What are *in vitro* diagnostics?

The term *in vitro* diagnostics (IVD) refers to tests that can be conducted on a cell culture or body fluid, such as blood, in what was traditionally a glass test tube. The phrase *in vitro* literally means "in glass" and diagnostics are the means used to identify or name the disease or condition affecting a patient. Common IVD tests include:

- pregnancy tests
- glucose monitoring for those with diabetes
- tests for infectious diseases, such as HIV or hepatitis
- cholesterol tests

Other diagnostic procedures, such as magnetic resonance imaging (MRI), X-rays and blood pressure screenings, are referred to as *in vivo* diagnostics – tests conducted on an entire organism or body.

Importance and value of diagnostics

Diagnostics is the common denominator in patient care. While more than 60 percent of all healthcare decisions are made using diagnostic test results, diagnostic testing only accounts for about 2 percent of worldwide healthcare costs.* Diagnostics are crucial in helping healthcare practitioners diagnose medical conditions early, enabling them to make better-informed treatment decisions for faster courses to health. Diagnostics provide a deeper understanding of disease and aid in the development of more effective treatment. Following diagnosis, diagnostics help predict disease progression, allowing for proactive therapy management and appropriate treatment.

The National Committee for Quality Assurance in 2004 found that low compliance with diagnostics-based quality measures for diabetes, cardiovascular disease, colorectal cancer and breast cancer alone was linked to more than 56,000 avoidable adverse health events, 34,000 avoidable deaths and nearly $900 million in avoidable healthcare costs. According to a report issued by Kalorama Information in 2008, the world market for *in vitro* diagnostics, estimated at $42 billion in 2007, is expected to grow 6 percent annually through 2012.

*Source: The Lewin Group, 2005.
The Value of Diagnostics: Innovation, Adoption and Diffusion into Health Care.

Additional Resources

Ortho Clinical Diagnostics Franchise

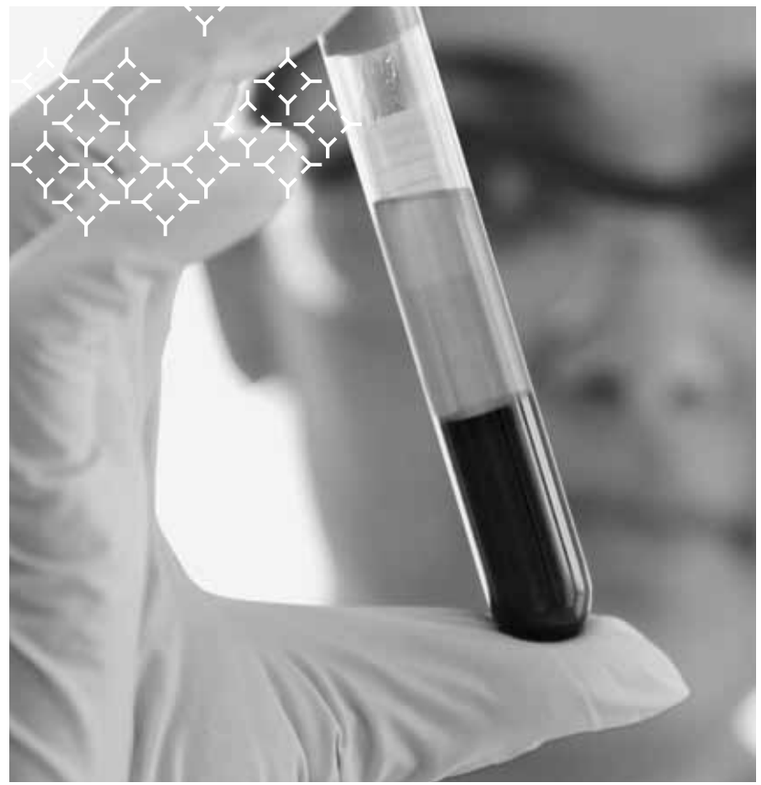
- Ortho-Clinical Diagnostics, Inc.
  www.orthoclinical.com
- Therakos, Inc.
  www.therakos.com
- Veridex, LLC
  www.veridex.com

Third Party Organizations

- AABB (formerly known as the American Association of Blood Banks)
  www.aabb.org
- AdvaMed, the Advanced Medical Technology Association
  www.advamed.org
- American Association for Clinical Chemistry (AACC)
  www.aacc.org
- American Society for Clinical Laboratory Science (ASCLS)
  www.ascls.org
- American Society of Clinical Oncology (ASCO)
  www.asco.org
- Association for the Advancement of Medical Instrumentation (AAMI)
  www.aami.org
- International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)
  www.ifcc.org
- International Society of Blood Transfusion (ISBT)
  www.isbt-web.org
- Medical Device Manufacturers Association (MDMA)
  www.medicaldevices.org

Ortho Clinical Diagnostics Franchise

A Journalist's Guide to Diagnostics



Diagnostics Process

The majority of diagnostic testing is carried out in hospital settings, with doctors' offices and centralized reference labs not far behind. Common terms for these various settings include:

- Commercial reference labs (large centralized diagnostic laboratories used by physicians and other smaller customers without their own lab facilities)
- Hospital central labs
- Point-of-Care (doctor's offices, hospital/nursing home bedsides)
- Patients/retail (home pregnancy test, STD tests mailed into a clinical lab)

Regardless of where the test is performed, there are three major steps to the process:

1

Samples + Reagents

Samples (blood, urine, saliva, etc.) are collected from the patient in an appropriate manner based on the nature of the sample.

The sample is combined with a **reagent,** a highly specific chemical or biological substance that reacts with the sample to detect, identify and measure a quantifiable substance. In the case of a home pregnancy test, the reagents are already on the test strips.

2

Diagnostic Instruments + Accessory Products

The samples and reagents are combined and analyzed on a **diagnostic instrument** that is able to detect, identify and measure the specific markers (glucose, cholesterol, diseases, etc.). The instrument could be as large and complex as a mainframe computer, or as simple as a glucose meter test.

Features like automation are often incorporated into high-volume diagnostic instruments to help the users run the tests more efficiently and accurately, and upload results into electronic medical records.

3

Test Results

The **results** of the test are analyzed by a lab technician, physician, or patient directly to aid and determine diagnosis.

Path to Regulatory Approval

United States

Similar to the regulatory process established by the U.S. Food and Drug Administration (FDA) for the approval of new medicines, a process has been established by the FDA's Center for Devices and Radiological Health (CDRH) and the Center for Biologics Evaluation and Research (CBER) for the approval of medical devices and diagnostics. Every type of device is assigned to one of three regulatory classes (Class I, II and III) based on its intended use and risk it poses to the patient. Class I includes devices with the lowest risk and Class III includes those with the greatest risk to patients.

Market submission options include:

- 510(k) Application and Clearance – From Section 510(k) of the Food, Drug and Cosmetic Act, a 510(k) application is a pre-market submission made to the FDA to demonstrate that Class I or II medical devices are at least as safe and effective (substantially equivalent or SE) as a legally marketed device intended for the same or similar use. The SE determination is usually made by the FDA within 90 days.

- Premarket Approval (PMA) – PMA is a more stringent type of marketing application and is required by the FDA to evaluate the safety and effectiveness of Class III medical devices. Class III devices are generally those that support or sustain human life or introduce a new technology. FDA regulations provide 180 days to review the PMA and make a determination.

Outside United States

- The European Economic Area (EEA) requires that products receive a CE Mark to be placed on a single market of a member state. This process requires the responsible organization to secure an EC-Declaration of Conformity (EC-DoC) and certify that the device meets European Union (EU) health, safety and environmental requirements.

- The Association of Southeast Asian Nations' (ASEAN) medical device regulatory committee has unified rules for medical devices, ASEAN Medical Device Directive (AMDD), which outline requirements for medical device safety and performance, a classification system for devices, a Common Submission Dossier Template (CSDT) and a post-marketing alert system.

- In Canada, manufacturers of products defined as "devices" under the Food and Drugs Act must secure a Medical Device License (MDL) for Class II, III and IV devices before they can be marketed.

Diagnostics Industry Glossary

- Antibody – A protein produced by the body, in response to a foreign substance, that fights the invading organism
- Antigen – A substance that evokes a response from the body's immune system, resulting in the production of antibodies or other defensive action by white blood cells
- Assay – A laboratory test to find and measure the amount of a specific substance
- Biomarker – A specific physical trait used to measure or indicate the effects or progress of a disease, illness or condition
- Cellular diagnostics – The ability to visualize a cell and clearly identify its type and any abnormalities
- Clinical chemistry – Scientific technique for identifying the chemical properties of a substance to help determine disease
- Diagnostics – Instruments or a technique used in medical diagnosis
- In vitro diagnostics (IVD) – The latin words meaning "in glass," — these processes or reactions conducted for medical diagnosis are conducted in an artificial environment, as in a test tube or culture media
- In vivo diagnostics – The latin words meaning "in the living body," — these are assessments for medical diagnosis conducted on an entire live being, as in an imaging scan
- Immunoassay – A test that uses the binding of antibodies to antigens to identify and measure certain substances; and may be used to diagnose disease and plan treatment
- Immunodiagnostics – Analytical methods using antibodies as reagents
- Immunohematology – More commonly known as "blood banking" — the area of laboratory medicine that ensures the accurate selection of appropriate and compatible blood components for transfusion
- Molecular diagnostics – Determines how genes and proteins interact in a cell and focuses on patterns — gene and protein activity patterns — in different types of cancerous or precancerous cells. Molecular diagnostics uncovers these sets of changes and captures this information as expression patterns
- Point-of-Care (POC) testing – Allows patient diagnosis near the patient, including, but not limited to a physician's office, an ambulance, the home, the field or in the hospital
- Personalized medicine – The use of new methods of molecular analysis to better manage a patient's disease or predisposition toward a disease
- Pharmacogenetics – The study of genetic factors that influence an organism's reaction to a drug (also referred to as pharmacogenomics)
- Reagent – A substance used (as in detecting or measuring a component, in preparing a product or in developing photographs) because of its chemical or biological activity