

GLOSSARY OF TERMS

A

adenovirus - a common virus that causes colds and sore throats. A defective adenovirus (one that cannot grow or cause adenovirus infections in humans) is sometimes used as a vector in HIV vaccines.

adjuvant - a substance that may be included in a vaccine to improve the body's ability to fight disease or infection.

adverse experience - A bad experience that may be related to receiving vaccine, such as fever, chills, rash, aches and pains, nausea, headache, dizziness, and fatigue.

antibody - an infection-fighting protein molecule in the blood or secretory fluids that tag, destroy, or neutralize bacteria, viruses, or other harmful toxins. Antibodies, known generally as immunoglobulins, are made and secreted by B lymphocytes in response to stimulation by antigens. An antibody is specific to an antigen.

antibody - mediated immunity - protection provided by antibodies (as opposed to cellular immunity) Also known as "humoral immunity."

Antibody dependant cellular cytotoxicity (ADCC) - When antibodies coat an HIV-infected cell identifying it as something abnormal that needs to be killed. This process activates the natural killer (NK) cells, which then kill the HIV-1 infected cell so it can't manufacture any more HIV.

antigen - a foreign substance (such as a virus) that enters the body causes the body's immune system to respond.

autoimmune disease - a disorder in which a person's immune system attacks parts of his or her own body.

B

B cells - white blood cells that produce antibodies which are important to the body's defense against foreign invaders.

broadly neutralizing antibodies (bnAbs) - Broadly neutralizing antibodies (bnAbs) against HIV are special antibodies that are able to block or "neutralize" many types or strains of HIV. Antibodies are part of the human immune system that protects someone from disease. BnAbs work by attaching to HIV and covering up the parts of the virus that it uses to attach to a person's cells, blocking HIV from being able to cause an infection. A bnAb against HIV could ideally protect a person from not just one type of HIV, but from many.

blinded study - a clinical trial in which the study participant is not told whether or not he/she is receiving a study product or a placebo.

C

CCR5 receptors - CCR5, called a co-receptor because it works with CD4 (see helper T cells), is the door that opens to allow HIV to enter the cell. Many people who are resistant to HIV have a mutation in the CCR5 gene called CCR5-delta32. Most forms of HIV cannot infect cells if there is no CCR5 on the surface.

CD4 - see helper T cells

CD8 - see killer T cells

cellular immunity - protection provided by the cells of the body's immune system (as opposed to humoral immunity).

chimera - A chimera is a combination virus constructed in the lab from pieces of different viruses. It has some features of each of the component viruses.

clade - a subtype or strain of HIV. Different HIV clades exist in various regions of the world.

clinical trial - a research study or experiment in humans (as opposed to animals) that is designed to answer specific questions.

control - a substance or product included in a trial that is used to compare its effect to that of the vaccine being studied. The control may be an inactive substance (placebo) or some other vaccine product.

cytotoxic T cells (CTLs) - a lymphocyte that is able to kill foreign cells marked for destruction by the cellular immune system. CTLs can destroy cancer cells and cells infected with viruses, fungi, or certain bacteria. CTLs can destroy virus-infected cells, whereas antibodies generally target free-floating viruses in the blood. Also known as "killer T cells" and "cytotoxic lymphocytes."

D

data safety monitoring board (DSMB) - an independent group that reviews data during the study and can recommend a study to be stopped if it appears the volunteers are being placed at risk.

DNA vaccine - a vaccine that uses genes made of HIV desoxynucleic acid (DNA) to trigger an immune response. In HVTN trials, vaccines using this method use only SOME genes of HIV, not the whole virus. Receiving a vaccine in an HVTN trial cannot infect a participant with HIV or AIDS.

double-blinded study - a study in which neither the investigator nor the participant knows whether the participant is receiving a vaccine or a control. Double-blinded studies are designed to prevent bias when conducting the trial or analyzing the results.

E

efficacy - the effectiveness of a vaccine, or how well it works. "Efficacy" is used in clinical trial settings, whereas "effectiveness" is used in real world (not carefully controlled) settings.

envelope (Env) - outer surface of a virus, also called the coat. Not all viruses have an envelope.

epitope - a specific part on the surface of a virus that is targeted for destruction by the body's immune system.

G

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.

gp140 (glycoprotein 140) - one of the viral surface proteins that forms the envelope of HIV.

gp160 (glycoprotein 160) - a precursor of HIV envelope proteins gp41 and gp120.

H

helper T cells (CD4) - a group of T cells that help produce antibodies, activate killer T cells (CD8), and make sure the immune system works smoothly.

HIV RNA testing - A form of HIV test that detects the presence of the actual virus rather than looking for antibodies to the virus.

HLA (human leukocyte antigen) - markers on the surface of a body's cell that identify the cell as one's own (as opposed to a foreign cell) and prevent the immune system from attacking itself.

humoral immunity - protection provided by antibodies (as opposed to cellular immunity) Also known as "antibody-mediated immunity."

I

immune system - the body system, made up of many organs and cells, that defends the body against infection, disease, and foreign substances.

immunogenicity - ability to protect against an infection, disease, and foreign substances.

immunosuppressive - capable of making the body unable to protect itself against infection or disease.

inactivated vaccine (killed vaccine) - a vaccine made from a whole virus or bacterium whose ability to grow or reproduce has been eliminated.

investigational vaccine - a vaccine that has been approved by the U.S. Food and Drug Administration (FDA) for experimental testing in humans, but has not yet been proven effective.

informed consent - the process of deciding whether or not to join a clinical trial, after learning enough information to make a responsible decision about participating. All trial participants must provide written agreement before entering a study.

injection - a shot.

institutional review board (IRB) - one of the groups that monitors HVTN trials. Each research institution (such as a university) has an IRB, that reviews studies to make sure they are scientifically and ethically

acceptable to the participant.

K

killer T cells (CD8) - a group of T cells that is activated by helper T cells (CD4) and have the ability to destroy cells infected by foreign invaders (such as viruses). Also known as cytotoxic T lymphocytes (CTLs).

L

live attenuated vaccine - a type of vaccine that uses a weakened version of an organism. An example is the Sabin polio vaccine. HIV vaccines do not contain live attenuated forms of HIV.

lymphocyte - a white blood cell present in the blood, lymph and lymphoid tissue that is essential in immune defense.

M

memory cell - a T or B cell that has been exposed to a specific invading organism and remembers the organism. Memory cells help the immune system respond faster when they encounter invading organisms for the second time.

microbe - a tiny living organism, such as a bacterium or virus.

mosaic vaccine - Mosaic HIV vaccines include inserts made from strings of amino acids (the building blocks of proteins). They are created by a computer program to optimally reflect the known circulating strains of HIV. They are also designed to produce proteins that physically resemble actual HIV proteins so that they will generate immune responses more like those seen in response to a real HIV infection. Mosaic vaccines typically include more than one amino acid sequence to help better cover the range of HIV variability.

mucosal membrane - moist (wet) tissue that lines body cavities or passages that have an opening to the external world, such as the mouth, nose, rectum or vagina.

mutation - a change in the genetic material (DNA) inside of a cell that results in a new characteristic. HIV is a virus that mutates frequently as it replicates, possibly resulting in a stronger and/or drug-resistant virus.

N

natural killer (NK) cells - a type of cytotoxic lymphocyte that constitute a major component of the innate immune system. NK cells play a major role in the rejection of tumors and cells infected by viruses. They kill cells by releasing small cytoplasmic granules of proteins called perforin and granzyme that cause the target cell to die by apoptosis (programmed cell death).

O

open label study - a clinical trial in which all participants know what product they are receiving. It is the opposite of a blinded study.

P

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

Phase I trial - an early clinical trial designed to study an experimental vaccine in humans. Phase I trials are generally small (less than 100 participants) and designed to see if the product is safe.

Phase II trial - an intermediate clinical trial for studying an experimental vaccine in humans. The goals of Phase II trials are usually to learn more about vaccine safety and to see if the vaccine generates an immune response. Phase II trials, which involve hundreds of participants, occur only after the experimental vaccine is shown to be safe in a smaller Phase I trial.

Phase IIb trial - A Phase IIb or test-of-concept trial is about finding out if the vaccine concept or the type of vaccine candidate being tested will be effective. A test-of-concept trial is not designed to establish the efficacy of a particular candidate but rather to help researchers decide if a candidate is worth testing in larger Phase III trials. These intermediate studies are also referred to as proof-of-concept trials. The number of volunteers required for such trials is smaller, around 2,000 to 5,000 volunteers, compared to over 10,000 for Phase III trials.

Phase III trial - an advanced clinical trial in humans designed to prove whether or not a vaccine is effective. Phase III trials involve thousands of participants and occur only after the experimental vaccine has successfully moved from a Phase I and Phase II trial.

placebo - an inactive substance designed to resemble the vaccine (or treatment) being studied. Participants taking a placebo form the control group in blinded clinical trials.

plasmid - A small, circular piece of DNA found outside the chromosome in bacteria. Plasmids are the principal tools for inserting new genetic information into microorganisms or plants.

preclinical - testing of a vaccine or drug in cells or animals before testing in humans.

principal investigator - the scientist in charge of a research team conducting clinical trials.

protocol - the plan for a research study.

R

randomized - assigned to a group by chance, like the toss of a coin. Whether a participant receives a vaccine or control will depend on which group he/she is in.

recombinant - an organism whose genome contains integrated genetic material from a different organism. Also used in relation to compounds produced by laboratory or industrial cultures of

genetically engineered living cells. Recombinant compounds often are altered versions of naturally occurring substances.

recombinant vaccine - vaccine that uses genetic material from a disease-causing organism to produce an immune response. For instance, an HIV recombinant vector vaccine uses a vector (a weakened virus or bacterium) to transport genetic material from man-made HIV proteins into the body.

rectosigmoidoscopy - a medical procedure to remove skin cells from the colon.

S

screening - the process clinicians use to see if a volunteer is eligible to participate in a clinical trial. Screening usually includes a medical history, including personal questions and laboratory tests.

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

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

subunit vaccine - a vaccine that uses one or more parts of a disease-causing organism, rather than the whole, to stimulate an immune response. The Hepatitis B vaccine is an example of a subunit vaccine.

T

t-cells - see memory cells, helper cells and cytotoxic T cells.

tolerability - the body's ability to support or withstand a vaccine or medicine.

toxicity - the extent, quality, or degree of harm to the body.

V

vaccine-induced seropositivity (VISP) - a false diagnosis of HIV infection based on a reactive HIV antibody test. HIV vaccines are designed to evoke antibody responses. Standard HIV tests look for the presence of antibodies rather than the virus. Trial participants who receive a vaccine product may develop HIV antibodies and show a reaction on antibody tests. The HVTN provides appropriate HIV testing in order to best avoid a misdiagnosis.

vaccine-induced seroreactivity (VISR) - see VISP.

vector - 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.

viral load – the amount of HIV in the body, usually measured in the blood, reported as virus particles per milliliter