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biotech focus

China's unique position in discovery and preclinical research

Roman Boutellier and Fredrik Ullman, fullman@ethz.ch

When considering China as a sourcing market from an outside perspective, it is difficult to get an idea of Chinese company variation regarding competence and quality; it all looks homogeneous. However, some US and European companies are more successful with their 'China strategy' outsourcing, offshoring or joint ventures (JVs) than others are. To better-understand this variation we tried to determine differences between possible collaboration partners. To do so, we interviewed personnel from 20 different companies that all perform research in Shanghai. Offshoring and JVs with Chinese companies were included in the survey. We noticed important inter-company differences that should be considered when doing research in China.

Four different business models for cooperation strategies

When conducting our interviews, we wanted to identify each company's strategic scope and organizational embedding. This information is relevant for the selection of a collaboration partner. By analyzing these two dimensions, we identified four different business models (Figure 1).

The first business model, the governmental laboratory, is managed by professors, and is fully dependent on the local Chinese university that the professors belong to. These laboratories serve as centres for technology-transfer, from academia to industry, and as a means to finance public research through contract research. Their

major goal is to produce publications and patents.

As a second group, we identified a hybrid business model used by companies financing their in-house research (i.e. first focus) with contract research organization (CRO) activities (i.e. second focus). These companies are focused on one specific core capability and, because they are not exclusively investing their profit into the expansion of their services but invest into their own research pipeline, they are characterized by slower growth than pure CROs, and their vision is to sell their own drug to the Chinese or world market.

The third business model identified is the pure CRO, focusing exclusively on specific services. Finally, the fourth business model identified is the offshored or JV model used by big pharma companies that have located part of their research capabilities in China.

There are >300 R&D CROs in China today, including hybrids, governmental laboratories and dedicated CROs. Most of them are active in clinical development and not in research. The number of offshored pharma and JVs in research is still low, but is growing fast. Our sample of companies (i.e. n = 20) represents all of these groups (i.e. 15% governmental laboratories, 30% hybrids, 25% CROs and 30% offshored pharma and JVs).

Governmental laboratories

The paradigm that short-term return on investment (ROI) is expected not only from private

research but also from public academic research is even more important in China than in western countries [1].

Consequently, academic institutions in China are often split into two units. One unit purely performs academic research and the commercial unit (e.g. the governmental laboratory), which is often located in a science park such as Zhang Jiang Hi-Tech park in Shanghai (Figure 2), facilitates technology transfer to industry.

The performance of these companies is measured by the number of publications and patents filed, and not by their profits. The managerial style is, therefore, more reminiscent of academic institutions than of process-driven companies. The work is performed by students and supervised by professors. Thus, it enables western companies to source high-quality scientific results at low cost – because these institutions are well-established research organizations with good track records. Furthermore, the intellectual property (IP) risk is low because they are non-profit-making organizations. Depending on the focus of research, these companies are used as partners for target identification based on genomic and proteomic technologies. If their research focus is in chemistry they are used to source new compounds as an alternative to combinatorial chemistry, literature or computer-aided drug design. For example, the Shanghai Institute of Materia Medica (SIMM) purifies secondary metabolites from plant extracts known in traditional Chinese medicine (TCM) to be effective in treating disease. Governmental laboratories are usually paid as a proportion of their output (e.g. number of compounds delivered to the customer), and not according to the number of full-time equivalents (FTEs) allocated to the client. They deliver the best results when the

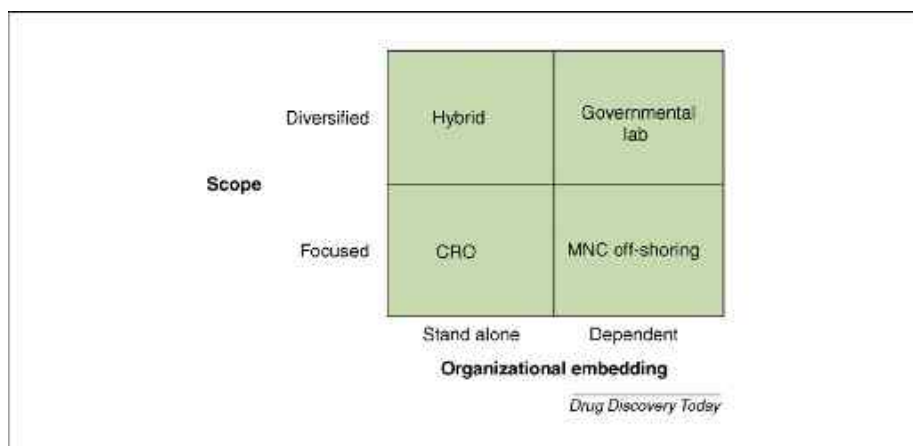


FIGURE 1

Scope and organizational embedding differentiate Chinese outsourcing partners.

work is closely related to the research interest of the professors, but are less-suited for time-critical activities.

Hybrid biotech companies

The business strategy of these companies is initially to supply big pharma with a particular process to generate positive cash-flow (e.g. synthesis of molecule scaffolds, chemical intermediates or cell-based-assay development and design) to finance in-house research. These companies aim to grow naturally through acquisition of core capabilities, ultimately to reach the status of a fully integrated pharmaceutical company incorporating R&D and manufacturing as well as marketing and sales.

The research performed for self purposes by these companies is mainly focused on compounds derived from TCM, the public domain,

discoveries by colleagues in western universities or new formulations of marketed drugs. This represents incremental rather than radical innovation and might, therefore, not be considered as real research (i.e. target identification through lead optimization) by western companies [2].

The standards of the Chinese food and drug administration (SFDA) and the FDA are different in terms of standards on new chemical and biological entities (NCEs and NBEs, respectively). If a substance originates from TCM, the level of compound purity has to be $\geq 50\%$ to satisfy the SFDA, which is much lower than any FDA approval. Consequently, some companies focus exclusively on the Chinese market.

The ultimate goal of these companies seems to be launching their own drug. They are driven by CEOs who returned from US companies or

universities, most of them from the San Francisco Bay area. Not surprisingly, business process standards and management approaches are similar to western companies. However, big pharma is sceptical about interacting with these companies because of potential conflicting goals and IP issues. With a strong need to grow, and often a lack of track records, these companies position their prices for a FTE – including laboratory space and chemicals – between US\$70,000 and US\$100,000, whereas fully dedicated CROs with good track records can charge up to US\$120,000. They are best at carrying out specific processes where IP is not an issue.

Fully dedicated CROs

Fully dedicated CROs are organized and managed like manufacturing sites. Researchers work in three shifts, capacity usage of expensive western technologies dictates the process, and on-time delivery is a major customer requirement. To keep such a system stable, and to respect the deadlines stipulated in contracts, predictability of process output in terms of time and quality is required. Therefore, customers can't expect too much creativity.

Responsiveness to customer needs is certainly a key strength of these companies. For example, it took WuXi Pharmatech six months from the decision to go into delivering analytical services until their first delivery to a customer in the USA. This six-month period included setting up a laboratory, hiring scientists and acquiring the needed technologies and equipment.

Pure CROs have hitherto focused on chemistry and carrying out *in vivo* assays. However, most are building up capabilities in biology, recruiting Chinese researchers from US pharma companies for leading positions. Cooperation with dedicated CROs is best-suited for getting work done quickly and inexpensively if the project matches the company expertise. They are good at repetitive activities.

Offshored big pharma

These companies are mainly companies associated with pharmaceutical firms either as a daughter company or a JV – performing research in China. This group is represented by a small sample because only few companies perform in-house preclinical research in China today [2]. However, this is changing because big pharma such as Roche, AstraZeneca, Pfizer, Novartis, Eli Lilly and Novo Nordisk are all investing in R&D in China today. Some have already established their own research facilities, often starting with focused activities.



FIGURE 2

Zhang Jiang Hi-Tech Park.

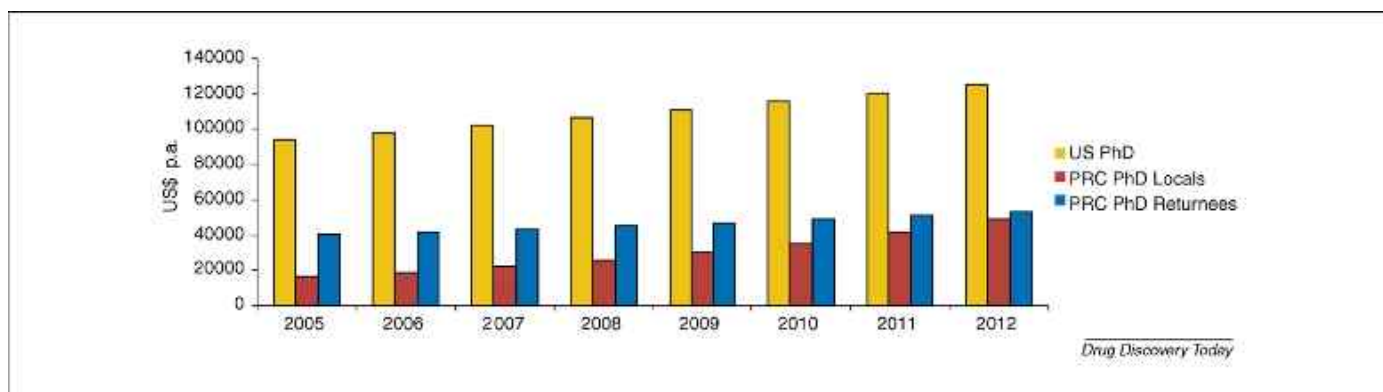


FIGURE 3

Estimated US and PRC wages of PhD chemists 2005–2012 [7]. Wages are given in US\$ per annum (p.a.).

Drivers of offshore research towards China are threefold: (i) a strong need to understand Chinese patients' genetic profiles to develop new therapies for China; (ii) a large naïve patient population suitable for clinical trials; and (iii) a large number of western-educated talented scientists who have returned to China [3].

In 2010 China should be the fifth-largest market for pharmaceuticals; and the third-largest market in 2020. Long-term commitment and building up trust is important in Chinese culture. Hence, if a company wants to gain a significant market share it will have to show commitment to the location (i.e. China) by creating job opportunities.

Lack of commitment from employees makes retention of good researchers difficult, which is a major challenge to expect when offshoring to China.

Cost of offshoring

To date, low costs have been the main driver towards manufacturing in China for many industries (e.g. the automotive industry). This is also partly true for science, however this is gradually changing. We compared the yearly wages of Chinese PhD chemists trained in China, Chinese PhD chemists trained in the West but working in China (i.e. returnees) and US PhD chemists working in the USA. In 2005, the average salary of a Chinese chemist was US\$10,000 and the average US chemist's salary was US\$94,000, whereas the returnee's average

salary was US\$40,000. Some years ago, however, the Chinese government lured back native Chinese from the USA with salaries up to 200% of those in the USA.

At present, the locally educated chemist's salary is rising between 15% and 20% per year, whereas US and returnee chemist's wages are rising less than 5%. If this growth was to persist, the gap between locals and returnees would be closed within six years (Figure 3). At the same time, many Chinese scientists return to China because of improving living standards in Chinese centres.

Because it will remain an advantage to have western education [4], we expect returnee wages to rise faster in the future, reducing the gap with US chemists. This should bring even more Chinese scientists home [4,5], and make cost savings as a driver to offshore preclinical research to China irrelevant within the next five years.

Concluding remarks

Preclinical CROs in China are focused on the generation of data [6] by carrying out assays or by synthesizing chemical intermediates. This is somewhat different from western CROs, which often sell expertise such as the analysis of data. However, there is not just one type of CRO in China: there are four generic types. Therefore, when seeking outsourcing opportunities, it is important to know exactly what process is to be

outsourced and to perform an in-depth analysis of potential partners. Note that it is not obvious which group a company belongs to based on its name or description of its activity. The major differences identified in this study reside in the management of efficiency, cost, goal congruence with the customer, the domain of expertise, the nature of the contract and the risk for IP issues (Table 1).

If the outsourced process is in early-phase discovery it is reasonable to seek a partnership with a governmental laboratory; whereas, if the requirement is *in vivo* assays, synthetic chemistry or biology the appropriate partner would be a pure CRO.

Dedicated CROs and governmental laboratories are commercially more successful than hybrids for three reasons:

- Profit is reinvested in expanding services for customers and no resources are allocated to their own pipeline.
- Emphasis is put on high efficiency.
- There are no conflicting goals, increasing the level of control needed.

Offshoring research to China is a major, long-term strategic investment. The main drivers are a large population of naïve patients for clinical trials, the great affluence of western-educated scientists and a fast-growing large market that can afford western medicine. Offshoring to China certainly builds up trust and mutual understanding, but a careful choice has

TABLE 1

Different laboratories have different strengths

	Efficiency	Cost	Goal congruence	Domain of expertise	Payment	IP risk
Governmental lab	–	++	++	Early discovery	Per compound or target	Low
Hybrid	+	+	--	Synthesis of intermediates for library generation	Per FTE	Medium–high
CRO	++	+	++	Broad skill base	Per FTE or fee for service	Medium–low
Offshore and/or JV	++	--	++	Focused activities	Internal transaction	Low

to be made when cooperating with CROs, governmental laboratories, hybrids or managing daughter companies in China.

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Roman Boutellier,
Fredrik Ullman
Technology and Innovation Management,
Kreuzplatz 5, ETH KPL, KPL H 7,
CH-8032 Zurich, Switzerland

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