CHARLES RIVER LABORATORIES INTERNATIONAL INC
Form 10-K
March 14, 2006

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2005

OR

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
FOR THE TRANSITION PERIOD FROM TO

Commission File No. 333-92383

CHARLES RIVER LABORATORIES INTERNATIONAL, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**06-1397316**
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
251 Ballardvale Street Wilmington, Massachusetts	**01887**
(Address of Principal Executive Offices)	(Zip Code)

(Registrant s telephone number, including area code): **(978) 658-6000**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.01 par value	New York Stock Exchange

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark whether the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes x No o

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No x

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 x 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 a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer x Accelerated Filer o Non-accelerated Filer o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No x

On June 25, 2005, the aggregate market value of the Registrant s voting common stock held by non-affiliates of the Registrant was approximately $3,410,397,382.

As of March 1, 2006, there were outstanding 71,991,729 shares of the Registrant s common stock, $0.01 par value per share.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant s Definitive Proxy Statement for its 2006 Annual Meeting of Stockholders scheduled to be held on May 9, 2006, which will be filed with the Securities and Exchange Commission not later than 120 days after December 31, 2005, are incorporated by reference into Part III of this Annual Report on Form 10-K. With the exception of the portions of the 2006 Proxy Statement expressly incorporated into this Annual Report on Form 10-K by reference, such document shall not be deemed filed as part of this Form 10-K.

CHARLES RIVER LABORATORIES INTERNATIONAL, INC.
ANNUAL REPORT ON FORM 10-K

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PART I

Item 1. Business

General

This Annual Report on Form 10-K contains forward-looking statements regarding future events and the future results of Charles River Laboratories International, Inc. that are based on current expectations, estimates, forecasts, and projections about the industries in which Charles River operates and the beliefs and assumptions of our management. Words such as expect, anticipate, target, goal, project, intend, plan, seek, estimate, will, likely, may, designed, would, future, can, could and other similar expressions that are predictions of or in and trends or which do not relate to historical matters are intended to identify such forward-looking statements. These statements are based on current expectations and beliefs of Charles River and involve a number of risks, uncertainties, and assumptions that are difficult to predict. You should not rely on forward-looking statements because they are predictions and are subject to risks, uncertainties and assumptions that are difficult to predict. Therefore, actual results may differ materially and adversely from those expressed in any forward-looking statements. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this document or in the case of statements incorporated by reference, on the date of the document incorporated by reference. Factors that might cause or contribute to such differences include, but are not limited to, those discussed in this Form 10-K under the section entitled Risks Related to Our Business and Industry. Except to the extent required by applicable law or regulation, we undertake no obligation to revise or update publicly any forward-looking statements for any reason.

Corporate History

Charles River has been operating since 1947 and since then we have undergone several changes to our business structure. Charles River Laboratories International, Inc. was incorporated in 1994. In 2000, we completed the initial public offering of Charles River Laboratories International, Inc. Our stock is traded on the New York Stock Exchange under the symbol CRL and is included in the Standard & Poor s MidCap 400 Index. We are headquartered in Wilmington, Massachusetts. Our headquarters mailing address is 251 Ballardvale Street, Wilmington, MA 01887, and the telephone number at that location is (978) 658-6000. Our Internet site is *www.criver.com*. Material contained on our Internet site is not incorporated by reference into this Form 10-K. Unless the context otherwise requires, references in this Form 10-K to Charles River, we, us or our refer to Charles River Laboratories International, Inc. and its subsidiaries.

This Form 10-K, as well as all other reports filed with the Securities and Exchange Commission, are available free of charge through the investor relations section of our Internet site as soon as practicable after we electronically file such material with, or furnish it to, the SEC. You may read and copy any materials we file with the SEC at the SEC s Public Reference Room at 100 F Street, NE, Washington, DC 20549. In addition, you may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site (*http://www.sec.gov*) that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC.

Overview

We are a leading global provider of solutions that advance the drug discovery and development process. We provide the animal research models required in research and development for new drugs, devices and therapies and have been in this business for more than 58 years. For over a decade, we have built upon our core competency of laboratory animal medicine and science (research model technologies)

to develop a diverse and growing portfolio of products and services. Our wide array of tools and services enables our customers to reduce costs, increase speed and enhance their productivity and effectiveness in drug discovery and development. Our customer base includes major pharmaceutical, biotechnology, and medical device companies, as well as many government agencies, leading hospitals and academic institutions throughout the world. We currently operate over 100 facilities in 21 countries worldwide. Our products and services, supported by our global infrastructure and deep scientific expertise, enable our customers to meet many of the challenges of early-stage life sciences research, a large and growing market. In 2005, our net sales were $1.12 billion and our operating income was $181.0 million.

In October 2004, we acquired Inveresk Research Group, Inc. Prior to the acquisition, Inveresk was a publicly traded company and a leading provider of drug development services to companies in the pharmaceutical and biotechnology industries. Through its preclinical and clinical business segments, it offered a broad range of drug development services, including preclinical safety and pharmacology evaluation services, laboratory sciences services and clinical development services. Much of our activities in 2005 has focused upon the integration of Inveresk, which has included unifying our products and services under the Charles River brand name and the harmonizing of best practices derived from the combination of the two companies.

The acquisition has broadened our portfolio of high-end products and services including general toxicology, specialty toxicology and clinical services. Overall the addition of Inveresk has impacted our Company dramatically, as follows:

- significantly expanded our overall corporate size;

- significantly increased the breadth of the products and services that we offer, including those that are highly complementary to the services Charles River had previously offered; and

- expanded and strengthened our global footprint in the growing market for pharmaceutical research and development products and services, particularly in key markets such as the United States, Europe and Japan, which better aligns us with our key pharmaceutical and biotechnology customers, who are increasingly seeking to outsource more of their preclinical and clinical research and development efforts and are seeking full service, global partners.

As part of the integration of Inveresk s business operations, in 2004 we changed our business reporting segments to better reflect our results of operations and facilitate understanding of our business, which has evolved since 1999 from a product-oriented focus to a service-oriented one. We currently have three reporting segments: Research Models and Services (RMS), Preclinical Services (which is a combination of Inveresk s preclinical business with our legacy preclinical business), and Clinical Services.

Research Models and Services (RMS)

With over 150 different stocks and strains, we continue to maintain our position as the global leader in the production and sale of research models, principally genetically and virally defined purpose-bred rats and mice, and have been supplying research models since 1947. We also provide a variety of related services that are designed to assist our customers in supporting the use of research models in drug development. With 20 facilities on three continents (North America, Europe and Asia (Japan)), we maintain production centers, including approximately 160 barrier rooms, strategically located near our customers. In addition, we anticipate expanding our existing U.S. West Coast capacity with additional construction which will partially open in the fourth quarter of 2006. In 2005, RMS accounted for 44.8% of total net sales and approximately 35% of our employees, including more than 160 science professionals with advanced degrees.

Research Models. A significant portion of this business is comprised of the commercial production and sale of animal research models, principally purpose-bred rats, mice and other rodents for use by

researchers. We provide our small animal models to numerous customers around the world, including most pharmaceutical companies, major biotechnology companies, many government agencies, and leading hospital and academic institutions. Our research models include genetically defined models and models with compromised immune systems, which are increasingly in demand as early-stage research tools. The United States Food and Drug Administration (FDA) and foreign regulatory bodies typically require the safety and efficacy of new drug candidates and many medical devices to be tested on research models like ours prior to testing in humans. As a result, our research models are an essential part of the drug discovery and development process.

Our rats, mice and other rodent species have been and continue to be some of the most extensively used research models in the world, largely as a result of our continuous commitment to innovation and quality in the breeding process. Our research models are bred and maintained in controlled environments which are designed to ensure that the animals are free of specific viral and bacterial agents and other contaminants that can disrupt research operations and distort results. With our barrier room production capabilities, we are able to deliver consistently high quality research models worldwide.

Our small research models include:

- outbred animals, which are genetically heterogeneous;
- inbred animals, which are genetically identical;
- hybrid animals, which are the offspring of two different inbred parents;
- spontaneous mutant animals, which contain a naturally-occurring genetic mutation (such as immune deficiency); and
- other genetically modified research models, including knock-out models with one or more disabled genes and transgenic animals, which contain genetic material transferred from a different species.

Since 2001, we have been offering new and proprietary, disease-specific rat models used to find new treatments for diseases such as diabetes, obesity, cardiovascular and kidney disease. We are presently focusing our disease model program on four areas of research: cardiovascular, metabolic, renal and oncology, which, in addition to providing overlapping disease modalities that support multiple uses of certain models, also will permit us to concentrate on focused sales and marketing efforts.

We believe that over the next several years, many new research models will be developed and used in biomedical research, such as transgenic models with modified genetic material, knock-out models with one or more disabled genes, and transgenic models that incorporate or exclude a particular gene. These more highly defined and characterized models will allow researchers to further focus their investigations into disease conditions and potential new therapies or interventions. We intend to build upon our position as a leader in this field to expand our presence in this market for higher-value research models.

In addition to our small research models, we also are a global leader in providing purpose-bred, high quality, SPF or disease free, large animal models to the biomedical research community, principally for use in their drug development and testing studies.

We also provide surgical services to our customers, utilizing over 50 full-time staff surgical technicians located in the United States, Europe and, commencing in 2006, Asia. This value-added service offering enhances the basic research model by allowing for repeated sample collection in the case of catheterized animals.

RMS also offers a variety of services, described below, designed to assist our customers in screening drug candidates faster, including those which are related to genetically defined research models for in-house research, as well as those services designed to implement efficacy screening protocols to improve the customer s drug evaluation process. These services address the growing need among pharmaceutical and

biotechnology companies to outsource the non-core aspects of their drug discovery activities. These services capitalize on the technologies and relationships developed through our research model business. We currently offer three major categories of research models services transgenic services, laboratory services, and preconditioning and surgical services. We also offer three other categories of products and services consulting and staffing services, vaccine support and *in vitro* technology products.

Transgenic Services. In this area of our business, we assist our customers in validating, maintaining, improving, breeding and testing research models purchased or created by them for biomedical research activities. While the creation of a transgenic model can be a critical scientific event, it is only the first step in the discovery process. Productive utilization of research models requires significant additional technical expertise. We provide transgenic breeding expertise, model characterization (including genotyping and phenotyping) and colony development, quarantine, embryo cryopreservation, embryo transfer and health and genetic monitoring. We provide these services to nearly 200 laboratories around the world from pharmaceutical and biotechnology companies to hospitals and universities, and maintain more than 1,000 different types of naturally occurring or experimentally manipulated research models for our customers.

Laboratory Services. We assist our customers in monitoring and analyzing the health and genetics of the research models used in their research protocols. We developed this capability internally by building upon the scientific foundation created by the diagnostic laboratory needs of our research model business. Depending upon a customer s needs, we may serve as its sole-source testing laboratory, or as an alternative source supporting its internal laboratory capabilities. We believe that the continued growth in model development and characterization and utilization of specific disease models and genetically engineered models will drive our future growth as the reference laboratory of choice for health and genetic testing of laboratory animals.

Preconditioning and Surgical Services. Augmenting our traditional model production and transgenic services described above, we believe there are emerging opportunities to provide customers with preconditioning services, which centers upon speeding the development process by preparing study-ready research models possessing necessary characteristics. Our veterinary medicine expertise makes us well positioned to create and monitor the research models for such studies, such as those focused upon obesity or hypertension. Additionally, models of subclinical disease can be created through surgical approaches, thereby providing a model for study that otherwise may not be commercially available.

Consulting and Staffing Services. Building upon our core capability as the leading provider of high-quality research models, we manage animal care operations on behalf of government and academic organizations, as well as commercial customers. Demand for our services reflects the growing necessity of these large institutions to outsource internal functions or activities that are not critical to the core scientific innovation process or for which they do not maintain the necessary resources in-house. In addition, we believe that our expertise in animal care and facility operations enhances the productivity and quality of our customers animal care and use programs. This area leads to additional opportunities for us to provide other products and services to our customers.

Vaccine Support. We are the global leader for the supply of specific pathogen-free, or SPF, chickens and fertile chicken eggs. SPF chicken embryos are used by animal health companies as self-contained bioreactors for the manufacture of live and inactivated viruses. These viruses are used as a raw material primarily in poultry, as well as human vaccine, applications. The production of SPF eggs is done under biosecure conditions, similar in many ways to our research model production. We have a worldwide presence that includes several SPF egg production facilities in the United States, as well as facilities in Germany and Australia, and a joint venture in Mexico. We also operate a specialized avian laboratory in the United States, which provides in-house testing and support services to our customers.

In Vitro Technology. Our *in vitro* business provides non-animal, or *in vitro,* methods for lot release testing of medical devices and injectable drugs. We are committed to being the leader in providing our

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customers with *in vitro* alternatives as these methods become scientifically validated and commercially feasible, and toward that goal we work with and support the European Center for Validation of Alternative Methods in these efforts. Our *in vitro* technology business produces and distributes endotoxin testing kits, reagents, software, accessories, instruments and associated services to pharmaceutical and biotechnology companies for medical devices and other products worldwide. We are a market leader in endotoxin testing, which is used for quality control testing of injectable drugs and medical devices, their components and the processes by which they are manufactured. Quality control testing for endotoxin contamination is an FDA requirement for injectable drugs and medical devices. Endotoxin testing uses a processed extract from the blood of the horseshoe crab, known as limulus amebocyte lysate (LAL). The LAL test is the first and only major FDA-validated *in vitro* alternative to an animal model test for endotoxin detection in pharmaceutical and medical device manufacturing. The process of extracting blood is generally not harmful to the crabs, which are subsequently returned to their natural ocean environment. Our Endosafe Portable Testing System (Endosafe® -PTS) is a portable endotoxin testing platform which allows endotoxin testing in the field, affording researchers accurate and timely results. We are currently pursuing FDA approval of our PTS system. We are also investigating expanding the use of the PTS system for endotoxin testing into other markets such as nuclear pharmacies, cell transplant, dentists/doctors offices, dialysis clinics, testing for sterile water and even environmental testing, as well as other ways to invest in the PTS platform, such as through additional biological assays.

Preclinical Services

Our customers are principally engaged in the discovery and development of new drugs, devices and therapies. Discovery represents the earliest stages of research in the life sciences, directed to the identification, screening and selection of a lead compound for future drug development. Discovery activities typically last anywhere from 4-6 years in conventional pharmaceutical research and development timelines. Development activities, which follow, are directed at demonstrating the safety, tolerability and clinical efficacy of the selected drug candidates. During the preclinical stage of the development process, a drug candidate is tested *in vitro* (typically on a cellular or subcellular level in a test tube or multi-well petri plate) and *in vivo* (in research models) to support planned or on-going human trials. The development services portion of our preclinical business segment enables our customers to outsource their critical regulatory-required toxicology and drug disposition activities to us. The demand for these services is driven by preclinical development programs for the smaller biotechnology companies, which traditionally have been outsourced, and key safety studies by the larger multi-national pharmaceutical companies. Because of the necessary investments in personnel, facilities and other capital resources required in order to efficiently partake in these activities, we believe that participants in these industries will prefer to focus on their core competencies of innovation, early drug discovery, and in the case of the larger pharmaceutical companies, targeted sales and marketing, and thus we believe the demand for our preclinical service offerings will continue to increase.

We are one of the two largest providers of preclinical services worldwide and are considered by many of our clients as market leaders in the conduct and reporting of general and specialty toxicology studies, especially those dealing with innovative therapies and biologicals. We currently provide preclinical services at 12 facilities in the United States, Canada and Europe. With Inveresk, we acquired high-quality, full research capability laboratories in Montreal, Canada and Edinburgh, Scotland, and, by the end of 2006 we expect to have initial occupancy of a new facility in Massachusetts, followed in 2007 by a fourth full-capability research facility in Nevada. Our Preclinical Services segment represented 43.5% of our total net sales in 2005 and employs over 4,000, or almost half, of our employees.

We currently offer preclinical services, in which we include both *in vivo* and *in vitro* studies, supportive laboratory services, and strategic preclinical consulting and program management to support product development from inception to market registration.

Toxicology. Once a lead molecule is selected, the stage of preclinical development begins where appropriate toxicology studies are conducted to support initial clinical trials. We offer all the standard models for general toxicity testing in the species typically required for regulatory submissions, but we also have particular expertise in specialty routes of administration, modes of administration (e.g., infusion, intravitreal administration, and inhalation). This is important not only for pharmaceuticals, but also for safety testing of medical devices, industrial chemicals, food additives, agrochemicals, nutraceuticals and other materials. Toxicology is clearly one of our core competencies and strengths. We offer services to fully evaluate the genotoxicity, safety pharmacology, acute, subacute, chronic toxicity and carcinogenicity potential to support first in man to first on the market strategies. In support of larger scale, human clinical trials, we believe that we are a world leader in the conduct and assessment of reproductive and developmental toxicology studies. We also offer services in important specialty areas like immunotoxicology, photobiology, ocular, and dermal testing. We have worked with all major therapeutic areas, and provide study design and strategic advice to our clients based on our wealth of experience in drug development. We have a strong history of aiding our sponsors in reaching their regulatory or internal milestones for safety testing, including studies addressing stem cell therapies, DNA vaccines, recombinant proteins, standard small molecules and medical devices. Within the requirements for preclinical safety testing are compliance with Good Laboratory Practices (GLPs) as outlined by the FDA as well as other international regulatory bodies. Our toxicology facilities operate in compliance with GLP requirements and are regularly inspected by U.S. and other GLP compliance monitoring authorities, as well as, our own and our customers Quality Assurance departments.

Pathology Services. In the drug development process, the ability to identify and characterize clinical and anatomic pathologic changes (within tissues and cells) is critical in determining the safety of a new compound. We employ highly trained pathologists who use state-of-the-art techniques to identify potential compound-related changes within tissues and cells, as well as, at the molecular level. Pathology support is critical for regulatory-driven safety studies, but also for specialized investigative studies, discovery support, and stand-alone immunohistochemistry evaluations for monoclonal antibodies. Key go/no-go decisions regarding continued product development are typically dependent on the characterization and evaluation of gross and microscopic pathology findings we perform for our clients.

Bioanalysis, Pharmacokinetics, and Drug Metabolism. In support of preclinical drug safety testing, our customers are required to demonstrate ample drug exposure, stability in the collected sample, kinetics of their drug or compound in circulation, the presence of metabolites, and with recombinant proteins and peptides, the presence of anti-drug antibodies. We have scientific depth in the sophisticated analytical techniques required to satisfy these requirements for a number of drug classes (including oligonucleotide and inhibitory RNAs). In the event that the sample analysis for preclinical study support translates to opportunities to analyze clinical samples for the same drug once human testing begins, we have opportunities to capture the benefits of bridging preclinical bioanalysis with later clinical development. Once the analysis is complete, our scientists evaluate the data to provide information on the kinetics (pharmaco-/toxico-) of the exposure to the drug, as well as complete evaluation of the distribution of the drug or metabolites by radio-labeled techniques. These studies are needed for the full preclinical assessment of the disposition of the drug and are used in the final preclinical safety evaluation of the compound.

Discovery Support. At the earliest stages of lead compound identification, our scientists are engaged in evaluating the activity of drug candidates in several important therapeutic and support areas, including: oncology (through our tumor xenograft models); asthma (through our specialized animal disease models); bone disease (using our state of the art imaging and pathology capabilities); ophthalmology (using our models of neovascularization); general cardiovascular and device testing (using our surgical models); and early drug formulation and bioanalysis support and method development. We offer lead optimization strategies including early pharmacokinetic, metabolism, and toxicology support to help in early integrative drug selection criteria.

Biopharmaceutical Services. We provide specialized, non-clinical quality control testing that is frequently outsourced by both pharmaceutical and biotechnology companies. These services allow our customers to determine if their human protein drug candidates, or the processes for manufacturing those products, are essentially free of residual biological materials. The bulk of this testing work is required by the FDA in order to obtain new drug approval, to maintain an FDA-licensed manufacturing facility or to release approved products for use in patients. Our scientific staff consults with customers in the areas of process development, validation, manufacturing scale-up and biological testing.

Clinical Services

The clinical services business represents a relatively new market and growth opportunity for us that originated through our acquisition of the Phase I-IV business of Inveresk. Our capabilities includes a premier Phase I clinic in Europe and an established international capability to manage Phase II-IV studies. Our clinical development business presently employs approximately 940 people and operates in 24 countries (from 17 facilities) located across North America, Europe, South America, Asia and Australia. In 2005, the Clinical Services segment accounted for approximately 11.6% of our total net sales. We are focused upon maintaining healthy profit margins in this segment through careful positioning of our clinical services including our core therapeutic areas of: cardiovascular, oncology, ophthalmology, respiratory and infectious diseases. From a strategic perspective we believe that our clinical services business is positioned to benefit from pull-through from our preclinical and laboratory services, particularly with our biotechnology customers.

Phase I Trials in Patients and Special Populations

We operate a 62-bed clinic in Edinburgh, Scotland, at which we conduct a wide range of Phase I clinical trials designed to move lead pharmaceutical candidates rapidly from preclinical development through Phase I tolerability assessment to explore human pharmacology. This facility is in close proximity to one of our laboratory sciences facilities, which is responsible for performing the analysis of biological samples generated by our Phase I clinic, facilitating fast response times. Our Phase I clinic, which focuses on first-in-man studies, is capable of conducting all types of studies and has experience across a wide range of therapeutic areas, including complex dose tolerance, radio-labeled, pharmacokinetics, pharmacodynamics and bioavailability studies. All of the clinic s volunteers are evaluated through an intensive screening process to ensure study suitability. The facility has an established quality assurance unit that monitors the conduct and reporting of Phase I trials to assure management that these trials are conducted in compliance with appropriate regulatory requirements.

Phase II-IV Clinical Development and Regulatory Support

From our 14 offices worldwide and business operations in more than 20 countries, we manage every aspect of clinical trials from clinical development plans and protocol design to New Drug Applications (NDAs) and post-marketing surveillance. We provide a comprehensive range of services as either a full-service package or as individual stand-alone services. In addition to conducting single site studies in many parts of the world, we have a proven track record of managing large international multi-center trials

culminating in regulatory filings. We have supported studies in over 34 countries. Our clinical trials management services include:

- strategy development;
- investigator recruitment;
- quality assurance;
- study monitoring;
- clinical data management;
- medical research and consulting; and
- study design;
- project management;
- patient recruitment;
- pharmacovigilance;
- biostatistical analysis;
- post-marketing/Phase IV studies.

We also have significant expertise in conducting patient and other outcomes registries, such as pregnancy registries, on behalf of the pharmaceutical industry, as well as regulatory support. Before a product may be launched in any country, it must be approved by the regulatory agency in that particular country. We offer comprehensive global regulatory product registration services at all stages of development for pharmaceutical and biotechnology products and have particular expertise with the regulations in Europe and North America. Through this service, we assist our clients in determining the feasibility of developing a particular product or product line.

Our Strategy

Our objective is to be the premier global company for advancing the search for drugs, devices and therapies from discovery through market approval. The products and services which we provide our customers are essential to the drug discovery and development process, and are almost universally mandated by law. Our business is primarily driven by the continued growth of research and development spending by pharmaceutical, biotechnology and medical device companies, the federal government and academic institutions and of outsourced services. According to a recent report by the Biomedical Industry Advisory Group, it takes 11 to 16 years and costs in the range of $180 million to $1.65 billion to bring a new drug to market. As the pressure to develop new drugs increases for these industries, so does the pressure to contain costs, implement research in multiple countries simultaneously and identify, hire and retain a breadth of experienced experts. In order to facilitate and speed their research, our pharmaceutical and biotechnology customers have increasingly strategically outsourced services which can be provided by high-quality service providers like Charles River. Outsourcing allows our customers to concentrate their resources on the basic drug discovery which only they can do, while continuing to advance their most promising products through the development pipeline. This creates opportunities for companies such as ours that can help speed the drug discovery and development process. Our strategy is to capitalize on these opportunities by continuing to build our portfolio of high end, value-added products and services through internal development, augmented by strategic bolt-on transactions.

In today s business environment, we particularly believe there is an advantage in being a large, global, high-quality provider of services throughout the drug discovery and development process. Many of our customers, especially large pharmaceutical companies, are attracted to Tier 1 contract research organizations with a full breadth of capabilities, and establish preferred provider agreements with only a small handful. We are focused on being recognized as a premier preferred provider and maintaining long-term relationships and strategic partnerships with our customers. Accordingly, with many of our largest customers, we have entered into global provider agreements that span two or three segments of our business.

We intend to continue to broaden the scope of our products and services primarily through organic growth, which will be augmented, as needed, through focused acquisitions and alliances. We believe our approach to acquisitions is a disciplined one that seeks to target businesses that are a sound strategic fit and that offer the prospect of enhancing stockholder value. This strategy may include geographic

expansion of existing core services, strengthening of one of our core services or the addition of a new product or service.

We believe that we are well positioned to exploit both existing and new outsourcing opportunities. We intend to focus our marketing efforts on stimulating demand for further outsourcing to gain additional market share. To take advantage of promising opportunities which are available to us as a result of continued growth of outsourced services, in 2006 we anticipate investing heavily in expanding our facilities capacity.

Customers

Our customers continue to consist primarily of all of the major pharmaceutical companies, as well as many biotechnology companies, animal health, medical device and diagnostic companies, leading hospitals, academic institutions, government agencies and other life sciences companies. Recently, as a result of the Inveresk merger and outsourcing trends, our commercial customer base (mainly pharmaceutical and biotechnology companies) has grown at a higher rate than our non-commercial customer rate. We have many long-term, stable relationships with our customers. During 2005, no single commercial customer accounted for more than 5% of our total net sales.

For information regarding net sales and long-lived assets attributable to each of our business segments for the last three fiscal years, please see Note 15 included in the Notes to Consolidated Financial Statements included elsewhere in this Form 10-K. For information regarding net sales and long-lived assets attributable to operations in the United States, Europe, Asia and other countries for each of the last three fiscal years, please review Note 15 included in the Notes to Consolidated Financial Statements included elsewhere in this Form 10-K.

Sales, Marketing and Customer Support

We sell our products and services principally through our direct sales force, the majority of whom work in the United States, with the balance working in Europe and Japan. Our primary promotional activities include organizing scientific symposia, publishing scientific papers, making presentations and participating at scientific conferences and trade shows in North America, Europe and Japan. We supplement these scientifically based marketing activities with trade advertising, direct mail, newsletters and our web site. The direct sales force is supplemented by international distributors for our products.

Our internal marketing/product management teams support the field sales staff while developing and implementing programs to create close working relationships with customers in the biomedical research industry. We maintain customer service, technical assistance and consulting service departments, which address both our customers routine and more specialized needs. We frequently assist our customers in solving problems related to animal husbandry, health and genetics, biosecurity, preclinical and clinical study design, regulatory consulting, protocol development and other areas in which our expertise is recognized as a valuable customer resource.

Research and Development

While there is some research and development activity involved in our in vitro technologies business, we do not maintain a fully dedicated research and development staff and therefore have not had any significant research and development costs in any of the past three fiscal years. Our approach to developing new products or services is to extend our base technologies into new applications and fields, and in some instances to license or acquire technologies to serve as platforms for the development of new businesses that service our existing customer base. Our research and development focus is principally on developing projects that improve our productivity or processes.

Industry Support and Animal Welfare

One of our core values is a concern for and commitment to animal welfare. We have been in the forefront of animal welfare improvements in our industry, and continue to demonstrate our commitment with special recognition programs for employees who demonstrate an extraordinary commitment in this critical area of our business. We created our own Humane Care Initiative, which is directed by our Animal Welfare and Training Group. The goal of the initiative is to assure that we continue as a worldwide leader in the humane care of laboratory animals. Laboratory animals are an important resource that further our knowledge of living systems and contribute to the discovery of life-saving drugs and procedures. We work hand-in-hand with the scientific community to understand how living conditions, handling procedures and stress play an important role in the quality and efficiency of research. As animal caregivers and researchers, we are responsible to our clients and the public for the health and well being of the animals in our care.

We support a wide variety of organizations and individuals working to further animal welfare as well as the interests of the biomedical research community. We fund scholarships to laboratory animal training programs, provide financial support to non-profit institutions that educate the public about the benefits of animal research and provide awards and prizes to outstanding leaders in the laboratory animal medicine field.

Employees

As of December 31, 2005, we had approximately 8,400 employees, including approximately 450 science professionals with advanced degrees including D.V.M.s, Ph.D.s and M.D.s. Our employees are not unionized in the United States, although employees are unionized at some of our European facilities, consistent with local customs for our industry. Our annual satisfaction surveys indicate that we have an excellent relationship with our employees.

Backlog

Our backlog for Preclinical Services and Clinical Services was approximately $448.2 million at December 31, 2005. We do not report backlog for the RMS segment because turnaround time from order placement to fulfillment, both for products and services, is rapid. Our preclinical and clinical services are performed over varying times, from a short period of time to extended periods of time, which may be as long as several years. We maintain an order backlog for these segments to track anticipated revenue from studies and projects that either have not started, but are anticipated to begin in the near future, or are in process and have not been completed. We only recognize a study or project in backlog after we have received written evidence of a customer s intention to proceed. We do not recognize verbal orders. Cancelled studies or projects are removed from backlog.

We believe our aggregate backlog as of any date is not necessarily an indicator of our future results for a variety of reasons. First, studies vary in duration (i.e., some studies that are included in 2005 backlog may be completed in 2006, while others may be completed in later years). Second, the scope of studies may change, which may either increase or decrease their value. Third, studies included in backlog may be subject to bonus or penalty payments. Fourth, studies may be terminated or delayed at any time by the client or regulatory authorities. Terminations or delays can result from a number of reasons. Delayed contracts remain in our backlog until a determination of whether to continue, modify or cancel the study has been made. We cannot provide any assurance that we will be able to realize all or most of the net revenues included in backlog or estimate the portion to be filled in the current year.

Competition

Our strategy is to be a leader in each of the markets in which we participate. We compete in the marketplace on the basis of quality, reputation, responsiveness, timeliness and availability, supported by our international presence with strategically located facilities.

The competitive landscape for our three business segments varies. For RMS, our main competitors include three smaller competitors in North America, several smaller competitors in Europe, and two smaller competitors in Japan. Of our main U.S. competitors, two are privately held businesses and the third is a government funded, not-for-profit institution. We believe that none of our competitors in RMS has our comparable global reach, financial strength, breadth of product and services offerings and pharmaceutical and biotechnology industry relationships.

We believe we are one of the two largest providers of preclinical services in the world, based on net service revenue. Our commercial competitors for preclinical services are both publicly-held and privately-owned companies. The clinical development services market is highly fragmented, with participants ranging from hundreds of small, limited-service providers to a few full service drug development services organizations with global operations. Our clinical services business competitors include a number of publicly traded and privately owned companies. In addition, both our preclinical and clinical businesses compete with in-house departments of pharmaceutical companies and universities and teaching hospitals.

Regulatory Matters

As our business operates in a number of distinct operating segments and in a variety of locations worldwide, we are subject to numerous, and sometimes overlapping, regulatory environments, as described below.

The Animal Welfare Act (AWA) governs the care and use of certain species of animals used for research. The United States Congress has passed legislation which permanently excludes rats, mice and chickens used for research from regulation under the AWA. As a result, most of our United States small animal research model activities and our vaccine support services operations are not subject to regulation under the AWA. For regulated species, the AWA and attendant Animal Care regulations require producers and users of regulated species to provide veterinary care and to utilize specific husbandry practices such as, cage size, shipping conditions, sanitation and environmental enrichment methods to assure the welfare of these animals. We comply with licensing and registration requirement standards set by the United States Department of Agriculture (USDA) for the care and use of regulated species. Our animal production facilities in the U.S. are accredited by The Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC), a private, nonprofit, international organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs. Portions of our preclinical business are also generally regulated by the USDA.

Our import and export of animals in support of several of our business units as well as our operations in foreign countries are subject to a variety of national, regional, and local laws and regulations, which establish the standards for the humane treatment, care and handling of animals by dealers and research facilities. We maintain the necessary certificates, licenses, detailed standard operating procedures and other documentation required to comply with applicable regulations for the humane treatment of the animals in our custody at our locations.

Our preclinical services business conducts nonclinical laboratory safety studies intended to support the registration or licensing of our clients products throughout the world. The conduct of these studies must comply with national statutory or regulatory requirements for Good Laboratory Practice (GLP). GLP regulations describe a quality system concerned with the organizational process and the conditions under

which nonclinical laboratory studies are planned, performed, monitored, recorded, archived and reported. GLP compliance is required by such regulatory agencies as the FDA, United States Environmental Protection Agency, European Agency for the Evaluation of Medicinal Products, Department of Health (DOH) in the United Kingdom, Health Canada, and the Japanese Ministry of Health and Welfare. GLP requirements are significantly harmonized throughout the world and our laboratories are capable of conducting studies in compliance with all appropriate requirements. To assure our compliance obligations, we have established quality assurance units (QAU) in each of our nonclinical laboratories. The QAUs operate independently from those individuals that direct and conduct studies and monitor each study to assure management that the facilities, equipment, personnel, methods, practices, records, and controls are in compliance with GLP. Our laboratory managers use the results of QAU monitoring as part of a continuous process improvement program to assure our nonclinical studies meet client and regulatory expectations for quality and integrity.

Our clinical services business conducts human clinical trials and provides services in support of our clients registration or licensing applications. Human clinical trials are conducted in a progressive fashion beginning with Phase I to IV trials. Phase I studies are the initial human clinical trials and are conducted with a small number of subjects under highly controlled conditions. Phase II and III trials are conducted with an increasing number of subjects and under actual clinical conditions, e.g., patients with the condition to be treated. Phase IV clinical trials are conducted after product approval with a large number of subjects under actual clinical conditions. These clinical trials and services are performed in accordance with the International Conference on Harmonization Good Clinical Practice Guidelines and in compliance with regulations governing the conduct of clinical investigations and the protection of human clinical trial subjects. In the United States, these trials and services must comply with FDA regulations and in Europe our clinical trials and services must comply with the clinical trials directive of the European Union. Neither FDA regulations nor the clinical trials directive requires a quality assurance program; however, our Phase I facility has an established quality assurance unit that monitors the conduct and reporting of Phase I trials to assure management that these trials are conducted in compliance with appropriate regulatory requirements. We also provide quality assurance oversight of our contracted clinical service activities and offer quality assurance inspections and audits as a contract service in Phase II through IV clinical trials.

Our manufacturing business produces endotoxin test kits and reagents and vaccine support products. Additionally, the analytical divisions of s