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## HIV Vaccine Glossary

### A

**ADCC (antibody-dependent cellular cytotoxicity):** an immune response in which an infected target cell that is coated with antibody is destroyed by an immune cell.

**adjuvant:** a substance sometimes included in a vaccine formulation to enhance or modify the immune-stimulating properties of a vaccine.

**adverse event:** in a clinical trial, an unwanted effect detected in participants. The term is used whether or not the effect can be attributed to the vaccine under study.

**adverse reaction (side effect):** in a clinical trial, an unwanted effect detected in participants and attributed to the study vaccine.

**AIDS (acquired immunodeficiency syndrome):** the late stage of HIV disease, characterized by a deterioration of the immune system and a susceptibility to a range of opportunistic infections and cancers.

**ALVAC-HIV™:** a genetically engineered HIV vaccine composed of a live, weakened canarypox virus (ALVAC™) into which parts of genes for non-infectious components of HIV have been inserted. When ALVAC™ infects a human cell, the inserted HIV genes direct the cell to make HIV proteins. These proteins are packaged into HIV-like particles that bud from the cell membrane. These particles are not infectious but fool the immune system into mounting an immune response to HIV. ALVAC™ can infect but not grow in human cells, an important safety feature. (See also **canarypox**.)

**amino acid:** any of the 26 chemical building blocks of proteins.

**anamnestic response:** the heightened immunologic reaction elicited by a second or subsequent exposure to a particular pathogenic microorganism (e.g., bacterium, fungus, virus), toxin, or antigen. (See also **memory cells**.)

**anergy:** the loss or weakening of immune response to an irritating agent or antigen. Anergy can be thought of as the opposite of allergy, which is an overreaction to a substance. The strength of the immune response is often quantitatively evaluated by standardized skin tests. A small amount of solution containing an antigen known to cause a response, such as tetanus, mumps, or candida, is injected under the skin and the area checked for a localized skin reaction after 48 to 72 hours. Healthy people will develop a measurable area of redness at the injection site; people who are immune suppressed, such as people with AIDS, will have no measurable response to these skin tests.

**antibody:** an infection-fighting protein molecule in blood or secretory fluids that tags, neutralizes, and helps destroy pathogenic microorganisms (e.g., bacteria, viruses) or toxins. Antibodies, known generally as immunoglobulins, are made and secreted by B lymphocytes in response to stimulation by antigens. Each specific antibody binds only to the specific antigen that stimulated its production. (See also **immunoglobulin**; **binding antibody**; **enhancing antibody**; **functional antibody**; **neutralizing antibody**.)

**antibody-mediated immunity:** also called humoral immunity. Immunity that results from the activity of antibodies in blood and lymphoid tissue.

**antigen:** any substance that stimulates the immune system to produce antibodies. Antigens are often foreign substances such as invading bacteria or viruses. (See also **immunogen**.)

**antigen-presenting cell (APC):** B cell, macrophage, dendritic cell or other cell that ingests and processes foreign bodies such as viruses and displays the resulting antigen fragments on its surface to attract and activate the CD4+ T cells that respond specifically to that antigen. (See also **dendritic cell** ; **macrophage**.)

**anti-idiotypic:** an antibody that recognizes and binds to the antigen-binding site of another antibody. In HIV vaccines, anti-idiotypic vaccines are made from antibodies generated against antibodies to the virus.

**apoptosis:** cellular suicide, also known as programmed cell death. A possible mechanism used by HIV to suppress the immune system. HIV may cause apoptosis in both HIV-infected and HIV-uninfected immune system cells.

**arm:** a group of participants in a clinical trial, all of whom receive the same treatment, intervention or placebo. The other arm(s) receive(s) a different treatment.

**attenuated:** weakened. Attenuated viruses are often used as vaccines because they can no longer produce disease but still stimulate a strong immune response, like that to the natural virus. Examples of attenuated virus vaccines include oral polio, measles, mumps, and rubella vaccines.

**autoimmunity:** in HIV vaccination, a theoretical adverse effect in which the vaccine causes immune responses that are inappropriately directed at a person's own tissues.

## B

**B lymphocyte (B cell):** one of the two major classes of lymphocytes, B lymphocytes are white blood cells of the immune system that are derived from the bone marrow and spleen. B cells develop into plasma cells, which produce antibodies.

**baculovirus:** an insect virus used in the production of subunit vaccines. By splicing a specific HIV gene(s) into the baculovirus genome, and then combining this construct with insect cells, mass quantities of the purified HIV protein(s) coded for by these two HIV gene(s) can be made by the cells for use as a vaccine. (See also **expression system**.)

**baseline:** the time point in a study just before initiation of intervention (vaccination) when starting measurements are taken. Measurements taken at later time points may be

compared with those taken at baseline to study variations.

**binding antibody:** an antibody that attaches to some part of HIV. Binding antibodies may or may not lead to the killing of the virus.

**blinded study:** a clinical trial in which participants are unaware as to whether or not they are in the experimental or control arm of the study. (See also **double-blind study**.)

**booster:** a second or later vaccine dose given after the primary dose(s) to increase the immune response to the original vaccine antigen(s). The vaccine given as the booster dose may or may not be the same as the primary vaccine. (See also **prime-boost**.)

**bDNA (branched DNA) assay:** laboratory test for measuring the amount of virus in blood plasma. The test detects an amplified luminescent signal whose brightness depends on the amount of viral RNA present.

**breakthrough infection:** an infection, which the vaccine is intended to prevent, that occurs in a volunteer during the course of a vaccine trial. Such an infection is caused by exposure to the infectious agent and may occur before or after the vaccine has taken effect or all doses have been given.

## C

**canarypox:** a virus that infects birds and is used as a live vector for HIV vaccines. It can carry a large quantity of foreign genes. Canarypox virus cannot grow in human cells, an important safety feature. (See also **ALVAC- HIV™**; **vector**.)

**CD:** abbreviation for "cluster of differentiation," referring to cell surface molecules that are used to identify stages of maturity of immune cells, for example, CD4+ T cells.

**CD4<sup>+</sup> T lymphocyte:** immune cell that carries a marker on its surface known as "cluster of differentiation 4" (CD4). These cells are the primary targets of HIV. Also known as helper T cells, CD4<sup>+</sup> T cells help orchestrate the immune response, including antibody responses as well as killer T cell responses. (See also **T cell**.)

**CD8<sup>+</sup> T lymphocyte:** immune cell that carries the "cluster of differentiation 8" (CD8) marker. CD8 T cells may be cytotoxic T lymphocytes or suppressor T cells. (See also **cytotoxic T lymphocyte (CTL)**; **T cell**.)

**cell-mediated immunity (cellular immunity):** the immune response coordinated by helper T cells and CTLs. This branch of the immune system targets cells infected with microorganisms such as viruses, fungi and certain bacteria.

**challenge:** in vaccine experiments, the deliberate exposure of an immunized animal to the infectious agent. Challenge experiments are **never** done in human HIV vaccine research.

**CHO (Chinese hamster ovary) cell:** a cell used as a "factory" in genetic engineering to make certain subunit vaccines. CHO cells are derived from mammals and are advantageous because they add carbohydrates (a sugar coat) to the protein, much like naturally infected human cells do.

**clade:** also called a subtype. A group of related HIV isolates classified according to their degree of genetic similarity (such as of their envelope proteins). There are currently two groups of HIV-1 isolates, M and O. M consists of at least nine clades, A through I. Group O may consist of a similar number of clades. (See also **isolate**.)

**cohort:** groups of individuals who share one or more characteristics in a research study and who are followed over time. For example, a vaccine trial might include two cohorts, a group at low risk for HIV and a group at higher risk for HIV.

**complement:** blood proteins that play an important role in the immune response. Generally, complement proteins amplify the effects of antibodies and inflammation.

**control:** in vaccine clinical trials, the control group is given either the standard treatment for the disease or an inactive substance called a placebo. The control group is compared with one or more groups of volunteers given experimental vaccines to detect any effects of the vaccines.

**core:** the protein capsule surrounding a virus' DNA or RNA. In HIV, p55, the precursor molecule to the core, is broken down into the smaller molecules p24, p17, p7 and p6. HIV's core is primarily composed of p24.

**correlates of immunity (correlates of protection):** the immune responses that must be present to protect an individual from a certain infection. The precise correlates of immunity in HIV transmission are unknown.

**cytokine:** a soluble, hormone-like protein produced by white blood cells that acts as a messenger between cells. Cytokines can stimulate or inhibit the growth and activity of various immune cells. Cytokines are essential for a coordinated immune response and can also be used as immunologic adjuvants. HIV replication is regulated by a delicate balance among cytokines.

**cytoplasm:** the living matter within a cell (excluding the nucleus) that is responsible for the function of the cell (for example, protein synthesis).

**cytotoxic T lymphocyte (CTL):** immune system cell that can destroy cancer cells and cells infected with viruses, fungi or certain bacteria. CTLs, also known as killer T cells, carry the CD8 marker. CTLs kill virus-infected cells, whereas antibodies generally target free-floating viruses in the blood. CTL responses are a proposed but unproven correlate of HIV immunity. (See also **CD8+ T lymphocyte**.)

## D

**deletion:** elimination of a gene either in nature or in the laboratory.

**dendritic cell:** immune cell with threadlike tentacles called dendrites used to enmesh antigen, which they present to T cells. Langerhans cells, found in the skin, and follicular dendritic cells, found in lymphoid tissues, are both types of dendritic cells. (See also **antigen-presenting cell**.)

**DNA (deoxyribonucleic acid):** the double-stranded, helical molecular chain found within the nucleus of each cell. DNA carries the genetic information that encodes proteins and

enables cells to reproduce and perform their functions.

**DNA vaccine (nucleic acid vaccine):** direct injection of a gene(s) coding for a specific antigenic protein(s), resulting in direct production of such antigen(s) within the vaccine recipient in order to trigger an appropriate immune response.

**domain:** a region of a gene or gene product. A neutralizing domain is a specific site on the virus to which a neutralizing antibody is directed.

**dose-ranging study:** a clinical trial in which two or more doses (starting at a lower dose and proceeding to higher doses) of a vaccine are tested against each other to determine which dose works best and has acceptable side effects.

**dose-response relationship:** the relationship between the dose of a vaccine and an immune or physiologic response. In vaccine research, a dose-response effect means that as the dose of the vaccine increases, so does the level of the immune response (antibodies and CTL activity).

**double-blind study:** a clinical trial in which neither the study staff nor the participants know which participants are receiving the experimental vaccine and which are receiving a placebo or another therapy. Double-blind trials are thought to produce objective results, since the researcher's and volunteer's expectations about the experimental vaccine do not affect the outcome.

**DSMB (Data and Safety Monitoring Board):** a committee of independent clinical research experts who review data while a clinical trial is in progress. The DSMB ensures that participants are not exposed to undue risk and looks for any differences in effectiveness between the experimental and control groups. The DSMB may review the data in such a way that they know which group received the vaccine and which group did not. This group may also recommend that a trial be modified or stopped if there are safety concerns or if the trial objectives have been achieved.

## E

**EBV (Epstein-Barr Virus) cell line:** a herpesvirus; in vaccine research, used to make target cells for CTL assays.

**efficacy:** in vaccine research, the ability of a vaccine to produce a desired clinical effect, such as protection against a specific infection, at the optimal dosage and schedule in a given population. A vaccine may be tested for efficacy in Phase 3 trials if it appears to be safe and shows some promise in smaller Phase 1 and 2 trials.

**ELISA (enzyme-linked immunoabsorbent assay):** a blood test that detects antibodies based on a reaction that leads to a detectable color change in the test tube. The HIV ELISA is commonly used as the initial screening test because it is relatively easy and inexpensive to perform. Because the HIV ELISA is designed for optimal sensitivity – that is, it detects all persons with HIV antibodies as well as some who don't have them (false positives) – a positive HIV ELISA test must be confirmed by a second, more specific test such as an HIV Western Blot.

**empirical:** based on experience or observational information and not necessarily on proven scientific data. In the past, vaccine trials have been performed based exclusively

on empirical data and without a full understanding of the disease processes or correlates of immunity.

**emulsion:** a suspension of droplets of one liquid in another liquid (such as oil and water). The two liquids do not actually combine but are instead suspended within one another.

**endpoint:** the results of an intervention such as vaccination compared among different study groups in a clinical trial. In early vaccine trials, common endpoints are safety and specific types and intensities of immune responses (neutralizing antibodies, CTL responses).

**enhancing antibody:** a type of binding antibody, detected in the test tube and formed in response to HIV infection, that may enhance the ability of HIV to produce disease. Theoretically, enhancing antibodies could attach to HIV virions and enable macrophages to engulf the viruses. However, instead of being destroyed, the engulfed virus may remain alive within the macrophage, which then can carry the virus to other parts of the body. It is currently unknown whether enhancing antibodies have any effect on the course of HIV infection. Enhancing antibodies can be thought of as the opposite of neutralizing antibodies.

**enzyme:** a protein produced by cells to accelerate a specific chemical reaction without itself being altered. Enzymes are generally named by adding the ending "-ase" to the name of the substance on which the enzyme acts (for example, protease is an enzyme that acts on proteins).

**env:** a gene of HIV that codes for gp160, the precursor molecule that breaks down into the envelope proteins gp120 and gp41. (See also **gp**.)

**envelope:** outer surface of a virus, also called the coat. Not all viruses have an envelope. (See also **virus**; **env**.)

**epidemiology:** the study of the frequency and distribution of disease in human populations.

**epitope:** a specific site on an antigen that stimulates specific immune responses, such as the production of antibodies or activation of immune cells.

**expression system:** in genetic engineering, the cells into which a gene has been inserted to manufacture desired proteins. Chinese hamster ovary (CHO) cells and baculovirus/insect cells are two expression systems that are used to make recombinant HIV vaccines.

## F

**functional antibody:** an antibody that binds to an antigen and has an effect that can be demonstrated in laboratory tests. For example, neutralizing antibodies are functional antibodies that inactivate HIV or prevent it from infecting other cells.

## G

**gag:** a gene of HIV that codes for p55, the core protein. p55 is the precursor of HIV

proteins p17, p24, p7 and p6 that form HIV's capsid or core, the inner protein shell surrounding HIV's strands of RNA.

**genetic engineering:** the laboratory technique of recombining genes to produce proteins used for drugs and vaccines.

**genome:** the complete set of genes present in a cell or virus.

**gp:** abbreviation for glycoprotein. A protein molecule that is glycosylated, that is, coated with a carbohydrate, or sugar. The outer coat proteins of HIV are glycoproteins. The number after the gp (e.g., gp160, gp120, gp41) is the molecular weight of the glycoprotein.

**gp41:** glycoprotein 41. A protein imbedded in the outer envelope of HIV that anchors gp120. gp41 plays a key role in HIV's infection of CD4<sup>+</sup> T cells by facilitating the fusion of the viral and cell membranes. Antibodies to gp41 can be detected on a screening HIV ELISA.

**gp120:** glycoprotein 120. One of the proteins that forms the envelope of HIV. gp120 projects from the surface of HIV and binds to the CD4 molecule on helper T cells. gp120 has been a logical experimental HIV vaccine because the outer envelope is the first part of the virus that encounters antibody.

**gp160:** glycoprotein 160, a precursor of HIV envelope proteins gp41 and gp 120.

## H

**half-life:** the time required for half the amount of a substance to be eliminated from the body or to be converted to another substance(s).

**helper T cell:** lymphocyte bearing the CD4 marker. Helper T cells are the chief regulatory cells of the immune response. They are responsible for many immune system functions, including turning antibody production on and off, and are the main target of HIV infection. (See also **CD4+ T lymphocyte**.)

**homologous:** similar in appearance, structure and usually function. For HIV, the same strain of the virus.

**host:** a plant or animal harboring another organism.

**HLA (human leukocyte antigen):** two major classes of molecules on cell surfaces.

**HLA class I:** molecules that exist on all nucleated cells and identify the cell as "self." In addition, if the cell is infected by a virus or other microbe, the cell displays the invader's antigens in combination with the cell's HLA class I molecules. The presence of the foreign peptide antigen with the HLA class I molecule activates CD8<sup>+</sup> CTLs specific for that antigen.

**HLA class II:** molecules that are found on antigen-presenting cells such as macrophages. These cells process soluble antigens such as toxins or other proteins made by microbes and then display them on their surface as peptide antigens in combination with HLA Class II molecules. Helper T cells specific for these antigens are

then able to be activated and respond to the presence of the invading microbe.

**humoral immunity:** see **antibody-mediated immunity**.

**hypothesis:** a tentative statement or supposition, which may then be tested through research.

## I

**immune complex:** the result of a reaction between an antigen and a specific antibody. This combination of antigen bound by antibody may or may not cause adverse effects in a person.

**immune deficiency:** a breakdown or inability of certain parts of the immune system to function, thus making a person susceptible to diseases that they would not ordinarily develop.

**immunity:** natural or acquired resistance provided by the immune system to a specific disease. Immunity may be partial or complete, specific or nonspecific, long-lasting or temporary.

**immunization:** the process of inducing immunity by administering an antigen (vaccine) to allow the immune system to prevent infection or illness when it subsequently encounters the infectious agent.

**immunogen:** a substance capable of provoking an immune response. Also called an antigen.

**immunocompetent:** capable of developing an immune response; possessing a normal immune system.

**immunogenicity:** the ability of an antigen or vaccine to stimulate immune responses.

**immunoglobulin:** a general term for antibodies, which bind to invading organisms, leading to their destruction. There are five classes of immunoglobulins: IgA, IgG, IgM, IgD and IgE. (See also **antibody**.)

**immunotherapy:** a treatment that stimulates or modifies the body's immune response.

**incidence:** the rate of occurrence of some event, such as the number of individuals who get a disease divided by a total given population per unit of time. (Contrast with **prevalence**.)

**inclusion/exclusion criteria:** the medical or social reasons why a person may or may not qualify for participation in a clinical trial. For example, some trials may exclude people with chronic liver disease or with certain drug allergies; others may include only people with a low CD4+ T-cell count.

**IND (investigational new drug):** the status of an experimental drug after the FDA agrees that it can be tested in people.

**informed consent:** an agreement signed by prospective volunteers for a clinical research trial that indicates their understanding of (1) why the research is being done, (2)

what researchers want to accomplish, (3) what will be done during the trial and for how long, (4) what risks are involved, (5) what, if any, benefits can be expected from the trial, (6) what other interventions are available, and (7) the participant's right to leave the trial at any time.

**intervention:** a vaccine (or drug or behavioral therapy) used in a clinical trial to improve health or alter the course of disease.

**in vitro:** an artificial environment created outside a living organism (e.g., in a test tube or culture plate) used in experimental research to study a disease or biologic process.

**in vivo:** testing within a living organism, e.g., human or animal studies.

**IRB (Institutional Review Board):** a committee of physicians, statisticians, community advocates and others that reviews clinical trial protocols before they can be initiated. IRBs ensure that the trial is ethical and that the rights of participants are adequately protected.

**isolate:** a particular strain of HIV-1 taken from a person.

## L

**LAI:** an HIV-1 isolate used in HIV vaccine development. LAI is also referred to as IIB or LAV. LAI belongs to clade B, the clade to which most HIV-1 found in America and Europe belongs. (See also **clade**.)

**live-vector vaccine:** a vaccine that uses a non-disease-causing organism (virus or bacterium) to transport HIV or other foreign genes into the body, thereby stimulating an effective immune response to the foreign products. This type of vaccine is important because it is particularly capable of inducing CTL activity. Examples of organisms used as live vectors in HIV vaccines are canarypox and vaccinia.

**lymphocyte:** a type of white blood cell produced in the lymphoid organs that is primarily responsible for immune responses. Present in the blood, lymph and lymphoid tissues. (See also **B cell** and **T cell**.)

**lymphoid tissue:** tonsils, adenoids, lymph nodes, spleen and other tissues that act as the body's filtering system, trapping invading microorganisms and presenting them to squadrons of immune cells that congregate there.

## M

**macrophage:** a large immune system cell in the tissues that devours invading pathogens and other intruders. Macrophages stimulate other immune cells by presenting them with small pieces of the invaders. Macrophages also can harbor large quantities of HIV without being killed, acting as reservoirs of the virus.

**mean:** the arithmetic average, or the sum of all the values divided by the number of values.

**median:** the midpoint value obtained by ranking all values from highest to lowest and choosing the value in the middle. The median divides a population into two equal halves.

**memory cell:** memory cells are a subset of T cells and B cells that have been exposed to specific antigens and can then proliferate (recognize the antigen and divide) more readily when the immune system re-encounters the same antigens. (See also **anamestic response**.)

**MHC (major histocompatibility complex):** the gene cluster that controls certain aspects of the immune response. Among the products of these genes are the histocompatibility antigens, such as HLA class I antigens, which are present on every cell with a nucleus and serve as markers to distinguish self from non-self. (See also **HLA**.)

**microencapsulated:** surrounded by a thin layer of biodegradable substance referred to as a microsphere. A means of protecting a drug or vaccine antigen from rapid breakdown. Microencapsulation may also enhance an antigen's absorption and the immune response to that antigen.

**MN:** an HIV-1 strain belonging to clade B, the clade to which most HIV-1 found in North America and Europe belong. MN is used in vaccine development. (See also **clade**.)

**monoclonal antibody:** custom-made, identical antibody that recognizes only one epitope.

**monocyte:** a large white blood cell in the blood that ingests microbes or other cells and foreign particles. When a monocyte passes out of the bloodstream and enters tissues, it develops into a macrophage.

**monovalent vaccine:** a vaccine that contains only one antigen.

**mucosal immunity:** resistance to infection across the mucous membranes. Mucosal immunity depends on immune cells and antibodies present in the linings of reproductive tract, gastrointestinal tract and other moist surfaces of the body exposed to the outside world.

## N

**nef:** a gene of SIV and HIV that regulates the production of the virus. Vaccines made of SIV virions from which *nef* has been removed (*nef*-deleted) have shown promise in monkeys.

**neutralizing antibody:** an antibody that keeps a virus from infecting a cell, usually by blocking receptors on the cells or the virus.

**neutralizing domain:** a section of HIV (most commonly on the envelope protein gp120) that elicits antibodies with neutralizing activity. (See also **V3 loop**.)

**NK cell (natural killer cell):** a non-specific lymphocyte. NK cells, like killer T cells, attack and kill cancer cells and cells infected by microorganisms. NK cells are "natural" killers because they do not need to recognize a specific antigen in order to attack and kill.

**nucleus:** the central controlling body within a living cell, usually a spherical unit enclosed in a membrane and containing genetic codes for maintaining life systems of the

organism and for issuing commands for growth and reproduction.

## O

**open-label trial:** a clinical trial in which doctors and participants know which vaccine is being administered to all participants.

**opportunistic infection:** an illness caused by an organism that usually does not cause disease in a person with a normal immune system. People with advanced HIV infection suffer opportunistic infections of the lungs, brain, eyes and other organs.

## P

**p24:** a protein in HIV's inner core. The p24 antigen test looks for the presence of this protein in a person's blood.

**parenteral:** administered intravenously or by injection. For example, medications or vaccines may be administered by injection into the fatty layer immediately below the skin (subcutaneous), or into the muscle (intramuscular). Medications, but not vaccines, can also be administered into a vein (intravenously).

**pathogenesis:** the origin and development of a disease. More specifically, it's the way a microbe (bacteria, virus, etc.) causes disease in its host.

**PBMC (peripheral blood mononuclear cell):** cells in the bloodstream that have one round nucleus; e.g., lymphocytes and monocytes. Usually, the majority of circulating PBMCs are lymphocytes.

**PCR (polymerase chain reaction):** a sensitive laboratory technique used to detect and repeatedly copy small amounts of RNA or DNA. Some PCR tests can also quantify the amount of RNA or DNA. PCR is used to measure viral load in persons infected with HIV.

**peptide:** a short compound formed by linking two or more amino acids. Proteins are made of multiple peptides.

**PHA (phytohemagglutinin):** a plant chemical used to stimulate the multiplication (proliferation) of T lymphocytes in laboratory tests.

**Phase 1 vaccine trial:** a closely monitored clinical trial of a vaccine conducted in a small number of healthy volunteers. A Phase 1 is designed to determine the vaccine's safety in humans, its metabolism and pharmacologic actions, and side effects associated with increasing doses.

**Phase 2 vaccine trial:** controlled clinical study of a vaccine to identify common short-term side effects and risks associated with the vaccine and to collect information on its immunogenicity. Phase 2 trials enroll some volunteers who have the same characteristics as persons who would be enrolled in an efficacy (Phase 3) trial of a vaccine. Phase 2 trials enroll up to several hundred participants and have more than one arm.

**Phase 3 vaccine trial:** large controlled study to determine the ability of a vaccine to produce a desired clinical effect on the risk of a given infection, disease, or other clinical

condition at an optimally selected dose and schedule. These trials also gather additional information about safety needed to evaluate the overall benefit-risk relationship of the vaccine and to provide adequate basis for labeling. Phase 3 trials usually include several hundred to several thousand volunteers.

**pharmacokinetics:** the processes of absorption, distribution, metabolism and excretion of a drug or vaccine.

**placebo:** an inactive substance administered to some study participants while others receive the agent under evaluation, to provide a basis for comparison of effects.

**plasmid:** an extrachromosomal ring of DNA, especially of bacterial origin, that replicates autonomously.

**pol:** a gene of HIV that codes for the enzymes protease, reverse transcriptase and integrase.

**polymerase:** an enzyme that creates genetic material, either RNA or DNA, from building blocks.

**polyvalent vaccine:** a vaccine that is produced from multiple viral strains, or is made to induce immune responses against multiple strains.

**prevalence:** the number of people in a given population affected with a particular disease or condition at a given time. Prevalence can be thought of as a snapshot of all existing cases at a specified time. (Contrast with **incidence**.)

**preventive HIV vaccine:** a vaccine designed to prevent HIV infection.

**priming:** giving one vaccine dose(s) first to induce certain immune responses, followed by or together with a second type of vaccine. The intent of priming is to induce certain immune responses that will be enhanced by the booster dose(s).

**prime-boost:** in HIV vaccine research, administration of one type of vaccine, such as a live-vector vaccine, followed by or together with a second type of vaccine, such as a recombinant subunit vaccine. The intent of this combination regimen is to induce different types of immune responses and enhance the overall immune response, a result that may not occur if only one type of vaccine were to be given for all doses.

**prophylaxis:** prevention of disease.

**protease inhibitor:** one of a class of anti-HIV drugs designed to inhibit the enzyme protease and interfere with virus replication. Protease inhibitors prevent the cleavage of HIV precursor proteins into active proteins, a process that normally occurs when HIV replicates.

**protocol:** the detailed plan for a clinical trial that states the trial's rationale, purpose, vaccine dosages, routes of administration, length of study, eligibility criteria and other aspects of trial design.

**pseudovirion:** a virus-like particle that resembles a virus but does not contain its genetic information and cannot replicate. In some viral diseases pseudovirions can interfere with infection by the real infectious virus.

## R

**randomized trial:** a study in which participants are assigned by chance to one of two or more intervention arms or regimens. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms.

**reactogenicity:** the capacity of a vaccine to produce adverse reactions.

**reagent:** any chemical used in a laboratory test or experiment.

**receptor:** a molecule on the surface of a cell that serves as a recognition or binding site for antigens, antibodies or other cellular or immunologic components.

**recombinant DNA technology:** the technique by which genetic material from one organism is inserted into a foreign cell in order to mass produce the protein encoded by the inserted genes.

**regulatory gene:** HIV genes (*nef*, *rev*, *tat*, *vpr*) that regulate viral replication in infected cells.

**retrovirus:** HIV and other viruses that carry their genetic material in the form of RNA rather than DNA and have the enzyme reverse transcriptase that can transcribe it into DNA. In most animals and plants, DNA is usually made into RNA, hence "retro" is used to indicate the opposite direction.

**reverse transcriptase:** the enzyme produced by HIV and other retroviruses that enables them to direct a cell to synthesize DNA from their viral RNA.

**RNA (ribonucleic acid):** a single-stranded molecule composed of chemical building blocks, similar to DNA. The RNA segments in cells represent copies of portions of the DNA sequences in the nucleus. RNA is the sole genetic material of retroviruses.

## S

**seroconversion:** the development of antibodies to a particular antigen. When people develop antibodies to HIV or an experimental HIV vaccine, they "seroconvert" from antibody-negative to antibody-positive. Vaccine-induced seroconversion does not represent an infection. Instead, vaccine-induced seroconversion is an expected response to vaccination that may disappear over time.

**serostatus:** positive or negative results of a diagnostic test, such as an ELISA, for a specific antibody.

**SF-2:** an HIV-1 strain used in vaccine development. SF-2 belongs to clade B, the clade to which most HIV-1 strains found in North America and Europe belong. (See also **clade**.)

**SHIV:** genetically engineered hybrid virus having an HIV envelope and an SIV core.

**side effect:** (See **adverse reaction**.)

**SIV (simian immunodeficiency virus):** an HIV-like virus that infects and causes an AIDS-like disease in some species of monkeys.

**statistical significance:** the probability that an event or difference occurred as the result of the intervention (vaccine) rather than by chance alone. This probability is determined by using statistical tests to evaluate collected data. Guidelines for defining significance are chosen before data collection begins.

**sterilizing immunity:** an immune response that completely prevents the establishment of an infection.

**strain:** one type of HIV. HIV is so heterogeneous, no two isolates are exactly the same. When HIV is isolated from an individual, and worked on in the lab, it is given its own unique identifier, or strain name (i.e., MN, LAI).

**stratification:** separation of a study cohort into subgroups or strata according to specific characteristics.

**subtype:** also called a clade. With respect to HIV isolates, a classification scheme based on genetic differences.

**subunit vaccine:** a vaccine that contains only part of the virus or other microorganism. HIV subunit vaccines produced by genetic engineering are referred to as recombinant subunit HIV vaccines.

**surrogate marker:** an indirect measure of disease progression. In HIV disease, the number of CD4<sup>+</sup> T cells per cubic millimeter of blood is often used as a surrogate marker.

**syncytia:** giant cells formed by the fusion of an HIV-infected blood cell with one or more uninfected ones.

## T

**T cell:** white blood cell critical to the immune response. Among these are CD4<sup>+</sup> T cells and CD8<sup>+</sup> T cells. The "T" stands for the thymus, where T lymphocytes mature. (See also **lymphocyte**.)

**T lymphocyte proliferation assay:** a test used to measure the memory of T cells to antigens or microbes, such as HIV.

**therapeutic HIV vaccine:** a vaccine designed to boost the immune response to HIV in a person already infected with the virus. Also referred to as an immunotherapeutic vaccine.

## V

**V3 loop:** a section of the HIV gp120 surface protein that appears to be important in stimulating neutralizing antibodies. (See also **neutralizing domain**.)

**vaccine:** a preparation that stimulates an immune response that can prevent an infection

or create resistance to an infection.

**vaccinia:** a cowpox virus, formerly used in human smallpox vaccines. Employed as a vector in HIV vaccines to transport HIV genes into the body.

**vector:** in vaccine research, a bacterium or virus that does not cause disease in humans and is used in genetically engineered vaccines to transport genes coding for antigens into the body to induce an immune response. (See also **vaccinia** and **canarypox**.)

**viremia:** the presence of virus in the bloodstream.

**virion:** a mature infectious virus particle existing outside a cell.

**virus:** a microorganism composed of a piece of genetic material – RNA or DNA – surrounded by a protein coat. To replicate, a virus must infect a cell and direct its cellular machinery to produce new viruses.

## W

**Western blot:** a blood test to detect antibodies to several specific components of a virus such as HIV. This test is most often used to confirm a positive ELISA.

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NIAID is a component of the National Institutes of Health (NIH), which is an agency of the Department of Health and Human Services. NIAID supports basic and applied research to prevent, diagnose, and treat infectious and immune-mediated illnesses, including HIV/AIDS and other sexually transmitted diseases, illness from potential agents of bioterrorism, tuberculosis, malaria, autoimmune disorders, asthma and allergies.

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