



## China: Assessing the Need for Outsourcing

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China offers significant cost advantages to companies that are looking to outsource their R&D activities

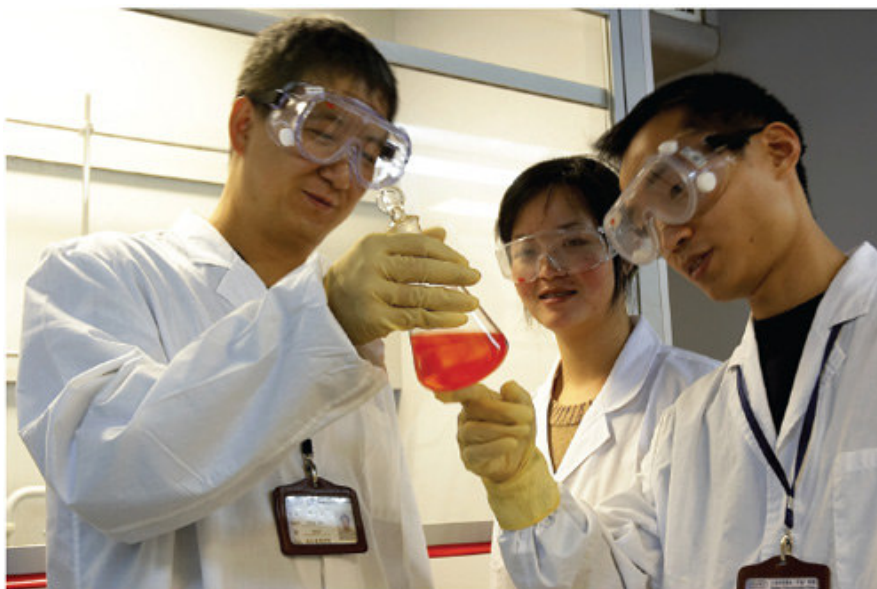
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The pharmaceutical and biotechnology industries have not been immune to the current financial crisis. It appears that the sector which is the hardest hit is the biotechnology R&D sector - in particular smaller drug companies that are in early stage drug discovery and/or development.

Since November 2008, more than 45 biotech companies have announced reductions in their workforce. The percentage of job cuts within these companies range from five percent to as high as 93 percent. Many have also announced the reprioritization of their R&D programs with more focusing only on late stage development. Several have completely terminated early stage programs including those still in discovery and preclinical research. Others are planning to close their R&D facilities or put their programs on hold.

However, it appears that most of the major pharmaceutical and biotech companies have not been affected by the crisis, probably because of their strong cash reserves. To some extent, many of them could benefit from it as they are poised to acquire more drug candidates which are in the advanced development stages, from the smaller biotech companies that are in financial trouble.



Outsourcing to China can help a company achieve a cost saving of at least 60 to 70 percent.  
(Source: JZMed)

## **Financial Considerations**

The present financial crisis has created a dilemma for R&D oriented drug companies. On the one hand, the nature of drug research and development requires these companies to have abundant cash reserves, which in the past was generally realized through rounds of fund raising.

On the other hand, the crisis has directly resulted in a funding shortage as many Venture Capitalists (VC) or investment institutions have either lost a large chunk of their investment elsewhere or have become stuck with their current investments. This has put them in a less advantageous position to take up other investments. VCs that still have cash in hand tend to be wary as it is unlikely for biotech companies to go public in the near future, given the overall financial situation. The overall climate has been reflected in the reportedly lowest number of biotech Initial Public Offerings (IPO) in 2008, in a year-by-year comparison for the period 2004 - 2008.

Small biotech companies that do not have strong financial resources, have to think about how they can survive the financial crisis as many VCs are cutting back on investment activities. Many in the industry believe that there are two options for these cash-strapped biotech companies to consider at this moment:

- 1) Selling their drug candidates or even the entire company at a significant discount.
- 2) Outsourcing R&D projects to low cost areas such as China, so that they can still continue their programs even with a limited cash reserve.

The first option works for companies that have developed a series of lead compounds. Some of them would have entered the development stages for drugs that are already demonstrated promising results. The situation is more challenging for those that are still in the discovery stage or early preclinical development stage, as some VCs who have invested in startups or early stage biotech companies are currently selling their stakes at a discount of 10- 60 percent of the original investment price. For such companies, the second option could be the better choice.

## **Outsourcing Overseas**

The offshore outsourcing of drug R&D programs to developing countries including China, has not been popular with many biotech companies. However, the abrupt change in the financial and investment environment may be a compelling factor for a shift in mindset. These regions offer significant cost savings, allowing such companies to continue their R&D programs even with limited cash reserves.

At present for example, outsourcing to China can help a company achieve a cost saving of at least 60 to 70 percent. For contract research projects in the lead discovery/optimization area, the current average Full- Time-Equivalent (FTE) rate in most Chinese Clinical Research Organizations (CRO) for a scientist located in Shanghai or Beijing is about US\$85,000- US\$100,000 per annum. In comparison, a scientist in a similar capacity in the US would cost about US\$260,000.

China also has abundant animal species such as rodents, rats, dogs, monkeys and other non-human primates - available at low cost. For example, a monkey in China only costs about US\$700-800. For preclinical testing, a two-month animal trial in primates costs about US\$25,000- US\$30,000.

Companies may also be able to achieve higher levels of productivity by outsourcing to China. They can take advantage of the 13-hour time difference and run their projects 24 hours a day. For example, their internal staff can design and revise the instructions of the project and then forward these to the Chinese service provider, whose scientists can conduct experimental investigations while the US site has closed for the night. Due to rapid development for over nearly a decade, there are currently a large number of service providers in China to choose from. This outsourcing environment provides flexibility to companies who require these services. For example, companies can begin the business relationship with a short term contract with a selected service provider. The initial size of the project can also be kept small. The scope of the projects can then be extended and expanded at a later time, if the outsourcing company feels comfortable with their Chinese partners.

### **Service Capabilities of China's Outsourcing Industry**

At present, the Chinese outsourcing industry is composed of about 250 professional service providers with various service capacities and capabilities. Although none of them are likely to be able to provide a fully integrated service yet, the industry as a whole can offer various types of services covering the entire value chain from drug discovery and development to manufacturing.

Beside this, there are about 50 multinational service providers that have service facilities in China. The entrance of these Multinational Organizations (MNO) has raised the service quality and capability of this industry segment. In addition, growing numbers of traditional Chinese pharmaceutical and R&D-oriented biotech companies are also joining the service community as "part-time" service providers, as they are being approached by a growing number of overseas drug companies.

#### **• Early Stage Drug Discovery**

China is one of the hot spots for pharma/biotech companies that are looking for compound libraries which possess the structural features of drug-like molecules. The country has a huge pool of skilled synthetic organic chemists and biochemists.

Companies specializing in the synthesis of specialty chemicals, scaffolds and building blocks as well as isolation and purification of natural products from the Traditional Chinese Medicines (TCMs) are spread out throughout the country. Rare chemicals that cannot be sourced elsewhere may be available in China. And because of low labor costs and less stringent environment protection measures, many chemicals and biological agents that cannot be profitably manufactured in other countries may be available in China at reasonable prices.

This service has been explored in the past by many major pharma/biotech companies. There are currently more than 30 such service providers that possess focused compound libraries of various sizes.

Besides these focused compound libraries, Chinese service providers 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.

#### • **Preclinical Research**

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. However, the quality of 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. For example, 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 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 and some have ended up acquiring their Chinese partner. For example, Charles River Laboratories has formed a joint venture with BioExplorer while MPI Research has formed a similar relationship with Medicilon.

#### • **Clinical Research**

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.

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. The majority of these medical personnel and other medical resources are located in major Chinese cities. 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 there. Pharmaceutical companies including Astra-Zeneca, Pfizer, GSK and Sanofi-Aventis also run clinical research centers. 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.

#### • **Process R&D**

Among the various service sectors in the Chinese pharmaceuticals 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 up-scaling.

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.

### **Geographic Distribution of Service Providers**

At present, China-based service providers are densely located in Shanghai and Beijing. These two cities (including their vicinities) house more than 90 percent of China's professional service providers. Shanghai has more CROs/ Contract Manufacturing Organizations (CMO) in chemistry-related services such as drug discovery research and contract manufacturing, whereas Beijing is more popular with CROs that provide biology related services such as preclinical and clinical research.



The issue of Intellectual Property (IP) protection has been the major concern to companies that are considering outsourcing to China. While the situation has been improved in recent years, companies may still need to address the following issues:

- Appropriately assess the projects to be outsourced: As rule of thumb, projects to be outsourced should be appropriately classified to determine their IP risk tolerance level. Based on this assessment, outsourcing companies can then decide on the activities that should be outsourced and which service provider to select.
- Identify the right service provider: When selecting a service provider, both the technical skills and service quality/reputation of an interesting vendor must be considered. However, larger CROs/CMOs may not necessarily be better than the smaller ones. It is advisable to obtain references from other companies that have previously engaged in outsourcing activities in China.
- Effectively manage outsourced projects: Once the outsourced project has started, it is critical for outsourcing companies to appropriately manage the outsourced projects, including developing a healthy relationship with the Chinese service provider.