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DNA SEQUENCING AND PCR 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

The focus of this study is to describe the landscape of DNA sequencing and polymerase chain reaction or PCR, two major technology platforms of value in life science research, drug discovery and clinical diagnostics. This report provides an in-depth analysis of key technology and market trends operative in the high-throughput sequencing space, while analyzing the main drivers of growth in markets for PCR products and applications. The markets for sequencing are extremely competitive, driven by rapid technological advancements coupled with aggressive price wars; markets are diversifying as manufacturers compete to offer sequencing equipment at attractive price points, creating niche markets for personal and desktop sequencers.

Once the domain of a few select groups, sequencing technology has become increasingly accessible, experiencing high growth as its markets continue to emerge and evolve. Next-generation sequencing (NGS) has already redefined the markets for genetic analysis, and is poised to enter the arena for high-throughput clinical diagnostics that will fuel future growth. As costs associated with sequencing continue to decline, the technology is rapidly gaining acceptance as the new benchmark in life science research, spawning applications in drug discovery, target validation, and drug development, in addition to the ag-bio and forensics sectors. Sequencing technology has potential applications in personalized medicine, clinical diagnostics, disease-screening and diagnostics, translational genomics, human genomics research and in screening and validation protocols in clinical trials.

PCR, one of the most popular techniques for analysis of nucleic acids, has applications in DNA amplification for sequencing, functional analysis of genes, diagnosis of hereditary diseases, identification of genetic fingerprints (used in forensic sciences and paternity testing), and the detection and diagnosis of infectious diseases. Recent advances in PCR technology enable greater sensitivity and precision in nucleic acid measurements, making it a perfect complement to next-generation sequencing, where it serves as the most adopted technique for sample preparation and validation. The markets for PCR are currently experiencing a revival fueled by a combination of technological improvements, rapid growth in molecular diagnostics and increasing interest in the genomics industry. TriMark Publications has focused this analysis on the emerging technologies in the DNA sequencing and PCR spaces and associated market opportunities.

1.2 About This Report

This report will:

- Identify viable technology drivers through a comprehensive look at various platform technologies for molecular sequencing, including advances in second, third, and fourth generation sequencing platforms.
- Provide an in-depth analysis of emerging markets for sequencing technologies.
- Provide a comprehensive analysis of the PCR space—the various technologies and the end-user applications driving this marketplace.
- Focus on global industry development through an in-depth analysis of the major world markets for DNA sequencing and PCR, including forecasts for growth.
- Study the market opportunity in the PCR space, especially qRT-PCR—the leading technology platform for quantitation and expression profiling.

1.3 Scope of the Report

The emphasis in this report is on those companies that are actively developing and marketing laboratory instrumentation and reagents and supplies for performing DNA sequencing and PCR. The reader should also consult other TriMark Publications reports at www.trimarkpublications.com for a detailed discussion of the important individual market segments that are related to the molecular diagnostics market. Emphasis is placed upon the DNA sequencing and PCR markets in important worldwide markets such as the U.S., Japan, BRIC, and Europe. The report focuses primarily on the research pharma and biotech market segments (life science research), and provides a description of the instruments, reagents and supplies marketed by major companies in this segment. The study also discusses the market size, growth rates and market components for instruments and reagents, controls and consumables used in this area.

What is generally characterized as immunochemistry instruments and reagents or molecular diagnostic markets is not covered, although many of the instruments, reagents and techniques in the molecular diagnostics market segment are intimately associated with these broader areas. The molecular diagnostics sector is covered extensively in TriMark's *Molecular Diagnostics Markets* report.

This review touches on the specialty markets in DNA sequencing and PCR, since these segments are frequently a part of the overall analytical focus of companies marketing general laboratory automation equipment. However, no effort is made to evaluate the size of this broader market. Companies that market and sell a limited number of instruments and equipment as an OEM part of a much larger clinical laboratory product line by other companies are not mentioned in detail. Moreover, the analysis here does not cover disposable plastic supplies, reagents, or consumables for use in research or clinical laboratories. All of these subjects are treated thoroughly in other TriMark Publications reports. Although this examination mentions related technologies (*e.g.*, microarrays) in passing, as well as techniques such as DNA extraction from serum, no extensive or in-depth treatment of this subject is presented. Such a discussion is outside the scope of this review.

The market for nucleic acid testing equipment and supplies with emphasis on the biotech, pharma and research markets, the reagents and instruments for analysis of nucleic acids, whether by screening, amplification, or sequencing, is reviewed. This market defines the dollar volume of sales, both worldwide and in the U.S. market, and analyzes the factors that influence the size and the growth of the market segments. The report details market sizes and growth rates, with projections for the U.S. and world market. All of the major companies known to be marketing, manufacturing or developing instruments and reagents for the DNA sequencing market in the U.S. and worldwide, are surveyed. Each company is discussed in depth with a section on the history of the company, the product line, business and marketing analysis, and a subjective commentary of the position of the company in its market. Certain areas are only touched upon since they are related to the major elements of this report, but are in and of themselves an entirely different field or market. An example is the point of care market and clinical chemistry testing instruments, which are covered in TriMark's *Point of Care Diagnostic Testing World Markets* and *Clinical Chemistry Analyzers* reports, respectively. These are very interesting and substantive areas which form the foundation of much of clinical diagnostic analysis, but in the interest of brevity and not including everything in molecular diagnostics remotely related to the point of care market segment or other diagnostic testing categories, these areas were not analyzed in depth here.

1.4 Methodology

The author of this report holds a Ph.D. in biochemistry from the University of Minnesota with many decades of experience in scientific writing and as a medical industry analyst. He has been a senior director of several large regional and national testing laboratories. He has over 30 years of experience in laboratory testing and instrument and reagent development technology, as well as an extensive experience in senior level positions in biotech and medical service companies. The editor holds a Ph.D. in life sciences from Jawaharlal Nehru University, with post-doctoral training from the University of Manitoba and Saskatoon Cancer Centre, respectively. She has authored several peer-reviewed articles on signaling pathways involved in cancer progression, and has over five years' experience as a scientific editor.

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), governmental entities like the U.S. Department of Health and Human Services (HHS), and U.S. federal agencies such as National Institutes of Health (NIH), Food and Drug Administration (FDA), and the Centers of 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 TriMark believes to be reliable, but TriMark does 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 and Sector Snapshots that TriMark publishes annually. TriMark extracts relevant data and analytics from TriMark's research in the past seven years as part of this data collection. TriMark also extracts qualified data feeds from e-questionnaire responses and primary research responses for this compilation.

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. The report conclusions are verified through intensive interviewing of the top ranking companies in the industry.

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:

- Completing an extensive secondary research effort on an important market sector, including gathering all relevant information from corporate reporting, publicly available databases, proprietary databases, direct meetings and personal interviews with the key personnel.

- Formulating a study outline with the assigned writer, including important items, as follows:

  - Market and Product Segment grouping and evaluating their relative significance.
  - Key Competitor 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 being analyzed.

1.5 Executive Summary

The worldwide market for next-generation sequencing platforms is currently estimated at $[redacted], with projected sales expected to grow to $[redacted] by [redacted]. The U.S. and Europe approached DNA sequencing based applications earlier, and exhibit higher market penetration than in other parts of the world. Uptake in these markets is projected to be slower due to the economic downturn coupled with reduced or flat government funding. Markets

for research instrumentation and consumables in the Asia-Pacific region rank higher in terms of growth, as do the BRIC nations, which are projected to grow at an overall compound annual growth rate (CAGR) of [redacted]%.

The markets for DNA sequencing and analysis products are characterized by rapidly advancing technology, evolving industry standards and emerging competition, accompanied by novel product introductions and aggressive pricing competition. In addition, there has been a distinct trend toward consolidation as market leaders seek to maintain their position by adding complementary emerging technologies to their portfolios through extensive licensing deals and/or acquisitions. Next-generation sequencing presents an exciting area of growth for life science tool vendors, including those providing sequencers, ancillary instrumentation, reagents and software.

Recent years have seen a dramatic drop in the costs of sequencing, which have almost attained the $[redacted] per human-genome goal. Sequencing platforms too have become increasingly affordable, with desktop sequencers available at attractive price points ($[redacted] to $[redacted]). TriMark predicts that as the costs of acquiring and operating sequencing machines continue to drop, the markets for DNA sequencing will continue to grow in size and scope. There has been an increasing demand for sequencing of human genomes, as evidenced by the reported backlog of orders placed with Complete Genomics (a wholly-owned subsidiary of BGI Shenzen). Complete Genomics, a company focused on providing human genome sequencing services, shipped out research-ready data for [redacted] human genomes in the first quarter of [redacted] alone. It reported a backlog of more than [redacted] sequencing orders as of August [redacted]. This increased demand is being driven in part by the lower costs of sequencing coupled with higher throughput and accuracy.

The current sequencing environment is highly competitive. In order to succeed, platform providers must continue to improve their instruments and employ innovative R&D efforts. As older systems turn obsolete in the face of new technology, players in the sequencing arena are engaged in increased efforts to secure their futures in the market where mergers, acquisitions and partnerships continue to shake up competitive dynamics. TriMark expects this trend of acquisitions of smaller start-ups and spin-offs from academic institutions to continue as new and innovative technologies continue to emerge. The overall leader in the next-generation sequencing segment is Illumina with ~[redacted]% market share. Other major players in this market segment include Life Technologies and Roche, with [redacted]% and [redacted]% market shares, respectively.

Another factor driving the markets for DNA sequencing is the rise in the number of applications for next-generation sequencing technologies. As the molecular diagnostics market continues to grow, TriMark expects human genetic testing, pharmacogenomics, and cancer testing to represent an increasingly larger percentage of this market in the near future. The markets for DNA sequencing products include all aspects of molecular biology research, including: basic human disease research, genetic analysis, pharmaceutical drug discovery and development, pharmacogenomics (research relating to how a person's genes affect the body's response to drug treatments), toxicogenomics (research relating to the measurement of gene expression as a predictor of toxicity) and agricultural research. In addition to research-oriented markets, an emerging applied testing segment represents molecular testing markets not related to human healthcare and academic or pharmaceutical research. This segment covers NGS applications in human identification and forensics, veterinary and food testing, cell therapy, regenerative medicine, and tissue engineering. End-users in this segment include many private and government laboratories such as law enforcement agencies, animal health organizations and veterinary testing laboratories, and food safety organizations. Some of the fastest growing categories within the life sciences research markets include quantitative PCR and next-generation sequencing technologies. The primary areas of market growth are expected to be genomics, ag-bio, non-invasive prenatal testing (NIPT), and molecular diagnostics.

Traditionally, NGS technologies have been employed primarily by life scientists who most frequently use amplification, cell culture, Western blots, gene expression technologies, cDNA analysis, light microscopy, cloning and sequencing in their research. However, over the last few years, adoption of NGS technologies has intensified; NGS tools are increasingly making inroads into the clinical diagnostics arena. Sequencing platform manufacturers have been strengthening their position through strategic acquisitions in order to take advantage of the promising markets for clinical diagnostics. Companies in the sequencing arena are attempting to penetrate the genomics-based diagnostics market as evidenced by Illumina's acquisition of BlueGnome and Verinata, and Life Technologies' purchase of Navigenics, exemplifying the progression from research-centric to clinical applications. Another important asset for companies choosing to enter the lucrative clinical diagnostics markets is Clinical Laboratory Improvement Amendments (CLIA)-certification. In [redacted], Life Technologies acquired Navigenics, with a focus

on acquiring and expanding its CLIA laboratory services. With acquisitions that were made in [redacted] including the cancer bioinformatics firm Compendia, and Pinpoint Genomics, Life Technologies' Medical Sciences business now offers a CLIA-certified test, Pervenio™ RS lung, which is designed to assist physicians improve risk stratification of patients with early-stage, non-squamous non-small cell lung cancer, as well as bioinformatics capabilities used by the pharmaceutical industry to identify novel gene targets for drug discovery and development in cancer.

The recent partnership between Roche and Pacific Biosciences also serves to illustrate the shift in the significance of sequencing technologies, from a research-oriented focus to applications in clinical diagnostics. In September, [redacted], Roche and Pacific Biosciences entered a partnership wherein PacBio will supply Roche with sequencing instruments and exclusive marketing rights to all clinical diagnostics developed using Pac Bio's Single Molecule, Real-Time (SMRT®) technology. Under this agreement, Pacific Biosciences will get $[redacted] upfront and potential milestone payments of $[redacted] down the road. Pacific Biosciences will also benefit from the marketing expertise Roche brings to the table. Roche is considered to be the world leader in *in vitro* diagnostics and tissue-based cancer diagnostics. The deal gives Roche inroads into the NGS market, which it has been trying to break into since its failed bid at acquisition of the NGS market leader, Illumina, last year. Next-generation sequencing technology will enable Roche to develop and market cutting-edge clinical diagnostics, reinforcing its leadership position in the *in vitro* diagnostics markets. In [redacted], Roche announced the closing its wholly-owned subsidiary [redacted] Life Sciences, a previously-dominant player in next-generation sequencing. This announcement follows a series of downsizing measures from Roche in the area of genetic sequencing over the past year.

Recent studies have revealed the magnitude of complexity of the human genome. Advances in sequencing technology are paving the way for genome analysis within applied markets such as personalized medicine, molecular diagnostics, ag-bio, food pathogen, and environmental and water testing. Some promising segments of the market for life sciences instrumentation and equipment include tools and instruments that aid in genomic analysis; in particular, the markets for next-generation sequencing are poised for high growth in the next five years. Going forward, the resequencing of human genomes for discovery of genetic variations, as well as repeat sequencing and expression analysis of cancer biopsies will continue to drive adoption of the technology. Concurrently, emerging applications for NGS technologies in clinical diagnostics, coupled with the development of more affordable platforms will be crucial drivers of growth. TriMark expects new competitors and technologies to continue to emerge as the market for NGS diversifies. Competition in the sequencing market is intense, marked by a high rate of M&A activity as companies try to gain traction in the highly competitive IP landscape. In [redacted], Thermo Fisher Scientific, Inc. proposed to buy Life Technologies Corp for $[redacted] in a deal that would make it one of the top two companies in the hot field of genetic testing. In [redacted], shareholders in Life Technologies Corp agreed to the terms of the takeover. Thermo expects the transaction to close early in [redacted], pending U.S. regulatory and shareholder approvals.

Promising new clinical applications of next-generation sequencing technologies include:

- In epidemiology, for surveillance and identification of infectious diseases to inform disease management and prevention.
- Comprehensive oncology panels that can screen entire oncology pathways.
- Noninvasive prenatal testing (NIPT).
- Identification of the root cause for previously idiopathic diseases.

In the gene expression monitoring and DNA analysis fields, competing NGS technologies include platforms provided by companies such as Life Technologies, Roche, Illumina, Complete Genomics, Helicos, Pacific Biosciences and Oxford Nanopore. Recent advances in molecular biology have resulted in the application of DNA microarrays and next-generation sequencing technologies to the field of genomic analysis. Though microarray markets have experienced a minor downturn with the advent of next-generation sequencing, microarray technology remains relevant in genomics. Sequencing-based genomics holds several advantages over microarray analysis, including depth and ease of analysis, throughput and cost-effectiveness; however, there remain several points of synergy between the two technologies. Optimal use of these tools will allow researchers to explore the information encoded within genomes to its full extent. Companies developing or marketing competitive DNA-array technology include: Affymetrix, Agilent Technologies, Molecular Devices, BD Biosciences, Clontech (part of the TaKaRa Bio Group), CombiMatrix Corporation, Febit AG, Illumina, Epoch Biosciences, Roche and Sequenom.

The DNA/PCR kit market for the research segment is highly fragmented and full of competitors. Companies in the DNA sequencing segment derive much of their revenue from the research and development expenditures of the pharmaceutical and biotechnology industry. Competition within the biomedical research market is even more fragmented than that within the pharmaceutical industry. There are hundreds of suppliers in this market, including major players like GE Healthcare, Life Technologies, Molecular Devices Corporation and Agilent. Genomic testing for variability in DNA can also be performed by products available from Affymetrix, Applied Biosystems, Clontech (part of the TaKaRa Bio Group), PerkinElmer Life Sciences and Sequenom, among others.

A direct-to-consumer (DTC) sequencing services market, catering to individuals and physicians, is expected to emerge over the next several years. This market is expected to involve service providers from both the next-generation sequencing services market and the DTC genetic testing market. Some established companies in this space include Foundation Medicine, 23andMe, and Illumina, which offers an Individual Genome Service for sequencing of clinically relevant genomes prescribed by physicians. In [redacted], 23andMe filed for FDA clearance for seven of its [redacted] genetics tests, the first 510(k) submissions from a DTC genetics business. 23andMe's bid to obtain FDA approval for its Personal Genome Service is built upon the fact that it processes DNA samples through a CLIA-certified provider, LabCorp. As the clinical market is seen to be more lucrative than the consumer market, former DTC companies as well as instrument manufacturers are increasingly looking to expand their CLIA-compliant facilities.

