

The In Vitro Diagnostics Market

Medical device products include disposable medical supplies, wound-management supplies and diagnostic products. In Vitro Diagnostics (IVD) is the medical device market segment that includes reagents, diagnostic test products, instrumentations and other related testing products supplied to both clinical and research laboratories. IVD refers to testing that aims for the identification of disease states outside the body, using such samples as body fluids (blood, urine) and tissues (biopsies and tissue sections). The IVD is a well-established market offering essential products used by physicians and other healthcare professionals.

The world market for IVD products was estimated at \$42 billion in 2007 and is expected to grow 6% annually to \$56.3 billion by 2012. This includes all laboratory, hospital-based and OTC testing product sales. North America, Europe and Japan are responsible for 44%, 26% and 11% respectively of these sales and make up 81% of the total IVD market. By 2012, their portion of the market is expected to decrease to 76%. Some of the total market growth derives from increased test usage in emerging countries.

**Worldwide In Vitro Diagnostic Reagent Sales by Country/Region
2007-2012**

	Sales 2007	%Mkt	Sales 2012	% Mkt	CAGR
N. America	\$18,450	44	\$23,090	41	5
EU 15/W. Europe	12,550	31	14,895	26	6
Japan	4,615	11	5,065	9	2
China	1,015	2	2,175	4	16
L. America*	830	2	1,695	3	15
India	520	1	1,000	2	14
E. Europe	710	1	950	2	9
ROW	4790	8	7446	13	9
Total	\$41,950	100	\$56,316	100	6

* includes Mexico

Source: Kalorama Information

Revenues of Selected IVD Companies, 2005-2007

	Country	2005*	2006*	2007*	%chg 05-07
THE TOP TIER					
Roche Diagnostics	Switzerland	6,594	7,057	7,480	4
Abbott Diagnostics	US	3,756	3,980	4,407	6
Siemens Medical	Germany	3,926	4,141	4,400	4
J&J - Ortho/Lifescan	US	3,275	3,507	3,911	6
Beckman Coulter	US	1,790	2,098	2,283	9
Becton Dickinson	US	1,638	1,705	1,936	6
Bayer Healthcare	US	1,077	1,215	1,425	11
bioMérieux	France	1,090	1,127	1,145	2
Sysmex	Japan	663	790	909	12
Inverness Medical	US	422	569	840	33
Bio-Rad	US	618	685	832	12
Novartis Diagnostics	US	556	625	707	9
Instrumentation Labs (IL)	Spain	455	500	525	5
Arkray	Japan	n/a	400	500	13
Cytac	US	362	402	500	13
Olympus	Japan	411	447	493	7
Total		26,633	29,248	32,293	7

Source: Kalorama Information Report 2008

As summarized in the table above in 2007, the top tier of IVD companies accounted for 78% of the global market, or \$32 billion, and will continue to dominate the market due to their global reach and multi-segment participation. However, their single-digit growth is compared to a 41% combined growth rate of the next tier of companies.

Immunoassay Market

Immunoassays are testing procedures that employ specific antibody binding for measuring an analyte in a test sample. Since the mid-1960s, immunoassays have made a major contribution to clinical lab work. In 2007, immunoassays of all kinds [automated, manual, enzyme-linked immunosorbant assay (ELISA), enzyme immunoassays, bead arrays, and microarrays] dominated the IVD product offerings and represented about a third of the testing in the clinical laboratory. Immunoassays have become one of the primary and indispensable tools in the diagnosis and monitoring of all areas of medicine.

In 2007, the world market for all immunoassay tests, including infectious diseases, was estimated at \$6.685 billion, excluding testing instrumentation. By 2012, the immunoassay-test market (excluding infectious diseases) will grow by 6% annually. The revenue of different immunoassay IVD companies as well as the sales in various market segments is illustrated in the following table as published in the Kalorama report in 2008:

**Revenue History of Leading Immunoassay Vendors, \$ million
2005-2007**

	2005*	2006*	2007*
Abbott	\$1,800	\$1,900	\$2,100
Siemens/Dade Behring	750	785	825
Siemens/Bayer	680	714	750
Beckman Coulter	402	484	596
Siemens/DPC	473	517	595
Roche	450	509	575
bioMérieux	353	362	363
Fujirebio	279	277	299
Ortho	160	190	200
Total	\$5,347	\$5,738	\$6,303

* estimated

Source: Kalorama Information

Cardiac Markers

With the incidence of cardiovascular disease going through the roof, cardiac markers are in huge demand. Physicians use cardiac markers in two ways: 1) to diagnose a cardiac event in a hospital emergency room (acute care) and 2) to evaluate the risk of a cardiovascular event occurring.

Traditional markers (CK-MB, troponin and myoglobin) are used in acute care while tests such as cholesterol are used to evaluate risk.

In the past two years, cardiac markers have been revitalized with tests such as myeloperoxidase (MPO), brain natriuretic peptide (BNP) and proBNP. Several other new markers [high sensitive C-reactive protein (hsCRP), homocysteine, Fatty Acid Binding Protein (FABP), Glycogen Phosphorylase isoenzyme BB (GPBB), urinary albumin, S-100 protein and hemoglobin A1c (hbA1c)] are becoming part of the acute-care test menu as well as part of the risk-evaluation toolbox.

The world market for cardiac markers was estimated at \$740 million in 2007, and with annual growth of 5%, it will reach \$1.05 billion in 2012. Until recently, the lead cardiac markers were troponin and CK-MB. Together, these two tests shared about 75% of the segment worth \$450 million in 2003. A number of new and developing markers are in the works.

Worldwide Lab-Based Immunoassay Sales by Analyte Type 2007-2012 (ID, Tumor Markers, Cardiac Markers, Diabetes/HbA1c, Thyroid, Proteins, Autoimmune, Anemia, Therapeutic Drugs, Fertility, Allergy, Drugs of Abuse)

	IVD Sales 2007	% Mkt	IVD Sales 2012	% Mkt	CAGR
Infectious Diseases	2,500	37	3,325	37	6
Tumor markers	740	11	1125	13	9
Cardiac markers	785	12	1050	12	6
Diabetes/HbA1c	370	3	590	7	10
Thyroid	365	6	465	5	5
Proteins	330	5	420	5	5
Autoimmune	250	4	410	5	10
Anemia	305	5	390	4	5
Therapeutic Drugs	310	5	335	4	2
Fertility	280	5	330	4	3
Allergy	260	4	290	3	2
Drugs of Abuse	190	3	200	2	1
TOTAL	6,685	100	8,930	100	6

Source: Kalorama Information Report 2008

Point-of-Care Market

The Point-of-Care (POC) test market includes the following segments:

- Patient self-testing / OTC products
- Rapid tests used in a professional setting—Physician Office Laboratory (POL), home care, clinic, etc.
- Rapid tests performed in the hospital

The estimates of IVD sales of POC tests include those in the home or OTC market and those used by professionals in the hospital, physician office labs (POL), clinic, etc. Professional POC includes all those in professional settings in hospitals, home care and clinics. This does not include workplace and criminal justice POC tests or services for drugs of abuse tests, which are estimated to have generated sales of approximately \$2 billion in 2007. It also does not include the diabetes testing market. In general, POC product sales represent about a quarter of all testing done.

The 2007 worldwide market for POC immunoassays designed for self and professional use is estimated at \$2.385 billion, self testing accounts for \$760 million and professional POC testing \$1.625 billion. The US market accounts for 55% (\$1.43 billion), the European market accounts for approximately 35% (\$835 million), Japan and Asia represents 5% (\$120 million), and the rest of the world accounts for the remaining 5% of the market.

Regional Breakdown of POC Immunoassay Market

Region	Sales (\$millions)
US	\$1311
EU	835
Asia	120
ROW	120
Total	\$2385

Source: Kalorama Information

The worldwide market for POC tests is projected to grow by an average of 11% per year to reach \$3.7 billion by 2012. The OTC market will see annual growth of 4%, partly because most tests require a blood sample, which is not especially conducive to self-testing. The need for close monitoring will help the professional sector grow 14% annually.

The POC tests most widely used by professionals in POL, clinics, home care etc. are glucose, prothrombin time and urinalysis strips. In Europe, numerous companies market small, table-top, chemistry systems for POLs and clinics. In the United States, this trend is emerging just now. For a number of years, POLs had resorted to performing only CLIA-waived tests. However, Moore Medical and PSS have begun distributing chemistry, hematology and immunoassays to POLs more aggressively in the past several years. The US medical market consists of approximately 900,000 physicians, with approximately 25,000 offices that have CLIA moderate licensure. However, there are approximately 200,000 potential POC test sites including physician offices and clinics.

The future use of lab-on-a-chip (LOC) and similar devices should make rapid, cost-effective assays for any assay available for POL. These are not expected to make any market impact until 2010. The most widely used POC tests used in the hospital are for drugs of abuse, blood gases and electrolytes, glucose, fecal occult blood, cardiac markers, pregnancy tests and infectious disease tests.

Worldwide, there is still the perception that POC tests are more expensive than lab-based tests and that patient test results are lost to the historical record. Further, once the patient leaves an acute care area such as the ER or an intensive care unit, the baseline testing done in that unit is relatively useless because, more often than not, the test results from POC devices do not correlate with lab-based systems or an algorithm to establish correlation has not been developed.



Professional POC

After many years of little growth, the professional POC test market is beginning to come alive. In 2006/07, demand for quicker test turnaround time spurred the launch of at least 15 new POC tests and devices, and at least another 15 are near market. The market for professional POC immunoassays is estimated at \$1.625 billion. With 14% growth, this market segment will reach \$2.77 billion in 2012. Most of the growth will come from increased use of cardiac markers and new assays for cancer markers and diabetes/cardiac disease markers.

Professional POC Testing 2005-2010 (Pregnancy, Cardiac Markers, Cholesterol/Lipids, HbA1c, Fecal occult blood, Cancer Markers, Drugs of Abuse, Other)

	2007	%Mkt	2010	%Mkt	CAGR
Pregnancy	\$110	3%	\$125	2%	3%
Cardiac Markers	425	11	850	15	15
Cholesterol/Lipids	250	6	475	8	14
HbA1c	300	7	550	10	13
Fecal occult blood	290	7	390	7	6
Cancer Markers	120	3	215	4	12
Drugs of Abuse	110	3	125	2	3
Other	20	1	40	1	15
Professional Total	\$1,625	41%	\$2,770	50%	14%

Source: Kalorama Information

Not all of the near-patient testing needs can be filled by strip-type, rapid tests. Increasingly, physicians are looking to increase the number of tests they offer in their offices. There is growing demand for small, easy-to-use and easy-to-maintain systems for near-patient sites and small clinical labs worldwide.

In the hospital setting, there is pressure for more rapid turnaround time and efficient patient management to minimize length of stay in hospitals; this provides an incentive for diagnostics companies to develop point-of-care testing technologies. The evidence for this supply/demand dynamic is evident in the continued growth in the market for critical-care analyzers and the new analyzers in development.

Cardiac Markers

The market for POC cardiac markers is one of the fastest growing segments of the IVD industry. By far, cardiac-marker testing is the most dynamic POC segment, and it will show the most change over the next few years. However, success often has the opposite effect than anticipated. The spectacular growth that could come in the area of POC cardiac-marker testing is tempered by the increasing popularity of automated lab-based systems. There are a number of reasons for this.

In 2007, most cardiac-marker testing was done in acute-care settings on patients in the midst of a cardiac event. The POC market for cardiac markers was estimated at \$325 million in 2007 and will increase to \$650 million by 2012. Physicians have begun testing patients during the office visit, and it is estimated that the world market for POL cardiac markers was approximately \$75 million in 2007 and that it will grow at an annual rate of 15%.

As more is learned about cardiovascular disease and its links to diabetes, lipid metabolism, and inflammation, the definition of a cardiac marker expands. Medical research will indicate the mix and match of various analytes according to specific cardiac conditions such as stroke, thrombosis, heart attack and cardiovascular risk. From the technology side, microfluidics and digital optics are the market enablers for this type of testing. Thus, the development of lab-on-a-chip or similar devices that drive lab-quality results will come into play.

The traditional cardiac markers (CK-MB, myoglobin and troponin I/T) have had their own shake-up with the emergence of new additions such as hsCRP and BNP. There are at least 20 companies that sell test strips for one or all of the above cardiac marker panels. Biosite is the leader of POC immunoassay testing, and product sales have increased from \$103 million in 2003 to \$208 million in 2007.

POC Market Penetration

Previously, infrastructure and reimbursement barriers were blamed for the poor track record of POC testing. However, payer groups have begun to provide reimbursement approval for POC tests. Many physicians use POC testing as a tool to provide improved patient care. Inside the hospital, the problems associated with quality control and training non-laboratory staff have scared off many would-be users.

According to the 2008 Kaloma Information Report, the most telling cause for POC's limited market penetration is technological. Most rapid POC tests are based on qualitative chromatographic

techniques with visual detection of results. However, as imaging and computational capabilities improve, there is a significant trend within the diagnostics industry to replace visual detection with digital and instrument-based methods. This relates to the technical aspects of near-patient testing. On the market acceptance side, the situation is less straightforward. Although benefits including advances in connectivity are driving POC instrument adoption, there are still a number of acceptance barriers. The primary factors relate to device maintenance and quality control. Here too, the new generation of one-test, lab-on-a-chip devices could make a difference. The goal of LOC devices is to go from sample to result in one easy step—put the sample on the device. Each LOC would have full calibration and quality control materials plus built-in connectivity.

Future of POC Immunoassay Platforms

The key to diagnosis is to measure the difference between normal and abnormal concentrations of potential disease markers. According to the 2008 Kalorama Information Report, “most immunoassay technologies in routine use in 2007 do not have the sensitivity needed to detect many of the new disease markers.” Thus, new ultra-sensitive test methodologies are needed to allow for detecting disease-specific markers for diseases such as diabetes, cancer, osteoporosis, arthritic conditions and cardiac disease. Immunoassay developers are on a continuous hunt to discover technologies that can detect nano-, pico- and even femto-molar concentrations of proteins in clinical samples.

The market significance of immunoassays is best shown by the intensive research that continues to bring new systems, technologies and tests to market. In 2007, Kalorama estimated at least 70 new immunoassays were in development or had come to market. Most of the new tests are for cancer testing, but they also cover a wide variety of diseases including: allergy, autoimmune, cardiovascular, sepsis proteins and transplant markers.

The demand for automated bench-top and POC (small footprint) immunoanalyzers is the impetus for the development of several new instruments. Many of these systems are obviously designed for POC testing, but they are also well-placed for use in small labs. Of particular interest is the investment manufacturers have made in new systems and technologies. Many of the new systems are being developed by major IVD companies, but most are held by smaller companies that will surely be looking for commercialization partners.

Two critical points are necessary for near-patient testing in the hospital to become more prevalent: data communication and correlation with lab-based results. The data communication aspect is under control. Every major POC system manufacturer now offers data management linking software and devices. For many assays such as coagulation and cardiac markers, though, correlation with lab-based results is still weak.

General IVD Market Trends

The IVD market is a well-established market for acquisition, collaboration and license agreements between small and large IVD firms. In 2006/2007, there were at least 100 acquisitions, some 25 distribution agreements and at least 80 collaborations and licensing deals. This is only a small portion of what is really happening as there are many more deals that have not been announced. A full list of all the public domain details of these agreements, acquisitions and licenses is available.

Major industry participants with immunoassay analyzers that offer a menu of test products include:

- Roche Diagnostics, Switzerland
www. Roche .com
- Abbott Diagnostics, Abbott Park, IL 60064
www. Abbott .com
- Siemens Medical Solutions Diagnostics, Deerfield, IL
www. diagnostics .siemens .com
- Johnson & Johnson, Ortho Clinical Diagnostics (OCD) division, Raritan, NJ
www. jnj .com
- Beckman Coulter Inc., Fullerton, CA
www. beckmancoulter .com
- Becton, Dickinson & Co., Franklin Lakes, NJ
www. bd .com
- bioMerieux SA, Marcy l'Etoile, France
www. biomerieux .com
- Bio-Rad Laboratories Inc., Hercules, CA
www. bio-rad .com
- Arkray Inc., Kyoto, Japan
www. arkray .co .jp
- Mitsubishi, Japan
www. mitsubishi .com