be measured from the date of randomization or enrolment.

**DOSE-RANGING STUDY:** A clinical trial in which two or more doses of an agent (such as a drug) are tested against each other to determine which dose works best and is least harmful.

**DOUBLE-BLIND STUDY:** A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, since the expectations of the doctor and the participant about the experimental drug do not affect the outcome; also called double-masked study. (See **Blinded Study, Single-Blind Study, and Placebo.**)

**DRUG RESISTANCE:** In cancer, the ability of a tumour or cancer cells to withstand the effects of treatment that should normally kill them.

**EFFECTIVE DOSE:** The dose of an investigational agent that produces the outcome considered "effective," as defined in the study protocol. This could mean a cure of the disease in question or simply the lessening of symptoms.

**EFFICACY:** A product's ability to control symptoms or produce beneficial effects on the duration or course of a disease. Efficacy is measured by evaluating the clinical and statistical results of clinical tests. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed. In general, Phase II clinical trials gauge efficacy and Phase III trials confirm it (See **Phase II Trials and Phase III Trials**).

**ELIGIBILITY:** Whether a person meets the criteria for entry into a clinical trial. Eligibility criteria are also called selection criteria. (See **Inclusion/Exclusion Criteria**).

**ENDPOINT:** An outcome or medical event that a clinical trial monitors. Common endpoints include severe toxicity, disease progression, death, or need for hospitalisation. For example, a clinical trial studying a new cancer drug might use death as an endpoint to determine if people getting the drug lived longer than those who did not get the drug.

**ETHICS COMMITTEE:** An independent group of both medical and non-medical professionals who are responsible for verifying the integrity of a study and ensuring the safety, integrity, and human rights of the study participants. Ethics Committees play a key role in the document evaluation process of clinical trials. The responsibilities of Ethics Committees are broad and include forming an opinion on the relevance of the clinical trial and the clinical trial design, the trial protocol, the suitability of the investigators and supporting staff, the investigators brochure, and the quality of facilities.

**EXPANDED ACCESS:** Refers to any procedures, such as compassionate use, parallel track, and treatment IND (investigational new drug), that distribute experimental drugs to participants who are failing on currently available treatments for their condition and also are unable to participate in ongoing clinical trials.

**EXPERIMENTAL DRUG:** A drug that is not licensed for use in humans or as a treatment for a particular condition (See **Off-Label Use**).

**FIRST LINE THERAPY:** Therapy to treat cancer that has never been treated before or as the first treatment for metastatic disease (cancer that has spread to distant parts of the body) when the disease may have already been treated by surgery, radiation therapy, and/or adjuvant therapy.

**GENERIC DRUG:** A medicinal product with the same active ingredient, but not necessarily the same inactive ingredients as a brand-name drug. A generic drug may only be marketed after the original drug's patent has expired.

**HAEMATOLOGIST:** A doctor who specialises in blood and bone marrow disorders.

**HYPOTHESIS:** A supposition or assumption advanced as a basis for reasoning or argument, or as a guide to experimental investigation.

**INCLUSION/EXCLUSION CRITERIA:** The standards determining whether a person may or may not be allowed to enter a clinical trial. These criteria are based on such factors as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. It is important to note that inclusion and exclusion criteria are not used to reject people personally, but rather to identify appropriate participants and keep them safe.

**INFORMED CONSENT:** The voluntary verification of a patient's willingness to participate in a clinical trial, along with the documentation of this decision. This verification is requested only after complete, objective information has been given about the trial, including an explanation of the study's objectives, potential benefits, risks and inconveniences, alternative therapies available, and of the subject's rights and responsibilities in accordance with the current revision of the

Declaration of Helsinki. Participants must also be provided with information throughout the study so that they can make informed decisions about remaining involved in the trial.

**INFORMED CONSENT DOCUMENT:** A document that describes the rights of the study participants and includes details about the study, such as its purpose, duration, required procedures, and key contacts. Risks and potential benefits are explained in the informed consent document. The participant then decides whether or not to sign the document. Informed consent is not a contract, and the participant may withdraw from the trial at any time.

**INTENT TO TREAT:** Analysis of clinical trial results that includes all data from participants in the groups to which they were randomised (See **Randomisation**) even if they never received the treatment.

**INTERVENTIONS:** Primary interventions being studied. Types of interventions are Drug, Gene Transfer, Vaccine, Behaviour, Device, or Procedure.

**INVESTIGATIONAL NEW DRUG:** A new drug, antibiotic drug, or biological drug that is used in a clinical investigation. This category also includes a biological product used *in vitro* for diagnostic purposes.

**IN VITRO TESTING:** Non-clinical testing conducted in an artificial environment such as a test tube or culture medium.

**IN VIVO TESTING:** Testing conducted in living animal and human systems.

**LONGITUDINAL STUDY:** A research study that involves observations of the same items over long periods of time, 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 in a patient's condition over time.

**LYMPHOMA:** Lymphoma is the name of a diverse group of cancers of the lymphatic system, a connecting network of nodes, organs, and vessels whose principle cell is the lymphocyte.

**MALIGNANT:** Cancerous cells capable of invading nearby tissue and spreading to other parts of the body.

**MAINTENANCE THERAPY:** Anti-cancer treatment given to patients in remission, after their initial or primary therapy, to delay or prevent a relapse.

**METASTASIS:** The spread of cancer cells to distant parts of the body. It is associated with more advanced disease and a poorer outlook.

**MULTICENTRE TRIAL:** A trial conducted in more than one location or city. Multicentre trials are generally larger than single-site trials and are often used for Phase III testing.

**NATURAL HISTORY STUDY:** Study of the natural development of something (such as an organism or a disease) over a period of time.

**NEUROPATHY:** Peripheral neuropathy is a condition of the nervous system that usually begins in the hands or feet with symptoms of numbness, tingling, burning and/or weakness.

**NEUTROPENIA:** Reduction in a subset of white blood cells leading to an increase in susceptibility to infection.

**NON-HODGKIN'S LYMPHOMA:** Blood cancer of the lymphatic system, which usually spreads throughout the body.

**OFF-LABEL USE:** A drug prescribed for conditions other than those for which it was approved.

**ONCOGENE:** A modified gene that increases the malignancy of a tumour cell. Some oncogenes, usually involved in early stages of cancer development, increase the chance that a normal cell develops into a tumour cell, possibly resulting in cancer.

**OPEN-LABEL TRIAL/STUDY:** A study in which all parties, (patient, physician and study coordinator) are informed of the drug and dose being administered. In an open-label study, none of the participants is given a placebo. These are usually conducted with Phase I & II studies, and often with Phase III.

**ORPHAN DRUGS:** Medications used to treat diseases and conditions that occur rarely.

**PEER REVIEW:** Review of a clinical trial by impartial experts for scientific merit, participant safety, and ethical considerations.

**PHARMACOECONOMICS:** The study of cost-benefit ratios of drugs with other therapies or with similar drugs. Pharmacoeconomic studies compare various treatment options in terms of their cost, both financial and quality-of-life. Also referred to as "outcomes research."

**PHARMACOKINETICS:** The processes (in a living organism) of absorption, distribution, metabolism, and excretion of a drug or vaccine.

**PHASE I TRIALS:** The first of four phases of clinical trials, Phase I studies are designed to establish the effects of a new drug in humans. These studies are

usually conducted on small populations of healthy humans to specifically determine a drug's toxicity, absorption, distribution and metabolism, as well as potential side effects and early evidence of effectiveness.

**PHASE II TRIALS:** After the successful completion of Phase I trials, a drug is then tested for safety and efficacy in a slightly larger population of individuals who are afflicted with the disease or condition for which the drug was developed. Phase II trials also help determine the common short-term side effects and risks.

**PHASE III TRIALS:** The third and last pre-approval round of testing of a drug is conducted on large populations of afflicted patients. Phase III studies are conducted after preliminary evidence suggesting effectiveness of the drug has been obtained, and they help gather additional information to evaluate the overall benefit-risk relationship of the drug. These studies usually test the new drug in comparison with the standard therapy currently being used for the disease in question. The results of these trials usually provide the information that is included in the package insert and labelling of the medication.

**PHASE IV TRIALS:** After a drug has been approved, Phase IV studies are conducted to compare the drug to a competitor, explore additional patient populations, or to further study any adverse events.

**PIVOTAL STUDY:** Usually a Phase III study that presents the data used to decide whether or not to approve a drug. A pivotal study will generally be well-controlled, randomised, of adequate size, and whenever possible, double-blind.

**PLACEBO:** A placebo is an inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness and rule out any psychological effects testing may present. (See **Placebo-Controlled Study**).

**PLACEBO-CONTROLLED STUDY:** A method of investigation of drugs in which an inactive substance (the placebo) is given to one group of participants, while the drug being tested is given to another group. The results obtained in the two groups are then compared to see if the investigational treatment is more effective in treating the condition. Placebo-controlled studies are rarely if ever used in clinical trials on cancer drugs.

**PLACEBO EFFECT:** A physical or emotional change, occurring after a substance is taken or administered, that is not the result of any special property of the substance. The change may be beneficial, reflecting the expectations of the participant and, often, the expectations of the person giving the substance.

**PRECLINICAL TESTING:** Before a drug may be tested on humans, experimental drugs must be tested in test tube or in animals to determine that the drug is safe.

**PREVENTION TRIALS:** Refers to trials to find better ways to prevent disease in people who have never had the disease or to prevent a disease from returning.

**PROTEASOME:** An enzyme complex found in all cells, responsible for breaking down proteins, including those involved in cell cycle regulation. Proteasome inhibition disrupts this process, leading to apoptosis or cell death.

**PROTOCOL:** A document and plan developed for each clinical trial. The plan is carefully designed to safeguard the health of the participants as well as answer specific research questions. A protocol describes what types of people may participate in the trial; the schedule of tests, procedures, medications, and dosages; and the length of the study. While in a clinical trial, participants following a protocol are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment (See **Inclusion/Exclusion Criteria**).

**QUALITY OF LIFE TRIALS (or Supportive Care Trials):** Refers to trials that explore ways to improve comfort and quality of life for individuals with a chronic illness, or an acute illness such as cancer.

**RANDOMISATION:** A method based on chance by which study participants are assigned to a treatment group. Randomisation minimises the differences among groups by equally distributing people with particular characteristics among all the trial arms. The researchers do not know which treatment is better. From what is known at the time, any one of the treatments chosen could be of benefit to the participant (See **Arm**).

**RECURRENCE:** The reappearance of a disease after a period of remission.

**REFRACTORY:** Disease that does not respond to treatment.

**RELAPSE:** The reappearance of a disease after a period of improvement.

**REMISSION:** When there is no evidence of cancer on examination. "Remission" is used instead of "cure" because doctors cannot be sure that the body is completely free of cancer.

**RISK-BENEFIT RATIO:** The risk to individual participants versus the potential benefits. The risk/benefit ratio may differ depending on the condition being treated.

**SCREENING TRIALS:** Refers to trials that test the best way to detect certain diseases or health conditions which do not have signs or symptoms of the disease or condition being studied.

**SERIOUS ADVERSE EVENT (SAE):** Any adverse event (AE) that is fatal, life-threatening, permanently disabling, or which results in hospitalisation, initial or prolonged.

**SIDE EFFECTS:** Any unanticipated actions or effects of a drug or treatment not related to the primary purpose of the drug. Negative or adverse effects may include headache, nausea, hair loss, skin irritation, or other physical problems. Experimental drugs must be evaluated for both immediate and long-term side effects. Also known as “adverse drug reactions” (ADRs) or “adverse events” (AEs). In clinical trials, side effects would also include any injuries by overdosing, abuse/dependence, and unintended interactions with other medicinal products. Researchers monitor for adverse reactions to determine a new drug's safety during a clinical trial. Onset may be sudden or develop over time.

**SIGNIFICANT OR STATISTICALLY SIGNIFICANT:** A statistical term indicating that the results of a study are stronger than would be expected from chance alone.

**SINGLE-BLIND STUDY:** A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking; also called single-masked study. (See **Blind** and **Double-Blind Study**).

**SPONSOR:** The entity responsible for conducting and financing a clinical trial. Sponsors can be governmental agencies, companies, medical or educational institutions, or even private individuals.

**STABLE DISEASE (SD):** Where patients neither improve nor get worse.

**STAGING:** Criteria used to determine the extent or stage of cancer.

**STANDARD TREATMENT:** A treatment currently in wide use and approved by regulatory agencies, such as the United States Food & Drug Administration or the Committee for Medicinal Products for Human Use (CHMP) in Europe, considered to be effective in the treatment of a specific disease or condition.

**STANDARDS OF CARE:** The benchmark or commonly accepted level/type of treatment for a disease.

**STATISTICAL SIGNIFICANCE:** The probability that an event or difference occurred by chance alone. In clinical trials, the level of statistical significance depends on the number of participants studied and the observations made, as well as the magnitude of

**STEM CELLS:** (Used in this context for blood stem cells.) Immature cells that give rise to all the normal components of blood. Stem cells are normally found in the bone marrow, but some will circulate in, and can be collected from the blood.

**STUDY TYPE:** The primary investigative techniques used in an observational protocol; types are Purpose, Duration, Selection, and Timing.

**TIME TO PROGRESSION (TTP):** The length of time after a disease is diagnosed (or treated) until the disease starts to get worse.

**TOXICITY:** An adverse effect produced by a drug that is detrimental to the participant's health. The level of toxicity associated with a drug will vary depending on the condition that the drug is used to treat. If toxicity prevents people from taking more of an experimental drug, the toxicity is called dose limiting.

**TREATMENT TRIALS:** Refers to trials which test new treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.

**WHITE BLOOD CELLS (WBC):** A general term for different types of blood cells that form part of the body's immune system.