



Next Steps Toward Globalization

China's services sector is expanding to meet the needs of its biopharmaceutical industry

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For years, China's domestic biopharmaceutical companies have completed in-house every step in the biopharmaceutical value chain. The domestic industry was not large enough to support a services segment. This situation is changing as China's pharmaceutical services sector expands to meet the emerging needs of the biopharmaceutical industry. As the country's domestic industry grows, it demands higher quality and more cost-effective external services from both home and abroad.

China's domestic companies have broad service needs, compared with the larger multinational organizations there, which typically have greater in-house resources and talent. Most domestic biopharmaceuticals are small-scale companies and are attempting to broaden their R&D-to-production value chain. This requires access to specialized talent.

Creating in-house expertise required for the broad array of services essential for a successful biopharmaceutical company is unrealistic for most Chinese companies (see Table 1). Also, China's services industry is at an early stage and the critical mass of customers required for such new services is not quite there.

REQUIRED EXTERNAL SERVICES

Today, most Chinese biopharmaceutical companies have realized the importance of external services and are looking for those that meet their needs and standards. This issue was discussed in detail with CEOs and senior execu-

tives at five Chinese biopharmaceutical companies: 3S Bio, Inc., Shanghai Sunway Biotech, Beijing Four Rings Biopharma, Beijing Tri-Prime Gene, and Shenzhen Interlong Biotech Co.

Most Chinese biopharmaceuticals are relatively small and there are not enough of them to sustain a robust services sector. According to

Dusheng Cheng, general manager at Beijing Four Rings Biopharma, "Most Chinese biopharmas are small and product distribution is relatively scattered, because most companies have only a few strong-selling products." Cheng says that additional funding would be required to enable companies to complete the entire pharmaceutical process value chain. More importantly, he believes, "Completing the process value chain

[internally] would be a waste of capital, manpower, and material. Some of the time-consuming, investment-demanding processes would become a big burden to companies [if they were brought in-house]." More and more Chinese biopharmaceutical companies are seeking external service providers to help complete the whole process.

Yongqing Cheng, general manager at Beijing Tri-Prime agrees, "Facing harsh competition in the domestic market, Chinese biopharmas certainly wish to invest their limited resources in ways that will allow them to be most competitive. Therefore, they really need external services."

Analytical testing, toxicology, and animal test services are among the services that have a great

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Table 1. Biopharmaceutical services required in China

Analytical Methods, Validation Services	Lyophilization
Analytical methods development	Packaging and labeling-clinical trials
Analytical testing	Packaging and labeling-commercial mfg
Assay development	Peptide synthesis
Bioprocess validation	Pharmacokinetics services
Custom protocols	Process R&D
Endotoxin removal	Process scale up
Endotoxin testing	Purification and filtration
Facility monitoring	Raw materials analysis
Gene therapy protocols	Strain improvement
<i>In vitro</i> testing	Technical services
<i>In vivo</i> testing	Business Services and Training
Lot release testing	Clinical research
Methods validation	Clinical trials management
Mycoplasma testing	CRO consulting services
Non-clinical research	Distribution services-clinical materials
PCR services	Distribution services-general
Process validation	Funding and financial services
Quality assurance services	General business consulting
Quality control services	Legal and patent services
Stability analysis and testing	Logistics analysis
Toxicology services	Nonclinical production
Validation services	Regulatory consulting
Biopharmaceutical Development and Scale up	Training
Biodiagnostic manufacturing	Drug Discovery and Lead Optimization
Biodiagnostic process development	Drug design and discovery
Biologics manufacturing-cGMP production	Drug screening
Biologics manufacturing-clinical	Genomics screening
Biologics manufacturing-preclinical	Pharmacogenomics
Biologics process development	Other Services
Cell culture optimization services	Cleanroom design and containment
Cell line construction and development	Construction and architecture
Chromatography, GC/MS; HPLC; LC; Other	Data management services
Cleaning services	Engineering and design services
DNA sequencing	Environmental monitoring
Downstream processing	Facilities services
Drug delivery	IND/NDA submission services
Electron microscopy services	Information technology services
Fermentation process services	Location and new site development services
Fill finish, sterile liquid	Utilities and waste management service
Formulation	

demand in China today. Four Rings Biopharma's Cheng believes that these services are critical because, "Chinese biopharmas find these assays are more strictly evaluated

by the State Food and Drug Administration (SFDA)."

Dr. Jing Lou, CEO of 3S Bio, Inc., notes that his company has already contracted out analytical testing

few companies.

Dr. HongLi Liu, MD, president assistant, at Shanghai Sunway Biotech Co., Ltd., also believes that despite a relatively rapid growth in

such as carbohydrate structure analysis of glycoproteins from mammalian cell-expressed process. Dr. Lou believes that such external services can help ensure *in vivo* activity in certain glycoproteins such as erythropoietin (EPO) and thrombopoietin (TPO).

Other services in demand include clinical research services, technology transfer, and cell line construction and development. According to Dusheng Cheng, though, "The companies providing these services are still early stage and large-scale professional service companies are not available." Moreover, quality management, training, and drug distribution services (contract sales) are sparse in China. Services that may be required in the near future, but are not in high demand yet, include contract manufacturing, formulation, and stability studies, which today are needed at relatively

the industry, “the expansion of China’s biotech industry still relies on the service providers...from Europe and the US to a great extent.” According to Liu, these imported services include technology transfer, capital market, and business marketing services, these are exactly the services that are needed urgently for domestic biopharmas and these are now readily available in Europe and the US. In particular, Liu believes commercial services are necessary as new drug marketing usually needs very strong market positioning. “In China, however, marketing talents are in short supply because only a few novel drugs have been marketed,” he informs.

Dr. Yan Wang, vice general manager, Shenzhen Interlong Biotech Co., Ltd., in Shenzhen also believes that more and more Chinese biopharmaceuticals now require external services and support. She finds that apart from lyophilization and data management services, where China’s biomanufacturers find current services adequate, most other services are needed in China. According to Wang, “In particular, stability study and cell line construction and development services are not available in China yet.” Other services required for addressing bottlenecks include: animal testing, formulation, technology transfer, cell line development, facility design, quality management, and marketing and distribution services.

THE IN-HOUSE SERVICES MODEL

Many biopharmaceuticals in China would like to have more services in-house to help complete their process value chain. However, China’s general ‘manufacturing’ orientation makes it somewhat unique. Beijing Four Ring’s Cheng explains, “Most Chinese biopharmas do their quality control, manufacturing, and marketing in-house

Table 2. Some biopharmaceutical nonclinical service providers in China

Service Provider	Ownership	Services
Wuxi PharmaTech	Private	Pharmaceutical R&D full services
Shanghai Genomics, Inc.	Private	Antibody production, protein expression, gene cloning, etc.
Bridge Pharmaceutical	Sino-US	Animal testing, formulation, and preparation
National Center for Safety Evaluation of Drugs	State-owned	Toxicological tests and preclinical drug safety evaluation
Beijing Joinn Pharmaceutical Center	Private	New drug safety assessment
Shanghai LeadDiscovery Pharma	Private	New drug R&D
Beijing Union-Genius PharmaTech, Ltd.	Private	New drug safety evaluation
Shanghai Medicilon, Inc.	Sino-US	Integrated Drug R&D
GeneMay, Inc.	Sino-US	Antibody custom services
Haxinpharm Co., Ltd.	Private	Drug R&D, preclinical studies, marketing service
AbMax Biotechnology Co., Ltd.	Private	Custom MAb service, protein expression, gene synthesis, etc.
Synergy PharmaTech	Sino-US	Toxicology test, disease model, DMPK, bioanalytical, formulations, etc.

today because these are production-based enterprises. Except for some government-supported companies, most lack R&D capabilities and thus expect to shorten the production-to-marketing period.”

Another reason some Chinese biopharmaceuticals would like to move more services in-house, according to Beijing Tri-Prime’s general manager Cheng, is the quality of services currently available, “The market has not been able to provide qualified services with a good performance–price ratio,” he says.

Many biopharmaceuticals in China strongly prefer to keep their R&D work in-house, including pilot experiments and stability studies, due to intellectual property (IP) sensitivity. Wang believes that “Chinese biopharmas are basically not willing to communicate and collaborate with outsiders, [out of concern for IP and trade secrets] this can be seen in some of China’s marketed genetically engineered products. These are mainly based

on prokaryotic and yeast expression because most cell line facilities, systems, and bioreactors must be imported. Hepatitis B vaccines, for example, can be produced from either yeast or CHO cells. In China, cell culture techniques lag behind those in developed countries, and hepatitis B vaccines are based on yeast expression.”

Another reason biopharmaceuticals in China tend to perform more work in-house is financial. Funding needed to outsource to external service providers is often not available. According to Shanghai Sunway’s Dr. Liu, “Due to the [relatively poor] capital markets in China, most work on new drugs including preclinical trials, production, clinical trials, and application must be completed in-house. Early R&D work may be contracted out. However, because domestic service providers are still growing and their professional level and specialization tend to be lower, Chinese biopharmaceuticals prefer to complete key R&D work in-house.”

BOTTLENECKS TO SUCCESS

External services may help bring China rapidly forward by addressing the bottlenecks caused by the current lack of R&D ability, innovation, and solid marketing channels.

Beijing Tri-Prime's Cheng agrees, "New product R&D and new technology platform construction services are key in China today. Other services of interest include data management and CRO services."

On the other hand, the big bottlenecks to the success of biopharmaceuticals in China, according to Wang, do not relate to the availability of outside service. These involve "the development of domestic innovative technologies with strong IP rights and a promising market perspective." Chinese companies prefer to avoid using external services at early stages because confidential technologies may be involved.

For the research-based innovative Chinese biopharmaceutical companies, such as 3S Bio and Shanghai Sunway, lack of effective capital support service poses a major challenge, because large investments are required to develop novel biopharmaceuticals. Shanghai Sunway's Dr. Liu says that the biggest obstacle is lack of funding due to limited venture capital (VC) services in China, "Domestic companies are able to complete new biopharmaceutical R&D...However, for small biotechs, insufficient VC support at early R&D stages, and a lack of link-up and transfer channels between VC's and long-term investors has placed hurdles in front of domestic biotech development. For larger companies, tech transfer is the key [bottleneck] that inhibits development."

Dr. Lou of 3S Bio points out, "China certainly has a lot of money, but not for biopharmaceu-

External services in demand in China include analytical testing, toxicology, animal test services, clinical research services, technology transfer, and cell line construction and development.

tical and biotech research companies, which can't price their quality products at a reasonable level [due to price controls]. Therefore, additional management services may be required."

EVOLVING SERVICES MODEL

Today, there is a limited, but growing number of service providers in China. Services in China began with contract research organization (CRO) services and low-risk discovery chemistry (lead optimization that might lead to claims on IP were typically done in the US or EU).

Early entrants, such as WuXi PharmaTech, have grown, and this has led to many new entrants into the services sector. Several of these companies are managed by 'returnees.' These additional services include animal pharmacology, good laboratory practice (GLP) toxicology services, and various lead optimization service providers. However, these new entrants may not be achieving the level of quality expected from a major international market participant.

GLP is a relatively new concept in China. It was only in January 2007 that all new drug safety evaluations were required to be conducted in GLP-accredited laboratories. To date, only 23 laboratories in China have been granted GLP certifications by the SFDA. These organizations are a part of state-owned organizations.

Their levels of service differ in scope and technical competence. Efforts are on to bring facilities to GLP standards. However, currently, few laboratories have passed the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) standards. These include Nanjing Laboratory-Next Century, Inc., National Research Center for New Drug Safety Evaluation (Shenyang), and AbMax Biotechnology Co., Ltd.

Also, there are no board-certified slide-reading pathologists in China. Many service providers also have limited real-world experience. For example, a US CRO might start 150 studies per month, whereas its Chinese GLP preclinical counterpart may be conducting 50 per year. There are also historical holdups. Many Chinese GLP facilities have experience in traditional chinese medicine (TCM) but have limited experience with new chemical entities (NCEs) or new biological entities (NBEs).

External service suppliers can offer a more efficient use of scarce resources and talent, which China's biopharmaceutical industry currently lacks. The availability of quality services can optimize the use of these resources, and may help speed China's industrial development. ♦