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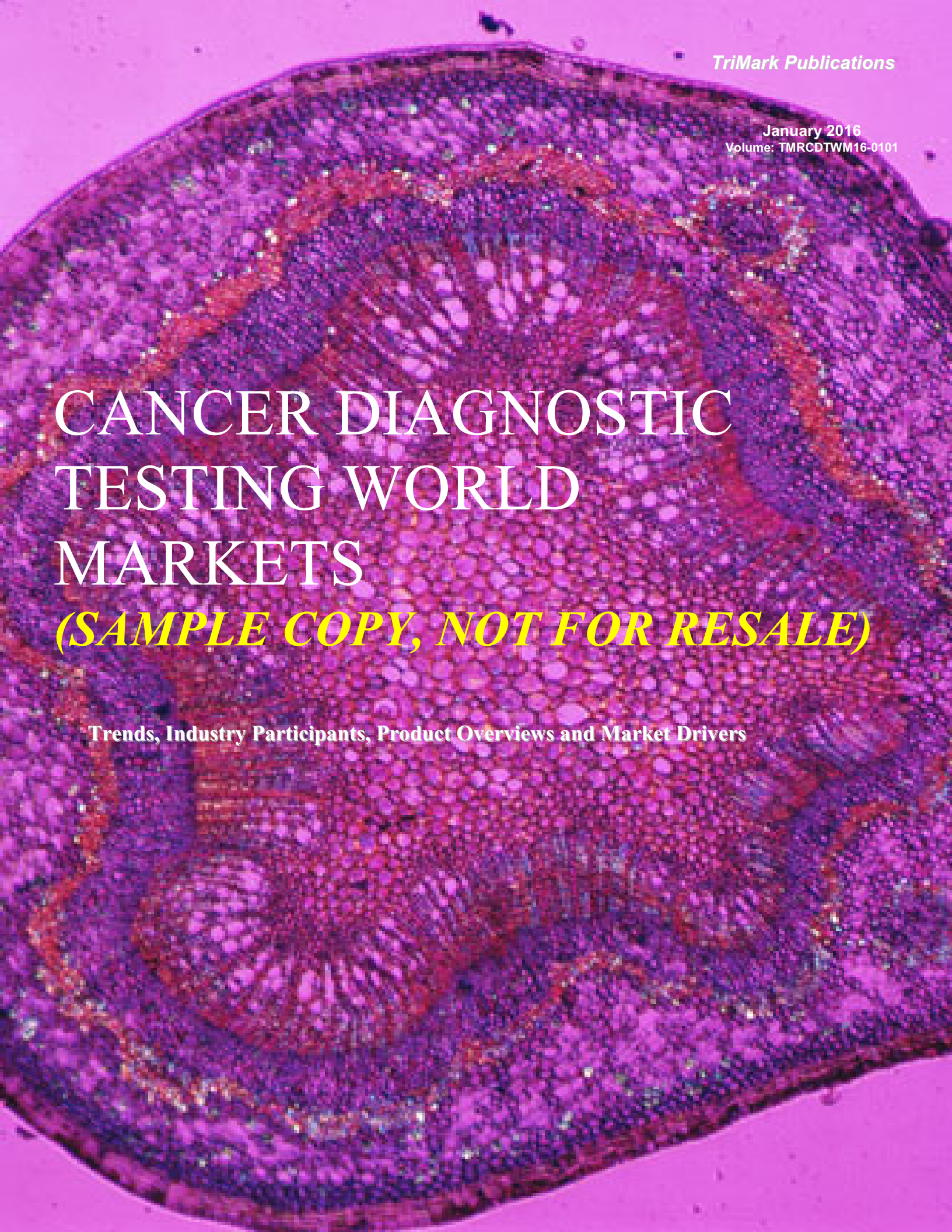

CANCER DIAGNOSTIC TESTING WORLD MARKETS

(SAMPLE COPY, NOT FOR RESALE)

Trends, Industry Participants, Product Overviews and Market Drivers

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1. Overview

1.1 Statement of Report

Cancer is a generic term for a large group of diseases that can affect any part of the body, characterized by uncontrolled growth and spread (or metastasis) of abnormal cells. As such, there is an urgent need for diagnostic tests to detect cancer earlier, allowing physicians to make more informed therapeutic decisions. Recently, the growth in this field has been extremely rapid with a large number of tumor markers being identified. Tumor markers are a group of proteins, hormones, enzymes, receptors and other cellular products that are over-expressed (*i.e.*, produced in higher than normal amounts) by malignant (cancerous) cells. Tumor markers are sometimes normal cellular constituents that are present at normal or very low levels in the blood of healthy individuals. The purpose of this report is to evaluate the technological developments that are occurring in the tumor marker testing segment of the cancer diagnostics market. This study reviews all of the generally-accepted clinical and research methods that are currently available for detection of cancer cells in patients. It examines the clinical measurement devices, including their reagents and supplies, utilized in hospitals, clinics, commercial laboratories and doctor's offices to diagnose and monitor cancer.

All cancers involve the malfunction of genes that control cell growth, division and death. As such, scientists are working hard to develop tests based on molecular and genetic RNA/DNA that can detect individuals at high risk for specific cancers. These include serological assays, cellular assays and molecular and genetic assays. Some of the most widely-tested and clinically-utilized diagnostic tumor markers include prostate-specific antigen (PSA) for prostate cancer, alpha-fetoprotein (AFP) for liver cancer, carcinoembryonic antigen (CEA) for colon cancer, carbohydrate antigen (CA)-125 for ovarian cancer, CA 19-9 for gastrointestinal cancer, the β sub-unit of human chorionic gonadotropin (β-hCG) in germ cell tumors, and CA 15-3 and CA 27.29 for breast cancer. With the rapid development of new systems and methodologies for diagnostic testing, early diagnosis and successful treatment of cancer is now a reality.

1.2 About This Report

This examination describes the analysis related to the common chemical constituents of blood, plasma or serum that are connected to the growth and progress of cancer. Emphasis is on those companies that are actively developing and marketing clinical laboratory instrumentation, reagents, supplies and products for performing tumor marker tests. The main objectives of this report are:

- Identifying viable technology drivers through a comprehensive examination of platform technologies for cancer diagnostics, including probe-based nucleic acid assays, microarrays and sequencing.
- Obtaining a complete understanding of the chief cancer diagnostics tests—*i.e.*, predictive, screening, prognostic, monitoring, pharmacogenomic and theranostic—from their basic principles to their applications.
- Discovering feasible market opportunities by identifying high-growth applications in different clinical diagnostic areas, focusing on the biggest and expanding markets in oncology.
- Focusing on global industry development through an in-depth analysis of the major world markets for cancer diagnostics, including growth forecasts.

By purchasing this analysis, the reader will have:

- An understanding of the most influential cancer marker market segments.
- The latest information on leading products and research and development (R&D) initiatives.
- Familiarity with recent developments and their effects on selected markets.
- Knowledge of the cancer marker market as an area of growth, research and investment.

The report defines the dollar volume of sales of the tumor marker testing segment, both worldwide and in the U.S., and it analyzes the factors that influence the size and growth of the market segments. Key questions answered in this study are:

- How can cancer marker measuring tools and technologies facilitate improved patient care?
- What are the main types of cancer marker technologies that are currently available?
- Who are the current key players in this marketplace?
- Which cancer marker market areas have the greatest potential for growth?
- What is the current state of the cancer marker market?
- Which biotechnology and diagnostic companies are investing in new cancer marker technology platform solutions?
- What are the main cancer marker business strategies adopted by leading companies?
- What are the benefits of various cancer marker technology platforms?

This review contains:

- Detailed analysis of recent trends in the cancer marker marketplace.
- In-depth profiles of the leading companies with cancer marker tools and technologies.
- Opinions on the cancer marker industry from leading industry experts.
- Analysis of potential new cancer marker applications in the clinical sector.
- Market predictions and trends analysis concerning U.S. expenditures on cancer markers.
- Projections of cancer marker market sizes for European and Asian markets.
- Projections for future applications of non-invasive tests in cancer marker screening.
- Analysis of commercial cancer marker business strategies, such as co-branding.
- A comprehensive overview and insight into cancer marker business strategies for growth in foreign markets.
- An in-depth examination of the subsections of each cancer marker market segment.
- An industry structure analysis including companies in the field and their focus.

Analysis includes charts and graphs measuring product growth and trends within the marketplace. Company-specific information, including sales figures, product pipeline status and R&D trends, is provided. Also, this report will:

- Assess cancer marker market drivers and bottlenecks from medical and scientific community perspectives.
- Discuss the potential benefits of cancer markers for various sectors of the oncology community.
- Establish the current total market size and future growth of the cancer marker market and analyze the current size and growth of individual segments.
- Provide current and forecasted market shares by company.
- Discuss profit and business opportunities by oncology segment.
- Provide strategic recommendations for near-term business opportunities.

The following questions will also be addressed in this study:

- What are the near-term business opportunities in the cancer marker market?
- What are the current and forecasted cell therapy market sizes in the U.S., European Union (E.U.) and Asia?
- What are the business models currently used by companies in the cancer marker market?
- How will manufacturers, researchers, physicians and patients influence this market?
- What are the drivers and bottlenecks influencing the cancer marker market?
- What are the barriers to entry for the cancer marker market?
- What are the key technologies used in cancer marker testing?
- Who holds the proprietary rights to the cancer marker technology platforms?
- How is this technology currently being applied and utilized?
- How will new cancer marker technologies reduce healthcare expenditures?
- How will new cell therapy technologies affect cancer therapy decisions?

The analysis contains:

- A comprehensive overview of several categories of cancer marker technology platforms that are of use as diagnostic tests in hospitals and doctor's offices.
- A chapter on each of the important cancer categories and applications of cancer marker tests to diagnosis and treatment.
- Full descriptions of the technologies involved and how these differ from existing and emerging technologies.
- Analysis of the technological approaches undertaken by various competitors, as well as industry, and end-user response to these products.
- Regulatory issues and legislation affecting use and marketing of cancer marker products.
- Complete review of the clinical uses of cancer marker tests.

1.3 Scope of the Report

This study emphasizes companies that are actively developing and marketing clinical laboratory instrumentation, reagents and supplies for performing cancer diagnostics tests. The reader should consult other TriMark Publications reports at http://www.trimarkpublications.com for detailed discussions of important individual market segments related to the cancer diagnostics market, such as *Biomarker Technology Platforms for Cancer Diagnoses and Therapies*, *Cancer Cell Therapy Markets*, *Cancer Therapeutics Markets*, *Companion Diagnostics in Personalized Medicine and Cancer Therapy*, *Cytology and HPV Testing World Markets* and *Molecular Diagnostics in Cancer Testing*.

The U.S., Japan and Europe—the world's three largest cancer 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 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.

Specialty cancer diagnostics testing is examined, since it is often part of the overall analytical focus of companies that market general laboratory automation equipment. However, no effort is made to quantify this broader market. In addition, this report does not cover disposable plastic supplies for the clinical laboratory. These subjects are discussed in other TriMark Publications reports.

1.4 Objectives

The goal of this survey is to review the market for tumor marker testing equipment and supplies using screening reagents and instruments for analysis of individual components in blood, serum or plasma. It defines the dollar volume of sales, both worldwide and in the U.S., and analyzes the factors that influence the size and growth of the market segments. Also examined are the subsections of each market segment, including the physician office labs, hospital labs and commercial laboratories. Additionally, the numbers of institutions using this type of testing and the factors that influence purchases are discussed. The study surveys almost all of the companies known to be marketing, manufacturing or developing instruments and reagents for the clinical oncology market in the U.S. Each company is discussed in depth with a section on its history, product line, business and marketing analysis, and a subjective commentary of the company's market position.

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 30 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. The editor of this report

holds a Ph.D. in biochemistry from the University of Liverpool and has many decades of experience in science writing and as a medical industry analyst.

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. Additionally, sources of information include the non-governmental organizations (NGOs) such as the World Health Organization (WHO) and the American Cancer Society (ACS), as well as governmental entities like the U.S. Department of Health and Human Services (HHS) and U.S. federal agencies such as the National Cancer Institute (NCI), 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 we publish annually. We extract relevant data and analytics from TriMark's 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 initially researches market share, market size and growth rate information from secondary sources. This gives a "feel" for the market. Analysts then contact individuals with the appropriate information (usually marketing product managers are the best source) from the leading suppliers and elicit information to either corroborate or reject data from the initial secondary searches. At the same time they will query them about the other aspects of the market, drivers, restraints, regulatory, etc. Secondary sources are many and varied and include websites of national governments, international organizations such as the World Trade Organization (WTO), trade and professional organizations *e.g.*, The Pharmaceutical Research and Manufacturers of America (PhRMA), etc.

A considerable amount of further information is obtained from numerous publications in the scientific and trade literature including information and data from Scrip, Clinica, etc. In addition, a significant amount of information has also been obtained from various national government sources who have kindly provided up-to-date information about the regulatory and legislative position on research funding in specific geographic regions. In addition to the use of corporate annual and quarterly reports, data was obtained from security offering prospectuses, Forms 10-K and 10-Q. This data was used along with other sources of data from investment analysts' reports, Reuters, Dun & Bradstreet, IMS and the CorpTech Directory.

Market Forecasts and Modeling

The numerical data on market size, growth rates and sales forecasts are obtained from a well-examined model based upon quantitative market information obtained from the leading global companies in the sector, private seminar presentations by company experts and public SEC filings. Many industry experts are also consulted to confirm these

market estimates. The numbers used are washed of discounts and returns, and represent the final sale numbers. In addition, global numbers are assessed by region components as well, taking into account differences in market conditions between the U.S., Europe and Asian markets in particular.

For projection for the future values and growth rates of specific markets, the analysts use a proprietary forecast spreadsheet, which takes into account a wide variety of market indices such as inflation rates, anticipated increases/decreases in funding of specific markets. Then other factors such as new market introductions, acquisitions, etc. are manually incorporated into the spreadsheet.

TriMark Publications Report, Research and Data Acquisition Structure

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

- 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.
- Launching a combination of primary research activities, including two levels of questionnaires, executive-direct focused, company-specific and region-specific communications to qualified and experienced senior executives worldwide.
- Completing a confirmatory primary research assessment of the report's findings with the assistance of expert panel partners from the industry.
- The final published report is reviewed by editors, fact checkers and proof readers, and then released by the Editor-in-Chief.

1.6 Executive Summary

People suffering from some of the most common forms of cancer are twice as likely to survive for at least ten years, compared with patients diagnosed in the early [redacted]. Breast, bowel and prostate cancer survival rates have shot up, as have those for non-Hodgkin's lymphoma (NHL) and leukemia. On average, [redacted]% of cancer patients are now expected to survive at least ten years, compared with [redacted]% in the [redacted]. Since peaking in the [redacted], cancer death rates have declined nearly [redacted]%. Approximately [redacted]% of survival gains in cancer are attributable to new treatments, including medicines. The improvement in survival reflects progress in diagnosing certain cancers at an earlier stage and improvements in treatment. Cancer testing is one of the most important growth opportunities in the diagnostics segment. The Agency for Healthcare research and Quality (AHRQ) estimates that the direct medical costs (total of all healthcare costs) for cancer in the U.S. in [redacted] were $[redacted].

- [redacted]% of this cost is for hospital outpatient or doctor office visits.
- [redacted]% of this cost is for inpatient hospital stays.
- [redacted]% of this cost is for prescription drugs.

Based on growth and aging of the U.S. population, medical expenditures for cancer in the year [redacted] are projected to reach at least $[redacted], an increase of [redacted]% over [redacted], according to a National Institutes of Health analysis. If newly developed tools for cancer diagnosis, treatment, and follow-up continue to be more expensive, medical expenditures for cancer could reach as high as $[redacted], said the researchers from the National Cancer Institute (NCI), part of the NIH. The analysis appeared online, [redacted], in the *Journal of the National Cancer Institute*.

The Pharmaceutical Research and Manufacturers of America (PhRMA) have estimated that in [redacted] a total of over [redacted] medicines and treatments are in development globally. Approximately [redacted] compounds are currently being studied in the U.S.—more than in any other region around the world. They estimate that in [redacted], [redacted] new medicines are currently under development to help treat cancer.

Furthermore, in a United Nations report it was published that cancer deaths will double by [redacted]. The director of the International Agency for Research on Cancer, Christopher Wild, said that by [redacted], there will be [redacted] cases of cancer diagnosed, the rate being highest in the developing countries, given the fact the rates of cancer would remain constant in next [redacted] years. The four leading causes of cancer death—lung, colorectal, breast and pancreas—are believed to have accounted for approximately [redacted]% of all cancer deaths in the U.S. in [redacted], or one in eight of every death.

The American Cancer Society (ACS) estimates that:

- About [redacted] new cancer cases are expected to be diagnosed in [redacted].
- In [redacted], about [redacted] Americans are expected to die of cancer, or about [redacted] people per day.
- In [redacted], almost [redacted] of the estimated [redacted] cancer deaths in the U.S. will be caused by tobacco smoking.
- Men and women who smoke are about [redacted] times more likely to develop lung cancer than non-smokers,
- Cancer is the second most common cause of death in the U.S., exceeded only by heart disease, and accounts for nearly one of every four deaths.
- The Agency for Healthcare Research and Quality (AHRQ) estimates that the direct medical costs (total of all healthcare expenditures) for cancer in the U.S. in [redacted] were $[redacted].

The World Cancer Research Fund estimates that about one-quarter to one-third of the new cancer cases expected to occur in the U.S. in [redacted] will be related to overweight or obesity, physical inactivity, and poor nutrition, and thus could also be prevented. Certain cancers are related to infectious agents, such as human papillomavirus (HPV), hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and *Helicobacter pylori*; many of these cancers could be prevented through behavioral changes, vaccines, or antibiotics. Many of the more than two million skin cancers that are diagnosed annually could be prevented by protecting skin from excessive sun exposure and avoiding indoor tanning.

The ACS estimated that approximately [redacted] new cancer cases were expected to be diagnosed in [redacted]. This estimate excluded basal cell and squamous cell skin cancers and *in situ* carcinomas except urinary bladder. The ACS have also predicted that about [redacted] Americans are expected to die of cancer, in [redacted], almost [redacted] people per day. Cancer is the second most common cause of death in the U.S., exceeded only by heart disease. In the U.S., cancer accounts for nearly one in four deaths. New technology in the diagnosis and treatment of these diseases and conditions should lead to attractive commercial opportunities. For example, the worldwide cancer treatment market currently is $[redacted] and growing at a rate of [redacted]% annually. The size and growth of the diagnostic tumor marker markets are influenced by a number of factors, including:

- Financing for biotech companies.
- Technological innovation in diagnostic practice.
- Government funding (including supplemental stimulus financing) for basic and disease-related research (for example, heart disease, AIDS and cancer).
- R&D spending by biotechnology and pharmaceutical companies.

The specific products in this segment include:

- Immunoassays for serum cancer markers, receptor assays and hormone assays.
- Mammography equipment.
- Clinical chemistry reagents (occult blood reagents, enzymes and serum proteins).
- Deoxyribonucleic acid (DNA) reagents.
- Cytological products.
- Histological reagents.
- Immunocytochemistry (ICC) products.
- Immunohistochemistry (IHC) reagents.

Biotechnology Associates estimates that the global product market for *in vitro* cancer detection products—including clinical chemistry reagents (occult blood reagents, enzymes, serum proteins), DNA reagents, cytological products, histological reagents, ICC products and IHC reagents—grew to over $[redacted] in [redacted]. The U.S. market for all *in vitro* cancer detection products, including the tumor marker category, is estimated to be $[redacted], or about [redacted]% of the total worldwide market.

The worldwide tumor marker product segment, comprising proteins detected with immunological technologies in serum or plasma, is expected to grow with a CAGR rate of [redacted]% and is expected to be valued at $[redacted] by the end of the forecast period in the year [redacted]. This market sector is primarily driven by the increasing number of people in the population who fall within the higher risk demographics of cancer and the increased marketing of new tests to doctors.

The tumor marker product segment in the U.S. is expected to grow with a CAGR rate of [redacted]% and is expected to be valued at $[redacted] by the end of the forecast period in the year [redacted]. During the first quarter of [redacted], however, the ACS has pulled back from previous PSA screening guidelines. The newer guidelines recommend that men whose PSA level is less than 2.5 ng/mL need only be screened every two years. The previous guidelines called for men with a PSA level of less than 4.0 ng/mL to be screened annually.

In general, the tumor marker product segment in the U.S. will be primarily driven by the increasing number of people in the population who fall within the higher risk demographics of cancer. The U.S. market is still constrained by the cost pressures from third-party payers who are reluctant to reimburse for new procedures, and the conservative stance of the FDA, which is slow to approve new diagnostic tests for cancer. The Japanese cancer marker market is recognized as being the second largest single market and has been valued at $[redacted] in [redacted], and is anticipated to continue to grow with a CAGR of [redacted]% over the forecast period reaching a value of $[redacted] by [redacted].

It is estimated that the tumor marker products market in Europe has been valued at $[redacted] in [redacted], and is anticipated to continue to grow with a CAGR of [redacted]% over the forecast period reaching a value of $[redacted] by [redacted]. Continued growth for tumor marker products is also expected for Germany and France in the European market. In fact, the European market uses a wider variety of cancer tumor markers, although the dollar volume is still third to the U.S. and Japan. Primarily because of marketing forces, the tumor marker nuclear matrix protein 22 (NMP22) sells very well in Germany.

It is estimated that the tumor marker products market in the Rest of the World has been valued at $[redacted] in [redacted], and is anticipated to continue to grow with a CAGR of [redacted]% over the forecast period reaching a value of $[redacted] by [redacted].

The existing FDA-approved assays which comprise the main tumor marker assay segment in the U.S. are:

- Diphtheria toxin A (DTA) and NMP22, which were approved for monitoring bladder cancer.
- CEA, which is used primarily for monitoring colorectal and breast cancers.
- PSA, which is used primarily for monitoring and screening prostate cancer.
- Truquant BR radioimmunoassay (RIA), which is used for monitoring breast cancer.

- hCG, for monitoring testicular cancers, trophoblastic tumors and choriocarcinoma.
- CA-125, used for the diagnosis and monitoring of ovarian cancer.

Serum PSA testing has revolutionized the diagnosis and management of prostate cancer and several million tests are performed every year in the U.S. to screen for this malignancy. It is estimated that over $[redacted] is now spent on PSA testing.

The market for cancer detection products generally encompasses diagnostic products companies like Johnson & Johnson, Abbott Diagnostics, Roche Diagnostics, Tosoh, bioMérieux and Diagnostic Automation/Cortez Diagnostics, Inc., which all market instruments and reagents for measuring serum protein tumor markers *in vitro*, *i.e.*, in the clinical lab. Another subsection of the cancer detection market consists of companies like General Electric, Siemens, Philips, Toshiba and Hitachi that market *in vivo* detection products. In addition, there are radionuclides (DuPont, Covidien and Bristol-Myers Squibb), X-ray contrast media (Covidien and Bristol-Myers Squibb) and X-ray film (DuPont, Agfa, Eastman Kodak, Fuji and 3M).

Tumor markers used and approved in the U.S. by the FDA include:

- PSA.
- Prostatic acid phosphatase (PAP).
- CA-125 for ovarian cancer (but only to follow the course of the disease).
- CEA in colon cancer.
- AFP in liver cancer and combined with β-hCG in germ cell tumors.
- Terminal transferase used in T-cell leukemia, tissue estrogen and progesterone receptors in breast cancer.
- CA 15-3 and CA 27.29 currently for breast cancer.

In other parts of the world, a wider variety of tumor biomarkers are used:

- CA 547, M26, M29, MCA for breast cancer.
- CA 19-9, CA 195, TAG72, CA 245, M43 for gastrointestinal cancers.
- Cytokeratin 19 fragment (CYFRA™) 21-1 in non-small cell lung cancer (NSCLC), neuron specific enolase (NSE) and calcitonin in neuroendocrine tumors.
- Squamous cell carcinoma antigen in squamous cell tumors of the cervix-uterus or head and neck.
- Non-specific markers like TPS, LSA and sialic acid.

The clinical value of serum tumor markers CEA, CA-50 and CA 242 in the distinction between malignant versus benign diseases causing jaundice and cholestasis is also being examined.

