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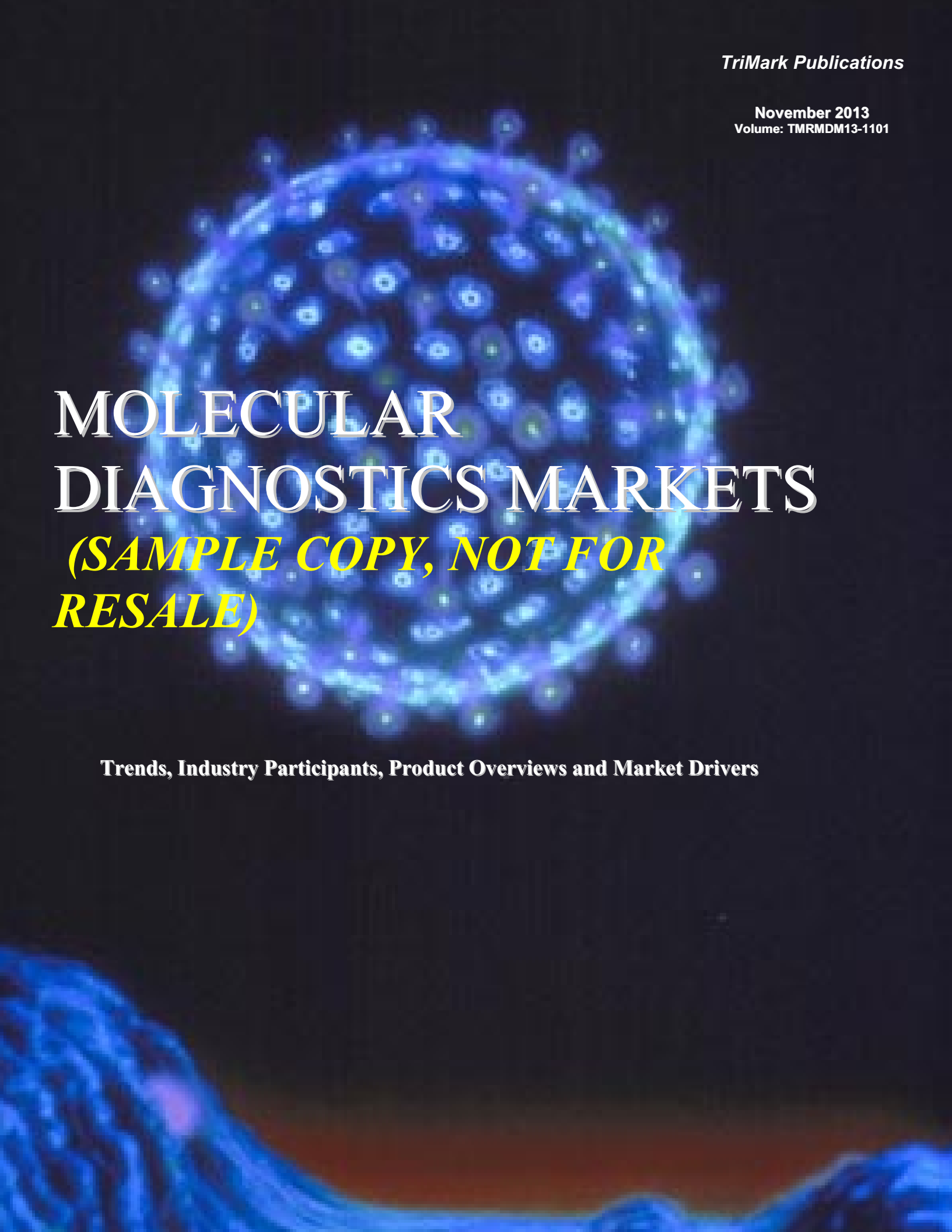

MOLECULAR DIAGNOSTICS MARKETS

(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 (MDx). In the current medical diagnostics market, molecular diagnostics offers the brightest promise for growth and innovation. The rapid development of this sector of the diagnostics industry has been driven by:

- The confluence of research breakthroughs in genomics such as the human genome project.
- The development of a wide variety of polymerase chain reaction (PCR)-based technology platforms.
- The rise of gene expression profiling.
- New developments in cancer diagnosis and treatment.
- The need for screening the blood supply for infectious diseases.
- Detection of infectious diseases in a hospital setting for intensive care units (ICUs) and other critically ill patients.
- The use of microarrays and multiplexing.

This review analyzes the size and growth of the MDx market, including the factors that influence the various market segments within it, the dollar volume of sales, both in the United States and worldwide. Also examined are:

- PCR technology platforms.
- Clinical applications of nucleic-acid-based testing.
- The market for molecular diagnostic tests.
- Companies participating in this sector.
- New instrumentation, technology platforms and diagnostic lab testing reagents.
- Trends in the MDx industry sector.
- The internal structure of the molecular diagnostics testing sector.

1.2 About This Report

This report:

- Examines all of the generally-accepted clinical analytical activities in use today in the MDx sector. It includes the prevalent clinical measurement devices and the accompanying reagents and supplies as utilized in hospitals, clinics, large reference laboratories and doctor's offices.

- Discusses the potential benefits of the MDx market for various sectors of the medical and scientific communities, and it assesses the market drivers and bottlenecks from the perspective of these communities.

- Establishes the current total market size and future growth of the MDx market and analyzes the current size and growth of various segments.

- Assesses various business models in MDx and provides strategic recommendations for near-term business opportunities.

- 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.

1.3 Scope of the Report

The goal of this study is to review the market for MDx 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 cutting-edge technologies to develop, validate and market molecular tests for clinical use?
- 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?
- How can regulatory oversight drive approval and adoption of new technologies?
- Which alliances show the greatest synergy in bringing MDx 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 MDx market, in both the U.S. and the world. Each leading 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., Europe and Japan, the world's three largest molecular diagnostics markets, are the focus of this report. Primary attention is paid to the hospital market segment and, separately, to the instruments, reagents and supplies marketed by the major companies in this segment. Market size, growth rates and market components for instruments, reagents, controls and consumables used in this area are also analyzed.

This analysis emphasizes the companies that are actively developing and marketing clinical laboratory instrumentation, reagents and supplies for performing molecular diagnostics tests. The emphasis in this report is on the clinical use of MDx tests.

1.4 Objectives

The main objectives of this analysis are:

- Identifying viable technology drivers through a comprehensive look at platform technologies for MDx , including probe-based nucleic acid assays, microarrays and sequencing.

- Obtaining a complete understanding of the chief MDx tests—*i.e.*, 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 diagnostic areas and by focusing on expanding markets, such as communicable diseases, cardiology and oncology.

- Focusing on global industry development through an in-depth analysis of the major world markets for MDx including growth forecasts.

One 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 blood, serum or plasma. Many new techniques in this space depend on the emerging developments in the genomic and proteomic spaces. The report also defines the dollar volume of sales, both worldwide and in the U.S., and analyzes the factors that influence the size and the growth of the market segments. The subsections of each market segment, including: commercial, hospital and specialty laboratories are examined. Additionally, the factors that influence purchases are also discussed.

This report will do the following:

- Assess the MDx market drivers and bottlenecks from the perspective of the medical and scientific communities.
- Discuss the potential benefits of the MDx market for various sectors of the medical and scientific community.

- Establish the current total market size and future growth of the molecular diagnostics market and analyze the current size and growth of various segments.
- Provide current and forecasted market shares by the company.
- Provide strategic recommendations for near-term business opportunities.
- Assess current commercial uses of the MDx market.
- Review the molecular diagnostics business models.

The emphasis in this report is on the clinical use of molecular diagnostics tests. The reader should consult other TriMark Publications reports on the TriMark Publications website 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 in Infectious Disease Testing*, *Molecular Diagnostics in Cancer Testing* and *Molecular Diagnostics in Genetic Testing*.

1.5 Methodology

The author of this report holds a Ph.D. in biochemistry from the University of Minnesota, with many decades of experience in science writing and as a medical industry analyst. He has over 40 years of experience as a director in laboratory testing and instrument and reagent development technology, as well as extensive experience in senior level positions in biotech and medical service companies. The editor of this report holds a Master's in immunology and has substantial experience in science writing and as a medical industry analyst. She also has many years of laboratory experience and has conducted laboratory testing and instrument and reagent development for biotech companies.

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 and accepted by the clinical community as CE marked and FDA approved tests. The technologies that come under the umbrella of MDx include first-generation amplification, DNA probes, second-generation biochips and microfluidics, and next-generation signal detection, biosensors and molecular labels. These technologies are profoundly influencing the discovery of new therapeutic molecules, the screening and diagnosis of patients, and the optimization of drug therapy during treatment. Over the past several years, this rapidly evolving field has seen several fascinating developments, including:

- Impact on pharmacogenomics and molecular epidemiology.
- Integration into central lab and point-of-care (POC) clinical practice.
- Impact on proteomics.
- Integration into therapeutics and diagnostics.
- Development of lab-on-a-chip devices.
- Novel relevant technologies, *e.g.*, new ways of labeling and signal detection.
- Gene expression profiling for cancer.
- High throughput detection of infectious disease in donated blood supplies.
- Improved detection of infectious disease.
- New assays for genetic diseases.

In [redacted], an estimated [redacted] MDx tests were performed at U.S. hospitals, clinics and laboratories, a figure that is projected to reach [redacted] in [redacted]. The following factors are driving the change from older technology to molecular testing:

- New technologies that permit the necessary quality control and data capture from PCR-based tests.
- Broader menu of available DNA-based tests.
- A greater understanding of the human genome.
- New developments in genomics.

- Exquisite sensitivity and accuracy of PCR-based testing.
- The confluence of research breakthroughs in genomics such as the human genome project.
- The development of a wide variety of PCR-based technology platforms.
- The rise of gene expression profiling.
- New developments in cancer diagnosis and treatment.
- The need for screening the blood supply for infectious diseases.
- Detection of infectious disease.
- The use of microarrays and multiplexing.

More than [redacted] companies market products in MDx. Most of these are relatively small, with annual sales between $[redacted] and $[redacted]. However, many major diagnostics companies, such as Abbott Laboratories, Siemens and Roche Diagnostics, have substantial market shares in each category of the MDx and dominate the market. A major outlet for novel diagnostics tests is through original equipment manufacturer (OEM) agreements with global platform suppliers such as Abbott Laboratories, Siemens, Beckman Coulter and Roche. Small and medium-size companies with innovative products have great opportunity for success in the field of MDx. 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. For this reason, mergers and acquisitions (M&As) activity is quite high in the MDx sector.

With the great potential for new testing modalities, infectious disease testing applications are currently paving the way, but there will also be applications in pharmacogenetics, cytogenetics, predisposition diagnostics and molecular cancer diagnostics. The molecular diagnostics industry is built around several basic competing technology platforms:

- PCR (polymerase chain reaction)
- TMA (transcription mediated amplification)
- Target amplification (MDA & MALBAC)
- Nucleic acid sequence amplification (NASBA)
- Ligase chain reaction (LCR)
- Branched chain reaction (bDNA)
- Gene sequencing (Next Generation Sequencing)
- Fluorescence *in situ* hybridization (FISH)
- DNA and oligonucleotide microarrays and chips

Worldwide, approximately $[redacted] was spent on MDx tools, assays and other products in [redacted]. Of this amount, approximately [redacted]% was spent on assays used for testing infectious diseases such as human immunodeficiency virus (HIV) and hepatitis C virus (HCV). The remaining [redacted]% was spent for other products, such as those used in genetic testing or cancer diagnosis and treatment. The global MDx market is forecast to grow $[redacted] by the end of [redacted]. As the MDx market continues to grow, TriMark expects human genetic testing, pharmacogenomics, and cancer testing to represent an increasingly larger percentage of this annual amount in the near future.

The molecular diagnostics testing market in the U.S. is the largest and most highly developed in the world. This market segment will significantly outperform the overall IVD market in the U.S., with sales of the U.S. MDx market growing from $[redacted] in [redacted] to $[redacted] in [redacted] (a CAGR of [redacted]%). European MDx market revenues are forecast to increase from $[redacted] in [redacted] to $[redacted] in [redacted], with a growth rate of [redacted]%. The Japanese MDx market was at $[redacted] in [redacted]. The projected growth rate is [redacted]% per year through [redacted], to reach almost $[redacted].

The global market for nucleic acid testing of infectious diseases was estimated to be $[redacted] by the end of [redacted]. With unsustainable high growth rates (about [redacted]% per year) and the dwindling supply of new high volume infectious diseases, this market segment should slow and mature during the forecast period. The largest segment of the PCR probe market for detection of infectious disease is HIV testing. The U.S. molecular diagnostic HIV testing market is estimated to be $[redacted] per year; globally it is a $[redacted] market. As a supplement to the HIV testing market, the market for determining viral load (the amount of virus in a person's blood) is beginning to grow, as

physicians are using the quantity of HIV virus in the blood as a marker for the effectiveness of antiviral therapy for acquired immunodeficiency syndrome (AIDS). Another significant area of infectious disease probe-based testing is sexually transmitted disease (STD) assessment.

The fundamental restructuring of healthcare delivery—such as downward price pressures and reimbursement cuts—occurring on an international level is impeding the entire diagnostics market, including the MDx sector. To be successful in the marketplace, tests must be novel, cost-competitive, clinically-relevant, reimbursable and capable of being conducted by lower-skilled technicians. This is particularly troublesome for the high-priced, technically difficult molecular diagnostic tests.

The use of molecular-based diagnostic solutions continues to expand to other diseases. For example, the viral load monitoring and genotyping techniques that have increased the life expectancy of HIV-infected patients have emerged as valuable tools for managing those patients infected with HCV. The molecular diagnostics market includes an extensive list of innovative products and tests. New developments, such as gene sequencing and nucleic acid amplification, have revolutionized the IVD industry in general. The future success of companies in the molecular diagnostics space depends on the speed at which they can find expanded applications for assays. For example, increasing insight into the ways in which genes influence a pathogen's response to therapy is ensuring tremendous growth in pharmacogenomics. Collaborations between diagnostics and pharmaceutical companies are expected to drive sales of both products. The dynamic U.S. molecular diagnostics market is highlighted by the growth of the cancer diagnostics and pharmacogenomics sectors. Changes in the industry include substantial moved to reagent driven sales over instrument intensive sales.

The largest market opportunities for PCR-based products will be in:

- Molecular clinical diagnostics of infectious diseases.
- Genomics and life science exploration of genetic codes as related to single-nucleotide polymorphisms (SNPs) for diseases.
- Drug discovery and pharmacogenomics.
- Cytogenetics.
- Personalized medicine and theranostics.

Additional products are being developed for areas such as infectious diseases, cancers, human leukocyte antigen (HLA) testing and genetic testing. A critical need exists for standardizing pre-analytical solutions, such as sample collection, stabilization, purification and handling. The clinical diagnostics segment is the fastest-growing part of PCR and molecular detection, at more than [redacted]% per year in reagent sales. As an example of the important trends in molecular diagnostics, TriMark believes the field of pharmacogenomics will become increasingly important in clinical trials and patient care. Through resequencing and genotyping technologies, DNA probe arrays could significantly reduce the cost and time required for high-volume polymorphism analysis, which is now performed using more labor-intensive techniques. The ability to predict which therapies are most likely to be effective for certain patients would constitute a powerful advance in diagnostic areas such as oncology.

Many drug companies without large diagnostic laboratories are concerned that genetic testing might upset the business models underlying many of their most successful products. Even as they have begun experimenting with pharmacogenomics, these companies are concerned that the FDA might use their data to limit the target patient population for potential blockbuster drugs. In view of this, major drug companies are likely to welcome a firm signal from the FDA that will reduce the questions surrounding this new field.

In another major trend, DNA microarrays have become indispensable tools in pharmacogenomics, toxicogenomics, developmental biology, cancer research and many other areas. A microarray is a collection of miniaturized test sites arranged on a surface that permits many assays to be performed in parallel. TriMark believes that nucleic acid testing (NAT) diagnostic assays will be used in the field of pharmacogenomics to screen patients prior to administering new drugs. The molecular clinical diagnostics sector can be divided into five main market opportunities:

- *Infectious Diseases*: This is the oldest and largest market opportunity, which still maintains good projected growth of up to [redacted]% CAGR. The actual growth rate may be higher if diagnostics-prescription applications emerge and drive incremental growth. It remains an exciting market, and any business that plans to be a player in nucleic acid testing needs to be involved here at some level.

- *Genetics*: The standard applications being followed in the field of genetics today include areas such as cardiovascular testing (which is being pursued almost universally), factor-5 and factor-2. Also, there are several applications, such as for cystic fibrosis and thrombophilia disorders. (Luminex xTAG® Cystic Fibrosis 39 Kit v2.)

- *Pharmacogenomics*: This is a separate market opportunity because it is technically more difficult to genotype a specific drug-metabolizing enzyme. Tests in this market may be a single test or a collection of perhaps a dozen different tests. Furthermore, the market relies on both nucleic acid technology and good bioinformatics.

- *Cancer*: Although current cytology applications use the FISH technique for cancer testing applications, new technologies based upon DNA/PCR are emerging such as the comparative genomic hybridization (CGH) array, and other array technologies, that are experiencing strong grow.

- *Blood Screening*: Blood screening for infectious disease.

Testing for chlamydia/gonorrhea, human papillomavirus (HPV), HIV and HCV viral load represents nearly [redacted]% of the total molecular diagnostic test volume in the U.S. Two of the biggest growth drivers are the continued expansion of cervical screening for HPV infection and anticipated growth in testing for hospital acquired infections (HAI). In the genetic testing segment, an estimated [redacted] tests were performed in [redacted]; most for cystic fibrosis and thrombophilia disorders. While existing genetic disorder tests will have slow to moderate growth during the forecast period, the continued discovery of disease related mutations, and the trend to direct-to-consumer (DTC) genetic testing may support the growth of the genetic testing landscape in the future.

The cancer testing segment, while small in comparison to infectious disease areas of molecular testing, will experience strong growth, as will the continued emergence of gene expression profiling and companion diagnostic tests for use in patient stratification and therapy selection. These tests are receiving premium pricing because of their high clinical value. There is strong growth in the use of FISH technology for cancer testing applications. Most cytogenetic labs use CGH arrays or plan to adopt use of CGH arrays in the near future. Clinical laboratories continue to expand their testing menus for molecular diagnostics with rapid additions of both new tests and technology platforms.

Geographically, the molecular diagnostic testing market is largely located in the U.S. and Europe, and to a lesser extent in Japan. However, there is a growing market in the so called BRIC countries as well. Latin America and the Pacific Rim countries as expected to have significant emergent markets in MDx by [redacted] and thereafter.

