

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, diagnostics test products, instrumentations and other related testing products supplied to both clinical and research laboratories. IVD refers to testing outside the body for the identification of disease states, using samples as body fluids (blood, urine) and tissues (biopsies and tissue sections). The IVD is a well-established market, offering essential products used by health care professionals.

The world market for IVD products is 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.

As summarized in the table above, in 2007, the top tier of IVD companies occupies 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 41% combined growth of the next tier 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 continue to make a major contribution to clinical lab. In 2007, immunoassays of all kinds (automated, manual, ELISAs, enzyme immunoassays, bead arrays, and microarrays) dominate the IVD products offerings and represent 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.

The 2007, world market for all immunoassay tests and including infectious diseases is estimated at \$6,685 million, excluding testing instrumentation. By 2012, the market for immunoassay test market (excluding infectious diseases) will grow by 6% annually.

Cardiac Markers

With the incidence of cardiovascular disease is increasing, cardiac markers are in huge demand. Physicians use cardiac markers in two ways; to diagnose a cardiac event in a hospital emergency room (acute care) or to evaluate the risk of a cardiovascular event occurring. Traditional markers (CK-MB, troponin and myoglobin) are used in the acute care and tests such as cholesterol were 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 and as part of the risk evaluation tool box.

The world market for cardiac markers is estimated at \$740 million in 2007 and with annual growth of 5% will reach \$1050 million in 2012. Up 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. A recent market report in 2013 estimates the total market of acute cardiac markers care of about US \$2 billion.

POINT-OF-CARE MARKET

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

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

The estimates of POC test sales include those in the home or OTC market and those used by professionals in the hospital, POL, clinic, etc. Professional POC includes all those in hospitals, home care and clinics settings. This does not include workplace and criminal justice POC tests and 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 \$2385 million, self testing accounts for \$760 million and professional POC testing \$1625 million. The U.S. market accounts for 55% (\$1430 million), the European market accounts for approximately 35% (\$835 million), Japan and Asia represents 5% (\$120 million) and the ROW accounts for the remaining 5% of the market.

The worldwide market for POC tests is projected to grow by an average 11% per year to reach \$3700 by 2012. The OTC market will see annual growth of 4%, partly because most tests require a blood sample that is not especially conducive to self-testing. The need for close monitoring will help the professional sector grow 14% annually.

Professional POC

The most widely POC tests used in physician office labs (POL), clinics, home care etc. are glucose, prothrombin time and urinalysis strips. In Europe, numerous companies market small tabletop chemistry systems for POLs and clinics. The U.S. medical market consists of approximately 25,000 offices with CLIA moderate licensure. However, there are approximately 200,000 potential POC test sites including physician offices and clinics 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 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 and infectious disease tests. The future use of lab-on-a-chip and similar devices should make rapid, cost effective assays for any test available for POL. 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.



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 has spurred the launch of at least 15 new POC tests and devices in the past few years and at least another 15 are near market. The market for professional POC immunoassays is estimated at \$1625 million. With 14% growth, this market segment will reach \$2770 million 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.

Not all of the near the 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 maintain small 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 that provide 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

Cardiac Markers

The market for POC cardiac markers is one of the fastest growing in the IVD industry. By far, cardiac marker testing is the most dynamic POC segment that 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 their increasing popularity on automated lab-based systems. There are a number of reasons for this.

In 2007, most cardiac marker testing is done in acute care settings on patients in the midst of a cardiac event. The POC market for cardiac markers is estimated at \$325 million in 2007 and will increase to \$650 million in 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 will grow at an annual rate of 15%. The traditional cardiac markers (CK-MB, myoglobin and troponins) have had their own shake up with the emergence of new additions as hsCRP and BNP. There are at least 20 companies that sell test strips for all or one of the above cardiac marker panel. Biosite is the leader of POC immunoassay testing with sales increasing from \$103 million in 2003 to \$208 million in 2007.

As more is learned about cardiovascular disease and its links to diabetes, 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.

POC Market penetration

According to a 2008 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.

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.

There are still a number of acceptance barriers for POC instrument adoption. The primary factors relate to device maintenance and quality control. The new generation of one device, one test lab-on-a-chip device could make a difference. Each LOC would have full calibration and QC materials plus built in connectivity.

Future of POC Immunoassay Platforms

According to 2008 published 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. Immunoassay developers are on a continuous hunt to discover technologies that can detect nano, pico and even femtomolar concentrations of proteins in clinical samples. The market significance of immunoassays is best shown by the intensive research that continues to bring new tests systems, technologies, and tests to market. Kalorama report estimates at least 70 new immunoassays are in development or have come to market.

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 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 developed by major IVD companies, but most are held by smaller companies that will surely be looking for commercialization partners.

General IVD market trends

The IVD market is 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 many more deals that have not been announced.

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