

# ***Global Outsourcing: Defining China's Leading Edge***

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## **Introduction**

The market for Research and Development (R&D) outsourcing in the biopharmaceutical industry represents a significant economic opportunity for China. The global outsourcing market, though, is highly competitive. In much of the industry literature, China is portrayed to be an increasingly important player in this market, but one that is lagging behind other developing markets, especially India.

This report offers a vision for China that reaches beyond the current models and drivers of outsourcing. This vision moves from the concept of outsourcing to one of strategic sourcing, thus paving the way to successfully competing in an industry where R&D will increasingly be performed by global companies that create nimble, virtual operating groups comprised of the best-in-class talent required for each project. How can the Chinese biopharmaceutical industry establish itself as the preferred partner in this type of competitive marketplace?

This report will address these critical issues, highlighting recommendations for the strategic positioning of China in its marketing and public relations efforts now, as well as priorities for market development over the next 5-10 years.

## **Market Opportunity**

R&D outsourcing in the biopharmaceutical industry has been steadily growing since the year 2000 and is expected to continue to grow at a rate of approximately 14% annually. By 2008, Thomson CenterWatch projects that the outsourcing industry will reach \$21 billion annually. Drivers of this growth include the need to:

- *Reduce cost*
- *Reduce time to market* – Clinical Research Organizations (CROs) reduce clinical testing times on average by 30%
- *Broaden access to specific expertise while focusing internal growth on core competencies*
- *Increase capacity to scale up and evaluate new lead compounds resulting from combinatorial chemistry and HTS techniques*
- *Increased access to new technologies*
- *Manage the regulatory requirements associated with the increasing complexity of clinical trials and regulatory submissions.* Regulators are also asking for more data to support claims, requiring more and larger trials. CROs are well positioned to manage this increase in trials size because they have ongoing relationships with patients and physicians.

Jeffries and Company, Inc. offers a market model for the R&D outsourcing industry through 2008 that breaks down the growth trends by phase (i.e., total outsourced development expenditure), as is illustrated in Table 1 below. The key assumptions underlying this model include: (1) early development strength; (2) more lucrative (in dollar terms) Phase II/III testing ramping slowly over the 2003-2008 period; (3) likely increase in safety testing following recent pharma industry product withdrawals; (4) bioequivalence testing demand sustained; and (5) central lab activity increases as more drug candidates advance in the pipeline.

Table 1

CRO Market Size and Year-over-Year Growth by Phase, 2003-2008E (\$mm)							
Year	Preclinical	Phase 1	Phase II/III	Phase IIIb/IV	Labs	Other	Total
2003	\$2,369	\$820	\$2,506	\$820	\$2,440	\$2,162	\$11,116
	24.10%	26.80%	5.90%	20.00%	19.80%	14.10%	16.60%
2004	2,934	978	2,731	1,003	2,750	2,441	12,837
	23.90%	19.30%	9.00%	22.30%	12.70%	12.90%	15.50%
2005	3,552	1,221	3,147	1,206	3,157	2,728	15,011
	21.10%	24.90%	15.20%	20.20%	14.80%	11.80%	16.90%
2006	4,034	1,502	3,667	1,424	3,603	3,008	17,237
	13.60%	23.00%	16.50%	18.10%	14.10%	10.30%	14.80%
2007	4,525	1,788	4,214	1,654	4,074	3,269	19,524
	12.20%	19%	14.90%	16.10%	13.10%	8.70%	13.30%
2008	4,957	2,079	4,741	1,839	4,450	3,480	21,636
	9.60%	16.30%	12.50%	11.20%	11.40%	6.40%	10.80%
CAGR (03-08)	15.90%	20.40%	13.60%	17.50%	13.20%	10.00%	14.20%

Source: MedAdNews, FactSet, Company reports, Jefferies & Company, Inc., estimates

The global R&D market represents a substantial economic opportunity for China. At present, though, China's current market share remains small, and its rate of growth is projected to lag behind that of other developing markets. In 2005, the global market for contract research was dominated by Western Europe; Eastern Europe comprised 10.7% while India accounted 0.7% and China made up 0.5%. By 2010, however, Eastern Europe will account for 13.3%, India, for 2.4% and China will represent 1.1%.

### The Future of Outsourcing

Historically, outsourcing of biopharmaceutical R&D has mostly commonly been tactical, as opposed to strategic. Tactical outsourcing tends to be a fall-back position when in-house resources unexpectedly prove to be inadequate to complete a project. A sponsor who attempts to maintain staff capable of performing all activities associated with a project may find itself with inadequate resources due to lay-offs, unexpected expansions of a study, unanticipated need for special expertise or services. Keeping work in-house is felt to enhance control. In addition, many sponsors think that using in-house resources reduce costs, although studies have not proven that point.

Tactical outsourcing has proven to have significant disadvantages:

- Last minute attempts to identify and contract with a CRO may delay the study.
- Pressure to quickly select a service provider runs the risk of a poor match.
- Little opportunity exists for the sponsor's staff to acquire the skills necessary to effective work with providers when they are needed.
- Staffing up for large Phase III studies is expensive and time-consuming.
- Work in a new therapeutic area may require hiring new personnel who have the targeted knowledge for that area.

- Termination of an unsuccessful project may result in lay-offs, severance packages, and relocation costs.

Strategic outsourcing, on the other hand, employs a deliberate mix of in-house and external resources with a view toward long term cost and resource management. The determination of which resources to use is carefully planned within the context of the long term strategic development plan for the company and its portfolio of pipeline products, as well as the short term needs for a specific project. The strategic model prioritizes longer term collaborative partnerships over short term project tasks with a vendor. This allows companies to focus on building core areas of excellence internally, while establishing reliable external partnerships to meet transient needs required to optimize productivity. Providers are selected according to projected sponsor needs and therapeutic expertise. They also tend to be selected for longer term relationships, across multiple projects. For example, if a provider has performed well on past projects, the sponsor may decide to help train its staff for a new therapeutic area rather than build this capability in-house.

Strategic outsourcing requires that sponsor personnel be trained in how to effectively manage a service provider, and the sponsor must ensure compatibility between its standards and procedures and those of the provider (e.g., ensuring that the databases for the early and later studies can be combined).

At present, about half of biopharmaceutical outsourcing is tactical, and the other half is strategic. Strategic outsourcing with the right provider and managed well by the sponsor has some compelling advantages. Anecdotally it is said that once a sponsor and provider have worked together on three projects, the efficiency and effectiveness of the relationship increases substantially. The pressure to expand the number of pipeline candidates requires parallel processing of multiple portfolio candidates.

The trend toward viewing carefully selected outsourcing providers as long-term strategic sourcing partners across a range of projects begins to make sense given the productivity challenges facing the industry. One of the early examples of this was that done by one of the authors when he was Executive Vice President and Head of Research and Development Hoechst Marion Roussel. In 1998, Dr Douglas formed a strategic outsourcing partnership with Quintiles and thus produced what became a 'triple win' situation. The newly formed Aventis ( the merger of Hoechst and Rhone Poulenc Rorer) wanted to exit one of its major sites in Kansas City, which had been headquarters for Marion Merrrel Dow, but could not afford to jeopardize the development of some important compounds, such as Allegra. Quintiles wanted to have a major presence in the Midwest, and ,of course, the employees in Kansas City wanted to maintain their jobs and complete the projects. This outsourcing relationship was highly successful and Quintiles not only took over the Kansas City operations and some 800 employees, but remains a strategic preferred partner for Sanofi- Aventis, a successor company of Hoechst Marion Roussel. (*Press Release: "Hoechst Marion Roussel and Quintiles announce Strategic Partnership Agreement." Dec. 14 1998*)

Taken to the next level, strategic sourcing can form the foundation for the development of start-up firms seeking to minimize investments in infrastructure, by establishing only core in-house capabilities and sourcing the majority of functions to external centers of excellence. One such life science company is IndUS, an entrepreneurial venture with research operations in India and

the US which has, in 18 months, with less than 20 employees and a small initial investment, developed a pipeline across three different therapeutic indications that includes five novel and patented lead compounds that are in preclinical development. By strategic and creative establishment of a number of partnerships, licensing agreements and vendor/client relationships, IndUS has successfully aggregated best-in-class resources and promising intellectual property from academia, government and industry on a global basis to optimize pharmaceutical R&D productivity. This innovative knowledge-integration biotech model avails cost efficiencies by leveraging the competitive strengths and niches of different geographies globally. It also offers an interesting approach to the challenges associated with technology transfer of intellectual property from academia to the commercial marketplace.

As Peter Drucker predicted "...the company of the future will be organized around knowledge rather than specific products." Pharmaceutical Contract Research Alliances (PCRAs), e-technologies, and emerging models of virtual drug development clearly are fueling the growth of the strategic sourcing industry. How can China position itself as a leader in a biopharmaceutical industry that is moving toward this vision of small, nimble, distributed operating units to optimize productivity and likelihood of success across the value chain?

### **Competitive Strengths of China**

#### ***Patients***

China has a number of compelling strengths that establish the foundation for a powerful strategic marketing campaign for its global outsourcing industry. The country's population of 1.3 billion is the largest in the world. By 2020, China is projected to surpass the US as the leading consumer of western pharmaceuticals as a result of the World Trade Organization's requirements to deregulate its domestic drug market. In addition, accessibility to patients is increasing as they move from rural to urban areas, and receive medical care through major centralized hospitals and affiliated networks of clinics.

Treatment naïve patients – highly desirable for many clinical studies – are significantly easier to access in China than in the US or the EU. In addition, the presence of unique gene pools in the population of China is valuable for pharmacogenomic studies.

Certain specific patient populations are more easily accessible in China than in other countries, providing an opportunity for the focused development of niche markets. Examples include gastrointestinal cancers (esophageal, gastric, and liver); hepatitis; nasopharyngeal cancers; neural tube defects, especially spina bifida; and nonsmokers with EGFR mutation.

And, finally, patients in China, for cultural reasons, tend to be more compliant with their medical care than is the case in the US and EU. This may well result in lower attrition rates in clinical trials, which would be a significant consideration for sponsors.

#### ***Industry***

Clinical studies in China have demonstrated, on average, a 70% cost savings over those done in the US due to lower per patient costs. In addition, many Chinese scientists who have worked in the pharmaceutical industry are returning, bringing with them cutting edge knowledge and skills. This trend, combined with the state-of-the-art research facilities and infrastructure position China well for taking a leadership role in the industry.

### ***Sociopolitical and Cultural Factors***

The physician investigators in China are highly educated and very motivated to participate in clinical studies. What they may lack in practical experience with clinical trials is more than balanced by their desire to learn and contribute to improving patient care.

Animal rights groups do not have a significant presence in China at this time, creating a climate that is not hostile to performing studies in a responsible manner in animals. Finally, intellectual property law has improved significantly in recent years, and enforcement of these laws is recognized by the government as a critical priority for enhancing competitiveness for the country.

### **Competitive Challenges for China**

#### ***Patients***

Because most patients are unfamiliar with clinical studies, they are often mistrustful about participating, which may significantly slow recruitment. In addition, recruitment may be further delayed by the fragmentation of the market of 64,000 hospitals, each with 3-4 affiliated outpatient clinics.

The racial dissimilarity of Chinese patients compared with Western patients leads to variation in drug performance. The genetics variations across this population are not yet well characterized, and represent a short-term disadvantage compared with India, whose population shares racial similarities with US and EU populations.

#### ***Industry***

Few within the Chinese biopharmaceutical industry have prior experience working in or with a western company, so the workforce is on a collective steep learning curve. In addition, the high rate of staff turnover in this industry leads to delays in projects and risks of information leaks.

### ***Sociopolitical and Cultural Factors***

The lack of familiarity with trial administrative procedures by physicians and hospital staff requires additional administrative time at study sites and represents a significant short time challenge.

Perhaps the greatest challenges, however relate to the legal and regulatory climate within China. The highly centralized regulatory model associated with the State Drug Administration (SDA) leads to long delays (average six months) in trial approvals; tight control of study site selection; and substantial delays in obtaining patents (average of 18-24 months).

In addition, historically the enforcement of patent protection has been very poor (note that 90% of the 3,000 Western medications sold in China are copies of foreign medicals). Anecdotally, executives in the biopharmaceutical industry have significantly less confidence in the government's ability to enforce patent protection in China compared with India at the present time.

Since blood products can not be transported out of the country, companies must work with clinical labs that are based in China. Identifying qualified labs, and establishing efficient and effective working relationship with them requires additional time and effort.

Another factor contributing to delays in product development and commercialization relates to the regulatory requirement that a product had to be launched in another country before a clinical trial could occur on the same product within China.

### **Signs of Progress**

Developments within the Chinese biopharmaceutical industry demonstrate important signs of progress in areas critical to positioning it competitively within the global marketplace.

For example, the SDA has recently designated 12 Good Clinical Practice (GCP) centers, mostly municipal teaching hospitals determined to have adequately trained investigators and appropriate staff and equipment to meet the defined quality standards. These centers take the lead on studies done at the 85 trial sites identified by the SDA to carry out clinical trials on western drugs by assigned therapeutic areas, and the 36 sites that perform trials on traditional Chinese medicines. These changes resulted in higher quality studies and increased the number of studies, now numbering hundreds each year.

The establishment of laboratory standardization that is aligned with Western standards has been another significant development in the area of quality. In 2005, Covance, in collaboration with its partner Center of Laboratory Medicine at Hua Shan Hospital, established the first central lab in China with Level I certification by the National Glycohemoglobin Standardization Program (NGSP). This certification ensures that the measure of glycosylated hemoglobin is precise, a critical quality factor for diabetes studies.

Overall, the growing number of collaborations between US companies and Chinese hospitals is enabling the mutual learning and experience required to improve collaborative performance, productivity, and quality within the industry. As early successes unfold, broadening of these partnerships is occurring as is the case with Quintiles in its ongoing expansion of services through its partnership with Peking Union Medical College Hospital.

Improved quality and capacity are also resulting from a commitment by the government to support infrastructure development. New biotech parks in Beijing (e.g., China Bio-Tech Research Center) is designed to meet FDA standards and to create the infrastructure to support the full continuum of growth needs for the industry, providing housing for start-ups, research centers, and venture capital firms.

As growing number of firms in China, led by experienced Chinese scientists returning from the US and EU, are instituting processes and procedures that are essential to attract business from Western pharmaceutical companies. For example, security measures applied to employees and regular video conference calls with overseas managers are becoming more common practices. There are a growing number of success stories as result of these types of changes. WuXi Pharmatech of Shanghai, through its successful master of such world class standards, now performs chemical R&D for 18 of the world's 20 largest pharmaceutical companies.

In addition, as the number of successful prosecutions of counterfeiters in the industry rises, confidence rises that that enforcement of patent protection may become business as usual in the coming years in China.

## **Recommendations**

Clearly the potential to build China as a leader in the worldwide market place of biopharmaceutical outsourcing is significant. Some of the recent developments in the industry indicate important trends and signs of progress. But there is an opportunity to aggressively drive the country to a leadership position in this competitive global market by establishing a shared vision, clear priorities, and cross-industry collaboration among key stakeholders including industry, government and academia. Important issues to consider both in terms of strategic marketing and public relations, as well as market development include:

### **1) Knowledge Needs**

- *Bioinformatics and pharmacogenomics* – the potential value of the unique gene pools present in the Chinese population can not be fully leveraged without a greater understanding of the correlations between genotype and phenotype with patient populations. Developing and applying this knowledge will require a major commitment from academia, industry, and government to collaborate in the area of bioinformatics and pharmacogenomics.
- *Epidemiologic data* – It will be critical to gain a greater understanding and ability to prospectively track the epidemiology of Western diseases in China. This information will be important for highlighting market expansion opportunities for existing Western drugs within the Chinese market.

### **2) Regulatory Issues**

- *Reduce delays due to regulatory environment* – any delay in initiating and completing a trial is very costly to the sponsor company. A critical priority for China will be to establish more efficient processes for approving clinical trials. In addition, an important strategic question for the government to consider is what is the right balance between centralization versus decentralization in trial approval and in site selection. In general, while centralization maximizes control and standardization, it also increases the likelihood of delays, and represents a major competitive disadvantage in the global marketplace.

### **3) Legal Issues**

- *Patent protection* – the need for dramatically improving enforcement of patent protection is clear. The more visible successful prosecutions can be in the media, the better in terms of marketing and public relations impact.
- *Patent approvals* – from the perspective of commercial competitiveness for the industry, there is a pressing need to reduce the time required to obtain patent approvals.

### **4) Education**

- *Patients* – an educational and public relations campaign targeting patients and focused on understanding the importance of clinical trials in developing new medical treatments would be valuable. Helping them understand informed consent processes and regulatory protections, as well as hearing stories from other patients who have had positive experiences with clinical trials would all be important components of this effort.
- *Investigators* – continuing to educate clinical investigators about GCP will be important to ensure quality and reduce management time required by study managers

- *Industry workforce* – continuing to promote strong English language skills among industry workers will be very important for building this market.

#### 5) **Marketing and Public Relations**

- *Competitive positioning* – it will be very important for marketing efforts of the Chinese biopharma industry to establish its competitive advantages rather than assume a defensive posture in the media coverage regarding the global outsourcing industry. For example, highlighting the size and increasing access to the population at large, as well as the unique gene pools and readily accessible niche market populations and treatment naïve patients are all compelling considerations given market demands in the current industry.
- *Outreach efforts* – while many companies in China approach marketing and outreach to global pharmaceutical companies by targeting individuals in remote office headquarters, a much more effective approach is likely to be building relationships with the local offices in China of target customers. This is true even if the type of service being marketed is different than the services provided by that local office. Relationship-based marketing is more likely to succeed, and local offices often have strong links – directly or indirectly - with headquarters.

It would be helpful to have a central listing of global biopharmaceutical companies with local offices, including names of senior staff members and the scope of activities performed in these offices. If such a directory does not currently exist, this could be provided by, for example, the Beijing Pharma and Biotech Center.

#### **Conclusion**

As global outsourcing in the biopharmaceutical industry grows across all components of the value chain, China offers a unique set of strengths that, if developed strategically and expeditiously, can position the country to become a world class player in this competitive marketplace. This will require the establishment of a shared vision and productive collaboration across key stakeholders groups including government, industry, and academia. It will also require development of broader expertise in clinical trials and regulatory standards and development of a ‘sourcing’ mentality on the part of the western companies that are interested in ‘outsourcing’.

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