

products from the Traditional Chinese Medicines (TCMs) spread out all over the country. Rare chemicals that cannot be sourced elsewhere may be available in China. And because of low labor costs, many chemicals and biological agents that cannot be profitably manufactured in other countries may be available in China at reasonable prices. This service feature has been extensively explored in the past by many major pharma/biotech companies. There are currently more than 30 such service providers in China that possess focused compound libraries of various sizes.

Beside these focused compound libraries, the services provided by Chinese companies also cover all areas of early stage drug discovery. For example, there are more than 20 companies that provide services related to target identification and validation such as DNA sequencing, elucidation of protein structures, reconstruction of proteins, preparation of recombinant proteins and disease modeling. In addition, there are more than 40 CROs providing services in medicinal chemistry related research such as lead discovery and optimization; assay and assay method development and pharmacological property studies such as the determination and optimization of Pharmacokinetics and Pharmacodynamics (PK/PD). Many of them also possess advanced techniques and experience in areas such as high-throughput screening, computer-aided drug discovery (CADD) and structure-activity-relationship (SAR) studies.

At present there is a group of about 37 China-based companies that provide services in preclinical research including *in vivo* efficacy testing, *in vivo/in vitro* Absorption, Distribution, Metabolism, and Excretion (ADME) screening, plasma protein binding studies, metabolite profiling and an entire scope of toxicity studies. More than 30 of them have received the AAALCA certification. However, the good quality service in this sector was not available until recently. The rapid change of landscape in this area is largely attributed to the entrance of experienced multinational CROs - all lured by the abundant animal species in a favorable regulatory environment as well as readily available manpower resources at low cost. Several CROs currently offering services in China are actually the service divisions, branches or subsidiaries of CROs based overseas. Examples include Bridge Laboratories and Crown Biosciences. The headquarters of these CROs are based in the Western countries (mostly in the US), but the bulk or all of their services are performed in China. In addition, several multinational CROs have formed joint ventures or partnerships with Chinese CROs and some have ended up with acquiring their Chinese partner. For example, Charles River Laboratories has acquired BioExplorer while MPI Research has formed a joint venture with Medicilon.

Contract clinical research has been conducted in China for more than a decade. In addition to a vast pool of treatment-naive patients, the nation also has specialized hospitals that possess medical facilities, specialists and knowledge in specialty areas such as cancer. The majority of these medical personnel and other medical resources are located in major Chinese cities. Drug companies have also realized that China has a pool of well-trained hospital physicians, thanks to the training provided by many Western companies including multinational CROs and major pharma companies. For

example, Astra-Zeneca has established a training center at Number Three Hospital of Beijing University to train physicians for clinical trials.

So far, most of the clinical trials conducted in China have been performed by major pharma companies or multinational CROs. Almost all multinational CROs including Quintiles, MDS, PPD and Covance have clinical trial centers in China. Pharmaceutical companies including Astra-Zeneca, Pfizer, GSK and Sanofi-Aventis also run clinical research centers there. An increasing number of locally-founded contract clinical research organizations have also emerged. At present, there are a total of 47 such CROs in China.

Among the various service sectors of the Chinese pharma outsourcing industry, process R&D and contract manufacturing of Active Pharmaceutical Ingredients (API) for developmental drugs are the most active. There are about 60 professional service providers in this sector. The majority of them also possess strong capabilities in process research and development with decent-sized process R&D teams as well as advanced pilot plants for step-by-step process scaling up. Their facilities are also generally supported by an internal Quality Control/Quality Assurance (QC/QA) laboratory equipped with advanced analytical instruments such as High Performance Liquid Chromatography (HPLC) with both regular and chiral columns, GC, LCMS, etc. The majority of them have production capacities that range from multi-kilograms to low-end metric tons (with reactor volumes ranging from 50L to 3,000L), and are able to handle a variety of chemical transformations. Technologies for certain special chemistry tasks such as large scale chiral resolution are also available.

3.2.2 Overall service capability of Indian pharma outsourcing industry

In the past ten years Indian pharma outsourcing industry has been growing in about 40% annually. Before 2002 there were only about 40 outsourcing service providers. The booming period of Indian pharma outsourcing industry was from 2002 to 2005. For example, at the end of 2005 there had been more than 200 CROs and CMOs in India. It is estimated that at present India has about 350 – 400 CROs/CMOs (including CRAMS organizations) in total.

Many Indian CROs are also young but growing fast. This is very similar to Chinese CROs. For example, Advinus Therapeutics was founded in 2005, but currently already has close to 350 scientists in multiple locations. It has collaborated with several major pharma companies including Merck. It also possesses internal drug R&D programs;

Most Indian CROs in drug discovery sector possess sophisticated capabilities in rational drug design and activity optimization. Unlike many of their Chinese counterparts whose primary focuses at present are still custom synthesis with less involvement in potency optimizations that are closely associated with biological activity testing, more

Indian CROs are able to help client companies optimize potency and pharmacological properties using the techniques such as the structure-activities-relationship (SAR) studies. Their daily work involves more biology than their Chinese counterparts.

However, there are limited numbers of Indian CROs that are able to conduct target identification/validation as well as sophisticated molecular biology research. Although the CRO industry started in India earlier than in China, the services in this area were not available until recently. For example, the earliest preclinical research service available in India was in 2003 and offered by Aurigene. Non-human clinical trial capability and facilities in Indian companies are much weaker and limited than in Chinese companies. At present there are only eight AAALCA-certified GLP facilities in India.

On the other hand, the service capabilities of Indian companies in clinical research are better than Chinese companies. For example, in the first quarter of 2008 alone there were a total of 139 applications received by Indian healthcare authority; whereas only 98 were approved in China during the same time period.

Currently, there are about 100 CROs in India's clinical research service sector with 757 certified clinical trial sites. India currently has about 50 institutes that offer clinical research programs to graduate students. Each year these institutes produce about 5,000 students to the industry. At present there are about 1,000 GLP certified clinical investigators all over the country.

MNCROs such as Quintiles, Covance, PPD, Parexel, ICON, Omnicare, Clintec, etc. all have subsidiaries in India. Among them, Quintiles was the first MNCRO that started clinical trial service in India in 1997. It has so far conducted more than 230 clinical trials in the country and currently has close to 1,000 employees throughout India (many of them are in data management and drug safety monitoring).

Major pharma companies that have had clinical trials in India include GSK, Johnson & Johnson, Eli Lilly, BMS, Pfizer, Sanofi-Aventis, Astra-Zeneca, Novartis, Merck, Roche (in a declining trend with GSK having conducted most clinical trials in India among all major MNCs). Many drug applications approved in the US and EU contain significant data achieved in India.

Most major Indian pharma companies have had more than ten years experience in API and formulated drug manufacturing and marketing in the regulated markets. Some of them such as Dr. Reddy's Lab and Ranbaxy have close to fifteen years experience in the Western markets. Their formulation strengths are in oil solid, liquids, injectables, which are considered complex to manufacture.

3.3 Head-to-head comparison of top 50 best outsourcing service providers in each country

3.3.1 Selection of top 50 best service providers in each country

To effectively compare these two countries and gain the objective results of which country is better in what area(s), we choose, from a large pool of pharmaceutical and biotech companies as well as professional outsourcing service providers, the top and the best fifty (50) companies in each country that are involved in outsourcing service. By comparing head-to-head the pharma outsourcing industry in these two countries in more than twenty areas including company size (both staff team and service revenue), industry distribution (numbers of pharma companies, biotech companies, CROs, CMOs, and even generic drug makers in each country), service capabilities, etc. we believe that the results from the comparison will tell the whole story of which country is better in what technical and service areas.

We believe that selecting the top 50 best service providers in each country as the basis of our comparison is appropriate as the size is not too big so that it is impossible to make the head-to-head comparison but it is still not too small that may make the comparison results inaccurate. Each country has more than 5,000 pharma and biotech companies (India has even more than 23,000 pharma-related companies but only about 1% of them are recognized as medium- to large-sized players). In addition to the large number of professional CROs and CMOs in each country, many pharma and biotech companies are also involved in outsourcing services. It is impossible to compare all of them. Also, majority of those small service providers play little roles in the industry. Many young companies (It is the feature at the present time in both countries!) also contribute little to the overall market size and development of the industry in each country. It is only those major and the best companies that represent the main stream of each industry sector and play key roles in it.

We therefore decide to choose only 50 companies that are either the largest or the best players in each country as the company pool for our comparison.

3.3.2 Criteria for selection of top 50 best service providers in each country

1. Selection criteria

The selected companies must have following characteristics:

- 1) Be publicly recognized as major players in their home country;