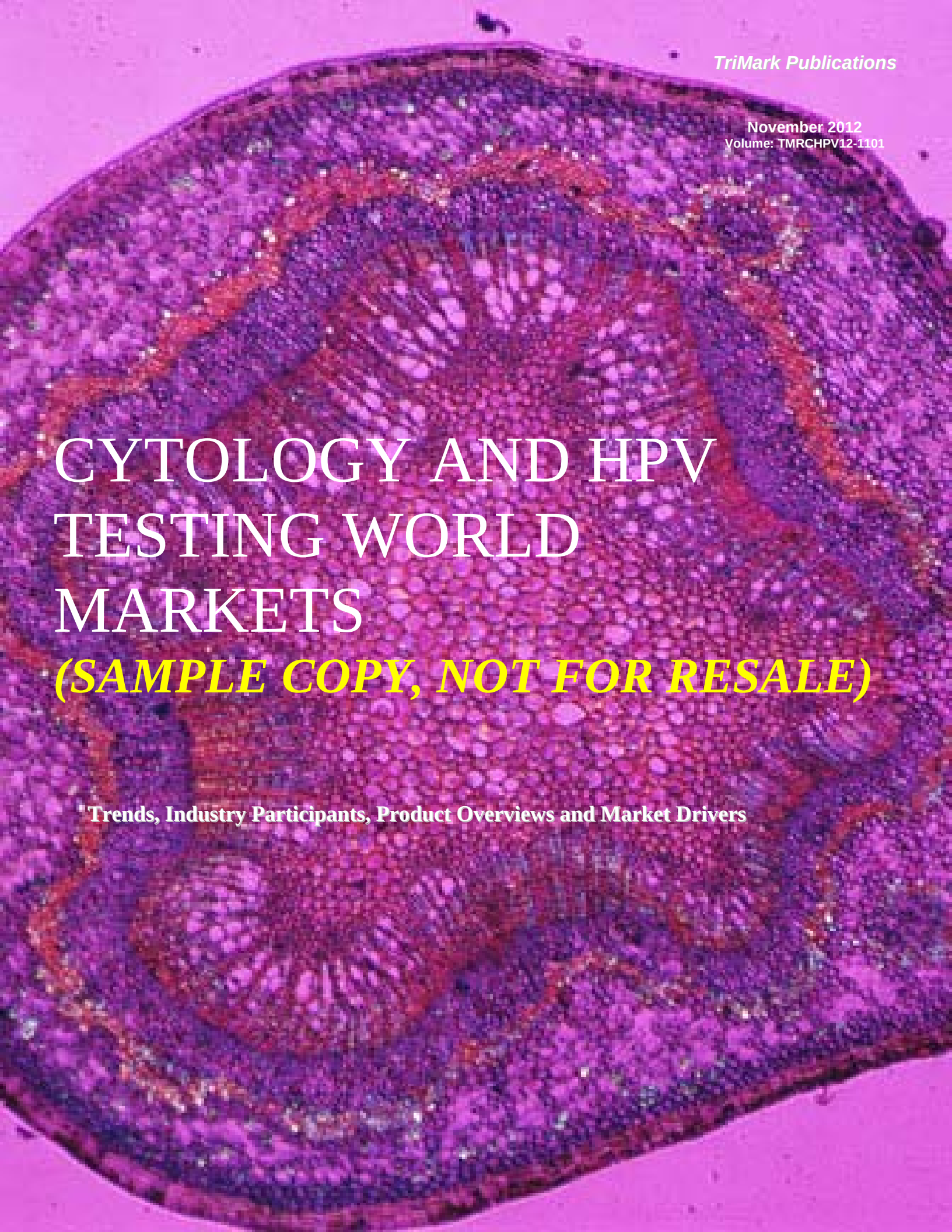
TriMark Publications

November 2012
Volume: TMRCHPV12-1101



CYTOLOGY AND HPV TESTING WORLD MARKETS

(SAMPLE COPY, NOT FOR RESALE)

Trends, Industry Participants, Product Overviews and Market Drivers

TABLE OF CONTENTS

1. Overview 6
1.1 Statement of Report 6
1.2 About this Report 6
1.3 Scope of the Report 8
1.4 Objectives 8
1.5 Methodology 8

2. Introduction to Cancer Biology and the Diagnostic Industry 11
2.1 Cancer 11
2.1.1 The Disease 11
2.1.2 Metastasis 11
2.1.3 Demographics and Statistics of Cancer 12
2.2 The Drivers of the Biotech and Diagnostics Industry 16
2.2.1 Top Ten Biotech Corporations Based on Innovation as Determined by FastCompany Magazine 17
2.2.2 Technological Innovation 18
2.2.3 Government Funding 18
2.2.4 Pharmaceutical Development 19
2.3 Outlook for Tumor Markers 21
2.4 The Cancer Market 21

3. Cervical Cytology Testing Overview 24
3.1 Sector Background 24
3.2 Cervical Cancer 24
3.3 Market Opportunity 25
3.4 Cytology-Based Screening for Cervical Cancer 26
3.4.1 Accuracy and Limitations of Pap Smears 29
3.4.2 Liquid-Based Pap Smear Technologies and Automation 30
3.5 New Guidelines for Cervical Cancer Screenings 31
3.6 Impact of New Screening Guidelines on the Pap Smear Market 31

4. Cytology Market Structure 32
4.1 Key Players 32
4.1.1 BD Diagnostics (Acquired TriPath Imaging) 32
4.1.2 Hologic, Inc. (Acquired Cytyc) 32
4.1.3 CytoCore, Inc. (Formerly Known as Molecular Diagnostics, Inc.) 33
4.1.4 Ventana Medical Systems, Inc. (A Member of the Roche Group) 33
4.1.5 Pap Smear Market Share 34
4.2 BD-TriPath Cervical Cytology Product Line 34
4.2.1 BD SurePath Pap Test 35
4.2.2 BD Cell Enrichment Process 35
4.2.3 BD PrepStain Slide Processor 35
4.2.4 BD FocalPoint Slide Profiler 36
4.2.5 BD FocalPoint GS Imaging System 36
4.2.6 Manufacturing of BD-TriPath Cytology Products 37
4.2.7 Molecular Oncology 38
4.3 Hologic Cervical Cancer Screening Products 39
4.3.1 The ThinPrep System 39
4.4 CytoCore, Inc. Products 42
4.4.1 SoftPAP Cervical Cell Collector 42
4.4.2 CytoCore Products in Development 43
4.5 Ventana (Roche) Cervical Cancer Screening—CINtec Plus Cytology Kit 43
4.6 Latest Advances in Cervical Cancer Screening Technologies and Products 44
4.6.1 Molecular Testing for Cancer Antigens 44

4.6.2 Flow Cytometric Analysis of Cervical Cells 44
4.6.3 LuViva® Advanced Cervical Scan 44
4.6.4 MarkPap® 45
4.6.5 oncoFISH® cervical 45
4.7 Marketing and Sales Strategies 46
4.7.1 BD-TriPath Marketing and Sales 46
4.7.2 Hologic Marketing and Sales 49

5. Human Papillomavirus Testing Overview 51
5.1 Human Papillomavirus 51
5.2 HPV Testing to Detect Cervical Cancer 52
5.2.1 New U.S. Guidelines include HPV Testing for Cervical Cancer Screenings 52
5.2.2 Benefits of Pap Smear and HPV Co-Testing 54
5.2.3 Primary HPV Testing 54
5.2.4 HPV Testing in Low-Resource Regions 55
5.2.5 Self-Sampling for HPV Testing 56

6. Human Papillomavirus Testing Market Structure 57
6.1 HPV Testing Market Overview 57
6.2 U.S. Market 57
6.3 European Market 58
6.4 Latin American Market 59
6.5 Asian Market 59
6.6 HPV Vaccines—Impact on HPV Testing 60
6.6.1 Cervical Cancer Vaccines on the Market 60
6.6.2 Cervical Cancer Screening Remains Vital in the Age of HPV Vaccination 61
6.7 Sales and Marketing Strategies—Lessons from QIAGEN 61
6.8 Competition 64
6.9 Market Challenges and Strategic Recommendations 67
6.9.1 Market Drivers and Restraints 67
6.9.2 Market and Technology Trends 68
6.9.3 Strategic Recommendations 70

7. Key Players and Products in the HPV Testing Market 71
7.1 QIAGEN (Acquired Digene) 71
7.1.1 QIAGEN HPV Testing Products 72
7.2 Hologic 76
7.2.1 Invader Chemistry 77
7.2.2 Cervista HPV HR 77
7.2.3 Cervista HPV 16/18 77
7.2.4 Hologic Acquires Gen-Probe and its Product Line 78
7.3 Gen-Probe (now part of Hologic) 78
7.3.1 APTIMA HPV Assay 78
7.4 Roche (Ventana) 79
7.4.1 cobas 4800 HPV Test 79
7.4.2 Linear Array HPV Genotyping Test 79
7.4.3 Amplicor HPV Test 79
7.4.4 INFORM HPV 80
7.5 Innogenetics' INNO-LiPA HPV Genotyping Extra assay 80
7.6 Greiner Bio-One GmbH's PapilloCheck® 80
7.7 GenoID Ltd.'s GenoID Assay 80
7.8 bioMérieux Clinical Diagnostics' NucliSENS EasyQ® HPV Test 81
7.9 Trovagene, Inc. 81

8. Business Trends in the Industry 82

8.1 Industry Consolidation 82
8.2 Breadth of Product Offering 83
8.3 Government Regulation of Medical Devices 83
8.4 Strategic Business and Marketing Considerations 84
8.5 Commercial Opportunities in Cancer Markers 84
8.6 Moderators of Growth 85
8.7 Biotechnology Industry Trends 86
8.8 Pharmaceutical Industry Trends 86
8.9 Acquisition, License Agreement and Partnerships 87
8.10 Sales and Marketing Strategies for Tumor Marker Tests 87
8.10.1 North American Market 88
8.11 Recent Industry Activity 88

9. Third-Party Reimbursement 90
9.1 Reimbursement Codes Classification 90
9.2 Reimbursement for the Cervical Cytology Product Line 91
9.3 Molecular Diagnostic Products and Imaging Systems 91

10. Barriers in Business 92
10.1 Barriers in the Business Section 92
10.1.1 Barriers for Hologic 92
10.1.2 Risk Factors for QIAGEN 96
10.1.3 Ventana Medical Systems (A Member of the Roche Group) 104

11. Acquisition Activity 107
11.1 Acquisition 107
11.2 Hologic, Inc. Acquires Cytyc Corporation 107
11.3 BD Diagnostics Acquires TriPath Imaging, Inc. 107
11.4 QIAGEN Acquires Digene Corporation 108
11.5 Hologic Acquires Gen-Probe 108
11.6 Roche Acquires mtm laboratories AG 108

12. Intellectual Property 110
12.1 BD-TriPath Proprietary Technology and Intellectual Property 110
12.2 QIAGEN Intellectual Property 110
12.2.1 Hybrid Capture Technology 110
12.3 Ventana (Now a Member of the Roche Group) Patents and Proprietary Rights 111

13. Outlook on the Women's Health Industry 112
13.1 Hologic 112
13.2 BD-TriPath 114
13.3 QIAGEN 115
13.4 Trends, Issues, Challenges and Opportunities: An Analysis 115
13.4.1 Hologic 115
13.4.2 BD-TriPath 118
13.4.3 QIAGEN 119
13.5 Competitive Landscape 120

14. Analytical Section 121
14.1 Company Strategies 121
14.1.1 QIAGEN 121
14.1.2 BD-TriPath 122
14.1.3 Hologic 122
14.2 SWOT Analysis 122
14.2.1 QIAGEN 122

14.2.2 BD-TriPath 124
14.2.3 Hologic 126

INDEX OF TABLES

Table 2.1: Drug Development by Type of Cancer 12
Table 2.2: Estimates for the Leading Types of New Cancer Cases and Deaths in the U.S. by Sex, 2012 12
Table 2.3: Organ-Specific Medicines in Development for Cancer 13
Table 2.4: Estimated Number of Cancer Cases and Deaths by World Area, 2008 14
Table 2.5: Cancer Death Rates per 100,000 Population (and Rank) for All Cancer Sites by Country 15
Table 2.6: Cancer-Associated Genes 15
Table 2.7: Carcinogens in the Workplace 16
Table 2.8: U.S. Government NIH Research Grant Funding, 2000-2011 18
Table 2.9: Global R&D Spending in the Pharmaceutical Industry, 2008-2012 19
Table 2.10: Pharmaceutical Companies Ranked by Total R&D Expenditures, 2011 19
Table 2.11: Leading Therapy Classes for R&D, 2012 20
Table 2.12: Women's Cancers in the U.S., 2012 21
Table 2.13: Five-Year Relative Survival Rates by Stage at Diagnosis 22
Table 3.1: Estimated Number of Pap Smears Performed by Country, 2011 26
Table 3.2: Bethesda System of Classifying of Pap Smear Test Results 28
Table 4.1: Pap Tests in Top European Markets, 2011 46
Table 4.2: Pap Tests in Top Asian Markets, 2011 46
Table 5.1: Conditions Associated with Different HPV Types 51
Table 5.2: New Guidelines for Cervical Cancer Screenings (2012) 53
Table 6.1: Global Market for HPV Molecular Diagnostic Testing, 2009-2017 57
Table 6.2: U.S. Market for HPV Diagnostic Testing, 2009-2017 58
Table 6.3: HPV Molecular Diagnostics Market Drivers 67
Table 6.4: HPV Molecular Diagnostics Market Restraints 68
Table 7.1: HPV Tests on the Market 71

INDEX OF FIGURES

Figure 4.1: Liquid-Based Pap Test Market Share 34
Figure 6.1: U.S. Market Share of HPV Molecular Diagnostic Market, 2011 65

1. Overview

1.1 Statement of Report

According to the Union for International Cancer Control (UICC), [redacted]% of the [redacted] million people diagnosed with cancer worldwide each year could avert the killer disease by protecting themselves against infections and changing their lifestyles. A [redacted] report by the Geneva-based UICC highlighted nine infections that can lead to cancer, with human papillomavirus (HPV) at the top of the list. On February 4, 2010—designated as "World Cancer Day" by the UICC—the International Agency for Research on Cancer (IARC), the Cervical Cancer Action (CCA) coalition and the UICC called for the implementation of comprehensive strategies to reduce cervical cancer. Cervical cancer is one of the leading causes of cancer among women in developing countries and is the second most common cancer in women worldwide. The most recent estimates suggest that each year, there are more than a quarter-of-a-million deaths from cervical cancer and over [redacted] new cases, most of which could be prevented. The World Health Organization (WHO) projects that without immediate action the global number of deaths from this disease will increase by nearly [redacted]% by [redacted], mostly in low- and middle-income countries.

Two HPV vaccines are now on the market for the prevention of cervical cancer. Both vaccines have been shown to be highly effective at preventing infection with HPV types [redacted] and [redacted], which are responsible for approximately [redacted]% of cervical cancer cases globally. Furthermore, HPV testing enables the initiation of diagnosis and treatment before cervical cancer can develop. With the aid of preventative screening and vaccines such as these, [redacted]% of cancers can be prevented, but these measures are not being used.. This report provides an overview of HPV testing and the key players involved in this market, with specific emphasis on each company's sales focus, product portfolio and research and development (R&D) pipeline. It also discusses the specific segment of the diagnostic market aimed at analysis of cytology specimens derived from the female reproductive tract.

1.2 About this Report

This study describes the analytical methods used to separate, isolate, characterize and quantitate cells, deoxyribonucleic acid (DNA) and protein complexes in biological systems related to the diagnosis and treatment of diseases of the female reproductive tract, such as the cervix, vagina, uterus and ovaries. The emphasis is on those companies that are actively developing and marketing products such as laboratory instrumentation and reagents and supplies for performing cytology and molecular diagnostic tests for HPV. The main objectives of this analysis are:

- Identifying viable technology drivers through a comprehensive look at platform technologies for cytology and HPV testing, including thin-film cytology techniques and molecular diagnostic technologies for HPV detection.
- Obtaining a complete understanding of the chief cytology tests from their basic principles to their applications.
- Discovering feasible market opportunities by identifying high-growth applications in different analytical diagnostic areas, concentrating on the biggest and expanding markets.
- Focusing on global industry development through an in-depth analysis of the major world markets for cytology technology, including growth forecasts.
- Presenting market figures regarding the current value of the cytology and HPV market, projections and growth rates. The source of this information is the most current data derived from the global diagnostic industry with cytology market forecasts.

By purchasing this study, the reader will gain:

- An understanding of the most promising cervical cancer screening market segments—current and future.
- The latest information on leading products and R&D initiatives.
- Familiarity with recent developments and their effects on selected markets.
- Knowledge of the cervical cancer screening market as an area of growth, research and investment.

Key questions answered in this review are:

- How can cytology tools and technologies facilitate other diagnostic tests like those for HPV?
- What are the main types of cervical cancer screening technologies that are currently available and used?
- Who are the current key players in this marketplace?
- Which cervical cancer screening market areas have the greatest potential for growth?
- What is the current state of the cervical cancer screening market?
- Which biotechnology and diagnostic companies are investing in cervical cancer screening solutions?
- What are the main cervical cancer screening business strategies adopted by leading companies?
- What are the benefits of cervical cancer screening technology platforms?

This report contains:

- Detailed analysis of recent trends in the cervical cancer screening marketplace.
- In-depth profiles of the leading companies with cervical cancer screening tools and technologies.
- Forecasts for the cervical cancer screening market in the biotechnology and diagnostic industries.
- Views and principles on the cervical cancer screening industry from leading industry experts.
- Analysis of potential cervical cancer screening applications in the life science sector.
- Market predictions and trends analysis concerning U.S. expenditure on cervical cancer screening solutions.
- Projections for future applications of molecular diagnostic tests in cytology-related screening.
- A comprehensive analysis, overview and insight into commercial cervical cancer screening business strategies.

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 study will:

- Analyze cervical cancer screening market drivers and bottlenecks from medical and scientific community perspectives.
- Discuss the potential benefits of cervical cancer screening for various sectors of the medical and scientific community.
- Establish the current total market size and future growth of the cervical cancer screening 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 segment.
- Provide strategic recommendations for near-term business opportunities in the cervical cancer screening market.
- Assess current commercial uses of the cervical cancer screening market.

The following questions will also be addressed in this analysis:

- What are the current and forecasted cervical cancer screening market sizes in the U.S., European Union (E.U.) and Japan, as well as in other key country markets?
- What are the business models currently used by companies in the cervical cancer screening market?
- Who holds the proprietary rights to the cervical cancer screening market technology platforms?

- How is this technology currently being applied and utilized?
- In the U.S., Japan and the E.U., what regulatory processes apply to cervical cancer screening technologies?
- How will new cervical cancer screening technologies change diagnostic screening testing paradigms?
- How will new cervical cancer screening technologies reduce diagnostic false-negatives and decrease costs of patient care?

1.3 Scope of the Report

This analysis emphasizes companies that are actively developing and marketing laboratory instrumentation, reagents and supplies for performing cervical cancer screening tests. The reader can consult other TriMark Publications reports at www.trimarkpublications.com for detailed discussions of important individual market segments related to the protein analysis market, such as clinical chemistry testing, high-growth diagnostic test markets, over-the-counter diagnostic testing markets and point-of-care testing.

The U.S. and Europe—the world's two largest cervical cancer screening markets—are the focus of this study. Primary attention is paid to the clinical 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 molecular diagnostic testing, such as that for HPV, is examined, since it is often a part of the overall analytical focus of companies that market cytology laboratory-automation equipment. This study does not cover disposable plastic supplies for the laboratory. These subjects are discussed in other TriMark reports.

An analysis of business trends, technology trends and developing areas of cytology and HPV testing is provided, along with a review of the market for cervical cancer screening equipment and supplies in the clinical and research market segments. This review defines U.S. and global market dollar-sales volume and analyzes factors that influence the size and growth of market segments. Market size and growth rates, with projections (where sensible) for the U.S. and global markets, are examined. Activity and trends in research markets, including the number of institutions that use cytology testing and the factors that influence purchasing, are also addressed in this report. Also discussed are trends that have stimulated this market and patterns of information processing in array testing instruments.

1.4 Objectives

The goal of this report is to review the market for cytology and HPV-testing equipment and supplies using screening reagents and instruments for analysis of individual components in tissue samples, 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 the growth of the market segments. The subsections of each market segment are also examined, including the research labs, hospital labs and commercial laboratories. Additionally, the number of institutions using this type of cervical cancer screening and the factors that influence purchases are discussed. The report surveys almost all of the companies known to be marketing, manufacturing or developing instruments and reagents for the cervical cancer screening market in the U.S. Each company is discussed in extensive 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 has 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 cancer testing laboratories. He has over 30 years of experience 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 degree in immunology, and has substantial experience in science writing and as a medical industry analyst. She also has many years of laboratory experience investigating cancer immunotherapies, 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. Additionally, sources of information include non-governmental organizations (NGOs), such as the World Health Organization (WHO), and governmental entities and U.S. federal agencies like the U.S. Department of Health and Human Services (HHS), the National Cancer Institute (NCI), the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the American Cancer Society (ACS) and the Centers for Disease Control and Prevention (CDC). Where possible and practicable, the most recent data available have been used.

Some 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 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.

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 U.S. Securities and Exchange Commission (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 in regional components as well, taking into account differences in market conditions between the U.S., European and Asian markets in particular.

TriMark Publications Report, Research and Data Acquisition Structure

The general sequence of research and analysis prior to the publication of a 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.

