



## Alere Glossary of Terms

### Cardiometabolic

**Acute Coronary Syndrome (ACS):** refers to any group of symptoms attributed to obstruction of the coronary arteries. The most common symptom prompting diagnosis of ACS is chest pain, often radiating to the left arm or angle of the jaw, pressure-like in character, and associated with nausea and sweating. It is estimated that, in the United States, >780,000 persons will experience ACS annually. Patients with ACS will be sub-categorized as having ST elevation myocardial infarction (STEMI), non ST elevation myocardial infarction (NSTEMI), or unstable angina (UA).

**Anticoagulants:** a class of drugs that work to prevent the coagulation or clotting of blood.

**Atrial Fibrillation:** an irregular and often rapid heart rate that commonly causes poor blood flow to the body. During atrial fibrillation, the heart's two upper chambers (the atria) beat chaotically and irregularly – out of coordination with the two lower chambers (the ventricles) of the heart. Symptoms include heart palpitations, shortness of breath and weakness.

**B-Type Natriuretic Peptide (BNP):** a 32-amino-acid polypeptide secreted by the ventricles of the heart in response to excessive stretching of heart muscle cells. The levels of B-type natriuretic peptide are elevated in patients with congestive heart failure, and correlate with both the severity of symptoms and the prognosis.

**Body Mass Index (BMI):** a weight-to-height ratio calculated by dividing one's weight in kilograms by the square of one's height in meters and used as an indicator of obesity and underweight.

**C - reactive protein (CRP):** a protein produced by the liver and found in the blood. CRP is not normally found in the blood of healthy people. It appears after injury, infection or inflammation and disappears when the injury heals or the infection or inflammation goes away.

**Chronic Disease:** a disease lasting three months or more, by the definition of the U.S. National Center for Health Statistics. Chronic Diseases generally cannot be prevented by vaccines or cured by medication, nor do they just disappear.

**CPK-MB Test:** a cardiac marker used to assist diagnosis of acute myocardial infarction. It measures the blood level of CK-MB, the bound combination of two variants (isoenzymes CKM and CKB) of the enzyme phosphocreatine kinase.

**Glycated Hemoglobin (HbA1c):** a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. It is formed in a non-enzymatic glycation pathway by hemoglobin's exposure to plasma glucose. Normal levels of glucose produce a normal amount of glycated hemoglobin. As the average amount of plasma glucose increases, the fraction of glycated hemoglobin increases in a predictable way.

**Heart Failure (HF):** occurs when the heart is unable to pump sufficiently to maintain blood flow to meet the needs of the body. Symptoms commonly include shortness of breath, excessive tiredness, and leg swelling.

**International Normalized Ratio (INR):** A system established by the World Health Organization (WHO) and the International Committee on Thrombosis and Hemostasis for reporting the results of blood coagulation (clotting) tests. Under the INR system, all results are standardized. For example, a person taking the anticoagulant warfarin (brand name: Coumadin) would regularly have blood tested to measure the INR. The INR permits patients on anticoagulants to travel and obtain comparable test results wherever they are. Commonly INR results are reported as a ratio with prothrombin time (PT) as PT/INR.

**Ischemic Stroke:** occurs when a blood vessel that supplies blood to the brain is blocked by a blood clot.

**Lipid panel:** a blood test that measures lipids, usually cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL). Elevated levels of cholesterol, triglycerides and LDL and low levels of HDL are linked to higher risk of heart disease. Other measurements that may be done for a lipid panel include very-low-density lipoprotein (VLDL) cholesterol level, the ratio of total cholesterol to HDL and the ratio of LDL to HDL.

**Myocardial Infarction (MI):** the medical term for an event commonly known as a heart attack. An MI occurs when blood stops flowing properly to a part of the heart, and the heart muscle is injured because it is not receiving enough oxygen. Usually this is because one of the coronary arteries that supplies blood to the heart develops a blockage due to an unstable build-up of white blood cells, cholesterol and fat. The event is called "acute" if it is sudden and serious.

**Myoglobin:** an iron- and oxygen-binding protein found in the muscle tissue of vertebrates in general and in almost all mammals. It is related to hemoglobin, which is the iron- and oxygen-binding protein in blood, specifically in the red blood cells. Myoglobin is only found in the bloodstream after muscle injury. It is an abnormal finding, and can be diagnostically relevant when found in blood.

**Prothrombin Time (PT):** a blood test that measures how long it takes blood to clot, commonly used to check whether an anticoagulant is working. Commonly PT results are reported as a ratio with International Normalized Ratio (INR) as PT/INR.

**Thrombosis:** the formation or presence of a blood clot within a blood vessel.

**Troponin:** a protein within a troponin complex that helps regulate the heartbeat and can be used as an indicator of myocardial infarction.

**Type 1 Diabetes:** an autoimmune disease that occurs when the T cells attack and destroy most of the beta cells in the pancreas that are needed to produce insulin, so that the pancreas makes too little insulin (or no insulin). Without the capacity to make adequate amounts of insulin, the body is not able to metabolize blood glucose (sugar), to use it efficiently for energy, and toxic acids (called ketoacids) build up in the body. There is a genetic predisposition to type 1 diabetes.

**Type 2 Diabetes:** a metabolic disorder characterized by hyperglycemia (high blood sugar) in the context of insulin resistance and relative lack of insulin. This is in contrast to type 1 diabetes, in which there is an absolute lack of insulin due to breakdown of cells in the pancreas. Type 2 diabetes makes up about 90% of cases of diabetes, with the other 10% due to primarily type 1 diabetes and gestational diabetes. Obesity is thought to be the primary cause of type 2 diabetes in people who are genetically predisposed to the disease.

### Diagnosics (General)

**Analyte:** a substance measured by a diagnostic test, for instance, a specific mutation or blood chemistry component.

**Biomarker:** a biological property or substance(s) that is: (1) A sign of a normal or abnormal process, or of a condition or disease; (2) Used to determine how patients respond to treatments.

**Diagnosics:** the use of clinical tests to inform clinical decision making for the purpose of disease prediction, screening, diagnosis, treatment selection, prognosis and monitoring.

**Clinical Sensitivity:** probability that the test gives a positive result among individuals that have the disease or condition of interest. Specifically, the ratio of true positives to the sum of true positives and false negatives.

**Clinical Specificity:** probability that the test will give a negative result among individuals who do not have the disease or condition of interest. Specifically, the ration of true negatives to the sum of true negatives and false positives.

**False Negative:** a test result that indicates that an individual does not have a specific disease when the individual actually does have the disease.

**False Positive:** a test result that indicates that an individual does have a specific disease when the individual actually does not have the disease.

**In Vitro Diagnostic Test (IVD):** a diagnostic test that is conducted outside of the body on specimens such as blood or tissue.

**Molecular Testing:** testing DNA or RNA, whether amplified or not, for specific targets whether it be pathogens, like bacteria or viruses, or particular genes from a person (chromosomes) but also proteins and other molecular biomarkers.

**Monitoring Test:** a test used to evaluate patient health status or disease state or to determine whether or to what extent disease has progressed.

**Point of Care Testing (POCT):** testing that occurs at the point of treatment or patient interaction with a healthcare provider (e.g., the bedside, home, or physician office).

**Polymerase Chain Reaction (PCR):** a testing technique where small segments of DNA or RNA are copied exponentially by a biochemical reaction to detectable levels. PCR would be a type of molecular test.

**Reagent:** a chemical substance (other than the specimen) used in conducting a diagnostic test/assay.

**Screening Test:** a test used to rule out a particular disease. The test can be evaluated on an asymptomatic person or particular symptoms, like coughing, where the results then have to be confirmed. Rapid HIV and influenza tests would be considered screening tests as positives would need to be confirmed.

an IVD test package that includes all of the reagents necessary to obtain test results (excluding the patient specimen/sample) and a protocol with instructions using the test kit.

## Infectious Disease

**Absolute CD4:** a measurement of how many functional CD4 T-cells are circulating in the blood. The lower the absolute CD4 count, the weaker the immune system. The absolute CD4 count is measured by a simple blood test and is reported as the number of CD4 cells per cubic millimeter of blood. HIV-negative people typically have absolute CD4 counts between 600 and 1200 CD4 cells per cubic millimeter. HIV-infected people have counts that are typically less than 500, and people with AIDS can have 200 CD4 cells per cubic millimeter or fewer.

**Amplicon:** the piece of amplified DNA that is made by a molecular enhancement method like PCR or NEAR.

**Antibiotic Resistance:** the ability of bacteria and other microorganisms to resist the effects of an antibiotic to which they were once sensitive. Antibiotic resistance is a major concern of overuse of antibiotics. Also known as drug resistance.

**Antiretroviral Therapy (ART):** the combination of several antiretroviral medicines used to slow the rate at which HIV makes copies of itself (multiplies) in the body.

**Blood-Borne Pathogens:** pathogenic microorganisms that are present in human blood and can cause disease in humans. These pathogens include, but are not limited to, Hepatitis B Virus (HBV) and Human Immunodeficiency Virus (HIV).

**Community-acquired:** an infectious disease acquired outside of a medical site as opposed to healthcare associated

**DNA (deoxyribonucleic acid):** the genetic blueprint for all living organisms. DNA can be amplified by a molecular method such as PCR or NEAR and detected for a highly sensitive test.

**Fourth Generation HIV Test:** a test like Determine™ HIV-1/2 Ag/Ab Combo that detects both the virus itself (p24 antigen) as well as the antibody response. The addition of p24 allows for detection earlier in infection than traditional HIV tests. Second generation tests, like OraSure, only detect IgG (the antibody response). 3rd generation tests, like Trinity, detect IgG and IgM. IgM is an antibody that appears earlier than IgG, but goes away.

**Group A Strep (GAS):** See Strep A

**Healthcare-associated infection (HAI):** an infection that is transmitted in a hospital.

**Hospital acquired infection (HAI):** an infection transmitted in a hospital, but now reclassified as healthcare-associated infection.

**Human Immunodeficiency Virus (HIV):** a lentivirus (slowly replicating retrovirus) that causes the acquired immunodeficiency syndrome (AIDS), a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive. Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate, or breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells. There are two major variants of the virus: HIV-1 and HIV-2.

**HIV-1:** the common and most pathogenic strain of HIV seen in most of the world, like the United States and Europe. The Determine Combo test detects the p24 of early infections with HIV-1 and later infections by detecting the person's antibody response to HIV-1.

**HIV-2:** HIV strain primarily seen in Western Africa. It is not normally seen in other parts of the world, but people from these areas or that have visited, may be at risk.

**HIV p24 Antigen:** a structural protein that makes up most of the HIV viral core, or "capsid" of HIV-1. High levels of p24 are present in the blood serum of newly infected individuals during the short period between infection and seroconversion, making the p24 antigen assays useful in diagnosing primary HIV infection.

**HIV Viral Load:** the number of copies of the HIV virus in the blood and in other parts of the body. The HIV viral load test involves taking a blood sample and then measuring the amount of HIV in the blood.

**iNAAT (or iNAT):** isothermal nucleic acid amplification technology. iNAAT is the generic term for amplifying DNA for detection using an isothermal reaction.

**Influenza (flu) Type A:** the virus that is capable of causing respiratory “flu.” Influenza A can be found in many animal species and is highly infectious within that species, but the virus does not cross species barriers well. Type A flu virus is constantly changing and can cause sporadic cases to outbreaks to global pandemics.

**Influenza (flu) Type B:** Unlike type A flu viruses, type B flu is found only in humans. Type B flu may cause a less severe reaction than type A flu virus, but occasionally, type B flu can still be extremely harmful. Influenza type B viruses are not classified by subtype and do not cause pandemics.

**Isothermal Reaction:** a molecular reaction that takes place at one temperature, thereby reducing the time. In traditional reactions known as PCR, the temperature has to be increased to unzip the DNA, lowered to have our primers bind, and then raised a bit to make new copies. This temperature cycle has to be repeated usually around 40 times.

**NEAR (nicking enzyme amplification reaction):** the reaction on which Alere i influenza is based. At one temperature (isothermal), it is able to amplify DNA from a few copies to trillions that can be detected.

**Nosocomial infection:** the original term for healthcare-associated infection.

**p24:** see *HIV p24 Antigen*

**Pharyngitis:** the medical term for a sore throat which can be caused by things like *Strep A* bacteria.

**Primer:** a small piece of DNA specific to what molecular tests are trying to detect, such as a bacteria or virus. The primer binds to the single stranded DNA allowing it to be amplified and eventually detected.

**Real time PCR:** a PCR reaction that is able to give results as the reaction is occurring.

**Recombinant Polymerase Amplification (RPA):** a second isothermal amplification technology owned by Alere and capable of going on the Alere i platform.

**Reverse transcriptase:** an enzyme that converts RNA into DNA. In most living systems, DNA is converted into RNA which then tells how a protein is to be made. In some viruses like HIV, reverse transcriptase is used to make their RNA into DNA. Molecular amplification assays use reverse transcriptase to change RNA into DNA so they can amplify it.

**Ribonucleic Acid (RNA):** in many living organisms, RNA is the message from DNA that then is used to make proteins. There are some viruses that have RNA as their primary genetic material rather than DNA.

**RT-PCR (reverse-transcriptase PCR):** converting RNA into DNA by reverse transcriptase and then amplifying it by PCR.

**Polymerase Chain Reaction (PCR):** the traditional way DNA or RNA was amplified for highly sensitive detection.

**Strep A:** the bacteria that is responsible for Strep throat. If a person has Strep throat, they should be given antibiotics. If negative, most often it is a viral infection and the patient does not need to be treated with antibiotics.

**Vector-Borne Diseases:** infections transmitted by the bite of infected arthropod species, such as mosquitoes, ticks, triatomine bugs, sandflies, and blackflies. These diseases include, but are not limited to, West Nile Virus, Dengue, Malaria and Lyme borreliosis.

**Window Period:** The time from infection to when a test for the disease works. In the case of HIV, it is the time between when a person is infected and when the test is positive. Since the Determine Combo HIV test detects both the virus and the antibody response, the window period is shorter with this test compared to antibody-only tests.

## Regulatory

**510(k) Clearance:** section 510(k) of the Food, Drug and Cosmetic Act requires device manufacturers to notify FDA of their intent to market a medical device at least 90 days in advance. Medical device manufacturers are required to submit a premarket notification [510(k)] if they intend to introduce a device into commercial distribution for the first time or reintroduce a device that will be significantly changed or modified to the extent that its safety or effectiveness could be affected. Such change or modification could relate to the design, material, chemical composition, energy source, manufacturing process, or intended use.

**CE Mark:** a mandatory conformity marking for certain products sold within the European Economic Area (EEA) since 1985. The CE mark is also found on products sold outside the EEA that are manufactured in, or designed to be sold in, the EEA.

**Clinical Laboratory Improvement Amendments (CLIA) Waived Tests:** include test systems cleared by the FDA for home use and those tests approved for waiver under the CLIA criteria.

For a list of waived tests sorted by analyte name, visit the FDA website at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfClia/analyteswaived.cfm>.

**Investigational Device Exemption (IDE):** allows the investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification [510(k)] submission to the Food and Drug Administration (FDA). Clinical studies are most often conducted to support a PMA. Only a small percentage of 510(k)'s require clinical data to support the application. Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated.

**Moderately Complex Test:** a test defined by the Clinical Laboratory Improvements Amendments of 1988 (CLIA) as one requiring basic lab knowledge and training for personnel performing the test. Moderately Complex Tests may require reagent preparation, limited pre-treatment of specimens, quality control, calibration, proficiency testing, some skill in troubleshooting and maintaining equipment, and some skill or judgment in interpretation of results.