



Biopharmaceutical Outsourcing in China: A Rapidly Changing Business Environment

Eric S Langer, BioPlan Associates Inc explores the growing opportunities to be



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Pressure to reduce costs is the driving force behind outsourcing in biopharmaceuticals. Outsourcing opportunities exist across the entire biopharmaceutical value chain, including drug discovery research, preclinical research, clinical trial study design and management, clinical supplies management, manufacturing, packaging, distribution and even marketing and sales. According to a newly released report, China is today a \$10-\$13 billion pharmaceutical market – putting it in the top 10 worldwide (1). And while global pharmaceutical markets grew seven per cent in 2005, China's pharmaceutical sales grew by 20.4 per cent, this being the third consecutive year that market has achieved more than 20 per cent growth. Forecasts indicate that China will become the fifth-largest pharmaceutical market in the next five years.

GOVERNMENT SUPPORT FOR BIOPHARMACEUTICAL INNOVATION

In addition to enhancing intellectual property protection, the Chinese government is focusing resources and investment on new domestic drugs that will encourage innovation, foreign investment and growth. By 2010, the Government plans to establish five large domestic pharmaceutical groups with sales of at least US\$625 million each, and 10 groups with sales of US\$375 million each. To achieve this, increasing funding for R&D, and improving innovation are key strategies. According to Zhang Guobao, Deputy Director of the State Development and Reform Commission, the commission goals for the 11th five-year plan (2006-2010) include: licensing five therapeutics in the US and the EU; producing up to 15 new Chinese-innovated drugs and

vaccines; AND directing that at least five per cent of income from pharmaceutical sales be reinvested in R&D.

This kind of state-level strategic planning has allowed China to become the 'world's manufacturer' for many labour-intensive products; however, pharmaceuticals are in a technically different class. To secure its competitive position, China is preparing plans to expand its outsourcing services across the board, but especially in life sciences and healthcare. Until recently, outsourcing of biopharmaceutical services has been a domain occupied by China's Asian rival – India. Now China is prioritising this sector to boost its overall services industry. The global service-outsourcing market will hit US\$1 trillion in the next few years, and China expects a share.

China's Ministry of Commerce is budgeting for projects to establish service outsourcing facilities over the next three years, according to *China Daily*. The goal is to bring in up to 100 foreign national companies in order to transfer technology and outsourcing business to China. This effort will create 1,000 domestic services enterprises.

Bernard Pepperstraete, a principal at MASA Life Science Ventures, a VC fund in Washington DC, also sees potential: "There is a cost advantage (in China) in infrastructure, raw materials and manpower that will last five to 10 years. Preclinical animal testing is 20 per cent of the cost of doing it anywhere else. And the Government there has invested \$1.5 billion in initiatives to build creativity, innovation and pursuit-of-patents. They are sending strong signals that they are addressing IP pitfalls. There is an enormous talent pool, and the cost of an equivalent experienced scientist in China is a third of what it would cost in the US. Although labour costs in Shanghai and Beijing are increasing, this differential should continue to exist, at least for the near-term."

GLOBAL OUTSOURCING MARKET SIZE AND GROWTH

Biopharmaceutical companies have increased their outsourcing expenditures dramatically over the last decade. An anticipated 40 per cent of pharmaceutical drug development expenditures are presently committed to outsourcing. Globally, the

Table 1: Biopharmaceutical* and pharmaceutical sales revenue in China

Year	Biopharmaceuticals		Pharmaceuticals		Share
	Billion RMB	Billion USD	Billion RMB	Billion USD	
2005	30.31	3.80	402.0	50.44	7.5%
2004	24.90	3.12	347.6	43.61	7.2%
2003	22.34	2.80	296.2	37.16	7.5%
2002	16.04	2.01	246.4	30.91	6.5%
2001	14.80	1.86	206.0	25.85	7.2%

*Biopharmaceuticals include both biological products and biochemical products
Exchange rate: USD:RMB=1:7.97

Source: BioPlan Associates, Inc, *Advances in Biopharmaceutical Technology in China*, September 2006

biopharmaceutical outsourcing industry is predicted to reach US\$60 billion over the next five years. Early drug discovery outsourcing is growing at an annual rate of 15 per cent with revenues expected to reach US\$7 billion in 2009. The worldwide CRO market size was estimated to exceed US\$12 billion by 2005, with revenue increasing at an annual rate of 14-16 per cent, according to CenterWatch estimates. IMS is forecasting the CRO market to rise to US\$28 billion by 2008.

The global market for biopharmaceutical contract manufacturing is predicted to reach US\$2.5 billion in 2006, yet only a small percentage of this work will be conducted in Asian countries. This percentage is expected to grow as pricing pressures in biotechnology markets increase and companies seek access to Asian markets.

COMPANIES CURRENTLY OUTSOURCING

AstraZeneca has become a major player in pharmaceutical R&D outsourcing, having spent US\$3.4 billion on 11 R&D centres in seven countries. In China, it currently has collaborations with 139 hospitals and research institutes, and has recently invested US\$14 million in a two year collaboration project with WuXi PharmaTech (Shanghai) for research services to support new drug development. This is part of AstraZeneca's plan to invest US\$100 million in drug innovation in China over the next three years. AstraZeneca also intends to establish an innovation centre in Shanghai. According to James Cai, Vice President of AstraZeneca China R&D, the company is setting up the innovation research centre not because of lower costs, but to focus on the Chinese healthcare market, and to "focus on the differences between Chinese diseases and Western ones".

In addition to AstraZeneca, many other Western pharmaceutical companies are establishing facilities, or outsourcing R&D or clinical programmes to China. China's biopharmaceutical talent pool and lower costs have made it attractive to biopharmaceutical companies worldwide. As a result, global leading biopharmaceutical companies, including Novo Nordisk, AstraZeneca, Eli Lilly, Roche, GlaxoSmithKline and Pfizer, have all established relationships with Chinese counterparts, or set up their own R&D facilities in China. Many have launched joint-venture operations in partnership with Chinese institutes or companies. The Chinese Government's efforts to expand their domestic biopharmaceutical industry through partnerships and enhancements of intellectual property protection are beginning to pay off.

"China has unparalleled cost advantages compared with developed countries, attracting multinational pharmaceutical companies to offer their outsourcing contracts to China", said Mr Xiaochuan Zhou, Director of China Chamber of Commerce of Medicines & Health Products Imports and Exports. In addition to significantly lower labour costs, "China is also very competitive in raw materials, energy and other auxiliary facilities. The overall production capacity of Chinese pharma manufacturers has increased significantly following the nationwide GMP certification (completed in 2004). This was the result of China's 4,000 pharmaceutical manufacturers investing US\$40 billion to (improve) their facilities."

BIOPHARMACEUTICAL MARKET IN CHINA

China's biopharmaceutical industry began in the 1980s and has experienced a rapid growth over recent decades. The BioPlan/SIM report indicates that China's biopharmaceutical sales revenue in the fiscal year of 2005 achieved US\$3.8 billion, a 30 per cent growth over the previous year, which accounted for 7.5 per cent of the country's total pharmaceutical sales. This growth in the Chinese domestic biopharmaceutical industry has also helped to fuel the development of its services sector.

Today, China has about 400 small-to-medium sized biopharmaceutical companies, which produce more than 2,000 biological products. Although the majority of Chinese biopharmaceutical manufacturers are still producing biogenerics, Chinese research-based biopharmas have recently launched and patented 10 novel recombinant products. These include Recombinant Human Ad-p53 Injection (Shenzhen SiBiono GeneTech), Recombinant Human Adenovirus Type 5 Injection (Shanghai Sunway Biotech), Recombinant Endostatin (Yantai Medgenn), Recombinant Human Brain Natriuretic Peptide (Chengdu Nodikang), and Recombinant Thrombopoietin Injection (Shenyang Sunshine).

FAVOURABLE ENVIRONMENT FOR OUTSOURCING TO CHINA

China's pharmaceutical industrial environment experienced tremendous changes since the late 1990s. One critical milestone was its entry into the World Trade Organization (WTO) in 2001 and the Government's commitment to welcome foreign investment, services and products while enforcing IP protection. This led to a booming of "offshoring" to China. Western pharmas started to establish production and research facilities there in order to take advantage of lower cost, skilled workers and the special tax exempt or deduction policies creating enterprises linked with foreign investment.

Hiring a research professional with a PhD degree obtained in the US in China might cost US\$20,000. This is much lower than in the Western countries. And while the economics are rapidly changing, this cost disparity will remain for at least the next 5-10 years.

The Chinese Government has listed biotechnology high on its national five-year plans since the 1980s and has poured in hundreds of millions of RMB to stimulate the expansion of this sector. China's State Food and Drug Administration (SFDA) continues to amend related policies to stimulate the outsourcing industry in China.

Excess production capacities in China have become a strong driving force for Chinese pharmas to seek contract manufacturing opportunities. The SFDA is also under pressure find a way to keep the 45 per cent of idle facilities running. Hence, China continues to develop favourable policies to attract foreign pharma. Chinese CROs and CMOs are also making efforts to improve their research and production level according to international standards. Currently, 259 products at 130 Chinese manufacturers have obtained cGMP certification from the US FDA and 50 manufacturers have obtained 90 European COS certificates. Among them, 10 finished drug manufacturers have received cGMP certification from the FDA.

Table 2: Supportive Factors for Outsourcing to China

Political	<ul style="list-style-type: none"> Increasing government investment on biotech R&D and training Relaxation of government policies associated with outsourcing Shorter and controlled approval process Growing government commitment to IP protection
Economic	<ul style="list-style-type: none"> Low R&D and production cost Low manpower cost
Technological	<p>R&D</p> <ul style="list-style-type: none"> Large biotech talent pool Plenty biotech research institutes Rich clinical/disease resource Shorter time to complete clinical trials <p>Production</p> <ul style="list-style-type: none"> Improved production facilities after GMP certification High production capacity
Market	<ul style="list-style-type: none"> Large market potential Double-digit growing market Increasing demand for medications

Source: BioPlan Associates, *Advances in Biopharmaceutical Technology in China*, September 2006

CHOOSING AN OUTSOURCING PARTNER IN CHINA

China has upwards of 1,000 domestic biotech and pharmaceutical research institutions and 400 biopharmaceutical manufacturers. These institutions and companies are open to contract research or manufacturing opportunities. In the BioPlan & SIM report, a database has been developed that details biopharmaceutical research institutes and manufacturers in China. This database was developed to help Western companies identify and locate potential outsourcing partners in China.

According to Dr Trent Carrier, Director of Business Development, Invitrogen BioManufacturing Services: “The number of qualified offshore service providers is growing, driven by the growth of Asian consumer markets. Biopharmaceutical developers are beginning to address the capital and technical limitations that have previously slowed the offshoring of biopharmaceutical development and manufacturing. The expansion will continue as more therapeutics companies look for third party service providers. A significant portion of this expansion will occur in new geographical regions.”

Since the 1990s, a growing number of CROs and CMOs have emerged in China to meet the increasing needs for clinical research and manufacturing services. Today, it is home to more than 300 CROs. These companies form an integrated service chain, offering a wide variety of services from the earliest stage of drug discovery and development through to clinical studies, new drug application and post-approval research. Biopharma CROs also provide services including nucleotide sequencing and synthesis, protein expression, chemical custom development and other chemistry-based services, drug screening, clinical

development and so on. Table 3 lists a few major Chinese CROs and their expertise.

CONSIDERATIONS WHEN OUTSOURCING TO CHINA

Despite the opportunities, however, there are still some substantial strategic and operational considerations to be managed.

Intellectual Property

Although the Government keeps IP protection high on its agenda following China’s entry to the WTO, enforcement of IP protection is still thought to be problematic. Some contradictory generic drugs still exist in the Chinese market. While intellectual property protection is improving, most investors remain cautious.

Immature Capital Market

One of the biggest problems for most Chinese biopharmaceutical companies is the lack of financing channels. According to Zero2IPO statistics of venture capital investment in the pharmaceutical industry in 2004, China’s pharmaceutical industry acquired only RMB270 million (US\$34 million) of venture capital. Overseas VCs remain hesitant to invest in the Chinese biopharma market and, according to the BioPlan study, a major concern is that China has not established an effective venture capital withdrawal system.

Management Talent

One of the major issues facing organisations is a limited pool of talented managers. The Chinese Government is addressing these issues by actively recruiting expatriates back to China. Incentives are provided to managers with Western experience and technical capabilities to return to China and lend their support to this growing sector.

Language Barrier

China had a closed-door policy to the outside world for decades prior to 1980s. Chinese people were not encouraged to learn foreign languages. As a result, today many Chinese, especially older generations, do not speak English.

CONCLUSION

China’s current drug market size has exceeded US\$11 billion and is growing at a double-digit rate. Although today, it currently

accounts for less than 2 per cent of the world market, the growth opportunity is large. With the world’s largest population, supportive government policies and rapid economic expansion, the environment for a strong biopharmaceutical outsourcing sector has formed. Chinese CROs and CMOs are preparing to embrace more outsourcing opportunities in the coming years. We have every reason to believe that biopharmaceutical outsourcing industry in China will continue to expand. ♦

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Table 3: CROs in China

CRO	Owner	Location	Service
Wuxi Pharma Tech	Chinese	Shanghai Pudong	Drug R&D
Shanghai Genomics Inc	Chinese	Shanghai Zhangjiang	Drug Gene R&D
Shanghai LeadDiscovery Pharma	Chinese	Shanghai Zhangjiang	Drug R&D
Shanghai Pharma Engine (CRO) Co	Chinese	Shanghai Zhangjiang	Regulatory, Clinical trial
Pharmaron (Beijing) Pharm Tech	Sino-US	Beijing	Organic synthesis, R&D
Excel PharmaStudies Inc.	Chinese	Beijing	Clinical study, regulatory
Guangzhou Pudu Pharma Sci & Tech Dev	Chinese	Guangzhou	Drug R&D
Quintiles Transnational Corp	US	Beijing, Shanghai	Clinical study, regulatory
MDS Pharma Service	US	Beijing	Clinical study
Beijing KendleWit Medical Consulting Co	Sino-US	Beijing	Clinical study, regulatory
Shanghai InCROM Pharma Dev Co	Japan	Shanghai	Clinical study
CCBR	Denmark	Beijing	Clinical study
Bridge Pharmaceuticals	US	Beijing	Animal experiment
VenturePharm CRO Service	Sino-US-Canada	Beijing	Clinical study