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Global Contract Research Organization (CRO) Industry: Overview and Trends, 2008

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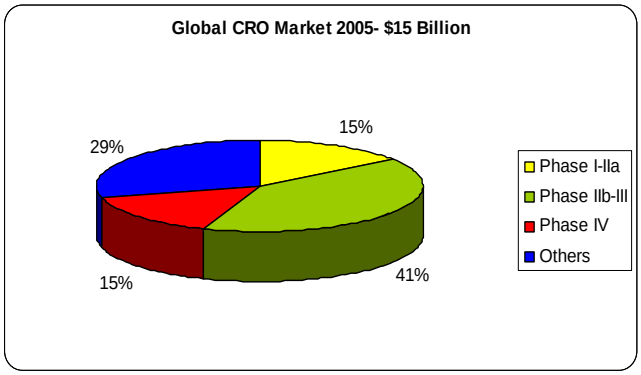


Source: Frost and Sullivan Analysis, 2006

Overview

Contract research is a multi-billion dollar industry. With demand for CRO services expected to increase by 16% annually over the next five years, the future appears rosy. The rise in foreign studies plus the increasing complexity and size of clinical trials fuels this growth.

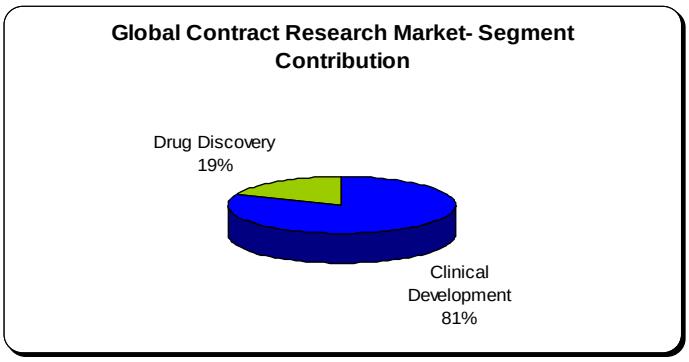
Rapid revenue growth encourages the formation of new CROs. As this trend continues, the market becomes highly fragmented, with hundreds of CROs vying for market share.

However, building a fully-functional CRO takes time. Thus, growth of the customer base tends to outstrip CRO capacity. Consequently, incumbents have no difficulty finding new customers. Their biggest challenge, typically, is managing rapid growth and maintaining cash flow needed to sustain capacity development.

In 2005, there were 269 CROs in the U.S., and 462 more in Europe. The top five CROs by market share laid claim to 36% of total industry revenues. This suggests that a few dominant CROs are arising, which is typical of an industry in the late growth phase. *(contractpharma.com/articles/2008/03/cro-market-view).*

CRO Industry Outlook

The US $9.57bn world market for contract clinical research services is growing at an annual 13.4%. This figure includes pre-clinical and phase I, II, and III clinical services provided by Contract Research Organizations (CROs) to pharmaceutical and bio-technology drug developers. Pre-clinical studies include toxicology and other safety studies, conducted both in vitro and in animal models. Phase I studies evaluate drug safety, determine safe dosage ranges, and identify side effects in small human groups of 20 to 80 volunteers. Phase II tests measure effectiveness and further evaluate safety in large groups of 100 to 300 patients. Phase III trials confirm effectiveness, monitor side effects, and compare the drug to other commonly used treatments in large patient groups of 1000 to 4000 or more individuals.



Source: Frost and Sullivan Analysis, 2006

Global vs. Regional Activity

There are more than 1,000 competitors in the CRO segment, offering various services. Companies range in size from small firms with revenues under US $1 million, to large, publicly traded entities.[1]

[1] Outsourcing in pharma industry: Global trends Viewed April 2, 2008. http://www.pharmabiz.com/article/detnews.asp?articleid=29682&sectionid=50

The trends that affect industry players tend to exist on a global rather than regional basis; there are, however, several key concentrations of market activity—particularly the United States, Europe and Asia. As of April 2008, the clinical research segment derives most of its revenues from U.S.-based projects, and more than 2/3 of the 1,000+ companies in the CRO segment are based in the United States. The U.S. predominance is due primarily to the status of the U.S. as the world's largest drug market and the favorable conditions which the U.S. presents for contract research.

Other regions are expected to see a slight decline or status quo in their market shares. Although Asia is expected to benefit from increases in clinical research activity, particularly in China and India, these revenues will remain relatively low in comparison to overall CRO sales because of the extremely low currency valuations in these regions.

South America and Africa are beginning to account for a small fraction of contract research fees. Like Eastern Europe and parts of Asia, these regions offer the ability to conduct clinical trials at a fraction of U.S. and Western European costs, while providing high quality patient populations that lead to high quality data. Many of the leading CROs – including Quintiles, Covance, Omnicare, and Parexel – are active in these emerging markets and often acquire local firms.

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Current Industry Trends[2]

The industry continues to evolve toward a full-service model, with CROs offering services from the earliest stages of development through clinical trials and post-approval research. Several large CROs are also seeing a fair amount of bundling of services. And, with the number of new products in the development pipeline steadily increasing, there's a greater premium on making efficient use of resources. The demand for services across the board has increased in the last year, with an upsurge in Phase II and III trials as well as a continued growth and expansion in Phase I. Also, mounting safety concerns have given rise to Phase IV and registry trials. Subsequently, with the FDA requiring more safety data and with trial sizes increasing, Pharma is outsourcing large global mega-trials now more than ever. The need for larger trials has added to the pressures CROs face in an increasingly global market. CRO services in the Biopharma sector have also surged in the last year, creating new full-service benefits/opportunities for both sponsors and CROs. *(contractpharma.com/articles/2006/05/cro-industry-update.php)*

Biopharmaceutical Product Pipeline

Productivity of drug manufacturers' R&D is an important issue that affects the health of the clinical CRO industry. Productivity is the key for supplying R&D pipelines with compounds to develop (and crucial in the long run for generating revenues to fund further R&D). Manufacturers' discovery units need to generate a steady stream of compounds (or in-license compounds) to keep the company growing and offset generic erosion. Too few compounds or compounds that fail

[2] CRO Industry Update Viewed April 2, 2008.
http://www.williamblair.com/documents/CROIndustryUpdate032206.pdf

during testing are threats to the growth of drug companies and ultimately the CRO industry.

Biopharmaceutical R&D Spending Growth

R&D spending growth by pharmaceutical and biotechnology companies is another measure and predictor of the clinical CRO market. Clinical trials are so large and they constitute such a large portion of drug companies' R&D budgets that as sponsors conduct more trials and spend more on each one (on average), overall R&D spending increases and business opportunities for CROs increase. The health of Pharma and biotech companies, and particularly their research budgets, is crucial because that is the source of funding for clinical CROs. William Blair and Company believe tracking R&D growth helps reveal where the industry is in the R&D cycle (i.e., expansion, plateau, contraction, or trough) and this metric can help point to the next stage of the R&D cycle.

Biotechnology Funding

William Blair and Company believe the R&D dollars of biotechnology companies are becoming a greater portion of the overall mix of R&D spending, as biological compounds become an increasing portion of the total industry pipeline. William Blair and Company also maintain that biotech companies generally outsource a greater portion of their development spending, given a lack of internal expertise and infrastructure as well as more limited financial resources. Therefore, they believe biotech funding is an important indicator for the future health of the CRO industry.

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Trends Affecting the CRO Industry[3,4]

The outsourcing of drug development activities by pharmaceutical and bio-technology companies has been increasing and will continue to increase as a result of the factors described below.

Cost Containment Pressures

Market forces and governmental initiatives have placed downward pressure on pharmaceutical and biotechnology companies' drug prices. Covance Inc believe that the pharmaceutical industry is responding to these pressures by converting some of the fixed costs of maintaining research and development personnel and facilities to variable costs, which can be increased or decreased as needed, by outsourcing drug development activities to contract research organizations. Pharmaceutical companies may find that they do not have sufficient internal development resources when a large number of prospective drugs emerge from the research process and need to undergo development. These resource shortages increase demand for the services of contract research organizations. Covance Inc also believe that many of these companies are attempting to shorten the new drug development cycle time by using

[3] Covance Inc. Viewed April 2, 2008.
http://sec.edgar-online.com/2000/03/03/14/0000912057-00-009690/Section2.asp

[4] PRA International. Viewed April 02, 2008.
http://209.85.175.104/search?q=cache:V-gpQZsnVfoJ:sec.edgar-online.com/2004/06/14/0000950133-04-002380/Section5.asp+globalisation+CRO+Industry&hl=en&ct=clnk&cd=7

contract research organizations, which may have greater expertise in a therapeutic area and/or offer greater efficiency at a lower cost.

Marketplace Globalization

Pharmaceutical and biotechnology companies are increasingly attempting to expand the market for new drugs by applying for regulatory approvals in multiple countries simultaneously rather than sequentially as they have in the past. Covance Inc believe that contract research organizations with a global presence will continue to benefit from these trends.

Revenue Enhancement

Covance Inc. believe that contract research organizations, by providing specialized development services, are often able to perform the needed services with a higher level of expertise or specialization, and more quickly than a pharmaceutical or biotechnology company could perform such services internally.

Pharmaceutical Company Consolidation

Business combinations such as mergers and acquisitions by pharmaceutical companies present an opportunity for contract research organizations, as companies resulting from business combinations often seek to reduce costs. Once combined, many pharmaceutical companies aggressively manage costs by reducing jobs, decentralizing the research and development process and outsourcing to contract research organizations in an effort to reduce the fixed costs of internal drug development.

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Increasingly Stringent Regulation

Regulatory requirements throughout the world have become more stringent and there is a trend toward global standardization of these requirements. This has led to an increase in the need for broader, global regulatory expertise. Covance Inc. believes that the pharmaceutical and biotechnology industries are outsourcing to global contract research organizations to take advantage of their capabilities and geographic presence.

Therapeutic Focus

Covance Inc. believes that the economics of the marketplace require increased research and development expenditures as pharmaceutical and biotechnology companies become focused on innovative new products. These include drugs for an aging population and drugs for the treatment of chronic disorders and life threatening conditions. The development of therapies for chronic disorders, such as Alzheimer's disease or arthritis, requires complex clinical trials to demonstrate the therapies' effectiveness and to determine whether the drugs cause any long-term side effects. Covance Inc believes that contract research organizations with the requisite therapeutic experience and the ability to manage complex trials will present an attractive development alternative for biopharmaceutical companies.

Increasing Competitive Pressures in the Pharmaceutical Industry

A report issued in late 1998 by the accounting firm PricewaterhouseCoopers stated that if recent trends continue, the research and development costs of the top 20

pharmaceutical companies will more than double by the year 2005. If the growth in research and development budgets keeps pace with revenue growth, which PricewaterhouseCoopers believes is more likely, they conclude that research and development costs per drug will have to be reduced to provide their shareholders with the investment returns they have experienced through much of the 1990's. We believe that to meet these pressures, large pharmaceutical companies will have to develop drugs more quickly and less expensively and that should lead to an increasing reliance on the services of CROs.

Biotechnology Industry Growth

The United States biotechnology industry has grown rapidly over the last twelve years and is introducing new therapies which require regulatory approval. Many biotechnology companies do not have the necessary capital, equipment or personnel experience to conduct preclinical studies and clinical trials. Accordingly, many biotechnology companies have chosen to outsource to CROs rather than expend significant time and resources to develop an internal preclinical or clinical development or bio-manufacturing capability.

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Leading CRO Players[5]

The key players in the global CRO market include the following:

Name	Headquarters	Annual Revenues	Products & Services
Charles River Laboratories International, Inc.	MA, USA	$ 1.2 billion* *Datamonitor PLC.	Research models and services: • Preclinical services • Biopharmaceutical services • Endotoxin and Rapid Microbiological Products • Agrochemical and veterinary services (Datamonitor plc)
Encorium Group, Inc.	PA, USA	$10.4 million* * Information Access Company	• Drug Development Consultancy • Project Management • Clinical Site Monitoring • Data Management • Biostatistics • Regulatory Affairs • Pharmacovigilance • Quality Assurance • Data monitoring committees and Endpoint Adjudication Committees • Medical Writing • Technology Solutions (remedium.com/services/index.html)

[5] Outsourcing in Drug Development: The Contract Research (CRO) Market Viewed April 02, 2008. https://www.leaddiscovery.co.uk/reports/124/Outsourcing_in_Drug_Development_The_Contract_Research_CRO_Market/

The US $9.57bn world market for contract clinical research services is growing at an annual 13.4%.

Name	Headquarters	Annual Revenues	Products & Services
Covance, Inc.	NJ, USA	$1.4 billion* *Standard & Poor's Corporate Descriptions plus News	Research products: • Antibody products and services • Nonclinical development services • Risk management services • Clinical pharmacology services • Central laboratory/ Covance local laboratory services • Cardiac safety services • Clinical development services • Commercialization service (covance.com/aboutcvd/index.php)
ICON Clinical Research	Ireland	$649.8 million* *Hoovers.com	• Laboratory testing services for clinical trials patients (through ICON Central Laboratories) • Clinical research staffing services (through ICON Contracting Solutions). (Hoovers.com)
Kendle International, Inc.	OH, USA	$373.0 million* *Datamonitor PLC.	• Clinical Development (Phases I to III) • Regulatory Affairs (Consulting and submission services, pharmacovigilance/ safety) • Biometrics (Clinical data management, biostatistics and scientific programming) • Late Phase (Phase IIIB/IV, health economics and outcomes, scientific events, education and publications. (kendle.com/what_we_do/what_we_do.php)
MDS Pharma Services	AZ, USA	$ 4.9 M* *Information Access Company	• Lead optimization • Pre-IND research • Early clinical research (bioequivalence, phases I-IIa) • Bioanalysis through global clinical development (phases II-IV) • Central lab and centralized cardiac services. (mdsps.com/Company/Default.aspx)

Name	Headquarters	Annual Revenues	Products & Services
Omnicare Clinical Research	PA, USA	$ 6.5 billion* *DatamonitorPLC.	• Project Management • Investigator Relations • Clinical Trial Services • Medical Affairs • Safety Surveillance • Data Management • Biometrics • Clinical Writing • Regulatory Affairs
Parexel International Corporation	MA, USA	$615.0 M (2006)* *Information Access Company	• Clinical development and consulting services, including strategy development, clinical trials, and biostatistics. • Computer database and file preparation • Medical writing services. • Products and services are sold to the medical industry. (www.parexel.com)
Pharmaceutical Product Development, Inc.	NC, USA	$1.3 billion (2007)* Information Access Company	• Compound Partnering • Resources spanning the R&D continuum to provide early compound assessment and development within a proven, innovative compound partnering program • Development Services: - Phase I clinic - Full service Phase II-IIIb clinical studies for multinational regulatory submissions - GLP bioanalytical, cGMP product analysis, biomarker and Phase I - IV global central labs - Therapeutic and specialty groups with dedicated project teams - Post-approval services including product safety and pharmacovigilance, risk management, Phase IV monitored studies, registries and observational studies, medical information and professional contact center services, and Rx-to-OTC switch - Clinical data management and information solutions, including consulting and propriety software tools to speed collection, analysis and reporting of clinical data

With demand for CRO services expected to increase by 16% annually over the next five years, the future appears rosy.

Of the large, global contract research providers, Quintiles is the market leader, with 14% of the global market share.

Name	Headquarters	Annual Revenues	Products & Services
Pharmaceutical Product Development, Inc. (continued)			- CSS Informatics (division of PPD) — consulting services and proprietary e-technologies for clinical and safety data management, validation and training services for Oracle Clinical - PPD Medical Device (division of PPD) — medical device development (http://www.centerwatch.com/professional/prv213.html)
Quintiles Transnational Corporation	NC, USA	$1.5 billion (2007)* *Information Access Company	• Phase I Services for early-phase human drug development. • Global Clinical Development Services, encompassing all Phase II-IV trial services, such as clinical trial management, medical and regulatory affairs, biostatistics, patient recruitment, ECG services, and drug safety and strategic research. • Global Central Labs to support all phases of clinical trials. • Global Data Management to capture, analyze and report patient-related data. • Global Consulting on product development; reimbursement and pricing; health outcomes; regulatory compliance (e.g., FDA enforcement, quality systems); and due diligence for pharmaceutical, biotech and medical device companies. • Medical Education involving the development and delivery of Continuing Medical Education (CME) programs for health care practitioners. (qtrn.com/AboutUs/Overview.htm)
PharmaNet Development Group	NJ, USA	$407 million 2006* *Datamonitor PLC	• Clinical-development solutions including consulting services, Phase I clinical studies, bioequivalency and pharmacodynamic studies, bioanalytical analyses, and Phase II, III, and IV clinical development programs • Technology tools for managing clinical trial data. (pharmanet.com)

The Future of CRO's[6]

Source: Frost and Sullivan Analysis, 2006

The total CRO market size is estimated at US $14bn in 2006 and is expected to grow at an annual rate of 14-16% to reach US $24bn through 2010.

- **Market Size & Scope**
  - The total CRO market size is estimated at US $14bn in 2006 and is expected to grow at an annual rate of 14-16% to reach US $24bn through 2010. The market is highly fragmented and the number of CROs worldwide has reached over 1,100 despite continued consolidation.
- **Market Leaders**
  - Of the large, global contract research providers, Quintiles is the market leader, with 14% of the global market share; followed by Covance and PPD, holding 10% each. The five largest CROs have increased their market share and now hold 45% of the total market.
  - The leading CROs are commodity full-service providers operating on a global scale. They act as "one-stop shops" for all services, from pre-clinical through marketing.
- **Competitive Advantages**
  - CROs provide substantial global capacity to drug developers and have become critical contributors to clinical trial activity. Clinical trials conducted by CROs are completed up to 30% more quickly than those conducted in-house by Pharma companies.
- **Strategic Growth Areas**
  - CROs and pharmaceutical companies are turning to strategic partnerships to gain a competitive edge in the global business environment.

[6] The CRO Market Outlook: Emerging Markets, Leading Players And Future Trends. Viewed April 02, 2008. http://www.marketresearch.com/product/display.asp?productid=1526872&g=1