Chasing opportunities in a changing Chinese market

Doing business with Chinese firms has been made more attractive by a wide-reaching series of reforms. But generics companies are failing to take full advantage, consultant Susan Capie told Aidan Fry.

The rise of China's pharmaceutical industry in recent years has clearly caused concern among some western generics companies. Having faced the competitive threat from Indian firms benefiting from low production costs, they are worried that Chinese companies will futher reduce prices in mature generics markets.

A recurring question at the 7th annual conference of the International Generic Pharmaceutical Alliance (IGPA) held in Prague earlier this year was at what stage would Chinese companies be in a position to file applications for finished-dosage forms in developed markets?

But in the meantime, western firms are having to decide what level of involvement they should have with Chinese industry. This covers not only supply deals for active pharmaceutical ingredients (APIs) and intermediates, but also joint-ventures and, in some cases, imports into the Chinese market.

Addressing many of these issues at the IGPA conference, Susan Capie – president of US-based consultancy PharmaVantage – told delegates that a potential long-term threat from Chinese firms in the finished-dosage form arena should not obscure immediate opportunities for partnerships and supply agreements for low-cost APIs and intermediates.

According to Capie – who has 20 years' experience in the Chinese pharmaceutical sector, primarily with Zuellig, and speaks fluent Mandarin – even the most progressive western generics firms have not fully exploited the opportunities.

Talking to **Generics *bulletin*** after the conference, she comments: "I am not sure if there is yet a single generics company that has maximised its strategy in China."

She cites European firms such as Ratiopharm, Sandoz and Stada – the last of which gained access to the Chinese market in 2001 by acquiring a 51% stake in Hong Kong company Health Vision – as being more active than their US counterparts in exploring both API sourcing from China and selling finished products into the country. Furthermore, India's Dr Reddy's, Orchid and Ranbaxy all have Chinese joint-ventures, Capie points out.

According to Capie, western generics firms can find sales opportunities in China, particularly if they can offer drugs in areas not currently well covered by domestic suppliers, such as paediatric formulations or novel drug-delivery systems. At present, domestic firms meet only half of China's demand for finished drugs, with joint-ventures providing 30% and imports 20%.

However, Capie warns, potential problems include: a lengthy procedure for obtaining import drug licences,which can easily take two years; getting onto reimbursement lists; import duties and 17% value-added tax; and stringent price cuts, like the recent reduction of over 20% for anti-infectives.

Furthermore, Capie says, competition from western brands is likely to increase as China strengthens its intellectual property provisions. Amendments to the patent law in 2001 allowed for statutory damages for patent infringement, based on losses to the patent holder or gains made by the infringer. And measures introduced following China's accession to the World Trade Organization (WTO) in the same year included 20-year patent terms, patent linkage and data protection regulations.

Capie argues that the looming threat of such imports of modern patent-protected drugs has increased Chinese companies' already strong desire to move beyond domestic supplies and to tap into lucrative western markets. All of the more ambitious Chinese firms, she says, are striving to gain approval for their facilities from European authorities and, in particular, from the US Food and Drug Administration (FDA).

FDA has approved 55 plants

At present, the FDA has approved only about 55 Chinese plants. "The low regulatory approval rate of factories in China," Capie stresses, "is not because they will not [take the necessary steps], it is because they do not know how to."

Western generics firms interested in partnerships with Chinese companies can, Capie points out, provide a valuable service by lending technical and regulatory support.

The regulatory departments set up by local firms to implement Chinese GMP regulations, Capie says, are now working on filing applications for drug master files (DMFs) in the US and certificates of suitability (CoS) in the European Union. However, she adds, they will take time to become well-versed in European and US GMP rules, observing that Chinese firms are increasingly hiring consultants and agencies to obtain API approvals.

For western generics companies, the more progressive Chinese firms can provide a low-cost source of APIs and intermediates, helping them remain competitive amid fierce price battles. Chinese statistics claim labour costs are up to 70% below those in developed nations, while raw material savings of at least 15% can be achieved.

But with around 3,000 well-established API suppliers spread across China, Capie says identifying potential partners can be a daunting task. Many of the leading Chinese companies do not have English-language websites, she notes, so finding even basic product information can be difficult.

"In addition, China is still a country in which personal relations are paramount and financial transparency is low," Capie points out. And with Chinese regulations constantly developing, she says, using third parties with strong local government and regulatory contacts can be useful.

Nevertheless, Capie stresses, many of the old barriers to entry presented by the local Communist regime and its planned economy have been broken down over recent years. The emergence of a market economy has shifted production decisions away from regional governments and towards firms, she notes, while factories are now negotiating exports directly rather than operating through state trading companies.

This exposure to customers has opened Chinese companies' eyes to market conditions, Capie says; while reducing and eliminating state subsidies has created a "sink or swim" climate.

At the same time, the Chinese government has made major regulatory changes. Last year, it cancelled local state regulations and set up a State Food and Drug Administration (SFDA), based on the US Food and Drug Administration (FDA). Increasingly stringent environmental regulations have been imposed, which larger companies are finding more difficult to circumvent. And the government has issued a flood of intellectual property regulations.

Another major constraint on China's industry has been implementing good manufacturing practice (GMP) regulations, based on guidelines from the World Health Organization (WHO). The initial June 2004 deadline for compliance has been extended for six months due to the large number of applications made to the SFDA.

But gaining GMP approval is only half the story."The Chinese still have to implement the practices, not just the paperwork," Capie maintains.

Nevertheless, Capie expects the GMP move to close about 1,000 Chinese firms by the end of this year, leaving about 3,000 API manufacturers. "A large number of the API factories that will lose their production licences are small in size and with few products," she comments, "[so] there will not be a substantial impact on China's overall production."

The emphasis on GMP, Capie observes, has already led to several mergers and acquisitions. Industry consolidation is part of the government's plan. It wants around 10-12 major Chinese pharmaceutical companies by 2010.

Capie believes this is not entirely realistic. But she points to major changes which have already occurred, such as the merger of five API firms and 12 finished-dose companies to create the Shanghai Pharma Group, which is building a facility in Shanghai's Spark development zone. This organisation is actively promoting to western firms its contract manufacturing capability in APIs and intermediates, as well as potential collaborations on new chemical entities.

Relaxed restrictions on investment

This consolidation has coincided with the Chinese government relaxing restrictions on foreign investment in state-owned enterprises and a more liberal view of privatisation, giving managers the motivation and funds to secure long-term partnerships with foreign companies and investors.

Capie acknowledges that Chinese law does not explicitly protect private property but insists that the government is highly unlikely to seize the assets of a successful, tax-paying pharmaceutical company, as it would deter further investment from foreign firms.

Indeed, she says, a handful of Chinese firms are seeking listings on the US NASDAQ stock exchange to raise funds and to improve financial transparency and investor confidence. Capie also highlights the exceptional example of AXM Pharma, a publicly-listed US company which focuses on marketing and distributing drugs in China.

According to Capie, many Chinese companies have risen to the challenge of the rapidly-changing pharmaceutical environment, upgrading their facilities to improve product quality, stepping up research and development investment from about 1% of turnover to over 5% in some cases, hiring non-Chinese employees to increase regulatory understanding, and embarking on new marketing strategies, such as setting up western sales offices.

All this, she maintains, has been made possible by significant changes in corporate culture. The old guard of bureaucratic overseers has been encouraged to retire, paving the way for younger managers, many of whom have been educated in the west and have worked for multinational firms before returning home to implement their ideas in China.

For western generics firms, this has brought the advantage that discussing collaborations in English is now much easier, not least because many of the Chinese managers have studied for masters of business administration (MBA) degrees.

"As the Chinese have become more westernised," Capie remarks, "they have become increasingly receptive to new ideas in both marketing and production." And, she says, each contact with a potential or existing client – including at trade fairs and conferences – helps Chinese companies to "raise the bar."

According to Capie, one of PharmaVantage's clients, Zhejiang Hengdian, has been audited by over half a dozen major western companies. Each time this has happened, the firm has developed a greater understanding of quality assurance and quality control procedures.

Weak communication and marketing

But, Capie admits, for all the improving fluency in English, communication and marketing techniques are often still weak. The legacy of China's planned economy can still be seen in sacrificing long-term profitability to reach short-term targets. Departments such as production and quality assurance are frequently segregated, while research and development projects can be poorly managed due to the difficulty of supervising multiple projects led by different external consultants.

Another weakness inherent in China's API sector is a lack of information on patents, particularly on polymorphs and salts, resulting in firms being reluctant to develop APIs for molecules covered by several valid patents.

"No Chinese company has patent attorneys on its staff," Capie comments, noting that limited resources force local API manufacturers to rely on data shared by potential customers or on information obtained easily via internet searches.

But tooking forward five to 10 years, Capie forecasts that progressive Chinese firms will be

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employing their own patent attorneys. They are also likely to have strong marketing networks, including overseas offices, to promote their aggressive DMF and CoS filings for APIs and advanced intermediates.

Vertical integration is also sure to continue, she believes, with groups such as Harbin Pharma, 999 Group and Shandong Xinhua already ensuring through acquisitions that they cover not only APIs and finished-dosage forms, but also retail outlets.

On the prospects of Chinese companies filing for approvals of finished-dosage forms in developed markets, Capie says this is "certainly a goal for the premier Chinese firms", pointing out "there is considerable interest from European and US firms in finding a Chinese partner capable of obtaining such regulatory approvals".

Furthermore, Capie adds, some Chinese firms are looking to acquire finished-dosage facilities in the US with the aim of reducing their immediate approval lead-times by five to 10 years.

According to Capie, Hisun Pharmaceuticals in the Zhejiang province – which has "by far the largest and best-qualified in-house regulatory staff of any Chinese manufacturer" – already holds several FDA and CoS approvals for APIs. It also offers a portfolio of tablets, capsules and injectable products locally "and it is moving forward with European and FDA finished-dosage form approvals".

Capie notes that Harbin Pharma has already registered several finished-dosage forms in South Africa. Shanghai Pharma Group is also intending to get some finished products approved, although its current focus is on upgrading its API facilities; while AXM Pharma is investing in a finished-dose facility compliant with US GMP regulations, although its primary focus is domestic sales.

Chinese companies' low cost base could give them a significant competitive edge if they are able to achieve approvals in developed markets. But Capie says labour costs are rising sharply in southern coastal regions, and firms are finding employee turnover rates are increasing with the higher wages.

"Western companies still gravitate towards the most westernised Chinese suppliers," she states, "so that most activity is still concentrated on the coastal areas, particularly Shanghai, Jiangsu and Zhejiang."

"The result of the rising labour costs," Capie says, "will be for western firms to be increasingly interested in exploring more inland and northern regions where costs are still significantly lower."

However, she warns, living standards inland do not compare favourably with those on the coast. "I imagine only the most cost-driven generic companies will be willing to leave the comforts of Shanghai for inland regions like Inner Mongolia," she predicts.

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The dates for forthcoming EGA and IGPA events have been confirmed as follows:

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Radisson SAS Portman Hotel, London, UK

■ 26-27 May 2005 **3rd EGA Symposium on "Biogenerics"**
Radisson SAS Portman Hotel, London, UK

■ 19-22 June 2005 **8th Annual IGPA Conference**
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