BIOVERIS CORP
Form 10-K
June 14, 2005

SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For Fiscal Year Ended	March 31, 2005
Commission File Number	000-50583

BioVeris Corporation

(Exact name of registrant as specified in its charter)

DELAWARE	80-0076765
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)

16020 INDUSTRIAL DRIVE, GAITHERSBURG, MD 20877
(Address of principal executive offices) (Zip Code)

(301) 869-9800
(Registrant s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:	NONE
Securities registered pursuant to Section 12(g) of the Act:	Common Stock $0.001 par value
	(Title of Class)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

Yes þ No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained to the best of the registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

Indicate by check mark whether the registrant is an accelerated filer (as defined on Rule 12b-2) of the Exchange Act.

Yes þ No o

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant as of September 30, 2004, computed by reference to the closing sale price of such stock quoted on The Nasdaq National Market on such date, was approximately $128,125,298.

The number of shares outstanding of the registrant s Common Stock as of June 1, 2005 was 26,726,950.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the definitive Proxy Statement for our 2005 Annual Meeting of Stockholders are incorporated by reference into Part III of this Form 10-K Report.

BIOVERIS CORPORATION

Annual Report On Form 10-K

For The Fiscal Year Ended March 31, 2005

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As used herein, BioVeris , we , us and our refer to BioVeris Corporation and its subsidiaries. M-SERIES, TRICORDER and BIOVERIS are our trademarks. This Form 10-K also contains disclosure relating to brand names, trademarks or service marks of other companies, and these brand names, trademarks or service marks are the property of those other holders.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

In addition to historical information, this Annual Report on Form 10-K contains forward-looking statements within the meaning of the safe harbor provision of the Private Securities Litigation Reform Act of 1995. All statements contained in this report that are not statements of historical fact, including statements about markets and potential markets, market growth for diagnostic products, potential impact of competitive products, our expectations regarding future revenue, the potential market for products in development, the description of our plans and objectives for future operations, assumptions underlying such plans and objectives, the need for and availability of additional capital and other forward-looking statements included in ITEM 7 Management s Discussion and Analysis of Financial Condition and Results of Operations (MD&A), are forward-looking statements. The words may, should, will, expect, could anticipate, believe, estimate, plan, intend and similar expressions have been used to identify certain of the forward-looking statements. In this Form 10-K we have based these forward-looking statements on management s current expectations, estimates and projections and they are subject to a number of risks, uncertainties and assumptions which could cause actual results to differ materially from those described in the forward-looking statements. The following factors are among those that may cause actual results to differ materially from our forward-looking statements:

changes in our strategy and business plan, including our plans for vaccines, the clinical diagnostics, biodefense, life science and industrial markets and other healthcare opportunities;

our ability to develop and introduce new or enhanced products, including incorporating multi/unit dose cartridges;

our ability to enter into new collaborations on favorable terms, if at all;

our ability to expand the distribution and increase sales of existing products;

changes in customer demand, the timing of significant orders or the demand for rapid testing products in each of our markets;

our ability to expand our manufacturing capabilities or find a suitable manufacturer on acceptable terms or in a timely manner;

our ability to develop our selling, marketing and distribution capabilities;

our and our licensees ability to obtain approvals from the U.S. Food and Drug Administration which we refer to in this Form 10-K as the FDA, and other governmental approvals for our and their clinical testing products or for vaccine products, including regulatory changes, uncertainties or delays;

the ability of our licensees to effectively develop and market products based on the technology we license to them;

our ability to win competitively awarded government contracts in the future and retain existing government contracts;

domestic and foreign governmental and public policy changes, particularly related to healthcare costs, that may affect new investments and purchases made by our customers;

competition from companies with greater financial and capital resources than ours;

availability of financing and financial resources in the amounts, at the times and on the terms required to support our future business;

dependence on a limited number of suppliers for materials used in the manufacturing of our products;

rapid technological developments in each of our markets and our ability to respond to those changes in a timely, cost-effective manner;

any potential future disputes regarding the scope, permitted use and other material terms of our license agreements, including those with Meso Scale Diagnostics, LLC., which we refer to in this Form 10-K as MSD;

our ability to receive payment over time from Meso Scale Technologies, LLC., which we refer to in this Form 10-K as MST, from the sale of our interests in MSD;

protection and validity of our patent and other intellectual property rights and the scope of third party patent rights;

relationships between us and certain companies with which we are affiliated; and

changes in general economic, business and industry conditions.

These factors are not necessarily all of the important factors that could cause actual results to differ materially from those expressed in any of our forward-looking statements. Other unknown or unpredictable factors could also have material adverse effects on future events. We disclaim any intent or obligation to update these forward-looking statements.

PART I

ITEM 1. BUSINESS

Summary

On February 13, 2004, IGEN and Roche Holding Ltd, which we refer to in this Form 10-K as Roche, consummated a merger and certain related transactions, which we refer to in this Form 10-K as the merger and related transactions, pursuant to which Roche acquired IGEN and IGEN simultaneously distributed shares of our common stock to its stockholders. The transaction occurred in the following steps:

IGEN restructured its operations so that we, a newly formed, wholly-owned subsidiary of IGEN at the time, assumed IGEN s biodefense, life science and industrial product lines as well as IGEN s opportunities in the clinical diagnostics and healthcare fields and the ownership of IGEN s intellectual property, IGEN s equity interest in MSD, cash and certain other rights and licenses currently held by IGEN; and

a wholly-owned subsidiary of Roche merged with and into IGEN, as a result of which IGEN became a wholly-owned subsidiary of Roche and we became an independent, publicly-traded company. Simultaneously with the completion of the merger, certain ongoing commercial agreements between certain affiliates of Roche and us became effective.

Diagnostics

We develop, manufacture and market our M-SERIES® family of products, which can serve as a platform for diagnostic systems to be used for the detection and measurement of biological or chemical substances. We incorporate

our technologies into our instrument systems, tests and reagents, which are the biological and chemical components used to perform such tests. Using the M-SERIES platform, we intend to integrate technologies and products to develop small, expandable and modular systems that can perform a wide variety of immunodiagnostic and nucleic acid tests for the following markets:

Clinical diagnostics. The clinical diagnostics market includes the testing of patient samples to measure the presence of disease and monitor medical conditions. We are developing products to be used in the clinical diagnostics market and believe that our products will be ideally suited for the immunodiagnostic and nucleic acid testing market segments of the clinical testing market.

Non-clinical diagnostics for the biodefense, life science and industrial markets. The non-clinical diagnostics market includes biodefense products for the detection of bacteria, viruses and toxins that may pose a military or public health threat; life science testing for drug discovery and development that is performed by pharmaceutical and biotechnology companies; and industrial testing for the detection of foodborne and waterborne disease causing pathogens.

We believe that the emergence of simple, more accurate and cost-effective clinical diagnostic products is shifting the site of clinical diagnostic testing from clinical reference laboratories and central hospital laboratories to decentralized patient care centers, such as physicians offices, ambulatory clinics, hospital emergency rooms, surgical and intensive care units, hospital satellite laboratories and nurses stations, which are collectively referred to as clinical point-of-care sites.

Our own product development efforts are focused on M-SERIES instruments and tests for the biodefense market and for the clinical diagnostics market, particularly for point-of-care sites. We are seeking to develop, market and sell products for the clinical point-of-care market segment through a combination of direct efforts and collaborative arrangements. We also are pursuing opportunities in the clinical reference laboratory and central hospital laboratory market segments through collaborative arrangements.

The first clinical diagnostic system being developed by us is an M-SERIES clinical analyzer that builds on the M-SERIES instruments we sell in the biodefense and life science markets. We are developing the assays using, among other things, improvements licensed from an affiliate of Roche. We believe that these improvements will reduce product development timelines. We also believe that the clinical analyzer will provide results to a physician rapidly with the same levels of sensitivity, accuracy or consistency as a large instrument in a clinical reference laboratory or in a central laboratory, thereby permitting the physician to make a more timely decision regarding the patient s course of treatment. Among the applications that we plan to develop is a proprietary approach for determining an individual s personal immune status through unique diagnostic panels. We will seek approval from the FDA for the clinical analyzer and other *in vitro* diagnostics products at the appropriate stage of their product development. There can be no assurance that such approval will be obtained.

Our M-SERIES instruments are used in biodefense programs for homeland security, including by the Department of Defense, or DOD. We believe there will be an increasing opportunity to sell our products for biodefense tools by commercial, governmental and military organizations around the world, as well as in the public health sector.

We are also selling two types of M-SERIES instruments for life science research to pharmaceutical and biotechnology researchers, as well as to scientists at academic and government research institutions. Immunogenicity testing is performed by pharmaceutical and biotechnology companies in order to characterize the ability of protein-based therapeutics to stimulate an immune response. We have recently introduced proprietary products for immunogenicity testing. Antibodies that result from an immune response to a protein-based drug can reduce its efficacy and cause significant side effects, such as allergic reactions. Because of serious side effects that have been reported over the last year, it has become increasingly necessary to determine if an immune response to protein-based drugs develops in patients by screening for the presence of antibodies, confirming their specificity, characterizing the type of antibodies present and determining whether they interfere with binding events. Immunogenicity testing is done during pre-clinical studies and may continue through the clinical trials required for regulatory approval. In some cases, the FDA requires additional testing after a drug has been approved. Our M-SERIES product line for the life science market is believed by us to be ideally suited to perform immunogenicity testing by measuring low affinity antibodies

with high sensitivity, all in the presence of the highly concentrated drug.

Vaccines

We have expanded our business model to target the field of vaccines. In conjunction with our efforts to determine an individual s personal immune status through unique diagnostic test panels, we have entered into an exclusive option agreement with Children s Hospital & Research Center at Oakland (CHRCO) for exclusive patent rights to a unique vaccine candidate for *Neisseria meningitidis* serogroup B, which causes meningitis. We believe that the availability of an effective vaccine that would prevent meningococcal serogroup B, for use by various population groups, could meet a significant unmet medical need.

We have also entered into an agreement with the National Research Council of Canada (NRC) for a license to patent rights to candidates for a group B streptococcus (GBS) Type II and Type V vaccine and a group B meningococcus (GBM) vaccine. Under the agreement with the NRC, we acquired worldwide, exclusive rights to commercialize products for possible use in the prevention, diagnosis and treatment of disease caused by GBS, a leading cause of sepsis, pneumonia, and meningitis among newborns. We received similar worldwide rights, with the exclusion of Canada, to NRC s GBM vaccine technologies for the prevention of meningococcal B meningitis and sepsis.

Recently, we entered into an option agreement with the University of Massachusetts at Amherst (UMA) for exclusive patent rights to a unique vaccine candidate for Chlamydia, the most frequently reported infectious disease in the United States. Under the agreement with UMA, we acquired a first option for exclusive rights to commercialize products for possible use in the prevention, diagnosis and treatment of all chlamydial infections, including the disease, chlamydia, caused by the bacterium, *Chlamydia trachomatis*.

Investor Information

We were organized as IGEN Integrated Healthcare, LLC, a Delaware limited liability company, on June 6, 2003, and converted to BioVeris Corporation, a newly formed Delaware corporation, on September 22, 2003. Our executive offices are located at 16020 Industrial Drive, Gaithersburg, Maryland 20877. Our Internet website is located at http://www.bioveris.com. Information contained on our website is not part of this Form 10-K or any other filing which may incorporate by reference this Form 10-K. We provide to the public on our website, free of charge, our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) of the Securities Exchange Act of 1934, as amended, as soon as practicable after such material is filed electronically with, or furnished to, the Securities and Exchange Commission which we refer to in this Form 10-K as the SEC. Any report, proxy statement or other information we file with the SEC may be read and copied at the SEC s Public Reference Room at 450 Fifth Street, N.W., Washington, D.C. 20549. Information on the operation of the Public Reference Room is available by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site (http://www.sec.gov) that makes available reports, proxy statements and other information regarding issuers that file electronically with it.

Our Strategy

Our strategy is based on the direct development and sale of products utilizing our technologies, while at the same time entering into collaborations with third parties that can assist us in product development, manufacturing and marketing efforts. Key elements of our strategy are to:

pursue collaborative relationships to accelerate new product development and enhance global manufacturing and marketing capabilities;

establish leadership positions in emerging markets;

develop and market product line extensions and an expanded menu of assays; and

maximize high value-added opportunities in vaccines.

Our Technology

Our M-SERIES family of products will incorporate a number of technologies, including:

ECL technology developed and owned by us;

various improvements to ECL technology developed by Roche Diagnostics GmbH, which we refer to in this Form 10-K as Roche Diagnostics, and licensed to us;

polymerase chain reaction technology developed by Roche Diagnostics and licensed to us for use in several specified markets, including the human and animal *in vitro* diagnostics markets, which we refer to in this Form 10-K as PCR technology; and

multi/unit dose cartridge technology for packaging reagents in a ready-to-use format that remains stable at room temperature.

In addition, we have rights to a unique vaccine candidate for *Neisseria meningitidis* serogroup B, which causes meningitis; to candidates for a GBS Type II and Type V vaccine and a GBM vaccine; and to commercialize products for possible use in the prevention, diagnosis and treatment of all chlamydial infections, including the disease, chlamydia, caused by the bacterium, *Chlamydia trachomatis*.

ECL Technology

ECL technology is based on electrochemiluminescence that is protected by patents in the United States and internationally. ECL technology permits the detection and measurement of a biological or chemical substance within a given sample. It works by labeling the targeted substance within a sample using a compound and binding the newly labeled substance to magnetizable beads. The beads can then be separated from the rest of the sample using a magnet. When this newly labeled substance is stimulated, the label emits light at a particular wavelength.

The light emitted by the label can be measured with a high degree of accuracy. The level of intensity of the light emitted by the label is determined by the amount of the targeted biological substance present in the sample for the label to attach itself to. Thus, the light emissions permit the accurate detection and measurement of the targeted biological or chemical substance.

ECL technology provides a uniform format that can be used to conduct a multitude of tests, including immunodiagnostic tests and nucleic acid tests. The essential component of an ECL technology-based system is the flow cell, which contains a magnet to separate the labeled substance from the sample being tested and a light detector to measure the electrochemiluminescence.

The flow cell has been designed so that it can be incorporated into a variety of instruments, ranging from large central laboratory random access systems to small batch systems.

We believe that the major features and benefits of ECL technology-based systems are:

Simplicity: uniform testing format reduces time and labor in performing a test or series of tests and permits complete automation of the testing process.

Flexibility: enables a single instrument to perform immunodiagnostic tests on large and small molecules and to perform nucleic acid tests, including in the form of DNA and RNA tests.

Cost: reduces the cost per test by minimizing the amount of expensive reagents needed and the number of steps required to prepare a sample for testing.

Speed: reduces time from test set-up to detection, producing rapid results and enabling high sample throughput.

Sensitivity: allows detection of targeted biological substances at very low concentrations.

Consistency: provides highly-reproducible measurements.

Accuracy: provides results that are identical or close to the standard reference measurement.

Stability: extends the shelf-life of the reagent that contains the label used in testing and improves measurement accuracy.

We believe that ECL technology is well suited for the continued development and sale of the M-SERIES family of instruments that can be used in all of our target diagnostic markets. We believe the technology will permit virtually all immunodiagnostic and nucleic acid tests to be performed on similar instrumentation using the same detection method.

ECL technology is well established in the market, evidenced by the fact that our licensees have developed multiple product lines based on ECL technology and through 2003 had sold or placed over 10,000 systems with customers worldwide which generate over $500 million in annual sales. Substantially all of these sales and placements have been made by Roche, one of the world s leading providers of clinical diagnostic products, which has a worldwide, non-exclusive, royalty-free license for our ECL technology for use with certain defined systems and immunoassay methods for the clinical diagnostics market. There can be no assurance that we will succeed in profitably developing, marketing and selling products based on ECL technology.

Improvements from Roche

As part of the merger and related transactions, we acquired from Roche Diagnostics and its affiliates an irrevocable, worldwide, non-exclusive, fully-paid, royalty-free, perpetual license under certain patents covering technologies based on:

Roche Diagnostics ECL instruments and all aspects of ECL assays developed prior to the completion of the merger between Roche and IGEN;

certain PCR technology; and

certain aspects of ECL technology and robotics used or developed prior to the completion of the merger between Roche and IGEN.

The license, which we refer to in this Form 10-K as the improvements license agreement may be used without a field restriction (except as set forth in the next sentence) to develop, make, reproduce, modify, use, sell and otherwise commercially exploit any product or service based on ECL technology. In addition, we are licensed to use certain intellectual property rights of Hitachi High Technology Corporation and its affiliates only outside the field defined in the improvements license agreement to develop, make, reproduce, modify, use, sell and otherwise commercially exploit any product or services based on ECL technology. Subject to an exception, the field in the improvements license agreement is the same as the field in the license agreement. We may sublicense rights under both of these licenses to affiliates and third parties.

The improvements license agreement does not permit us to develop, use, manufacture, sell or otherwise commercialize instruments based on ECL technology that meet certain specifications and use specific intellectual property, in the field. In addition, the license does not permit us to develop, use, manufacture or sell ECL assays that contain labeling that make them useable on ECL instruments manufactured, sold or placed by Roche Diagnostics or its licenses or resellers, in the field.

PCR Technology

PCR technology includes the amplification of specific nucleic acid sequences to a sufficient quantity of the nucleic acid sequence to permit detection and quantification. The process of nucleic acid amplification is commonly used for diagnostic procedures involving infectious agents, such as the AIDS virus, because of the need to detect the smallest

amount of virus possible in the blood or other clinical samples.

The PCR license agreements obtained by us from Roche Diagnostics and its affiliates will allow us to develop nucleic acid tests for several specified markets, including the human and animal *in vitro* diagnostics markets. We believe that nucleic acid tests are currently one of the fastest growing segments of the clinical diagnostics market and would complement our immunodiagnostic product line. We do not currently sell any product based on the PCR technology licensed from Roche. For more information about the license fee and royalty payments in connection with the PCR license agreements, see ITEM 8 Consolidated Financial Statements and Supplementary Data Notes to Consolidated Financial Statements Note 1.

Multi/Unit Dose Cartridge Technology

We have a unique technology utilizing a disposable, multiple dose or unit dose cartridge that we expect will be inexpensive to manufacture and contains all the reagents necessary to perform several different immunoassays on a single sample of blood from a patient. These reagents will be packaged so that they remain stable at room temperature for several months. This method of packaging reagents differs from the typical method of packaging reagents in a container that holds reagents for 100 to 200 tests for a single type of immunoassay and usually must be refrigerated. We have demonstrated that the test results using the multi/unit dose cartridge are accurate and consistent with the results obtained using conventional instruments and kits used in central hospital laboratories. We believe the ease of use, room temperature stability, accuracy and consistency of test results associated with this technology are important features for use in clinical point-of-care sites and biodefense applications.

Vaccines

We have entered into an exclusive option agreement with CHRCO for exclusive patent rights to a unique vaccine candidate for *Neisseria meningitidis* serogroup B, which causes meningitis. We believe that the availability of an effective vaccine that would prevent meningococcal serogroup B, for use by various population groups, could meet a significant unmet medical need.

We have also entered into an agreement with the NRC for a license to patent rights to candidates for a GBS Type II and Type V vaccine and a GBM vaccine. Under the agreement with the NRC, we acquired worldwide, exclusive rights to commercialize products for possible use in the prevention, diagnosis and treatment of disease caused by GBS, a leading cause of sepsis, pneumonia, and meningitis among newborns. We received similar worldwide rights, with the exclusion of Canada, to NRC s GBM vaccine technologies.

Recently, we entered into an option agreement with the University of Massachusetts at Amherst (UMA) for exclusive patent rights to a unique vaccine candidate for Chlamydia, the most frequently reported infectious disease in the United States. Under the agreement with UMA, the Company acquired a first option for exclusive rights to commercialize products for possible use in the prevention, diagnosis and treatment of all chlamydial infections, including the disease, chlamydia, caused by the bacterium, *Chlamydia trachomatis*.

Products and Markets Using Our Technology

The following table summarizes the range of products that we have licensed, developed or are developing. We expect that our future products will incorporate other technology, which may include the improvements from Roche, PCR technology and multi/unit dose cartridge technology.

BioVeris Products Diagnostics	Customer Application	Market	Status
M-SERIES (Clinical analyzer and clinical diagnostic tests)	Screen, monitor and diagnose medical conditions	Clinical	Development
BioVeris Detection System and Reagents	Detection of bacteria, viruses and toxins	Biodefense	Product sales
	Drug discovery and development	Life science	Product sales
M-SERIES (M384 Analyzer and Reagents)	Drug discovery and development	Life science	Product sales
M-SERIES (M1M Analyzers)	Drug discovery and development	Life science	Product sales
	Detection of food and beverage contaminants and bacteria, viruses and toxins	Biodefense	Product sales
Test Panel for BioVeris Detection System	Detection of food and beverage contaminants	Industrial	Product sales
Cell Culture Reagents	Biological research	Life science	Product sales
Vaccines			
Neisseria meningitides serogroup B	Preventative medicine	Vaccine	Pre-clinical research
Group B streptococcus Type II and Type V	Preventative medicine	Vaccine	Pre-clinical research
Group B meningococcus	Preventative medicine	Vaccine	Pre-clinical research
Chlamydia	Preventative medicine	Vaccine	Pre-clinical research

The following table summarizes the range of products that our licensees have developed using our ECL technology. In general, we will receive royalties or other payments as a result of product sales by our licensees other than Roche. For a description of the commercial arrangements and license agreements that we have with our licensees see Business-Collaborations and License Arrangements.

Licensee Products	Customer Application	Market	Status	Licensee
Elecsys 2010/1010/ ECL module of E170	Screen, monitor and diagnose medical conditions	Clinical	Product sales	Roche

NucliSens/NASBA QR	Screen, monitor and diagnose medical conditions	Clinical	Product sales	bioMérieux
	Screen, monitor and diagnose medical conditions	Life science	Product sales	bioMérieux
Picolumi	Screen, monitor and diagnose medical conditions	Clinical	Product sales	Eisai (Japan)
Sector product line	Drug discovery and development	Life science	Product sales	MSD

Our Products and Markets

Clinical Diagnostics

We plan to manufacture and sell products utilizing our technologies for the clinical *in vitro* diagnostics market either ourselves or through additional licensees. *In vitro* diagnostic testing, which is the process of analyzing blood, urine and other samples to screen for, monitor and diagnose diseases and other medical conditions or to determine the chemical and microbiological constituents of the samples is one type of testing used by the clinical diagnostics market. We believe that ECL technology is ideally suited for the blood-based immunodiagnostic and nucleic acid testing segments of the clinical diagnostics market. Clinical diagnostic testing is performed in many locations, including testing by clinical reference laboratories, central hospital laboratories, and blood banks, as well as testing at clinical point-of-care sites. Our products for the clinical *in vitro* diagnostics market will generally require approval or clearance by the FDA prior to the marketing of the products, which we will seek in the appropriate stage of product development. There can be no assurance that such approval will be obtained. See ITEM 1 Business Government Regulation Clinical Diagnostic Products for a more detailed description of the government regulations to which we are subject in connection with products for the clinical *in vitro* diagnostics market.

Point-of-Care Systems. Many diagnostic tests performed today involve a follow-up treatment decision by the physician, but the test and treatment process are usually decoupled. In most situations, samples of blood are drawn from a patient in the physician s office, emergency room or hospital room and sent to a laboratory at another location where the tests are performed. Test results are returned to the physician several hours or even several days later. We believe that there is demand among physicians, patients and third-party payers for clinical diagnostic products that reduce turnaround time by bringing laboratory testing closer to the patient and providing the physician with fast, quality and cost-effective results thereby permitting the physician to deliver prompt feedback to the patient.

Most immunodiagnostic systems for clinical point-of-care sites have had limited market penetration because of the lengthy turnaround time for test results, the need for skilled labor to perform the tests and the high cost of the tests. We believe that the emergence of simple, more accurate and cost-effective diagnostic products is shifting the site of *in vitro* diagnostic testing from clinical reference laboratories and central hospital laboratories to alternative sites.

We are developing a new instrument system, a clinical analyzer that would be a part of our M-SERIES family of instruments. We plan to integrate ECL, PCR, and other technologies into a small, expandable and modular system for the performance of immunodiagnostic and nucleic acid tests. The clinical analyzer is being designed for ease of use and the ability to provide fast results and is expected to be marketed to clinical point-of-care sites bringing laboratory testing closer to the patient thereby providing the associated benefits described above. We believe that the clinical analyzer may also be used in clinical reference laboratories, central hospital laboratories, and blood banks, which presently constitute the majority of the clinical diagnostics market. Currently available immunoassay tests for use at the clinical point-of-care sites are often not as sensitive, accurate, or consistent as similar tests run in a central laboratory. We believe the clinical analyzer can provide rapid turn-around time with the same levels of sensitivity, accuracy and consistency as a large instrument in a clinical reference laboratory or a hospital central laboratory.

Diagnostic testing of an individual s immune status will provide information about a person s susceptibility to infectious diseases including diseases for which vaccines exist or are being developed. In addition, the establishment of a database on immune status and vaccination history may assist in identifying certain population groups, such as school children, college students, military personnel and the elderly, which are at risk for diseases such as pneumonia and meningitis that can be prevented by vaccination. We expect to be able to offer unique and proprietary diagnostic test panels that would assess an individual s personal immune status and establish a database for individuals in various population groups. Such products and services should support initiatives such as the strategic plan of the Centers for Disease Control, which is developing an immunization registry and the recent Health Information Technology

Initiative of the U.S. Department of Health and Human Services.

We are exploring collaborative business arrangements to accelerate the development, manufacture and marketing of ECL technology-based products for clinical point-of-care applications.

Clinical/Reference and Central Hospital Laboratory Systems. One of the significant applications of ECL technology is in large, highly automated clinical immunodiagnostic systems used in clinical reference laboratories, central hospital laboratories and blood banks. These laboratories currently constitute the vast majority of the clinical diagnostics market. To serve these laboratories, systems must be able to perform a wide variety of immunodiagnostic tests on a large number of samples consistently, cost effectively and quickly. Although we do not currently manufacture or sell products for the clinical diagnostics market, we intend to pursue opportunities for the clinical reference and central hospital laboratory market segment through collaborative arrangements.

Non-Clinical Diagnostics

Biodefense. We are commercializing products in the emerging market segment for biodefense, which involves the detection of bacteria, viruses and toxins that may pose a military or public health threat, as well as for the detection of foodborne and waterborne disease causing pathogens. Our currently available instruments include the BioVeris Detection System and the M-SERIES M1R and M1M instruments. We believe there will be an increasing opportunity to use our products as a biodefense tool in commercial, governmental and military organizations around the world, as well as in public health, due to the early adoption of our products by key decision makers. We expect that our nonclinical products for biodefense will generally not require the approval of a U.S. government agency prior to marketing of the products in the United States. See ITEM 1 Business Government Regulation Biodefense and Industrial Testing Products for a more detailed description of the government regulations to which we are subject in connection with our biodefense products.

U.S. Army scientists at Fort Detrick and the Edgewood Chemical Biological Center (ECBC) have developed ECL technology-based biological tests designed to measure specific agents and toxins in environmental samples. We have a contract with the DOD pursuant to which the DOD may purchase these tests from us. Under the contract, the DOD may, at its option, make purchases of up to $23.0 million over a period of up to 48 months through June 2007. As of March 31, 2005, the DOD had purchased approximately $7.8 million of products under the contract. The tests are used by various laboratories and field sites of the DOD, as well as other U.S. government agencies. For risks related to our contracts with the government see ITEM 1 Risk Factors Risks Relating to Regulation and Government Contracts.

In June 2004, we introduced for sale our new M-SERIES M1M Analyzer which is designed to function in demanding field environments, as well as in the laboratory. The M1M is an automated analyzer designed for use with our BioVerify test kits for the detection of botulinum neurotoxins, anthrax, ricin, and staphylococcal enterotoxins A and B, among others. The system has easy-to-use sample handling and can detect biological agents quickly and with high sensitivity. System software reports positive or negative results automatically in a standard format. The M1M Analyzer was built with specification and configuration inputs from our customers and is designed to meet the needs of field, mobile and centralized laboratories. We also introduced the M-SERIES M1M Analyzer for use by first responders, such as trauma centers, emergency medical workers, firefighters and police.

The Automated Biological Agent Testing System (ABATS) program at the ECBC, Aberdeen Proving Ground, in conjunction with us and Beckman Coulter, has integrated an M-SERIES instrument system with Beckman Coulter s SAGIAN and Biomek® FX lab automation systems to automate sample preparation and plate handling for ECL technology-based immunoassays. This program is designed for high throughput detection of biological agents and incorporates reagents that are being manufactured by us. In 2004, the ABATS was transferred to Stations of Robotic Monitoring (STORM), a mobile, high-throughput laboratory that can be deployed rapidly to the scene of an accident or terrorist event.

We expect to continue to work with commercial and U.S. governmental agencies to expand the use of ECL technology-based products in a variety of homeland security and biodefense initiatives, including the development of reagents for the detection of biological agents, such as anthrax, staphylococcus enterotoxin B and botulinum, or toxins

in environmental samples.

We are also engaged in initiatives for product development for this market, including:

- the Cooperative Research and Development Agreement with the U.S. Army Medical Research Institute of Infectious Diseases for the development of tests for the detection of biological toxins;

the Cooperative Research and Development Agreement with Brooke Army Medical Center for the development of tests for the detection of clinical markers of disease; and

continued integration of ECL technology into the Air Force biological testing program.

Certain of our U.S. government contracts contain provisions that grant to the U.S. government a non-exclusive, non-transferable, irrevocable, paid-up license to use inventions made by us in the course of performing such contracts, or have such inventions used by or on behalf of the U.S. government, for research or other government purposes. See ITEM 1 Risk Factors Risks Relating to Regulation and Government Contracts.

Our presence in the biodefense market also provides the opportunity to sell products to other diagnostics markets. In addition to manufacturing specific tests for the detection of biological agents or toxins for the DOD, we have developed our own line of tests that can be sold to the pharmaceutical, biotechnology and food industries. These products include tests for the detection of botulinum toxins A, B, E and F, staphylococcal enterotoxins A and B, ricin and anthrax. We intend to expand this product line to meet the demands of the market. We believe that tests developed for the biodefense field may also have utility in the clinical diagnostic markets by providing tests for patients exposed to biological agents or toxins.

Industrial. We manufacture and sell a panel of tests for the detection of foodborne and waterborne disease-causing pathogens, such as E. coli O157, Salmonella, Campylobacter and Listeria. These tests are used as a quality control method for testing food and beverage products, such as meat used in hamburger, for bacteria that have caused numerous outbreaks of gastrointestinal and kidney-related disease worldwide.

We expect that our products for industrial testing will generally not require the approval of a government agency prior to marketing of the products in the United States. See ITEM 1 Business Government Regulation Biodefense and Industrial Testing Products for a more detailed description of the government regulations to which we are subject in connection with our products for industrial testing.

Life Science. We provide products and services for the discovery and development of new drugs to the life science market. Our product development and marketing efforts center on two M-SERIES instruments the M384 and the M1M instruments each of which build on the ECL technology-based applications provided by the M-SERIES systems and the BIOVERIS Detection System.

Our products can be used by pharmaceutical and biotechnology companies, universities and other research organizations in most phases of drug discovery, including:

validating targets identified through genomics;

screening of large numbers of compounds generated through combinatorial chemistry;

re-testing and optimization of lead compounds; and

clinical trial testing of drug candidates.

After identifying disease targets and synthesizing chemical compounds, researchers attempt to find compounds that are drug candidates. This drug discovery process involves developing an assay to determine whether a particular compound has the desired effect on a target and then screening compounds using that assay. We believe that the need of pharmaceutical and biotechnology companies to rapidly identify therapeutic targets, screen thousands of compounds per day against those targets and then optimize the leads has created new opportunities for ECL technology-based systems in the pharmaceutical and biotechnology industry. Our M-SERIES instruments are compatible with multi-well microplates that are commonly used in drug discovery and development laboratories and

can be fully integrated with many existing automation and robotic systems. These instruments were designed to enable researchers to test new biological targets against potential drug compounds with higher levels of accuracy and sensitivity. We believe they may also perform highly sensitive tests more quickly at a lower cost and this may permit a drug candidate to move more rapidly into the later stages of drug development, clinical trials and ultimately into the market.

We believe that the sensitivity and accuracy of these M-SERIES systems create advantages over many competitive detection technologies. They permit the user to:

more quickly adapt the ECL technology to develop and then perform the specific, desired assays, compared to the longer periods required by other existing competing technologies;

reduce the use of rare components, such as proprietary compounds, antibodies or clinical trial samples, that must be used to run assays; and

have more confidence in the results the tests produce.

Our expertise in developing assays allows us to assist customers in determining whether a proposed assay is feasible and to assist with the development and performance of assays that comply fully with the FDA s Good Manufacturing Practices.

Immunogenicity testing is performed by pharmaceutical and biotechnology companies in order to characterize the ability of protein-based therapeutics to stimulate an immune response. We have recently introduced proprietary products for immunogenicity testing. Antibodies that result from an immune response to a protein-based drug can reduce its efficacy and cause significant side effects, such as allergic reactions. Because of serious side effects that have been reported over the last year, it has become increasingly necessary to determine if an immune response to protein-based drugs develops in patients by screening for the presence of antibodies, confirming their specificity, characterizing the type of antibodies present and determining whether they interfere with binding events. Immunogenicity testing is done during pre-clinical studies and may continue through the clinical trials required for regulatory approval. In some cases the FDA requires additional testing after a drug has been approved. Our M-SERIES product line for the life science market is believed to be ideally suited to perform immunogenicity testing by measuring low affinity antibodies with high sensitivity, all in the presence of the highly concentrated drug.

Our M-SERIES life science customers include many of the major pharmaceutical and biotechnology companies in the United States and Europe. In addition to the M-SERIES instruments we sell or lease, we typically receive commitments from customers for purchases of proprietary reagents. We market the M-SERIES product family directly through our own sales, marketing and applications teams. Instrument systems originally designed for the life science market are now being used in biodefense and may be used in the clinical diagnostics market as well. We believe that our presence in the life science market provides us with the opportunity to identify novel tests that may have utility in the clinical diagnostics market.

While continuing to support our existing bio-pharmaceutical and academic customers, we may selectively pursue other commercial opportunities in the life science or other markets in support of our overall corporate strategy. Our products that will be sold only for research use in the life science market generally do not require the approval of a government agency prior to marketing of the products in the United States. See ITEM 1 Business Government Regulation Life Science Research Products for a more detailed description of the government regulations to which we are subject in connection with our products for the life science market.

Vaccines

We have expanded our business model to target the fields of vaccines. In conjunction with our efforts to determine an individual s personal immune status through a unique diagnostic test panel, we have entered into an exclusive option agreement with CHRCO for exclusive patent rights to a unique vaccine candidate for *Neisseria meningitidis* serogroup B, which causes meningitis.

Meningococcal disease is a bacterial infection that strikes approximately 1.2 million people worldwide each year, causing meningitis or sepsis in the majority of cases. Approximately 10 percent of the individuals who contract meningococcal disease will die. Of the survivors, up to 20 percent suffer long-term permanent disabilities such as hearing loss, brain damage and limb amputations. Meningococcal disease often begins with symptoms that can be

mistaken for common viral illnesses, such as the flu. It can progress very rapidly and kill an otherwise healthy young person in 48 hours or less. Communitywide outbreaks of meningococcal disease can persist for several months and controlling them remains a major challenge in public health. Currently, there is no effective vaccine available against disease caused by meningococcal serogroup B, which is responsible for one-third of meningococcal disease in the United States and up to 70 percent in Europe and Canada. The availability of an effective vaccine that would prevent meningococcal serogroup B for use by various population groups is expected to be in high demand for both mass immunization and catch-up vaccination programs.

We have also entered into an agreement with the NRC for a license to patent rights to candidates for a GBS Type II and Type V vaccine and a GBM vaccine. Under the agreement with the NRC, we acquired worldwide, exclusive rights to commercialize products for possible use in the prevention, diagnosis and treatment of disease caused by GBS, a leading cause of sepsis, pneumonia, and meningitis among newborns. We received similar worldwide rights, with the exclusion of Canada, to NRC s GBM vaccine technologies for the prevention of meningococcal B meningitis and sepsis.

Approximately 25 percent of pregnant women are carriers for GBS and the newborn infection is predominantly transmitted from mother to baby during labor. Although antibiotic intervention has been used during labor to reduce the rate of disease, the incidence of GBS early-onset disease remains at 0.5 per 1000 live births, and the incidence of late-onset disease remains at 0.3 per 1000, with an overall mortality rate of approximately 4 percent. In addition, GBS accounts for 4 to 7 cases of serious disease per 100,000 non-pregnant adults, with a mortality rate of approximately 20 percent. As a result, the Centers for Disease Control have stated that intrapartum chemoprophylaxis is not a permanent or comprehensive strategy for GBS disease prevention, and that further work on GBS vaccine development is warranted.

The meningococcal B vaccine technology developed by the NRC broadens the technology provided under our option to license exclusive patent rights to a unique vaccine candidate for *Neisseria meningitidis* serogroup B from CHRCO. We now have access to a broad use of the meningococcal B polysaccharide compositions for vaccine development.

Recently, we entered into an option agreement with UMA for exclusive patent rights to a unique vaccine candidate for Chlamydia, the most frequently reported infectious disease in the United States. Under the agreement with UMA, the Company acquired a first option for exclusive rights to commercialize products for possible use in the prevention, diagnosis and treatment of all chlamydial infections, including the disease, chlamydia, caused by the bacterium, *Chlamydia trachomatis*.

Chlamydia is a sexually transmitted disease caused by *Chlamydia trachomatis*. According to the Centers for Disease Control and Prevention, Chlamydia is the most frequently reported infectious disease in the U.S., with estimates of nearly 3 million cases annually, resulting in a total healthcare cost, estimated by the Institute of Medicine, of more than $2 billion. Although antibiotic therapy is available, chlamydia is a silent disease, showing no symptoms in three quarters of infected women and half of infected men. If left untreated in women, 40% of the infections will cause pelvic inflammatory disease with permanent damage, resulting in chronic pain, infertility and potentially fatal ectopic pregnancy. Infected pregnant women may transmit the infection to the eyes and respiratory tracts of their newborn, resulting in pneumonia and conjunctivitis. It has been estimated that by age 30, half of all sexually active women have been infected. Screening is recommended annually for all sexually active women under 26 years of age, as well as older women with certain risk factors and all pregnant women.

There is no vaccine currently available to protect against Chlamydia. The UMA vaccine technology would be expected to cover all chlamydial infections, including those caused by *Chlamydia psittaci*, which often results in pneumonia and endocarditis in humans, and *Chlamydia pneumoniae*, which is responsible for some pneumonia, bronchitis, pharyngitis, laryngitis, and sinusitis. In addition, *C. pneumoniae* infections have been implicated by some investigators to be associated with atherosclerotic vascular disease, Alzheimer s disease, asthma, and reactive arthritis.

It is our intention to continue to license rights to or acquire certain vaccine candidates.

Collaborations and License Arrangements

We expect to explore and negotiate collaborative business arrangements to accelerate the research, development, manufacture and marketing of ECL technology-based products and vaccines. In addition, we have license

arrangements with Roche Diagnostics, bioMérieux, Eisai and MSD.

Roche Diagnostics

In connection with the merger and related transactions, Roche, one of the world s leading providers of clinical diagnostic products, has obtained a worldwide, royalty-free, non-exclusive license, which we refer to in this Form 10-K as the license agreement, to develop, make, reproduce, modify, use, sell and otherwise commercially exploit certain clinical

immunoassay instruments and assays using defined ECL technology owned by us in the human *in vitro* diagnostics field, including the continued sale and further development of its Elecsys products. We will not receive royalties or other payments as a result of product sales by Roche in accordance with the license agreement.

Under the improvements license agreement with Roche, we have a worldwide, non-exclusive, fully-paid, royalty-free, perpetual license under certain patents covering and technologies based on:

- Roche Diagnostics ECL instruments and all aspects of ECL assays developed prior to the completion of the merger with IGEN;
- certain PCR technology; or
- all aspects of ECL technology and robotics that, prior to the completion of the merger with IGEN, Roche Diagnostics or any of its affiliates used or developed to be used in performing ECL testing (other than specific antibodies, antigens and reagents).

In addition, we are licensed to use certain intellectual property rights of Hitachi High Technology Corporation and its affiliates only outside the field defined in the improvements license agreement to develop, make, reproduce, modify, use, sell and otherwise commercially exploit any product or service based on ECL technology.

bioMérieux

bioMérieux, Inc. or bioMérieux, has a license from us for the development and worldwide development, use, manufacture and sale of ECL technology-based nucleic acid test systems on a co-exclusive basis for certain segments of the clinical diagnostics market and on a non-exclusive basis for certain segments of the life science market. bioMérieux specializes in products for central hospital laboratories and blood banks and has incorporated its proprietary nucleic acid sequence-based amplification technology and ECL technology into its NucliSens line of diagnostic virology products, which are marketed with test kits for the detection of HIV-1 RNA and CMV (cytomegalovirus). The agreement with bioMérieux extends until the expiration of the patents we license to bioMérieux, and we receive royalty payments from bioMérieux on the relevant product sales by bioMérieux.

Eisai

Eisai Co., Ltd., or Eisai, a leading Japanese pharmaceutical company, has a license to manufacture and market a class of ECL technology-based diagnostic systems for the clinical diagnostics market in Japan on a non-exclusive basis. Eisai introduced its first ECL-based product under the trade name Picolumi in 1997. We receive royalties on the relevant product sales by Eisai. The agreement with Eisai extends until the later of May 2010, or the expiration of the patents we license to Eisai. Eisai is obligated to make royalty payments to us at a reduced royalty rate for a period of seven years after expiration of the agreement.

MSD

As part of the merger and related transactions, we assumed IGEN s interest in MSD, a joint venture formed in 1995 by IGEN and MST, which is a company established and wholly-owned by Mr. Jacob Wohlstadter, a son of our chief executive officer. An independent committee of IGEN s board of directors, with the advice of independent advisors and counsel, negotiated and approved the MSD agreements.

MSD develops, manufactures, markets and sells products utilizing a combination of MST s multi-array technology and our ECL technology. MSD s Sector line of instrumentation is used in drug discovery for high throughput screening, high content screening, multiplexing and target validation. MSD also manufactures and markets a line of its own

reagents, assays and plates that are used on these systems. During the period from January 1, 2004 through December 13, 2004 (the date of the sale of our interests in MSD), MSD had revenues of $12.3 million and a net loss of $17.7 million.

The joint venture agreement among MSD, MST and us, which we refer to in the Form 10-K as the MSD joint venture agreement, expired upon completion of the merger and related transactions. As a result, MSD and MST had the right to purchase our interests in MSD and pursuant to the settlement agreement we entered into with MSD, MST and Jacob Wohlstadter in August 2004, which is referred to in this Form 10-K as the settlement, on December 13, 2004 MST

purchased our interests in MSD. For a more complete description of this purchase and the MSD agreements, see ITEM 7 Management s Discussion and Analysis of Financial Condition and Results of Operations and ITEM 8 Consolidated Financial Statements and Supplementary Data Notes to Consolidated Financial Statements Note 3. See ITEM 3 Legal Proceedings for a description of litigation and the related settlement with MSD.

Patents and Other Proprietary Rights

We pursue a policy of seeking patent protection to preserve our technology and our right to capitalize on the results of our research and development activities and, to the extent it may be necessary or advisable, to exclude others from appropriating our technology. We will also rely on trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position.

We intend to prosecute and defend our intellectual property, including our patents, trade secrets and know-how. We plan to regularly search for third-party patents in our fields of endeavor, both to shape our patent strategy as effectively as possible and to identify possible collaborations and licensing opportunities.

We own approximately 83 issued U.S. patents, and own or have exclusively licensed approximately 32 pending U.S. patent applications in the diagnostics field. Additionally, we own or have exclusively licensed approximately 165 granted foreign patents and approximately 88 pending foreign patent applications in the diagnostics field. These patents and patent applications are important to our business and cover various aspects of ECL technology and products, as well as the methods for their production and use.

The pending patent applications in the diagnostics field may not be granted and others may challenge our patents. Certain ECL patents will begin to expire in 2006; however, patent coverage for certain key aspects of our ECL technology will continue through 2022. We plan to continue to protect our technology with new patent filings, which could further extend our patent coverage.

Our business could be harmed if we lose our patent protection or if pending patents are not issued to us.

Government Regulation

The research and development, manufacturing, marketing, sale and distribution of both existing and future products based on ECL technology are subject to comprehensive government regulation. Government regulation by various Federal, state, and local agencies, which includes detailed inspection of, and controls over, research and laboratory procedures, safety, clinical investigations, manufacturing, marketing, sampling, labeling, distribution, record keeping, storage and disposal practices, substantially increases the time, difficulty and costs incurred in obtaining and maintaining the clearance or approval to market newly developed and existing products. In particular, government regulatory actions can result in, among other things, delays in the release of our and our licensees products, injunction, seizure or recall of our or our licensees products, suspension or revocation of the authority necessary for their production and sale, and other civil or criminal sanctions, including monetary penalties that could be substantial.

International sales of products by us and our licensees will also be subject to a significant degree of government regulation, including export regulations, international standards (such as those set by the International Organization for Standards), European Union directives and other country-specific rules and regulations. For example, many countries, directly or indirectly through reimbursement limitations, control the cost of most clinical diagnostic products. Furthermore, many developing countries limit the importation of raw materials and finished products. International regulations may also have an impact on U.S. regulations. In addition, the FDA, the Commerce Department or the State Department regulate the export of products from the United States.

Biodefense and Industrial Testing Products

Our biodefense products are subject to stringent Federal, state, local and foreign laws, regulations and policies governing their manufacture, storage, sale, distribution and export. In addition, the U.S. government has adopted, and is expected to continue to adopt, laws, regulations and rules governing the research, development, procurement and handling of pathogens that may be used in a bioterrorist attack or other agents that may cause a public health emergency and to permit government inspection and oversight of facilities engaged in the research, development, manufacture or sale of select

agents. Under several statutes recently enacted, the Department of Homeland Security, the FDA, the Department of Commerce and various other regulatory authorities have been charged with establishing and implementing programs designed to enhance the security of food and water supplies, as well as the environment, from terrorist attacks. These legislative initiatives include recordkeeping, registration, notification, import, export, manufacturing and various other compliance measures. This is a rapidly evolving regulatory landscape and many of the possible rules and regulations have not yet been proposed or adopted. We may be required to incur significant costs to comply with such laws and regulations in the future, and such laws or regulations may have a material adverse effect upon our ability to do business.

Life Science Research Products

Our products that will be sold for life science research use only, including the M-SERIES instruments used in the life science market, must be properly labeled as for research use only - not for use in diagnostic procedures , as required by the FDA, but do not generally require FDA approval prior to marketing. Research does not include clinical investigations and is narrowly defined by the FDA to apply to the early development of product concepts. The FDA has begun to impose new distribution requirements and procedures on companies selling research use only products, such as the requirement that the seller receive specified certifications from its customers as to the customers intended use of the product. We expect that the FDA will develop additional restrictions of this nature some of which may adversely affect us.

Clinical Diagnostic Products

The FDA and other Federal, state, local, and foreign governmental authorities, regulate, among other things, the development, clinical testing, manufacture, packaging, labeling, storage, distribution and promotion of medical devices, including products intended for clinical diagnostic purposes. The FDA imposes specific requirements on the conduct of clinical studies and requires approval of the study by an institutional review board and, in some cases, by the FDA, depending upon the product and its use. Before a new device can be introduced into the market, the manufacturer must generally obtain marketing clearance through a section 510(k) pre-market notification or approval through a pre-market approval application. The testing, preparation of necessary applications and processing of those applications by the FDA is expensive and time-consuming.

Our clinical diagnostic products and the clinical diagnostic products of our licensees will be regulated as medical devices. Significant difficulties or costs may be encountered to obtain FDA clearances or approvals and that could delay or preclude us or our licensees from marketing products for clinical diagnostic purposes. Furthermore, the FDA may request additional data following the original submission. Delays imposed by the governmental review process may materially reduce the period during which our or our licensees will have the exclusive right to exploit our products or technologies.

The FDA will clear a device under section 510(k) if the submitted information establishes that the proposed device is substantially equivalent to a legally marketed class I or II medical device, or to a class III medical device for which the FDA has not yet called for a pre-market approval application. Commercial distribution can begin only after the FDA issues an order that the device is substantially equivalent to a device that is legally marketed and not subject to a pre-market approval requirement. The FDA may determine that a proposed device is not substantially equivalent to a legally marketed device, in which case a pre-market approval will be required to market the device, unless additional information can be submitted to support a substantial equivalence determination, or the FDA, pursuant to a timely request, makes a risk-based determination that a device that is not a substantially equivalent device can be classified into class I or II. An FDA request for additional data could require that clinical studies of the device s safety and effectiveness be performed. Clearance, if obtained, may be conditioned on labeling restrictions or conducting a lengthy post-market surveillance study.

A pre-market approval application must be filed and approved before a device can be marketed if a proposed device is not substantially equivalent to a legally marketed device, as discussed above, or if it is a class III device that was in commercial distribution prior to May 28, 1976, for which the FDA has called for pre-market approval. A pre-market approval application must be supported by valid scientific evidence, which typically includes extensive pre-clinical data and well controlled or partially controlled clinical trials, to demonstrate the safety and effectiveness of the device. Obtaining approval can take several years and approval may be conditioned on, among other things, substantial restrictions on indications for use and the conduct of postmarket surveillance studies. Generally, the pre-market approval process requires much more extensive pre-filing testing than does the section 510(k) pre-market notification procedure and involves a significantly longer FDA review after the date of filing. In responding to a pre-market approval application, the FDA may grant marketing approval, may request additional information, may set restrictive limits on claims for use or may deny the application altogether.

After the pre-market clearance or approval for the medical device has been received, it may still be withdrawn if compliance with regulatory standards is not maintained or if problems occur after the device reaches the market. The FDA may require post-market surveillance programs to monitor the effect of medical devices that have been sold, and has the power to prevent or limit further marketing of medical devices based on the results of these post-marketing programs. In addition, the FDA s medical device reporting regulation requires reports to the FDA whenever information reasonably suggests that a marketed device may have caused or contributed to death or serious injury, or when a device malfunctions and if the malfunction were to recur, the device would be likely to cause or contribute to a death or a serious injury.

In addition to obtaining FDA approval for each medical device, under the pre-market approval application procedures, we or our licensees must seek FDA approval of their manufacturing facilities and procedures. The FDA will also inspect clinical diagnostics companies on a routine basis for regulatory compliance with its Good Manufacturing Practices regardless of whether the product was cleared under section 510(k) or approved under pre-market approval.

We and our licensees clinical diagnostic products will be affected by the Clinical Laboratory Improvement Amendments of 1988, which is intended to insure the quality and reliability of medical testing and may have the effect of discouraging, or increasing the cost of, clinical diagnostic testing.

The regulations establish numerous requirements applicable to clinical diagnostics. Under these regulations, the specific requirements that a laboratory must meet depend upon the complexity of the tests performed by the laboratory. Under the clinical laboratory improvement regulations, all laboratories performing moderately complex or highly complex tests will be required to comply with stringent standards and requirements. Because the regulations interpretation is uncertain, it is possible that certain of our licensees products may be categorized as highly complex tests, in which case penetration of the point-of-care market would be reduced because not all laboratories would meet the standards required to conduct such tests. In addition, future changes in regulations or interpretations made by the U.S. Department of Health and Human Services, FDA, Centers for Medicare & Medicaid Services or other regulatory bodies may adversely affect us and our licensees.

In addition to the foregoing, we will be, and our licensees are, subject to numerous Federal, state and local laws and regulations relating to such matters as safe working conditions, laboratory and manufacturing practices, fire hazard control, and environmental protection, including disposal of haza