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The Global Pharmaceutical Industry and China's Position

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Discussions of China's pharmaceutical industry in the WTO framework cannot be separated from an analysis of the global pharmaceutical industry. The global pharmaceutical industry has never played a more important role than it does today in addressing the mortality and morbidity of global populations, given the threatening increase of global pandemics and emergent health issues, such as HIV/AIDS, avian flu, SARS, TB, hepatitis and debilitating chronic diseases (cancer, diabetes, Alzheimer's disease and so on). Global developments will inevitably have an impact on the position of the Chinese pharmaceutical industry as China is integrated into the global market by the WTO. The purpose of this chapter is to examine prospects for the global pharmaceutical industry, China's pharmaceutical industry and its position in the global market, and the major benefits and challenges facing China's pharmaceutical sector.

Potential of China's pharmaceutical market

China's potential in pharmaceutical development is widely recognized; it is expected to become the fifth-largest drug market in the world by 2010. Growth will be driven by factors such as an increasingly ageing population, the increase in life expectancy, the large market size (urban and rural), government support for restructuring the highly fragmented industry, and improved IPR policies. Beyond demographic factors, it is obvious that the market reform has led to the emergence of a large middle class (the size of the total US population). This middle class is health conscious and has an expanded range of health needs. Yet the potential of the health care market has not been fully realized. According to a global estimate in 2000, the average pharmaceutical consumption in the globe was US$50 per person: including an average of US$300 in the USA, US$400 in Japan, and US$40–50 in middle-income countries. In comparison, China in 2000 spent an average of less than US$10 per person and was therefore believed to have much room to grow. Rising incomes and fast-paced economic

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growth is likely to change this picture, however. It was noted that China's pharmaceutical market was worth US$19 billion in 2000 and will increase to US$60 billion by 2010, with more than US$24 billion in revenues. In 2020, China's pharmaceutical market will gross US$120 billion, above that in the USA (see *Chinapharm*, 2002, 'The development of three ventures in China in globalization framework: Series four', 6 March 2002; see also KWA Pharmaceutical Services, 2006; and an interview with Dr Wei Zhang, Beijing University, 20 January 2006). On the whole, China will remain an attractive market for foreign drug companies for many years to come, because China offers many advantages in terms of the size of its market place, its low labour cost, and its unrealized market potential.

The major impetus for China's pharmaceutical growth comes from larger contextual factors. China has made considerable progress towards macro-economic growth, which has led to improved living standards, increasing concern about health issues, more disposable income for health needs, and increasing demands for better health services. The market for high-quality, patient-orientated healthcare services is small, but growing steadily. There is no universal health care in China and most Chinese lack health insurance. Only a small fraction of the population, mainly those in major cities, can afford top-end Western medical care. Currently, there are many successful foreign and joint venture health care service providers that have been operating in China since the early 1980s. Their experiences point to growing opportunities in the pharmaceutical sector.

The global pharmaceutical industry and China's position

Global pharmaceutical production includes the discussions about raw materials, formulations, Chinese herbal medicines, Chinese herbal formulas, antibiotics, biotech productions, radioactive products, medical equipment, health care devices, and pharmaceutical production facilities and equipment, pharmaceutical packaging materials and trade marks. Overall, global pharmaceutical consumption has increased rapidly year by year. In 2000, the total was more than US$368 billion and reached more than US$550 billion by 2004. The annual growth rate was about 7 per cent in the 2000s (IMS Health, 2006; see also *Chinapharm*, 2 July 2004). 'A review of the planning of pharmaceutical sector in the Tenth Five-Year Plan'. Major global events and trends have also influenced this picture: (i) the increase in the ageing population in developed countries, which has increased pharmaceutical needs; (ii) Increasing health care costs reduce the number of days for in-patient care for which the insurers are willing to pay. The use of pharmaceuticals to relieve the burden of hospital care is useful to the industry; (iii) new diseases and epidemics provide new opportunities for pharmaceutical development; (iv) the potential of biotechnology has provided unlimited opportunities for developing testing devices, vaccines

and pharmaceuticals; and (v) Increases in generics, food supplements and preventive care products also increase the room for growth.

In this environment, the global pharmaceutical business is facing both challenges and opportunities. Several facts are worth noting. First, it is estimated that the cost of developing a drug averages more than US$800 million and is increasing. Second, only three out of ten drugs are able to generate profits. Third, on average, it takes about ten years to develop a new drug. Fourth, the pharmaceutical business is not a purely commercial pursuit: it has a public health component. Fifth, the pharmaceutical market is expected to grow by some 6–9 per cent each year between 2005–9; in comparison, the biotech sector is likely to increase by 20 per cent, but with very risky prospects (Gerbino, 2006; Verret, 2006).

The developments in China's pharmaceutical sector have a two-directional interaction with the global market; that is, China's pharmaceutical market will have an impact on the growth of the global pharmaceutical industry, and similarly global pharmaceutical progress will affect China's pharmaceutical domestic supply and demand. Globally, by 2000, the top ten pharmaceutical companies held 50 per cent of market share in prescription drugs, which had decreased to 47 per cent by 2004. Several global trends are worth noting:

(i) In terms of global market competition,
   (a) smaller pharmaceutical companies have been growing at a faster pace;
   (b) pharmaceutical manufactures, especially those in China, India, Pakistan, Brazil and Indonesia are expanding;
   (c) biotechnology businesses are growing at a faster pace than conventional pharmaceutical companies – for example, the US company Amgen has grossed more than US$ 10 billion and been ranked in the top 500; and
   (d) the rate of rolling out new products is slow because of setbacks during the clinical trial stages of promising new drugs unexpected side effects of such drugs and the nearing of expiration of profitable brands.

   These trends have both direct and indirect effects on the returns of multinationals.

(ii) In terms of pricing and market share, developed countries are still the major markets, but most of the disease burden is in developing, resource-poor countries. India, China, Africa, Latin America and Eastern European countries share most of the disease burden, and they also share the greatest risk of emergent diseases. It has been noted that pharmaceutical prices have increased four times more than the global increase of GDP. Pharmaceutical production in the USA, Japan, Germany, France and the United Kingdom combined accounted for

two-thirds of global production. Competition in generics is increasingly intense, but profits derive mainly from brands. In the USA, generics account for more than 50 per cent of sales. Multinationals on the whole control global pharmaceutical production and marketing. On average, the multinationals have seen their sales increase by 30 per cent in China, but a slower rate is expected in over-the-counter products (OTCs) and generics.

(iii) Research and development of new products remains the key factor for sustainable profits for all pharmaceutical manufactures (*Chinapharm*, 2005).

The future of the pharmaceutical industry is promising, but the complexity and diversity of global health issues presents many challenges to the sector. The 1990s saw major breakthroughs in pharmaceutical developments but it is questionable whether that golden age will be repeated in the twenty-first century, for several reasons: (i) decreasing R&D investment by multinationals; (ii) a distorted investment structure. For example, it was noted that only 10 per cent of investment targeted 90 per cent of the major health issues in the global community, while 90 per cent was invested in only 10 per cent of human health problems. The increasing share of marketing and advertising in pharmaceutical expenditure has also been criticized; and (iii) increasing costs in developing drugs and a high failure rate in clinical trials. The cost of developing new drugs, compounded by the increasingly rigorous standards demanded in developed countries before approving them, is making it more difficult to increase investment in new drugs. This might explain why the numbers of new compounds approved by the Food and Drugs Administration (FDA) have decreased since 2000, from thirty-eight in 2000 to twenty-three in 2004. The advancement in human genetics and biotechnology has provided a glimmer of hope for the industry, albeit under certain conditions, such as the need to lower R&D costs and provide a faster translation between upstream and downstream development. In this global environment, the collaboration between conventional pharmaceutical businesses and new biotechnology research centres, and between multinationals and pharmaceutical businesses in developing countries, is inevitable.

Overall, the major motors for growth in the global pharmaceutical industry are: innovation in biotechnology, an increase in the ageing population, and emerging geographical centres, such as China and India. These phenomena have motivated pharmaceutical companies to increase collaboration with biotech companies to share their expertise, products and operations to overcome the productivity gap and increase growth (*Business Insights*, 2005). The key issues facing global pharmaceutical industries in China in the WTO framework will be:

(i) the market entry principle: based on principles of non-discrimination and fair competition;
(ii) manufacturing principles: price, safety and efficacy;
(iii) the protection of pharmaceutical IPRs;
(iv) marketing, advertising and distribution issues;
(v) understanding the demographic needs and disease profiles of populations (see *Chinapharm*, 2001).

In a very competitive global market, the greatest threats to fully realizing sales and marketing effectiveness of all pharmaceutical businesses, including those in China, are competition and price containment. Biotech will be the focus of attention in this picture. Biotech is currently the fastest growing sector in the pharmaceutical industry globally, and is forecast to have record sales of US$ 250 billion by 2015 (20.3 per cent of the global market). Biotech in the USA grew at a rate of almost twice that of the overall drug market in the second quarter of 2004. About 91 per cent of industry executives believe pharma–biotech mergers will increase during the next ten years, and 69 per cent also believe there is likely to be increased consolidation between companies within the biotech sector (*Business Insights*, 2005, p. 131). It is believed that by 2015, the large pharmaceutical companies will synergize their R&D networks with biotechs and focus on their core competitive sales and marketing (ibid.). China has taken note of this trend and made major investments in developing biotech products. Its recent progress in cancer drugs was an important step for the growth of its biotech-related pharmaceuticals.

As mentioned earlier the global pharmaceutical market is expected to grow by 6–9 per cent between 2005–9 (Gerbino 2006; Verret 2006). At the time of writing, China accounts for about 1.5–2 per cent of the global pharmaceutical market and this market share is likely to increase to 5 per cent by 2010–15. China is expected to rank eighth in the global market, with 13 per cent to 16 per cent of annual growth (*Chinapharm*, 2005). In 2004 alone, China's pharmaceutical market was worth US$9.5 billion, a record 28 per cent growth over 2003, but this was still a small percentage compared to the global picture; for example, the USA reached US$ 248 billion, accounting for 45 per cent of global growth (IMS Health, 2006).

China's pharmaceutical industry

Despite the fact that pharmaceuticals manufacturing was not previously thought of as a pillar of Chinese economic development, the Chinese government has articulated a detailed framework for the overall development of the pharmaceutical sector in the Tenth Five-Year Plan (March 2001). The conceptual framework outlines the following guidelines for increasing the competitiveness of the pharmaceutical sector: the Chinese pharmaceutical

sector will continue to support Chinese social development and focus on structural adjustment. It will be market and private-sector-orientated. China will also focus on developing its niche areas in pharmaceutical growth. It will support public health and improve the quality of health for its population through the development of preventive medicines. It will filter out high-polluting, energy-consuming and low-efficiency products. It will improve pharmaceutical informatics through digitalizing monitoring and surveillance systems, accounting systems, and population informatics. It will develop the as yet unrealized market potential in the inland region and improve pharmaceutical access there. It will upgrade the technology capacity of the sector, especially for biotech products and Chinese herbal medicines, with the ultimate goal of improving product quality and increasing China's position in global competitiveness. It will globalize its production, marketing, distribution and capital investment. The key areas selected for government support are: biotechnology, Chinese herbal medicines and niche raw materials. The substantive goals are:

(i) pharmaceutical manufacturing is expected to grow by at least 12 per cent;
(ii) value-added products in the pharmaceutical sector are expected to grow by at least 13 per cent;
(iii) the sale volume of pharmaceutical-related products is expected to grow by 9 per cent;
(iv) pharmaceutical exports are expected to grow by 6 per cent; and
(v) the profit margins for the pharmaceutical industry are expected to grow by 13 per cent (*Chinapharm*, 2004).

To reach these targets, China will engage in major structural adjustment in product composition, R&D upgrades, and improvements in capital investment and organizational structure. On product composition, China will aim to increase the share of high-end products in the market. For example, China plans to hold the patents of about ten new brands that will enter the global market place. About fifty new drugs will be at the clinical trial stages. About ten to fifteenth biotech products are expected to enter the global markets. More than twenty Good Manufacturing Practice (GMP)-certified facilities will be completed to process multiple pharmaceutical tasks. Exports of Chinese herbal medicines will grow. Chemical raw materials, such as artemisinin and Vitamin C, will increase their global market share. The percentage of formulations in total share of exports market will increase from the current 0.2 per cent to 5 per cent. On R&D upgrades, large-scale pharmaceutical businessess will establish their R&D centres and it is expected that they will increase from the current 2 per cent to 5 per cent. The biotech sector is expected to make major progress in genetic engineering, such as recombinant technology. The technology for chemical

production, especially for artemisinin and Vitamin C, will be enhanced. On capital investment and organizational structure, China will focus on the establishment of large-scale pharmaceutical businesses through both vertical and horizontal integration, such as IPOs (Initial Public Offerings), mergers, joint ventures, and reorganizations. It was noted that efficiency was a major issue prior to 2004. For example, in 2003, on average, only 44–60 per cent of production capacity was realized in the pharmaceutical sector. The excessive number of small pharmaceutical companies has decreased China's global competitiveness. In contrast, the global top ten 'pharmas' accounted for 47 per cent of pharmaceutical production across the world; in India, the top twenty pharmaceutical producers accounted for 50 per cent of all revenue; in the USA, the top three wholesalers accounted for more than 90 per cent of medicines (*Chinapharm*, 2003). The opening of the financial sector will allow an increase of venture capital in pharmaceutical investment. China is determined to streamline pharmaceutical production in the areas of unrealized production capacities, unhealthy competition among small-sized producers for duplicated products, and lack of efficiency. It will strengthen its enforcement and control of pharmaceutical quality control. It is expected that the ten largest manufacturing businesses, grossing more than US$6.25 billion each, will own 30 per cent of the market share in China. China will facilitate the formation of large-scale distributors, each of which is expected to have a capital investment of more than US$2.5 billion. China will also be instrumental in the establishment of ten large retail chains, each owning more than 1,000 stores as well as smaller regional chains that are expected to own more than 100 stores each *Chinapharm* 2004).

China's pharmaceutical development has shown a large growth potential:

(i) it has been noted that its growth since in the 1980s has outpaced the increase in China's GDP. The fact that its total value accounts for 5.5 per cent of China's GDP, less than the 10–15 per cent of the total GDP share for the industrialized countries, shows that it still has much room to grow (*Chinapharm*, 2005; *see also China Pharmaceuticals*, 2002). In one estimate, in the early 1990s, the pharmaceutical sector in China was calculated to account for only 1.83 per cent of its total industrial value, and was ranked at only 22 out of 37 sectors; by 1999, the value had increased to 2.1 per cent and ranked 19; and in 1999, its value was 2.4 per cent and it was ranked 17th. In 1999, the total profits, profit return rate, cost return rate and production efficiency were ranked 7th, 5th, 4th, and 8th respectively (*Chinapharm*, 2004); and
(ii) despite some operational issues in China, the country is still the fastest-growing pharmaceuticals market in the world. Between 1978

and 2005, the gross value of China's pharmaceutical industry increased by 17 per cent annually, one of the fastest-growing industries in China (*Chinapharm*, 2005). In another estimate, the pharmaceutical market was calculated to have increased by 28 per cent between 2000 and 2005, compared to a 7 per cent global growth. The total pharmaceutical needs were estimated to be more than US$2.7 billion (*Chinapharm*, 2005). It was predicted that, at the current growth rate, China is likely to be the fifth-largest pharmaceutical market in the world, and will exceed the market volume of Germany and France, respectively, by 2015. The major areas to have shown a large potential are Chinese herbal medicines and raw chemicals. Domestic pharmaceutical investment has also been increasing through the capital accumulated in the stock market. Most of the pharmaceutical stocks received positive ratings because of lower risks compared to other stocks. It is also hoped that the influx of venture capital to the Chinese market will encourage dynamic growth in this sector (*China Pharmaceuticals*, 2002).

The presence of multinationals in China is increasing. Since China approved the first joint venture in pharmaceuticals in May 1980, the top twenty pharmaceutical multinationals have all established their presence in China. After China's WTO entry, the multinationals could not wait to capitalize on this potential. For example, as early as 2002, the Boehringer Ingelheim International Group, the world's largest private medicine manufacturer, invested US$41 million in Asia's second-largest pharmaceutical plant, in Pudong, China (*China Health Sciences Newsletter*, 2002). The multinationals entered the Chinese market either individually or as joint ventures. It was estimated that drugs produced by joint ventures claimed 30 per cent of the market share, and imported drugs accounted for 23 per cent, by 2002 (Hong Kong Development Council, 2002). Overall, the foreign pharmas' position in China's market has changed significantly, having decreased from an average rate of 20 per cent sales growth and quick returns to a lower rate. Before the WTO accession, China's laws were more protective of domestic producers, but since WTO membership, the competition for profits has led to more domestic–foreign partnerships, such as in the form of foreign-invested enterprises (FIEs). By 2005, the value of foreign investment was about US$2 billion in the pharmaceutical sector (Gross, 1998).

A related point is that capital composition in China's pharmaceutical industry has also changed tremendously since 1978. Joint ventures accounted for 18.8 per cent in 2004, increasing from 15 per cent in 1995; private producers accounted for 33.2 per cent, rising from 12 per cent in 1995, and state-controlled businesses have decreased from 55 per cent to 36.1 per cent since 1995 (*Chinapharm*, 2004). By 2004, China already saw more than

200 retail pharmaceutical businesses controlling more than 5,000 retail pharmacies. On the whole, multinationals have the most influence on global economic development, and it has been estimated that they accounted for one-third of the world's GDP and controlled 50 per cent of world's trade, 80 per cent of patents, and 75 per cent of technology transfer by 2001. This is also true for the pharmaceutical sector. According to an estimate by Forbes, there were fourteen pharmaceutical multinationals in the top 500 Fortune companies. Each of the top three (Merck, Pfizer and Novartis) grossed more than the combined revenues of all the pharmaceutical manufacturers in China in 2000. All nations and businesses considered, multinationals accounted for the top 50 per cent of the GDP in the world. And the total revenues of Chinese pharmas was less than the sheer volume of Pfizer's in 2005 (*Chinapharm*, 2002).

To recap, the major advantages of Chinese markets are the size of its market, emerging health care issues and disease profiles, potential for R&D, human resources, the government's commitment to improving the health sector, the relatively easy access to patients available for clinical trials, and lower clinical trial costs (*Research and Markets*, 2005; *Digital Vector*, 2005, p. 360). For example, because of changing lifestyles and changing demographic needs, China's demand for cardiovascular drugs and cancer treatment have grown at a fast pace in 2004, and it was estimated that up to 2009, both production and demand will continue to grow (AMID, 2003).

China has continued to improve its international competitiveness and has changed its strategy towards the pharmaceutical market, from acquiring a market share to comprehensive competition. Biomedicine is growing steadily, with major input for research and development, and traditional Chinese medicine is being modernized but still faces major challenges (see related discussions in Okokok Research Centre, 2005). In 2004, China ranked as the seventh-largest pharmaceutical market globally, with a value of US$ 14 billion (up from US$4 billion in 1996), compared to India's US$4.5 billion (*Business India*, 2005, p. 92). Pharmaceutical imports have been growing at a rate of 20 per cent since the early 1990s and exceeded US$930 million by 2000. In 2004, China's pharmaceutical industry continued to maintain its growth momentum, achieving a stable rise in both output and sales revenues.

Looking to the future, China is expected to become the fifth-largest drug market in the world by 2015, with an estimated value of US$24 billion (*Business India*, 2005, p. 92). It is also expected to become the world's largest pharmaceutical market by 2020 (Gross, 1998). As discussed earlier, the major drivers of growth are changing demographic trends, the disease and health profile in China, and socioeconomic changes, such as economic growth and increases in incomes, population growth, an increasingly ageing population, increasing pharmaceutical consumption per capita,

market size (urban and rural), government support in restructuring the highly fragmented industry, IPR policies, increasing life expectancies, HIV, lifestyle changes, and liberated sexual behaviour.

Improvements in living standards, reduced levels of poverty and strong macroeconomic growth, also affect the health care market as a whole. These developments have both positive and negative consequences for health. Many developments also mean tremendous potential for the growth of pharmaceuticals consumption among the population. For example, in 2004, pharmaceuticals consumption was less than US$10 per capita in China; in comparison, it was more than US$300 in the USA and other industrialized countries. With health care reform, both the public and private sectors will pay more for their pharmaceutical needs, and the Chinese government is determined to implement universal health care in all villages by 2008. Urbanization has also increased pharmaceutical needs. For example, about 460 million Chinese lived in cities and towns in 2000 and this trend is increasing by 2.7 per cent each year – more than 10 million population are added to the cities annually. Pharmaceuticals consumption has a ratio of 7:1 between urban and rural populations, and urbanization will also increase the size of the pharmaceuticals market. China's population grew to more than 1.3 billion by 2005. In addition, the ageing population is increasing by 3 per cent each year. The regulatory environment has also helped the pharmceuticals market, and it is estimated that retail pharmacies are increasing in number by 15 per cent each year. As mentioned earlier, the decrease of tariffs in the WTO framework will also help both domestic and multinational producers. The market for high quality and patient-orientated health services is small, but is growing steadily. Most Chinese do not have health insurance. Only a fraction of the population can afford high-end Western medical care.

Economic development and demographic trends are conducive to pharmaceutical growth, and the total volume of China's pharmaceutical industry is growing. By 2005, about 6,000 domestic pharma manufacturers controlled roughly 70 per cent of the pharmaceuticals market (*Business India*, 2005, p. 92). There are about 17,000 joint ventures with China, including all the leading pharmaceutical companies. By the end of 2004, 3,731 pharmaceutical manufacturers in China were GMP-certified (*Chinapharm*, 2005), By July 2004, China had about 3,613 pharmaceuticals-related manufacturers, in which only 423 (11.7 per cent), were considered to be large-scale producers. The majority of producers were small-scale, lacked distinct products and brand recognition, had an out-of-date, traditional management style and were loosely organized. They produced more than 15,000 kinds of pharmaceutical-related materials, totalling 430,000 tons annually (*Chinapharm*, 2004). They also produced 34 formulations and more than 4,000 kinds of drugs. The top 60 businesses accounted for 35.7 per cent market share in China while in contrast top

20 global producers accounted for 60 per cent of global market (ibid.). About 97 per cent of the products are generic. On average, each batch of raw material can make three formulations. In contrast, the multinationals can make 18–80 formulations (ibid.). By 17 February 2004, there were 7,486 pharmaceutical wholesalers, including 6,936 business owners and 551 partners. In comparison, in the USA there are ten, and in Sweden, two. The preferred global standard for retailers is that there should be less than 7 minutes' walking distance between a neighbourhood and a pharmacy. China is below this standard. China now has 15,1760 retailers, and 719 chains. In total, the total number of stores and chains that sell pharmaceutical products is 230,000 (*Sina News Taiwan*, 2004). In 5–10 years, it is believed that generics will account for 70 per cent and prescriptions 30 per cent of China's pharmaceutical market (*Chinapharm*, 2005). China's potential for pharmaceutical production and consumption was recognized in the 1990s.

China's pharmaceutical sector is experiencing a multi-directional dynamic to improve its domestic positioning. China's pharmaceutical industries are catching up to global competition by forming alliances, and employing horizontal and vertical integration. For example, in the first half of 2005, LAMP acquired New World for US$14 million; the Green Valley Group's US$6.25 million developed a strategic alliance and R&D investment with Chinese Academy Sciences; TaiGen partnered P&G Pharmaceutical to develop a novel antibiotic to address drug-resistant pathogens; and the Shanghai Pharmaceutical Group Co. Ltd (SPGC) invested US$12 million to launch a joint venture in Chongquing with a local drug firm, the Mokom Group, and SPGC plans to hold a 60 per cent stake in the new company, Shanghai Pharmaceutical Mokom. The Chongqing Mokom Group will retain 40 per cent in return for contributing its infrastructure. This will allow the SPGC to expand its sales networks into rural markets. Mokom has the third-largest chain of drug stores in Chongquing and major sales network in the rural markets of South-west China. An alliance of five major pharmaceutical holding companies aims to pool resources and share regional distribution rights and channels to increase competitiveness and cut costs. Each of the five alliance members – Shanghai Pharmaceutical Holdings Ltd; Beijing Pharmaceutical Holdings Ltd; Tienjing Pacific Group Ltd; Chongqing Pharmaceutical Holdings Ltd; and Guangzhou Pharmaceutical Group Ltd is one of the top ten revenue producers in its segment. AXM Pharma Inc., the owner of AXM Pharma Shenyang through a wholly-owned subsidiary of Werke Pharmaceuticals, Inc., reached a distribution agreement with Sinopharm Holding Guangzhou Co. Ltd, an affiliate of China National Pharmaceutical Group Corp. The agreement was for an expected US$6.5 million in sales of Elegance feminine hygiene products by December 2005, and the sales territory includes regions in Southern China (BGCG, 2005, p. 17). It was noted that feminine hygiene products have a

major potential in China. This kind of dynamic is likely to help domestic producers increase their R&D and management capacity, and in return the multinationals can gain domestic distribution channels.

Creative partnerships are being generated to build competitive capacity in China. For example, TaiGen Biotechnology Co., a privately held biotech with headquarters in Taiwan and with subsidiaries in mainland China, has completed a project with Procter & Gamble Pharmaceuticals (P&G). This agreement will take advantage of TaiGen's network of clinical investigators and be responsible for the Phase IB and Phase II clinical testing of a novel, non fluorinated-quinolone antibiotic from P&G. P&G retains the right to evaluate the product given positive Phase II studies, and with TaiGen may seek another pharmaceutical company for Phase III development and commercialization. For its risk-sharing, TaiGen will be rewarded with a share of the financial rewards from the re-partnering of the Phase III-ready antibiotic and will retain the rights of this compound in China, Korea and Southeast Asia. Procter and Gamble has obtained US$133 billion market capitalization. But risks remain for both companies: for example, for P&G, anti-infectives are not a core strategic focus for its revenues, and it needs to lower development costs. It also needs access to patients for clinical trials. Partial collaboration with a focused target is also a clever strategy. For example, PharmaEngine, another Taiwan life science company focusing on cancer, immunology and infectious disease therapeutics, obtained exclusive rights to Xenova Group PLC's brain cancer treatment, TransMID, in China and South Korea. What Xenova gets is an advance payment as well as milestone and royalty payments and it will retain manufacturing rights and the exclusive supplier right of TransMID to PharmaEngine. At the time of writing, TransMID is in Phase III clinical trials for the treatment of glioblastoma multiforme (GBM). PharmaEngine's current prospects include one Phase I candidate for cancer and one Phase II candidate for both asthma and chronic obstructive pulmonary disease (COPD) (BGCG, 2005, p. 17). In April 2005, the Shanghai Institute of Materia Medica (SIMM) at the Chinese Academy of Sciences Shanghai Life Science Institute made a joint announcement with the Green Valley Group about a partnership and co-development agreement for traditional Chinese medicine (TCM). The Green Valley Group will invest US$6.25 million as start-up funding for projects in cancer and cardiovascular diseases. Green Valley specializes in marketing and selling TCM products. It has offices and subsidiaries across China and owns two state-of-the-art GMP manufacturing facilities in Shanghai and Xian, with a third being built in Shanghai (Green Valley Financial Services, 2005).

China has also become a centre of outsourcing for multinational pharmaceuticals, including R&D. To access the Chinese market and its low-cost manufacturing capabilities, the Lam Pharmaceutical Corp. of Lewiston, NY, signed an agreement in January 2005, to acquire privately-held New World Kellerton in Xinyang for US$14 million in cash and stocks. The New World's leading product is Hipreomycin, approved for treating TB in China

and India. This also has the potential to be exported to other developing countries. Ciba Specialty Chemicals has opened a new US$20 million R&D centre in Shanghai. It will bridge chemical knowledge with formulation science to create new products and solutions for both Asia and the world at large. Besides the R&D centre, Ciba already has six branch offices, twelve production sites and three trading companies. Ciba's Chinese operation accounted for 7 per cent of its US$5.8 billion global sales in 2004. China is also making an effort to reach global markets. Yangzijiang Pharmacy Corp. reached an agreement with Stanford University in the USA to build a research facility in Shanghai for new drugs. This is the second R&D facility after its collaboration with Merck to build a similar centre in Beijing, where its investment totalled US$2.25 million. The Shanghai project will focus on cardiovascular medication. Yangzijiang will provide the funding facilities and testing and Stanford the intellectual expertise. Yangzijiang will have first claim to any products developed (BGCG, 2005, p. 17).

China has increased its quality control in pharmaceutical production incrementally, especially in GMP and GSP (Good Scientific Practice) certification. On average, GMP certification costs about US$2.5–3.75 million. By 2003, between 1,800 and 2,000, companies, about a third of all manufacturers in China, spent more than US$6.25 billion on becoming GMP certified (*Chinapharm*, 2003). By 2004, 60 per cent of all manufacturers (controlling 90 per cent of total production) were GMP certified. Those who did not have GMP or GSP certification, (including more than 2,000 businesses, 900 whole salers and 5,000 retailers), were told to close down their company (*Chinapharm*, 2004).

Foreign pharmaceuticals have taken note of China's need to deal with emergent diseases, and that tackling infectious diseases is at the top of China's public health agenda. Sinovac Biotech Ltd (SVA), a leading biotech company in China, has obtained encouraging results from its clinical trials of a SARS vaccine. The Chinese CDC (Centre of Disease Control) revealed that, in initial clinical trials, the SARS antibody was found in all volunteers six months after receiving the test vaccine. SVA also received Chinese marketing and sales approval for its Slit Influenza vaccine and for Bilive, a combined hepatitis A and B vaccine (BGCG, 2005, p. 17).

Yet China's pharmaceutical sector is also facing grave challenges, which will be further discussed later. However, in the WTO-regulated economy, the possible opportunities facing Chinese pharmaceutical makers can also be enormous (Access China Management Consulting Ltd, 2005, p. 39).

The competitive advantages of China's pharmaceutical sector

Overall, China's pharmaceutical sector and market has several major advantages, as mentioned earlier: mainly the size of its market, lower costs for labour, production and clinical trials, and quicker drug approvals, a

talent pool, policy environment and commitment to health care improvement, and emerging health issues. As became obvious after China's entry into the WTO, the country's pharmaceutical industry is at a major turning point. China has become a multi-tasking centre for global pharmaceutical products (*World Journal*, 2003).

Specifically, China's major advantages are as follows.

A future R&D and global manufacturing centre for new drugs

It is estimated that in the USA and Europe, developing a new drug costs an average of US$800 million to US$1 billion because of the high cost of clinical trials and the high attrition rate, which means that only 15 per cent of new drugs entering development eventually reach the market (Tufts Center for the Study of Drug Development, 2002; see also Kemani, and Findlay, 2000). Finding themselves in this disadvantageous position, Western pharmaceutical companies are constantly looking for ways to cut costs, such as identifying new pathways to develop new molecular medicine and accelerating targets by using new technologies. This explains why most major pharmaceutical companies, such as Pharmacia-Upjohn, Glaxo SmithKline, Novartis and so on had established their R&D centres in China by the early 2000s. Yet, the challenge to global pharmaceutical businesses is to find innovative operational models for drug development. This new framework of thinking puts China in an advantageous position:

(i) *Cost-effectiveness*: China's research scientists are paid a fraction of the salaries of their Western counterparts, which lowers the overall cost of developing new drugs, testing drug compounds and manufacturing in a highly scalable fashion. Even compared with other developing countries, China's labour advantages cannot be underestimated. For example, China's labour costs are a third or a quarter of those in Brazil or Mexico (*Sina News,* 2006).
(ii) *A vast research talent pool*: The return of a large number of Western-trained talent in the pharmaceutical sector increases China's competitiveness (Wang, 2005). By September 2005, more than 200,000 had returned, most of them highly educated having received advanced training in the West, especially the USA.
(iii) *Increasing expertise*. In highly specialized areas, such as biopharmaceutical discovery research and clinical development.
(iv) *Increasing investment*. China's increasing investment through public and private expenditure on drugs.
(v) *An increasing share of the pharmaceutical market.*

However, for China to become a formidable player in a globally competitive environment, it needs to address the following issues: (1) it needs to improve its drug development infrastructure to comply with international

regulatory standards if it wishes to become part of the fully integrated global 'virtual drug development model'. China has moved in the right direction with its mandatory implementation of Good Laboratory Practice (GLP) in September 2003, which require that all data for the safety evaluation of new drugs must come from GLP approved labs; and (ii) China needs such channels as 'the Life Sciences Bridges' to facilitate the bi-directional transfer of knowledge, technology, capital and other resources between its own tech hubs and other life science hubs in the world. China needs major information channels to absorb up-to-date biomedical scientific discoveries in the West and to transfer its own discoveries to the West to realize the full commercial value of its pharmaceutical research (BGCG, 2005, p. 14). Invitrogen's acquisition of Chinese competitor Bio Asia in December 2004 shows that life science R&D capacity in China has been noted by foreign competitors in biotech research equipment and reagents. It also shows that China has made some progress in integrating itself into the new global drug development paradigm.

Overall, (i) the traditional costly drug development paradigm is being evaluated by Western pharmas. Multinationals need to assess the cost-effectiveness of this model and final alternatives to reduce production costs; (ii) China can provide a new paradigm for drug development that 'leverages the most efficient drug development resources worldwide' (BGCG, 2005, p. 15); and (iii) China's engagement in infrastructure and capacity building to comply with global standards is a good first step to becoming a respectable partner in the global arena.

In terms of manufacturing, low-cost prescriptions and generics have multiple global markets. The role of such emerging pharmaceutical producers as China, India and Brazil are worth noting. The USA and Japan are the largest pharmaceutical exporting countries, but also the largest importing countries of pharmaceuticals. US pharmaceuticals sales accounted for 18.4 per cent in the global market place in 1976, and 52 per cent or more since 2000. EU sales total more than 26 per cent; Japanese sales grosses more than 10 per cent, but Chinese sales are about 2 per cent (*China Pharmaceuticals*, 2005). High income countries, which account for more than 15 per cent of the global population consume more than 90 per cent of the pharmaceuticals, and pharmaceutical consumption in the least developed countries has been decreasing, from 3.5 per cent in 1985 to 2.9 per cent in 1999. Pharmaceuticals sales in these countries decreased from 0.98 per cent in 1990 to 0.64 per cent in 2000. Yet, pharmaceuticals sales and consumption have been increasing in middle-income countries, including China. In terms of access, about a quarter of the global population had less than US$5 available for pharmaceutical expenses. More than half of the global population had difficulty in paying for medicines, and in China, more than 60 per cent population had problems in paying for health care. There is about a 100 times difference between high-income and low-income coun-

tries. On average, pharmaceuticals accounted for 15 per cent of total health care cost for global populations, while in China they accounted for more than 60 per cent. Pharmaceuticals are a major health care expenditure for most Chinese people (ibid.).

As well as those markets in developed countries, the potential in developing countries cannot be ignored by producers in China. These markets are not a source of profit for multinationals and are therefore not the focus of their attention. According to a 2004 WHO report, more than 2 billion people did not have access to essential medicines, including 1 billion in China. Essential medicines are exempt from tariffs in all but ten countries, but in those ten countries, imported raw materials for essential medicines are taxed at 23 per cent, while an average rate of 12 per cent is levied on finished products. Most middle-and low-income countries still purchase their medicines from other low- and middle-income countries. Like Brazil and India, China is well-positioned to enter those markets with essential medicines, low-cost generics and herbal medicines. China's largest competitor in this area will be India, whose pharmaceutical products are priced at 60 per cent less than Chinese products (ibid.).

A rapidly growing market

China has changed its position from being ranked eleventh in 1996 to seventh in 2002, and is projected to be the fifth by 2010, with estimated sales of US$24–26 billion per year. The sheer size of population and the demographic trends of the Chinese population offer a growing potential for pharmaceutical products, as mentioned earlier. In 2004, prescription sales grossed more than US$10 billion, with a rate of increase of 27 per cent over the previous year. As a whole, China's pharmaceuticals retail totalled more than US$97 billion; hospital pharmacies sales totalled US$141.4 billion; and pharmaceutical advertising totalled US$20.5 billion. Profits were US$30 billion for the pharmaceutical industries; US$11.7 billion for retail; and US$44.4 billion for hospital sales (ibid.).

Several specific demographic characteristics and trends in China are: (i) the size of population is 1.36 billion and it is increasingly conscious of its health needs; (ii) since 1998, pharmaceuticals sales have increased by at least US$500 million; (iii) the ageing population leads to increased pharmaceutical consumption. According to China's 2000 census, about 10 per cent of the Chinese population were aged over 60 years old, and this population is increasing by 3 per cent every year. For the purpose of comparison, the Japanese are the second-largest pharmaceutical market because of the high percentage of elderly people in its demographic composition; (iv) the rapid pace of urbanization in China has also increased the pharmaceutical need for OTCs in retail pharmacies, especially the need for imported medicines. Urbanization increased by 4.4 per cent between 1990 and 1995, and by 30.89 per cent between 1998 and 1999. If this trend continues, there will

be plenty of room for the growth of pharmaceutical products (BGCG, 2005, p. 1). The long-term prediction is that, by the middle of the century, drug sales in China will outstrip those in every other region (see also 'Analysis of strategies and markets for multinationals', *China Pharmaceuticals*, 2002).

Cost advantages

China's low production costs are its major advantage. These include the costs of labour, facilities and equipment, raw materials, distribution, marketing and advertising. Certainly, the most conspicuous is the cost of labour, as mentioned earlier. China is known for having one of the largest, most inexpensive, and best-trained labour forces. It has been estimated that the average salary for a Ph.D.-level scientist in China was US$25,000 a year – about 10 per cent of a corresponding US compensation package. In addition, the large number of returning scientists from the West adds a further advantage to China's cost calculations. A global human resource firm, Watson Wyatt, found that the annual salary before tax for R&D professionals in China was even lower than in South America. In contrast, it was estimated that 80 per cent of total R&D costs typically pay for the salaries of research scientists in the West. This explains the increasing interest of the West in turning to Chinese scientists to conduct new drug research.

Centres of clinical trials

The cost of conducting clinical trials, including the associated hospital fees, is also much less in China than in the West. According to some conservative estimates, clinical trials costs in China are a third of those in the USA. (PriceWaterhouseCoopers, 2004). On average, for the drug development processes in China, the preclinical cost is approximately 20 per cent of that in the USA. It has been estimated that it costs about US$120 million to develop a new drug in China (*General Biologic*, 2004). It was noted that that more than 800 drugs, most of which are new drugs in Phase III of clinical trials, are tested annually in China. Usually, more than 500,000 Chinese are involved in the process (*World Journal*, 2005).

The scientific research tradition

(i) China has a long history of scientific research and has developed its talents over a twenty-year period. Scientists of Chinese origin have won four Nobel prizes in science-related fields, and the third and fourth generations of Chinese leaders were all from science backgrounds. China has a well-established universal education system, generated about 1.87 million undergraduate degree holders and 111,000 postgraduates in 2003, according to the Chinese Ministry of Education. It has a talent pool of more than 50,000 research scientists. In addition, each year, about 500–1000 Chinese who have obtained doctorate degrees from overseas institutions return to China, providing

major support for large research institutions (see *Asia Pacific Biotech News*, 2005). The Chinese government also implemented a policy that encouraged collaboration between the private sector and universities, to develop patentable products. This policy has provided a major impetus for research institutes. For example, the Shanghai Institute of Materia Medica, China's leading centre for pharmaceutical research and development, is also a major target for collaboration by multinationals.

(ii) A large number of pharmaceutical researchers in US pharmas came from China, and a good percentage of them have returned to China, as mentioned earlier.

(iii) The Chinese ethnomedical system, which has been practised for more than 3,000 years, has provided many innovative ideas for drug development. It suggests great potential for future new drug developments.

(iv) There have been many successful collaborations between Chinese research institutes and multinationals since the 1978 economic reform. Their profit returns have been the major drivers for the multinationals' stay in the Chinese market (*Chinapharm*, 2001).

Government support

The Chinese government is supportive of pharmaceutical development. Since the late 1990s, government policies have encouraged foreign investment in the pharmaceutical sector in China. For example, (i) China offered special tax incentives for pharmaceutical investors, reducing the levy on their capital gains from 33 per cent to 17 per cent; (ii) there was no limit on the maximum investment that foreign investors could transfer from the gains of their previous investment into pharmaceutical investment; and (iii) the government includes such products as genetic engineering, vaccines and advanced biotechnology in the government's purchasing priorities, but Chinese herbal products remain the monopoly of local manufacturers (*see also China Pharmaceuticals*, 2002).

In 2000, the Chinese government made further endeavours to improve the policy environment to make it conducive to multinational investment, through legislation such as the People's Republic of China Joint Investment Law, People's Republic of China Joint Ventures Law, and People's Republic of China Foreign Ventures Law. On 1 December 2002, China also passed the Qualified Foreign Institutional Investor Act (QFII), which allowed foreign entry to Chinese stock markets. This made it possible for foreign capital to be an engine of growth for Chinese businesses, including the health care sector (*China Pharmaceuticals*, 2002). In January 2003, the Chinese government also abolished a wide range of limitations on foreign investments, such as the volume of stocks in which foreign parties could invest, the Chinese government's protection of multinational rights, and the amount of commission charged for pharmaceutical investment. This

step was crucial to funnelling foreign funds into high-growth sectors, such as pharmaceuticals.

In this environment, on 29 September, 2003 the largest pharmaceutical retailer, Medicine Shoppe International Inc., entered the Chinese market (ibid.). China also approved the first foreign multinational, Roche Pharmaceuticals, to enter Chinese retail market, on 16 May 2003, which demonstrated China's fulfilment of its WTO commitments. Prior to this deal, Roche had already set up a subsidiary in Shanghai (in the early 1990s), which covered more than 100 cities and 400 hospitals. The framework of Roche's entry was through a joint venture with the Chinese pharmaceutical company Shing Hsing, in which Roche provided 49 per cent of the investment. The possible targets of this joint venture included hospitals, retail pharmacies, and pharmaceutical imports and wholesaling. It was also noted that foreign investment accounted for a higher growth rate in China's exports (*China Pharmaceuticals*, 2003).

As mentioned earlier, the Chinese government also provides support for research institutes and universities. The major agency in charge of science and technology policy and resource allocation is the State Science and Technology Commission. With an overall R&D budget of US$18.7 billion in 2003 (1.31 per cent of GDP), China has increased its annual investment in science and technology. This rapid progress in science and education since 1978 arose from the policy directive issued by the Chinese Communist Party Central Committee and the State Council, on 6 May, 1995 entitled the 'Decision of the Central Committee of the Chinese Communist Party and the State Council on the Acceleration of Progress in Science and Technology'. The 'Decision' aimed at both public and private sectors reaching Chinese R&D spending equivalent to 1.5 per cent of GDP by the year 2000. This was a breakthrough decision that urged scientific academies and institutes of higher education to establish their own high-tech companies. The 'Decision' paid attention to special development issues, such as population control, food security, environmental protection (including pollution abatement technologies), and public health (such as pharmaceuticals development). The State Council also suggested that science should move out of the institutes and into private enterprise. Government research institutes should join Chinese and foreign companies in co-operative ventures, decide their own research focus and be responsible for profit management. The flow of personnel, information and capital are expected to improve to meet the market's need for research (Wikipedia, 2006; see also Louet, 2004; BGCG, 2002, p. 1). This policy was conducive to China's high-tech research.

The investment in biotechnology began in 1986 with the launch of the 863 Programme for high-tech investment, which has reached US$500 million per year and includes major infrastructure building in research institutes, laboratories, centres and universities. About fourteen of

the eighteen genetically engineered drugs approved by the state were sponsored by the 863 Programme. Other programmes are the 'Torch Programme' and the 'Natural Science Foundation', which enabled China to strengthen its research capacity in genome sequencing, bio-agriculture, traditional Chinese medicine, tissue engineering and gene therapy, which have strong potential for future growth (BGCG, 2002, p. 12). In this environment, genetic engineering has made progress in China. China's Genome Project is headquartered in Shanghai. Since 1993, the Chinese Genome Project has carried out structural analyses of genomes, collected samples from Chinese minorities for a national depository, and developed techniques for human genome research informatics. The project started with the rice genome and expanded to human genome research, with a focus on disease-causing genes. A liver cancer gene project that began in 1993 is now focusing on chromosome 17. Other groups focus on genes associated with oesophageal cancer and psychological disorders. A research group at the Institute of Medical Biology at the West China University in Chengdu is looking for disease-causing genes in several cell lines. Twelve institutes and nineteen research groups are involved in the human genome project. Large cities with sufficient infrastructure have become major scientific hubs, thus, Shanghai has become a leading Chinese centre for biotechnology and human genome research (Wikipedia, 2006). The South Centre of Human Genome Research has participated in the international undertaking of the sequencing of the human genome, and the Beijing Global Biotechnology Centre has made a major investment in developing an international biotechnology research park in Hangzhou (ibid.).

China's participation in biopharmas is also worth noting. There are now 139 drugs in China's biopharma pipeline, 60 biologics, 43 generics, 19 antibodies and 11 vaccines (*China Pipeline*, 2004.). Of the 139 drugs, 96 (69 per cent) are at a preclinical stage, while only about 13 (9 per cent), are at Phase III, compared to 700 biologics in clinical development worldwide, 150 of which are in a late clinical stage (Anscomb, 2004). China's biopharmas are likely to expand in an environment of increased government-sponsored research, increasingly available private venture capital investment, and innovative R&D in the biopharma sector (BGCG, 2005, p. 1).

Transgenetic research

Innovative research thrives in a flexible policy environment. Chinese research institutes, such the Centre for Stem Cell Biology and Tissue Engineering in Guangzhou, are establishing a new primate research centre that aims to create transgenic primates for use as models of human disease and as a global source of primate stem cells. The USA used about 57,000 primates in 2000, and China is a major supplier, which is conducive to the clinical trials business that China is establishing. Conducting animal testing close to its source could save a large amount on the costs related to breeding and

transportation. The use of non-human primates is a source of major political controversy and a target for attack by animal rights supporters in the West, which gives China the opportunity to become a major animal testing centre for clinical trials. However, it is also important that China develops mechanisms in transgenetic research that can answer the concerns of animal rights supporters.

Liberal attitudes and fewer ideological interventions in scientific research

The debate about stem cells and therapeutic cloning research in the USA is less contentious in China. When China approved Gendicine in December 2003, developed by Shenzhen's SiBiono GenTech, China was the first country in the world to officially approve a gene therapy for head and neck squamous cell carcinoma. In total, in 2004, there were about ten gene therapy products in development in China, compared to forty-three in the USA and ten in Europe (see *Nature News*, 2004; see also *Asia Pacific Biotech News*, 2004). Similarly, China's approval of genetic medicines for the treatment of cancer in 2006 also showed China's advantage in prioritizing scientific research without ideological baggage.

The changing demands of domestic markets

The demands for biomedicine have increased, especially for drugs that deal with ageing, chronic diseases and infectious diseases globally. To meet these demands, pharmaceutical research, especially biotech medicine, has also received increasing support for research and development. The case of Gendicine was instructive. It has become the first genetically modified medicine approved by China's regulatory authority. The growth in biomedicine in general has been steady over recent decades in China. The largest growth has been in biomedicine and the manufacture of equipment designed for pharmaceutical industry. The growth of traditional Chinese medicine was slower than the average rate because of difficulties in the modernization and industrialization process. Medical apparatus and equipment in manufacture decreased from a growth rate of 50 per cent in 2002 to 7.76 per cent in 2003. Sales revenue in 2002 was US$40.05 billion, a 16.4 per cent increase over 2001, with a profit margin of 22.02 per cent. Imports in these categories increased steadily from 2002 to 2005 (see *China Industry Development Report*, 2003).

Policy environment

As mentioned earlier, the Chinese government is supportive of multinationals conducting R&D in China. The most important policy was 'Item 863', which was approved by Chinese leader Deng Xiao-ping in March 1986 and encourages technology transfer from industrialized countries and scientific research in various sectors. Deng approved about US$1.2 billion of investment in scientific and technology research from China's public

funds. This policy has important implications for China's pharmaceutical sector. For example, in 2000, China's SFDA allowed exemptions from import duties and other customs taxes, to encourage R&D by multinationals. China has also listed biotech as a priority sector to enlist foreign investment in its *Catalogue for the Guidance of Industries for Foreign Investment*. This will render foreign companies eligible for a lower rate of corporate income tax, about half of the 33 per cent paid by domestic companies. Foreign R&D can import equipment without tariffs, and the revenues reinvested in research are tax-free. It is believed that multinational investment in R&D can support the bottom line in their global budgets as well as strengthen the financial performance in their Chinese operation (BGCG, 2005, p. 12). The Chinese policy environment is believed to be one explanatory factor for the increase of R&D in drug development. About 96 per cent of the 8,000 new drug applications submitted to China's SFDA in 2003 were manufactured by local companies, and about 40 per cent of the new drugs are imitations (see Vasella, from BGCG, 2005). Since 2002, central government has mapped out a plan to encourage innovation in the pharmaceutical industry. The Chinese government set out to invest US$120 million between 2002 and 2005, ten times higher than the period 1996–2000, to strengthen research and development of new drugs, instead of duplicating current generics. Traditional Chinese medicine is treated equally in this investment. The pursuit of patent ownership should be a priority for the Chinese government because Chinese ownership of pharmaceutical patents is sparse. For example, in 2002, Chinese pharmaceutical developers owned only 2 per cent of the patents of the medicines sold on the domestic market (China Internet Information Centre, 2002).

Challenges

China's pharmaceutical sector is facing challenges in several areas, such as in the need for R&D, a lack of patented pharmaceuticals developed domestically, the enforcement of intellectual property rights, a scattered geographical layout, duplicated production processes, the need to modernize manufacturing technology and management structure, a lower market concentration in international trading competitiveness, and its position in the world's pharmaceutical industry and the regulation environment under WTO.

Policy and the legal environment

(i) Since early 2000, China has been moving steadily towards improving the legal and policy environment by encouraging innovation and increasing patent protection. By 2002, China was producing 1,350 types of crude pharmaceuticals, in 24 categories, among which 97 per cent do not have patent protection. To date, China has only two inno-

vative drugs, arteannuin and sodium dimercapto-succinate, that had international patents (Hong Kong Development Council, 2002):

(ii) Manufacturers should decrease duplication of products and streamline the pharmaceutical business. By 2001, China had 5,164 or fewer companies producing crude drugs, medicine and chemical reagents, and preparations. It was believed that there was excessive duplication in the production of pharmaceuticals. At the time, questions were raised about the competitiveness of such a large number of indigenous pharmaceutical companies in the face of strong foreign competition. It was suggested that the government should raise the threshold for the entry of new pharmaceutical enterprises. The other solution – vertical and horizontal integration – is important to decrease the number of indigenous pharmaceutical companies. This strategy is working gradually. In the 1985–98 period, there was a sharp addition of 500 new companies to the list of pharmaceutical production. In 1999, there was an increase of only additional five companies; 17 in 2002, and 23 in 2001. It was also mandated by the new law that other institutions or companies would not be allowed to replicate similar production once a new application had passed the first step of the application process. Third, the new law also made it difficult for small pharmaceutical companies not meeting the GMP standard to continue by changing the drug production certification process or enforcing GMP authentification. In 2001, about 10 per cent of smaller businesses were eliminated in this way.

(iii) China should enforce GMP standards. Enforcing these standards has been crucial to upgrading the pharmaceutical industry in China. In 2002, China's State Drug Administration set a timetable for all Chinese pharmaceutical companies to qualify for GMP authentication by 30 June 2004. All medicines, preparations and crude drugs had to conform to GMP standards and gain GMP certificates. It was a crucial step for quality control in Chinese pharmaceutical companies. Although this has caused smaller, less competitive pharmaceutical companies into bankruptcy and forced mergers of others, it has been beneficial to the industry overall;

(iv) The government should facilitate the flow of distribution channels, implement a classified drug management system, and separate the medical treatment from drug management. Retail pharmaceuticals are mainly sold through two types of outlet: hospitals and pharmacies. It was estimated that about 85 per cent of drug sales were through hospitals. Since 2000, Chinese government has mandated the use of a classified drug management system, and the separation of prescription and OTC drug sales was tried out in a number of venues, to encourage the development of pharmacies/drug stores. There is also a policy that encourages retail drugstores to set up chains and large medical retail

enterprises to expand trans-regional business. China has also gradually improved the OTC (over-the-counter) system. A system of 'medical insurance designated drugstores' with measures 'separating medical treatment from drugs' has also been introduced. Now, with doctors' prescriptions, patients can buy drugs outside hospitals. This encourages the expansion of retail pharmacies. These policy directions will also open up distribution channels for pharmaceutical companies;

(v) The government should improve centralized bidding and efforts to reduce drug prices. Centralized bidding through hospitals was designed to reduce doctors' backdoor dealings when purchasing drugs – so-called 'grey income' – and to decrease expenses for patients. But, this policy was found to have serious defects. As mentioned earlier, the Chinese government has made strong efforts to cut pharmaceutical prices. Since 1997, the State Development and Planning Commission has cut the prices many times of more than 200 varieties of centralized managerial drugs and reagents. The goal was to cut retail prices while wholesale prices remain the same. This policy was hard to implement because the reduction of retail prices hurt the profits of hospitals and drug wholesalers, shifting the loss of profits bade to pharmaceuticals producers.

Creating brand awareness

In this area, the major issues facing China are: the protection of intellectual property rights (IPR); a lack of finance; a lack of state-of-the-art drug development infrastructures; a lack of management talent; difficulty in exiting; poor corporate governance; currency exchange; reduction of tariffs; domestic harmonization and compliance with WTO regulations at the central and local levels; competitiveness of domestic pharmaceutical industries; product registration regulation; the regulation of the Chinese herbal industry; the competitive advantages of biochemical medicines; and the public–private sector partnership (BGCG, 2005, p. 1).

IPR protection

According to the Pharmaceutical Research and Manufacturers Association, the IPR situation in China remains a concern. Major challenges include 'a lack of date exclusivity protection, counterfeiting, and inconsistent administrative protection'. In 2004, Pfizer's patent on Viagra (Sildenafil/citrate) was overturned in July 2004; and GlaxoSmithKline abandoned an attempt to defend its patent on Avandia (Rosiglitazone maleate) in August 2004 (BGCG, 2005, p. 1). The case of Pfizer aroused some concerns. In 2001, Pfizer's patent of Viagra was invalidated by China's State Intellectual Property Office after it was challenged by Chinese drug makers on the basis that Pfizer had not supplied enough laboratory data in its original application (*Business India*, 2005, pp. 92–3). The resolution by the Chinese Court

that Pfizer should be awarded its Viagra patent in 2006 was a good sign for the Chinese government's credibility in IPR enforcement.

Under the WTO, the Chinese government has worked hard to improve IPR-related issues. It has had the positive effect of encouraging major global companies to build upon their initial involvement in China. In a survey (BGCG, 2005), more than two-thirds of the thirty-five senior executives of multinational pharmaceutical companies questioned said that they expect the WTO agreement to strengthen IPR protection in China. The fact that multinationals are expanding the R&D capabilities – multinationals such as Novartis, Roche and Eli Lilly, who have operated in China for a significant amount of time – suggests that China's IPR issues are not serious enough to diminish China's strengths (BGCG, 2005, p. 1). Chinese government officials believe that intellectual property rights issues are improving in China and that they have been overly politicized (*Sina News*, 2006).

The issue of R&D merits an in-depth discussion

The major challenge facing all pharmas operating in China is R&D: (i) domestic producers need to harmonize their R&D practices. It has been noted by some analysts that Chinese researchers engaged in different R&D processes from the multinationals in drug development, such as developing detailed research plans, establishing well-defined targets and timetables, and discussing progress with colleagues (BGCG, 2005, p. 11); and (ii) China needs to strengthen its drug development capabilities. It was noted that most of its drug development facilities do not reach global standards. GLP was recently introduced in China, but the end of May 2005, the total number of GLP-compliant facilities in the country was still fewer than twenty. It was pointed out that China lacks innovative drugs, and most domestic producers in China still rely on copying existing drugs rather than developing new ones. Between 1985 and 1996, most patented drugs were raw materials or herbal medicine products. As mentioned earlier, China has had only two drugs, arteannin and sodium dimercapto-succinate, approved internationally (Wang, 2002).

The issue of R&D is particularly important in biopharmaceuticals. China's biopharma industry is highly fragmented, with 4,000 producers. The fact that few domestic manufacturers are large enough to run effective R&D programmes shows that integration is necessary. The domestic bio-pharmas need to spend a higher percentage on R&D, given the fact that leading multinational companies spend around 15 per cent of their revenues on R&D. On average, Chinese companies spend less than 5 per cent (ibid.).

The niche of traditional Chinese medicine

Traditional Chinese medicine has been found to be effective in treating some long-term, chronic diseases, but it needs major research investment

as well as improvements in marketing and manufacturing, which will be further discussed later. For example, in 2002, active ingredients of only 2,000 (out of 10,000 or more popular medicines) were known to the researchers. In the Chinese herbal industry, local researchers own more than 80 per cent of the patents, but most of them are about a combination of herbs (China Internet Information Centre, 2002).

Enforcement of pharmaceutical laws and regulations

The issue of counterfeited drugs merits discussion in China. Worldwide, counterfeiting is a major issue facing global health. It affects the legitimate pharmaceutical industries; wastes health care resources; causes increased health care expenses; decreases medical effectiveness; it can cause fatal results. In the environment of globalization and internet trade, conventional regulations on pharmaceutical trade are no longer powerful enough. The internet makes it much easier for consumers to compare prices and obtain prescriptions. The global pharmaceutical counterfeiting business, without effective control, will be a serious threat to global health. It has been estimated that 10 per cent of drugs in the global market and 50 per cent of the drugs sold in developing countries are counterfeit. Most counterfeit drugs are advertised as cures for obesity, impotency, baldness, or malaria. The production chain for counterfeit drugs is complex: the ingredients might be found in country A, while the final product is manufactured in country B. Counterfeiting requires global collaboration. The World Health Organization (WHO) has established an emergency communication system providing a platform to update information on counterfeit drugs, and this can provide a model for monitoring Chinese counterfeit drugs (Lee, 2005).

Counterfeit drugs are a major public health issue in China. For example, in Suanzhou City, the local FDA confiscated twenty-seven illegal drugs that claimed to have therapeutic effects in cardiovascular diseases, prostate problems or impotency. The labels were misleading, and frequently the companies listed on the labels do not exist (*World Journal*, 2005).

In a major city in China's North-west region, Viagra was sold for the equivalent of US60¢ per tablet. With similar packaging as that produced by Pfizer, Chinese counterfeit Viagra cost thirty times less than the American version. In another pharmacy in Henan, Viagra was sold for US$20 per pack and no prescription was required. The Chinese medical authorities have increased their surveillance over counterfeit drugs yet challenges remain formidable. For example, collaborating with the police, the provincial Food and Pharmaceutical Supervision and Management Office reported 17,664 violations, and confiscated illegal medical equipment and pharmaceuticals worth a total of US$900,000. Yet counterfeit drugs are now sold in health food stores. Locally-made Viagra is a major source of profit for sellers of counterfeit drugs. It was reported that, by August 2000,

about 500,000 counterfeit Viagra pills had been produced in Zhejiang Province, and by the time the manufacturer was arrested, 80 per cent of the pills had already been sold in the market. Counterfeiters usually buy real Viagra from licensed sellers, analyse the active ingredients and counterfeit the drug in their own factories. In many cases, the counterfeit Viagra is just coloured sugar pills.

In particular, Henan Province has become a major centre for counterfeiting, with counterfeiting manufacturers even gaining name recognition among Chinese consumers. Some consumers have mistaken the 'Henan made' mark for quality assurance. The counterfeit drugs have also gained some share of the overseas market via mail order to about ten countries including the USA, Britain, and as far as Israel. The king of counterfeit Viagra, Mr Mo Huei Biao, sold most of it via the internet. He was able to produce 10,000 pills a day, at a production cost of US$0.28 per tablet. Local post office clerks, who were part of the operation, received a commission from the counterfeiters. Some local government clerks even became accomplices in this business. Now, local food and drug supervision and management authorities work with a wide range of government offices to stem the flow of counterfeit drugs. These include the police department, the post office, telecommunications, banking and mobile communications. In the face of the government's high-pressure tactics, the counterfeiting operations have also diversified their operations. The manufacturing, packaging, transportation and payment are now dispersed to different locations (*Sina News Beijing*, 27 September 2005).

Related to counterfeiting is the issue of the recall and disposal of expired drugs. This problem is widespread in Chinese villages despite the efforts by the Chinese government to issue a national mandate to recall and dispose of all expired drugs. Some recalled drugs have been repackaged and sold in remote villages (*Sina News Beijing*, 24 May 2005). The price attracts poorer consumers because it is usually some 50 per cent less than the drugs' original price (*Sina News Beijing*, 16 May 2005).

Control of classified drugs

On 6 November 2005, 1,360,000 pills of triazolam were sold to the black market by the 'Jinling Pharmaceutical Company' in Jilin Province. Triazolam, a Class I classified drug, is one of the most strictly regulated pharmaceuticals in China because of its anesthetic effects. It is used clinically to treat insomnia but it is often used as a rape or robbery drug by criminals. Jingling Pharmaceutical Company was one of only two companies permitted by the Chinese government to produce triazolam. In a routine inspection in May, 2005, local authorities found that only 18 per cent had been sold to licensed pharmaceutical wholesalers; the rest went to illegal sellers. The problem stemmed from the lack of vigilance on the part of the sales agents at the pharmaceutical company. The sales agents did not

inspect the licences of the buyers, and most were counterfeits sold on the street for US$1.7 (*World Journal,* 6 November 2005).

Evidence-based pharmaceutical tracking and consumer protection

China needs a system to supervise retailers in the tracking and monitoring of drug use. In the past, consumers could not sue pharmacists for malpractice when suffering severe side effects caused by pharmacist error in dispensing drugs. The experimental application in a Guanzhou drug store of tracking patients' drug reactions history can improve this problem. Monitoring and tracing side effects is especially important when assessing the effectiveness of pharmaceutical products.

Misuse and abuse of prescriptions

Abuse of prescription drugs is on the rise in China. For example, it was reported that prescriptions used for human problems were sold at veterinary clinics at ten times the original prices. The overpricing and misuse of veterinary medicine is prevalent, especially in large cities such as Beijing. Beijing city mandates that all pet dogs should be vaccinated in public clinics, as private clinics often use illegal vaccines. The danger of using human prescriptions for veterinary problems is that, once the disease crosses the species barriers, it poses a grave risk to humans. The epidemics of SARS and avian flu, where viruses have crossed the species barrier, should be instructive to Chinese pharmaceutical control officials.

Regulating clinical trials

China has become a major clinical trials centre for multinational pharmaceutical companies. Yet this trend might have an adverse effect on China's participation in this business if it is not closely monitored. As mentioned earlier, it was estimated that more than 800 drugs in Phase IV of clinical trials are tested annually in China, directly or indirectly involving more than 500,000 Chinese in the process. There has been a lack of coherent policy and regulatory framework to monitor the clinical trials business in China. It is reported that many multinationals engaged in Phase III and IV trials labelled 'free physical examinations' or 'free cures', with the collaboration of local state health agencies. The victims were often poor farmers. The most appalling incident involved a Korean drug manufacturer. The Korean cancer drug manufacturer reportedly engaged in clinical trials on a group of 593 farmers between 1997 and 2001. All of them became seriously ill or died during the process (*World Journal*, 22 May 2005).

Pharmaceutical pricing control

Pricing is a challenging issue facing Chinese pharmaceutical regulators and other stakeholders. It has serious implications for all parties involved. In May 2005, the Pharmaceutical Association in twenty-one provinces in

China appealed to the Chinese government for pharmaceutical discount (*Sina News Beijing*, 19 May 2005). An issue related to pricing is access. There need to be more pharmacies in rural and remote areas offering affordable medicines. Large cities and towns benefit compared to small towns and rural villages in the quality and quantity of services they receive, while rural health care is falling apart. Access to quality medicine is a serious issue in the villages. There needs to be major infrastructure building and public–private partnerships to improve the distribution channels of pharmaceuticals in remote areas (*Business India*, 2005, p. 92).

The Chinese authorities are in a difficult position *vis-à-vis* pharmaceutical price controls. On the one hand, they have to meet public health objectives and social solidarity goals; but on the other, they are concerned about the impact of such measures on local pharmaceutical producers. For example, in June 2005, the Chinese government took measures to lower the prices of six antibiotics and six other drugs on the state health insurance list. The rate of reduction reached more than 60 per cent for domestic drug manufacturers, but less for joint ventures or foreign ventures. On, average, the reduction rate on brand names was 20 per cent. The main purpose of this was to lower drugs costs in hospitals, but it was said to have had a major impact on local drug manufacturers rather than on the foreigner pharmas, because antibiotics sales accounted for about 30 per cent of pharmaceutical sales. It was estimated that most large Chinese pharmaceutical companies saw their profits from antibiotic sales reduced by around 50 per cent (*World Journal*, 23 May 2005). More often than not, the well-intended price control measures did not achieve the intended effect of reducing the burden on the patients, as hospitals might in fact recommend more profitable drugs to patients.

China's public health objectives cannot be ignored in this discussion. On the whole, the Chinese Medical Reform Commission has made a deliberate plan to improve pharmaceutical access, and the lowering of prices for antibiotics was just the first step. The Medical Reform Commission aims to solve the issues of pharmaceutical overpricing, providing more pricing flexibility, and stopping the abuse of antibiotics. The role of doctors and hospitals in the use of pharmaceuticals is a major issue in overpricing. Generally, doctors and hospitals tend to charge a commission for pharmaceutical products. Unlike the situation in the USA or the EU, medical practice is not separate from pharmaceutical sales in China. Since China's economic reforms, hospitals receive fewer subsidies from the government and have to rely on the profits made on pharmaceuticals to pay for hospital operations. The lower discount rate for joint ventures and foreign drug makers is to take into account the high R&D cost for those producers. Yet these public health measures have not achieved their intended effects.

This plan resulted from consultations with experts and local pharmaceutical vendors, the Ministry of Health and China's State Department. The

publicly-owned Chinese pharmaceutical industries are apprehensive that this measure would allow their competitors to erode their discount drug market and shrink the share of the domestic pharmaceuticals market held by publicly-owned pharmas in China. The domestic pharmas believed that shrinking profits would force them out of the market while joint ventures or foreign pharmas would maintain their profit margins. According to the China Pharmaceutical Sales Association, in 2004, the average sale prices for pharmaceuticals decreased overall; for example, in three major pharmaceutical categories prices were lowered by 4.98 per cent. Pharmaceuticals produced by Chinese domestic manufacturers showed the greatest rate of decrease, which seriously affected their profit margins. This trend was felt painfully by such major domestic pharmaceutical industries as Ha Pharmaceuticals, Northern China Pharmaceuticals and New China Pharmaceuticals. In the first quarter of 2005, profits of twenty-three state-owned pharmaceuticals decreased by 12.1 per cent compared to the first quarter of 2004. These industries face the combined challenges of rising prices of raw materials and policy pressure. Some were forced to decrease antibiotics production, streamline or change that product structure, reduce production costs by moving facilities to the villages, increase exports, or move into health foods businesses. In fact, the health foods industry can be a potential growth area for domestic state-owned pharmas if they cannot cope with the competition in the conventional pharmaceuticals sector. One major potential market is villages, which house for some 80 per cent of the Chinese population. New policies by the Chinese government to support a reformed health care system in the villages provides room for discounted drugs. According to one study, the market at the country and village level reached about US$630 million by 2005. The other possibility is to enlarge the export market (Jing, 2005).

In consequence, pharmaceutical pricing reforms are likely to:

(i) filter out domestic pharmas that are not competitive;
(ii) lead to a concentration of ownership of antibiotic makers, allowing for horizontal integration;
(iii) allow pharmaceutical producers that are strong in R&D to gain larger market share;
(iv) increase partnerships between multinationals and domestic pharmaceutical companies;
(v) change the marketing strategy among competitors; and
(vi) this will also be likely to increase generics and decrease the effort made to produce branded drugs.

Yet, it is important to note that the pricing issue is just the tip of the iceberg. The main problem is the financing of China's health system, especially the use of pharmaceutical profits to support the cost of hospital operations.

In conclusion, this chapter has offered an in-depth analysis of China's pharmaceutical industry, its potential in the global market, and the major advantages of and challenges facing the Chinese pharmaceutical sector. Overall, global pharmaceutical development is supportive of China's position in the global market place. China's domestic market also offers tremendous opportunities for global stakeholders. It is widely anticipated that within fifteen (around 2020) years, China's will be the largest pharmaceuticals market in the world. China's advantages lie in the size of its market; lower costs for labour, production clinical trials and quicker drug approvals; a talent pool; policy environment and commitment to health care improvement; and emerging health issues. Yet the challenges are also enormous, such as a need for R&D, a lack of patented pharmaceuticals developed domestically, the enforcement of intellectual property rights, a scattered population geographically duplicated production processes, the need to modernize manufacturing technology and management structures, a lower market concentration in international trading competitiveness, and a weak position in the global pharmaceutical industry, and the regulatory environment under the WTO. The next chapter will offer an analysis of the ways in which the WTO would have an impact on the major stakeholders in China's pharmaceutical sector.