

The background of the cover is a microscopic image of cells. A large, central cell is in sharp focus, showing its nucleus and cytoplasm. Other cells are visible in the background, some out of focus. The overall color palette is dominated by purples, pinks, and greens.

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MOLECULAR DIAGNOSTICS IN CANCER TESTING *(SAMPLE COPY, NOT FOR RESALE)*

Trends, Industry Participants, Product Overviews and Market Drivers

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1. Overview

1.1 Statement of Report

This report describes the specific segment of the *in vitro* diagnostics (IVD) market known as molecular diagnostics (MD), with a specialization in the MD tests for cancer. In the current medical diagnostics market, molecular diagnostics for cancer testing offers one of the brightest areas for growth and innovation. The confluence of breakthroughs in genomics, proteomics, and the development of microarray devices to measure analytes in the blood and various body tissues, has led to this revolutionary market segment offering the power of advanced analytical techniques to the diagnosis and treatment of cancer.

This market report analyzes the size and growth of the molecular diagnostics market in its applications for cancer detection and therapy, examining the factors that influence the various market segments and the dollar volume of sales, both in the United States and worldwide. The cancer market has been divided into the following parts for examination:

- Breast cancer molecular diagnostics market.
- Colorectal cancer molecular diagnostics market.
- Prostate cancer molecular diagnostics market.
- Other cancer molecular diagnostic market segments.

This segregation is based upon the available technology platform advances and the number of companies interested in that segment of the cancer market.

1.2 About This Report

This report includes the following features:

- It examines the generally-accepted clinical analytical activities in use today in the molecular diagnostics sector for diagnosis and management of cancer. It includes the prevalent clinical-measurement devices such as genomic profiling analysis (IVDMIA) and the accompanying reagents and supplies as utilized in hospitals and large reference and specialty CLIA licensed laboratories.
- It discusses the potential benefits of the molecular diagnostics technique for various sectors of the medical and scientific communities, and it assesses the market drivers and bottlenecks for MD tests from the perspective of these communities.
- It establishes the current total MD market size and future growth of the molecular diagnostics market for cancer management, and analyzes the current size and growth of various segments.
- It assesses various business models in molecular diagnostics for cancer, including CLIA licensed specialty labs, general reference labs and reagent kit marketing, and provides strategic recommendations for near-term business opportunities.
- It examines the products offered and roles played by companies that have invested significantly in this market, and it provides current and forecasted market shares by these companies.
- Discusses new collaborative business models that bring together diagnostics and therapeutics.
- Evaluates the role that cancer prognostic assays can play in partnership opportunities in personalized medicine.

1.3 Scope of the Report

The goal of this study is to review the market for molecular diagnostics testing equipment and supplies using reagents and instruments for analysis of individual components in body tissues and fluids. Toward this goal, this review answers the following key questions:

- Which companies are utilizing new, cutting-edge technologies to develop, validate and market molecular tests for clinical use in cancer management?
- What are the current impediments to incorporating promising molecular tests into clinical practice?
- Which new molecular diagnostics tests show the most promise for approval?
- What are the economic challenges to gaining approval? And what kind is best?
- How can regulatory oversight drive approval and adoption of new technologies?
- Which alliances show the greatest synergy in bringing molecular diagnostics tests to market?
- Which shared technologies are driving the most encouraging development?

This examination surveys most of the biotech companies known to be currently marketing, manufacturing or developing instruments and reagents for the molecular diagnostics market for cancer management, in both the U.S. and the world. Each company is discussed in depth, with sections on its history, product line, business and marketing analysis, and a subjective commentary of the company's market position.

The U.S. is the focus of this report. Primary attention is paid to the specialty and reference lab market segment and, separately, to the instruments, reagents and supplies marketed by the leading companies in this segment. Market size, growth rates and market components for instruments, reagents, controls and consumables used in this area are also analyzed.

1.4 Objectives

The main objectives of this analysis are:

- Identifying viable technology drivers through a comprehensive look at platform technologies for molecular diagnostics in cancer management, including probe-based nucleic acid assays, microarrays and sequencing.
- Obtaining a complete understanding of the chief characteristics of molecular diagnostics tests—namely, predictive, screening, prognostic, monitoring, pharmacogenomic and theranostic tests—from their basic principles to their applications.
- Discovering feasible market opportunities by identifying high-growth applications in different clinical cancer diagnostic areas (breast cancer being the leading one).
- Focusing on global industry development through an in-depth analysis of the major world markets for molecular diagnostics for cancer management, including growth forecasts.

The emphasis in this report is on the clinical use of molecular diagnostics tests for cancer diagnosis and management. The reader should consult other TriMark Publications reports at <http://www.trimarkpublications.com> for detailed discussions of important individual market segments related to the molecular diagnostics market or routine testing. In addition to this report, TriMark Publications offers a complete suite of market reports aimed at the molecular diagnostic space including: *Molecular Diagnostics Markets* and *Molecular Diagnostics in Infectious Disease Testing*.

1.5 Methodology

The author of this report holds a Ph.D. in biochemistry from the University of Minnesota and has had post doctoral experience at the University of Connecticut School of Medicine. He has taught at Quinnipiac University and the Tufts School of Medicine, and has been a senior scientist at Pfizer Pharmaceutical Laboratories in drug development. He also has many decades of experience in science writing and as a medical industry analyst. He has over 25 years of experience in laboratory testing and instrument and reagent development technology as a licensed clinical laboratory director, as well as extensive experience in senior level management positions in biotech and medical service companies. He was the first director and a founder of Dianon Laboratories, now part of LabCorp, and was a pioneer in bringing cancer diagnostic tests, including an early PSA, to the clinic.

Company-specific information is obtained mainly from industry trade publications, academic journals, news and research articles, press releases and corporate websites, as well as annual reports for publicly-held firms. Additional sources of information include non-governmental organizations (NGOs) such as the World Health Organization (WHO) and governmental entities such as the U.S. Department of Health and Human Services (HHS), the National Institutes of Health (NIH), the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC). Where possible and practicable, the most recent data available have been used.

Some of the statistical information was taken from Biotechnology Associates' databases and from TriMark's private data stores. The information in this study was obtained from sources that we believe to be reliable, but we do not guarantee the accuracy, adequacy or completeness of any information or omission or for the results obtained by the use of such information. Key information from the business literature was used as a basis to conduct dialogue with and obtain expert opinion from market professionals regarding commercial potential and market sizes. Senior managers from major company players were interviewed for part of the information in this report.

Primary Sources

TriMark collects information from hundreds of Database Tables and many comprehensive multi-client research projects, as well as Sector Snapshots that it publishes annually. TriMark extracts relevant data and analytics from its research as part of this data collection.

Secondary Sources

TriMark uses research publications, journals, magazines, newspapers, newsletters, industry reports, investment research reports, trade and industry association reports, government-affiliated trade releases and other published information as part of its secondary research materials. The information is then analyzed and translated by the Industry Research Group into a TriMark study. The Editorial Group reviews the complete package with product and market forecasts, critical industry trends, threats and opportunities, competitive strategies and market share determinations.

TriMark Publications Report, Research and Data Acquisition Structure

The general sequence of research and analysis activity prior to the publication of every report in TriMark Publications includes the following items:

- Completing an extensive secondary research effort on an important market sector, including gathering all relevant information from corporate reporting, publicly-available data and proprietary databases.
- Formulating a study outline with the assigned writer, including important items, as follows:
 - Market and product segment grouping, and evaluating their relative significance.
 - Key competitors' evaluations, including their relative positions in the business and other relevant facts to prioritize diligence levels and assist in designing a primary research strategy.
 - End-user research to evaluate analytical significance in market estimation.
 - Supply chain research and analysis to identify any factors affecting the market.
 - New technology platforms and cutting-edge applications.

- Identifying the key technology and market trends that drive or affect these markets.
- Assessing the regional significance for each product and market segment for proper emphasis of further regional/national primary and secondary research.
- Completing a confirmatory primary research assessment of the report's findings with the assistance of expert panel partners from the industry being analyzed.

1.6 Executive Summary

Molecular diagnostics is a rapidly-advancing area of research and medicine, with new technologies and applications being continually added. The technologies that come under the umbrella of molecular diagnostics include first-generation amplification, DNA probes, fluorescent *in-situ* hybridization (FISH), second-generation biochips and microfluidics, next-generation signal detection, biosensors and molecular labels, and gene expression profiling using microarrays. These technologies are improving the discovery of therapeutic molecules for cancer, the screening, diagnosis and classification of cancer patients, and the optimization of drug therapy. Over the past several years, this rapidly evolving field has seen several fascinating developments, including:

- Impact on pharmacogenomics and molecular epidemiology.
- Integration of specialty labs and gene expression profiling into clinical practice.
- Integration into therapeutic choices for cancer and the use of diagnostics for predicting disease recurrence.
- Development of lab-on-a-chip devices.
- Development of companion diagnostics for drug development.
- Use of gene expression profiling for determining the efficacy of therapeutic drugs for cancer.

More than █ companies market products in molecular diagnostics. Most of these are relatively small, with annual sales between \$█ and \$█. However, several major diagnostic companies, such as Abbott Laboratories, Siemens and Roche Diagnostics have substantial market shares in each category of the molecular diagnostics market, including cancer testing. On the other hand, small and medium-sized companies like Genomic Health and Myriad, with innovative products and technology platforms, have great opportunities for success in the field of molecular diagnostics as applied to cancer. The exciting thing here is that this market segment is characterized by unprecedented growth rates, which stand in contrast with the low or even negative growth rates of mature laboratory-testing segments in fields such as hematology and microbiology.

Research in genomics has led to a new healthcare paradigm, where a disease is understood at the molecular level, allowing patients to be diagnosed based on genetic their own unique information and then treated with drugs designed to work on specific molecular targets for cancer. Gene expression profiling will continue to increase as companies in the pharmaceutical industry work with diagnostic companies to accelerate their drug discovery and development efforts in cancer therapeutics by using companion diagnostic tests in clinical trials, and later as guides to optimum efficaciousness during cancer therapy through targeted drugs. These efforts are expected to create a demand for increasingly effective cancer diagnostic tests. Among the most important questions that future genomics research will address are:

- How do genetic polymorphisms—the variations in DNA sequences among individuals—contribute to susceptibility to chronic diseases such as cancer?
- How do genetic variations influence individual responses to drug therapies?
- How do differences in gene expression in various tissues affect development of diseases like cancer?
- How does gene expression contribute to health, and how do changes in gene expression contribute to long term development of cancer?
- How does gene expression regulate recurrence of cancer?

Most industry experts believe that over the next few decades, the use of molecular diagnostics will grow rapidly, in the order of █% to █% per year, and will have a revolutionary impact on the way clinical medicine is practiced. A particularly important emerging area of focus for molecular diagnostic services is cancer. In the U.S. alone, the

American Cancer Society indicates that [REDACTED] individuals are diagnosed with cancer annually, and this rate is expected to grow rapidly as the overall population, including the “baby boomer” generation, ages. Advances in genomics are making it possible to choose therapy appropriate to an individual’s genetic makeup. The translation of genomic information into novel molecular diagnostics products is taking place at both the gene and protein levels.

The cancer segment of molecular diagnostics, while not the largest, is growing the fastest. As molecular diagnostics technologies continue to grow, they offer the potential to move from diagnostics to prognostics and theranostics. Still, the molecular diagnostics market for cancer is difficult to estimate, as it overlaps with the broader IVD market and includes the more routine, older serum tests for cancer (CEA, PSA, Ca125, etc.) and is less well-defined than the pharmaceutical or device markets. However, molecular diagnostics is now being used in cancer management in real clinical situations to evaluate patients. Factors that drive the molecular diagnostics business are:

- Personalization of diagnosis and therapy by identifying genes associated with complex diseases, optimizing the drug response, and reducing side effects and failure rates (pharmacogenetics).
- Need for faster methods of diagnosing disease states and medical disorders earlier, and for a powerful, reliable tool for therapy decisions.
- Need for an automated analysis and data evaluation.
- Need to contain or decrease healthcare costs without compromising accuracy or reliability.

Molecular diagnostics using genomic technologies are being used to characterize tumors at the molecular level, and several clinical successes have shown that such information can guide the design of drugs targeted to a specific tumor type. Emerging classes of cancer biomarkers such as microRNAs and epigenetics are also important in this context the emerging cancer personalized medicine market landscape includes:

- Cancer diagnostic tests on the marketplace and in development that are developed as companion-diagnostics (coupled with a therapeutic regimen).
- Landscape of *In Vitro* Diagnostic Multivariate Index Assays (IVDMIAs)—multigene predictors with prognostic/predictive value.
- Key personalized medicine products in the breast cancer, colon cancer, etc. market spaces—together with the characteristics/features of these products—HER2, Oncotype DX™, MammaPrint®, UGT1A1, K-RAS, EGFR, etc.

One of the main barriers to further progress is identifying the biomarkers of cancer that predict who will benefit from a particular targeted therapy. The market for advanced cancer diagnostic testing will increase from an estimated \$ [REDACTED] in [REDACTED], to over \$ [REDACTED] by [REDACTED]. Business factors influencing advanced oncology testing services are:

- Demographic shifts to an older (> [REDACTED] years) population.
- An increased incidence of cancer within an aging population.
- New cancer therapies.
- An expanding test menu for prediction and efficacy.
- Recent trends indicate that treatment decisions are likely to involve the assessment of a complex panel of protein and gene based testing, rather than a single test.
- Diagnostic and predictive testing for these therapies will likely become increasingly complex, and there will be increased demand for sophisticated tests.
- Advanced molecular tests will also require additional expertise to interpret test results and/or assist pathologists in such interpretations.
- Pharmaceutical companies’ demand for high potential targeted therapies will continue to grow under pressure from the FDA for more effective drugs.
- Four thousand hospitals and healthcare networks in the U.S. together with their oncology and pathology staffs constitute a large readymade market.
- One thousand biopharmaceutical companies developing new drugs and partnering with large pharma companies for targeted therapies.
- Emergence of CLIA certified specialty labs for advanced testing services.

Pharmaceutical companies are investing billions of dollars in the development of high-potential targeted therapies, one of the fastest growing segments of oncology drug development. Many of these therapies will require a specific test (referred to as a “theranostic” or “companion diagnostic”) to assist physicians in selecting the right drug for the right patient. The theranostic is likely to accelerate the process for drug approval and market introduction by guiding selection of the most appropriate patients for the clinical trials. The Food and Drug Administration’s “Critical Path Initiative” is facilitating a national effort to modernize the scientific process through which a potential human drug, biological product or medical device is transformed from a discovery or “proof-of-concept” into a medical product.

A classic example of a targeted therapy that uses a companion diagnostic test is Genentech, Inc.’s Herceptin[®], used to target breast tumor cells that have a significant amount of HER2/neu protein on the cell membrane. The National Comprehensive Cancer Network (NCCN), a not-for-profit alliance of ■ of the world’s leading cancer centers, currently mandates that all new breast tumors be tested for HER2/neu status levels. Cancer diagnostic companies provide a wide range of cancer diagnostic and consultative services which include technical laboratory services and professional interpretation. Specific diagnostic products categories comprising the cancer diagnostic market are:

- Immunoassays for serum cancer markers, receptor assays and hormone assays.
- Mammography equipment.
- Clinical chemistry reagents (occult blood reagents, enzymes, serum proteins).
- DNA and gene expression reagents and products (microarrays and chips).
- Cytological products.
- Histological reagents.
- Immunocytochemistry products.
- Immunohistochemistry reagent.

There are five basic business models for entry into the cancer diagnostic market:

- Pure play IVD/MIA specialty tumor analysis: Myriad, Genomic Health, Agendia, DxS, Clariant, etc.
- Mixed specialty cancer diagnostic labs offering cytology, flow cytometry, anatomic pathology, immunohistochemistry, around microarray specialty MD testing: Neogenomics, Redpath, Genoptix, etc.
- General clinical reference labs (national and community): Quest, LabCorp, etc.
- Diagnostic device and reagent developers: Exact Sciences, Abbott, Roche, etc.
- Companion diagnostics development in partnership with a pharmaceutical company.

Market trends in cancer testing:

- Rapidly growing market segment in cancer diagnosis.
- Expansion of Pharma DX collaborations.
- Strong growth of esoteric testing.
- Strong move toward targeted therapies for cancer.
- Expansion of molecular diagnostics to drive therapy decisions.
- Minimal pressure on reimbursements.
- Lack of capital will increase opportunities to license markers.
- Emerging opportunity for molecular pathology space.
- Focus on delivering companion diagnostic information for cancer therapies.
- Tumor types represent ■% of ongoing Phase II and Phase III therapeutic trials.
- Use of cancer profiles for reporting data (Clariant Insight DX).
- Increased M&A activity.

Molecular diagnostics cancer market; market drivers ranked in order of impact:

- Core genetic testing industry growth (CAGR ~■%).
- Increased sensitivity for detection of analytes.
- Faster detection and analysis times (increased TAT).
- Higher accuracy of detection, particularly in complex mixtures.
- Ease of use for previously esoteric assays (*e.g.*, HPV).
- Ability for the molecular diagnostic nucleic acid technology platforms to be developed for assay of new analytes.
- Applicability of molecular diagnostic techniques to pharmaceutical industry development needs, *e.g.*, companion diagnostics for drug development.
- The rapid expansion of genomics and genetic testing.
- The clarification of much proteomic research and development (R&D) through improvements in data handling.
- Continuing breakthroughs in cancer diagnosis and therapy.
- New analysis needs for biosafety and homeland security.
- Trend to increased penetration through more tests ordered per requisition for lab orders.
- Increased M&A activity.
- Partnering with large diagnostic companies (Abbott, Roche, etc.).

Molecular diagnostics cancer market—market restraints ranked in order of impact:

- Increased cost of assays.
- Changes in analysis paradigm, particularly in the movement of tests to specialized CLIA labs.
- Inaccessibility of many molecular diagnostic tests to standard laboratory instrumentation, and therefore the need for labs to acquire additional hardware for high throughput automated analysis.
- High cost of test results and lack of third-party reimbursement.
- Lack of understanding of molecular tests by oncologists and other physician groups.
- Stringent licensing requirements by CLIA and state governments.
- Complex mix of third-party payors.
- Competition from hospitals and community pathologists.

Strategic recommendations on molecular diagnostic sector business functions:

- Cancer testing will become a significant growth area during the forecast period.
- Small diagnostic companies will only succeed in partnership with large diagnostic companies with significant marketing reach; general clinical labs are overdue for consolidation.
- Funding for promising technology platform start ups will become increasingly more difficult to obtain and licensing will dominate to entry of new test procedures.
- Funding for on-going small companies who have used up their initial funding will be extremely problematic.
- The cancer testing sector of molecular diagnostics will see a significant increase in the number of active players in the mixed specialty and pure play testing labs.
- Pharmacogenomics of older well used drugs (*i.e.*, Warfarin), although a popular topic with researchers, will not break through into general use in the medical community within the next five years.
- Companion diagnostics for new pharmaceutical drugs will be a grow area for molecular diagnostics as it is driven by increasingly strict FDA requirements for marketing approval.
- Niche areas for diagnostic tests on less tested diseases like lymphoma, leukemia, and women's health determinations will become an important place for small companies to survive and grow.
- Biosecurity testing will become an important source of funding in response to government funding for Homeland Security.