



## The Future of Biotech in China

### Will China Overcome Its Barriers?

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**R**ecent trends in the pharmaceutical industry show an increase in the development and manufacturing of biological products. Although biopharmaceutical manufacturing has been greatly facilitated by the development of new technologies, difficulties persist in regulating biological products manufactured in different facilities, particularly ones at a great distance from the sponsor's "home office." However, because biopharmaceuticals are very costly to develop, many Western companies are increasingly considering transferring manufacturing to developing countries that offer lower production costs. Furthermore, as non-Western countries gain experience in biopharmaceutical research and development, biopharmaceutical manufacturing, and testing of biotech products, they have notably increased their offshoring activities.

At the same time, some Asian countries, particularly China and India, have exhibited substantial growth in biopharmaceutical manufacturing. In addition to significantly reduced production costs in these countries, their experience in manufacturing generics, evolving regulatory environments, and recent government focus on the industry are all contributing factors. As regulatory issues in China evolve, and because Chinese employee wages are reportedly less than those for equally qualified Indian employees, China is expected to overtake India's current position as a leader in biopharmaceutical offshoring by 2015.<sup>1</sup> Currently, China is responsible for 60% and 65% of the world's annual production of penicillin and terramycin, respectively.<sup>2</sup> In addition to biopharmaceutical manufacturing, China is expanding its research and development and testing facilities.

Although China is one of the most prominent countries in biopharmaceutical offshoring, and is predicted to play an even greater role over the next couple of decades, recent manufacturing problems, including quality control, contamination, corruption, and counterfeiting, have dampened China's reputation. In an attempt to control the escalating situation, the Chinese government in 2007 sentenced China's former director of State Food and Drug Administration (SFDA), Zheng Xiaoyu, to death for accepting bribes in exchange for approval of untested drugs.<sup>3</sup> Although this helped to restore some confidence in Chinese products, China's manufacturing problems have not been entirely resolved. China's biotech expansion continues, however, fueled by the Chinese government's efforts to establish a strong economy based on high-tech indus-

try and by sponsors' reactions to the high cost of drug development in the West.

## China's Biotech History

China has a history of sound scientific research. Deng Xiaoping, leader of the communist party from 1978 to 1990, was primarily responsible for economic reform policies that helped restore China's science and technology sectors. Between 1997 and 2002, the number of biotech companies increased exponentially, largely due to China's work in two areas: the global Human Genome Project (HGP) and the sequencing of the rice genome. The goal of the global HGP was to sequence 1,000 human genomes worldwide, a portion of which was completed in China.<sup>4</sup> Having gained experience from the HGP, China moved on to become the first to map the rice genome. Together, these projects accounted for the most significant scientific research activity since the Chinese Cultural Revolution, with large genome research centers opening in Beijing and Shanghai and an influx of expatriates with biotech experience returning to work in China.

More recently, in response to an increasing worldwide demand for more affordable prescription medications, there has been significant growth in China's biogenerics production. Biogenerics in China currently account for 95% of biologics manufacturing, and include products such as the interferon series, erythropoietin, colony-stimulating factor series, tumor necrosis factor, insulin, growth hormone, and interleukin-2.<sup>5</sup> Although most biogenerics have been developed in Western countries, such as the United States, this is gradually changing as China increases its research and development capabilities.

Between 2001 and 2005, the Chinese government made substantial investments in the biotech industry, shifting to include innovation, rather than focus solely on manufacturing foreign products. The development and pro-

duction of the new cholera vaccine tablet, one of the world's first approved gene therapy products (a technique for correcting defective genes responsible for disease development), reflects China's emerging role in biotech research and development.<sup>6</sup>

Currently, China produces eight of the world's top 10 genetically engineered therapeutics and vaccines.<sup>7</sup> Among the most commonly manufactured Chinese biopharmaceuticals are protein therapeutics, gene therapy products, vaccines, antibodies, blood products, and diagnostic agents. In addition, many multinational biotech companies have started to work with Chinese biological-service providers because of the expertise and lower labor costs that they offer.

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## The Offshoring Challenges

China offers several advantages in biopharmaceutical offshoring; however, many Western companies maintain that the risks outweigh the benefits. Advantages include a highly skilled workforce of returning scientists as well as Chinese-educated scientists, ultra-modern facilities, substantial government investment in the biotech sector, and significantly reduced labor and manufacturing costs. The most common concerns include inadequate intellectual property (IP) protection laws, regulatory issues, and language and cultural barriers. IP protection laws are still evolving, especially fol-

lowing China's entrance into the global market. Although regulatory legislation has improved significantly, issues such as quality control have not been entirely resolved. Technology and infrastructure are inconsistent throughout China, and only major cities such as Beijing and Shanghai provide adequate facilities.

In addition, the logistics of transferring biologics manufacturing to China, in contrast with conventional pharmaceuticals, are a hurdle. Moreover, language and cultural differences continue to pose significant barriers with the West, despite recent implementation of English-language programs and the influx of many Western-educated, Chinese-born scientists. Thus, despite the advantages of offshoring in China and the potential of the Chinese biotech industry, significant barriers remain.

## IP Protection Laws

China's biopharmaceutical product patent laws are fairly recent, having been established in 1993. After China's entry into the World Trade Organization (WTO) in 2001, the Chinese government made great efforts to improve IP protection and harmonize China's patent system with that of other WTO member countries. However, progress has been slow due to various factors, including serious problems with piracy and counterfeiting. China's internal corruption, limited resources, and lack of public awareness concerning the impact of counterfeiting and piracy have been identified as major barriers.<sup>8</sup>

As new precedents are set in Chinese courts favoring foreign patents, greater confidence in China's IP system will evolve. Already, examples of positive outcomes for foreign investors have begun to set positive precedents. For example, in 2006, Pfizer won its Viagra patent case.<sup>9</sup> As more Chinese companies go to court to protect their IP rights, the Chinese business environment is also improving at the domestic level.

IP protection laws are continually evolving, and significant government support of China's biotech industry over the last 10 years has facilitated greater foreign investment.<sup>10</sup> Many foreign biopharmaceutical companies with independent patents are increasingly considering offshoring in this newly emerging Chinese market. However, weak regulations, lack of sufficient precedents, and poor enforcement continue to pose barriers. As a result, successful IP protection in China must include both offensive and defensive elements.<sup>11</sup>

## Regulatory Environment

Chinese regulatory legislation is also gradually evolving. As part of a Cabinet-restructuring plan to better monitor the country's food and drug safety, China's SFDA was recently put under the aegis of the Ministry of Health.<sup>12</sup> Although the regulatory environment has improved significantly over the past decade, issues of quality control continue to ail the Chinese manufacturing industry. There are several examples of recently recalled Chinese products, including the well-publicized cases of contaminated children's toys, pet food, toothpaste, and baby formula. Furthermore, a recent U.S. Food and Drug Administration (FDA) investigation into the cause of several deaths in the United States from Chinese-manufactured heparin revealed contaminated products.<sup>13</sup> This has raised well-founded concern regarding the lack of regulatory oversight for quality control procedures in China.

In response to China's manufacturing problems, an initiative to help ensure that Chinese exports meet FDA quality and safety standards was recently put into place. In November 2008, the Secretary of Health and Human Services and the FDA Commissioner opened their first offices in China.<sup>14</sup> In addition, to foster further exchange of information and facilitate cooperation between U.S. and Chinese regulatory agencies, Health and Human

Services recently signed legal agreements with FDA counterparts in China. The Chinese government's continued efforts to better control manufacturing quality and its recent agreement to adhere to FDA guidelines for safety and efficacy are good indicators that quality control procedures in China will improve. The final outcome, however, remains to be seen.

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## Infrastructure and Technology Base

China's biotech infrastructure is still evolving; although some cities offer biotech facilities, the intellectual workforce and most reliable services are concentrated in Beijing and Shanghai.<sup>15</sup> Large biotech centers, such as Zhangjiang Hi-Tech Park in Shanghai, are increasingly common offshoring locations for Western biotech companies because of their modern laboratory facilities and highly skilled personnel.

However, because of the unique challenges involved in the manufacturing of biologics, Western companies are still concerned about transferring biotech manufacturing to facilities in China. Biologics manufacturing is already a complicated process, and additional variables such as geographic distance, linguistic challenges, and cultural differences create further barriers. Many companies maintain that close interaction between scientists and plant workers, primarily during scaling-up, limits some of the potential risks involved in biologics production. As a result, they prefer to keep biomanufacturing facilities nearby.

Despite their reservations, companies are finding it difficult to manage product development costs and, if not already doing so, are considering

offshoring. Although multinational pharmaceutical companies have had activities in China for many years, several recently added research and development facilities and expanded their manufacturing capabilities. Many major biopharmaceutical companies have transferred a portion of their biotech to Chinese facilities, including Amgen, AstraZeneca, Biogen Idec, Eli Lilly & Co., Genzyme, Johnson & Johnson, Novartis, Novo Nordisk, Pfizer, Roche, and Wyeth.<sup>15</sup> This trend is largely due to the fact that drug development costs are about 80% lower in China than in the United States (i.e., salaries for research scientists in China are one-fifth to one-tenth less than in North America).<sup>15</sup>

## Language and Cultural Barriers

Mandarin Chinese, the official language of mainland China, is the primary language of communication and the written language for official documents. In addition to Mandarin, several other languages are common in China, including Cantonese, Taiwanese, Japanese, and Korean. In an effort to overcome language barriers with Western countries that conduct business predominantly in English, many Chinese companies have added English-language programs for their employees. In addition, there is significant government funding of several university English-language programs.<sup>15</sup> Further efforts to improve English proficiency occurred during preparation for the 2008 Olympics in Beijing.

Despite these efforts, much of the population does not speak English as a second language. All documentation for manufacturing in China must be translated into Mandarin Chinese, as must all clinical trial applications<sup>16</sup>, since most local biopharmaceutical employees are not adequately proficient in English. As noted by an expert in offshoring, Lionel Carrasco, managing director and global vice president of strategic solutions and alliances for Neoris, "The challenge for China's

growth will be business domain expertise and huge language and cultural barriers. India has the British heritage and China has the Great Wall of China that remains conceptually.”<sup>1</sup>

In addition to language barriers, there are many differences in acceptable business methods between China and the West. For example, Chinese cultural attitudes may prevent employees from discussing problems with their Western managers, making it difficult to resolve issues. Hierarchy and authority are strongly emphasized in company structure. One of the biggest differences is in project management styles. Chinese attitudes about business have been changing, and a better understanding of cultural differences is evolving.<sup>15</sup> Moreover, when Western companies create offshoring bonds, they must share in the responsibility of overcoming cultural barriers. Thus, implementing localization strategies and hiring local translators who are familiar with the culture are crucial elements in achieving effective communication.

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Over the past few years, primarily because of greater work opportunities in China, there has been a “reverse brain drain” from the West. An increasing number of highly educated, Western-trained Chinese scientists, referred to as *hai gui* or “the returning sea turtles,” are returning to work in China. In a study conducted by the Public Policy Institute of California, 43% of Chinese-born scientists interviewed in San Francisco said that they would consider returning to live in China.<sup>17</sup> Ge Li, chairman and CEO of WuXi PharmaTech in Shanghai, is one such example. Ge Li spent 12 years in the United States earning a doctorate

in organic chemistry at Columbia University and subsequently cofounding a New Jersey pharmaceutical company, Pharmacopeia. In 2001, Dr. Li moved to Shanghai and founded WuXi PharmaTech, a contracting chemistry company that deals mainly with U.S. and European companies.<sup>18</sup>

Returning scientists will definitely play an important role in bridging the gap between China and the West. Their presence has facilitated the growth of transnational partnerships between Western and Chinese companies. The advantages of partnering with Chinese-born scientists who are well accustomed to speaking in English and working in the West are further incentives for Western companies considering offshoring in China. Many of these expatriates have completed their graduate and postdoctoral education in the West and have experience conducting research in Western biotech companies; therefore, they are well equipped to deal with the challenges of bringing Eastern and Western industries together. Jonathan C.K. Knowles, head of global research for Roche, explained Roche’s comfort with transferring facilities to China: “U.S. academia had been run by Chinese postdocs for the last 10 years, if not 15.”<sup>18</sup>

The growing presence of returning scientists in the industry, however, does not eliminate the need for translation and localization experts. Despite the abilities of expatriates to communicate well in both Mandarin Chinese and English, language barriers among many Chinese employees remain an issue. Furthermore, cultural barriers exist even between many returnees and Chinese-educated scientists, especially as the returnees make the transition to working in China. Although the growing number of expatriates, particularly in biotech management positions, will be an added advantage in overcoming these barriers, large language and cultural differences remain among the majority of Chinese-educated employees in the industry.

## Conclusions

China is expected to become a world leader in biopharmaceutical manufacturing. Its biogenerics sector is one of the most dominant in the world. Over the next decade, even more foreign biopharmaceutical companies are expected to expand their biotech capabilities into China. Especially as future offshoring trends foster greater multinational access of resources and expertise, China will further its ties with the West.

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Government funding, cost benefits, improved regulatory legislation, and the influx of Western-trained scientists have all greatly facilitated growth of the Chinese biotech industry. However, the Chinese government’s substantial efforts to promote new biotech product development cannot always keep potential international investors from being hindered by an uncertain financial situation, continuing doubts about the Chinese government’s approach to quality control, and concern about inadequate IP protection. Moreover, language and cultural differences continue to create a major barrier to international investment in China’s biotech industry, despite the growing presence of Chinese returnees.

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