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The World Trade Organization, and the Present and Future of China's Pharmaceutical Industry

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China's pharmaceutical industry is experiencing a period of high growth, in which global stakeholders have played an important role. The WTO framework has opened up new opportunities and challenges for the stakeholders in this sector. The purpose of this chapter is to examine the WTO and Trade Related Aspects of Intellectual Property Rights Agreement (TRIPS) rules related to the pharmaceutical industry as a whole; the WTO's challenges to the regulatory and legal system in China, especially surrounding the patents issue, pharmaceutical quality control, price control, and the potential of Chinese herbal medicines; and the WTO's overall impact on the development of indigenous pharmaceutical and biotech industries.

The WTO, TRIPS and pharmaceuticals

In the WTO framework, the TRIPS Agreement has had the most impact on the pharmaceuticals industry, mainly through the regulations on pharmaceutical patents (WTO, 2005). WTO definitions on patents and related issues affect the way the pharmaceutical industry operates across the globe.

The foundations of the TRIPS agreement are: Uruguay Round negotiating objectives for TRIPS, 1986 Punta del Este Declaration, and the 1988/89 Mid-Term Review.

A patent is defined as 'an exclusive right granted for an invention, which is a product or a process that provides, in general, a new way of doing something, or offers a new technical solution to a problem'. The patent protects the inventor so that the new invention cannot be commercially made, used, distributed or sold without the patent owner's consent. The enforcement of the patent rights resides in the authority of the court. A third party can challenge the original patent owner, and if the challenge succeeds, the patent to the original owner will be declared invalid.

The right of patent ownership: a patent owner has the right to decide which party may – or may not – use the patented invention for a specific period of time in which the invention is protected; twenty years in TRIPS.

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Licensing allows the patent owner to grant permission to other parties to use the invention on mutually agreed terms. The owner may also sell the right to the other party, who will then become the new owner of the patent. The protection of the patent rights ends once it expires. Once the invention enters the public domain, others can use the invention commercially.

The overarching principles for the WTO are national treatment (treating one's own nationals and foreigners equally) and most-favoured-nation treatment (equal treatment for nationals of all trading partners in the WTO). It is important to note that national treatment is honoured in other international intellectual property rights agreements.

TRIPS is also underlined by the principle that it encourages innovation, technology transfer and social development. Article 7, entitled 'Objectives', according to which the protection and enforcement of intellectual property rights should contribute to the promotion of technological innovation and to the transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge and in a manner conducive to social and economic welfare, and to a balance of rights and obligations. Article 8, entitled 'Principles', recognizes the rights of Members to adopt measures for public health and other public interest reasons, and to prevent the abuse of intellectual property rights, provided that such measures are consistent with the provisions of the TRIPS Agreement.

Related to the previous point is that there are exceptions to the patent protection. One is for inventions contrary to public order or morality (Article 27.2). Patent protection is exempted if the protection is dangerous to human, animal or plant life or health, or seriously prejudicial to the environment. Accessing HIV medicine is a most significant case in point. The use of this exception is to protect public order and morality. The second exception is on diagnostic, therapeutic and surgical methods for the treatment of humans or animals (Article 27.3(a)). The third is that Members may exclude plants and animals other than micro-organisms and essential biological processes for the production of plants or animals other than non-biological and microbiological processes. However, any country, in exercising exceptions in plant varieties from patent protection, must provide a *sui generis* system of protection, which is also subject to review four years after the coming into force of the Agreement in a WTO Member Country (Article 27.3(b)). Members may provide limited exceptions to the exclusive patent rights if the exceptions do not conflict unreasonably with a normal exploitation of the patent and do not prejudice unreasonably the patent owner's and the third parties' legitimate interests (Article 30).

The exclusive rights that must be conferred by a product patent are the ones of making, using, offering for sale, selling, and importing for these purposes. Process patent protection must give rights not only over the use of the process but also over products obtained directly by the process.

Patent owners shall also have the right to assign, or transfer by succession, the patent, and to conclude licensing contracts (Article 28).

Other treaties governing pharmaceutical production that are equally important are: the convention of the World Intellectual Property Organization, the Paris Convention for the Protection of Industrial Property, the Berne Convention for the Protection of Literary and Artistic Works, the International Convention for the Protection of Performers, Producers of Phonograms and Broadcasting Organizations (Rome Convention), and the Treaty on Intellectual Property in Respect of Integrated Circuits (IPIC Treaty).

The persons or parties protected by the agreement: Article 1.3 defines who these persons are. These persons are referred to as 'nationals' but include persons, natural or legal, who have a close attachment to other Members without necessarily being nationals.

On the technical terms of intellectual property rights, Articles 3, 4 and 5 include the fundamental rules on national and most-favoured-nation treatment of foreign nationals, which are common to all categories of intellectual property covered by the Agreement. These obligations cover not only the substantive standards of protection but also matters affecting the availability, acquisition, scope, maintenance and enforcement of intellectual property rights, as well as those matters affecting the use of intellectual property rights specifically addressed in the Agreement.

It is also required that patents be available and patent rights enjoyable without discrimination as to the place of invention, and whether products are imported or locally produced (Article 27.1).

Patent applicants must disclose the invention in a sufficiently clear and complete manner for the professionals to carry out the application (Article 29.1).

Compulsory licensing and government use without the authorization of the patent right holder are permitted if they meet the conditions of protecting the legitimate interests of the rights holder, such as an attempt to obtain voluntary licensing not being successful and adequate compensation.

The protection of undisclosed information is particularly relevant to the pharmaceutical industry. The TRIPS Agreement requires the protection of undisclosed information, such as through trade secrets. It also stipulates conditions on undisclosed test data and other data whose submission is required by governments as a condition of approving the marketing of pharmaceutical or agricultural chemical products using new chemical entities. The government concerned is legally obligated to protect the data against unfair commercial use. In addition, WTO members must protect such data against disclosure, except under such conditions as the protection of the public.

Doha Declaration, 2001*

Several stipulations are important to the pharmaceutical industry in this declaration:

1. WTO rules should not pose a barrier to the protection of human, animal or plant life or health, or of the environment. The WTO will continue to co-operate with the United Nations Environment Programme (UNEP) and other international agencies regarding sustainable development issues.
2. The WTO continues to work toward the liberation of services. The General Agreement on Trade in Services (GATS) are to regulate, and to introduce new regulations on, the supply of services with the goal of promoting the economic growth of all trading partners and the expansion of developing and least-developed countries by continuing the work started in January 2000 under Article XIX of the General Agreement on Trade in Services.

17. The TRIPS will be interpreted in such a way as to support public health by promoting both access to existing medicines, and research and development into new medicines.

19. In accordance with Article 27.3(b), Article 71.1 and paragraph 12 of the Doha declaration, the WTO will examine the protection of traditional knowledge and folklore, and other relevant new developments. The WTO will take into account Articles 7 and 8 of the TRIPS Agreement in examining the development dimension. (This is pertinent to the producers of traditional medicines, such as Chinese medicines.)

Specifically, on health-related issues:

1. The WTO recognizes the gravity of the public health problems afflicting many developing and least-developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics.
2. The WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS Agreement) should be part of wider national and international action to address these problems.
3. The WTO recognizes the effects of intellectual property rights on the prices of medicines.
4. The TRIPS Agreement should not prevent members from taking measures to protect public health. Accordingly, the TRIPS Agree-

*Doha WTO Ministerial 2001: Ministerial Declaration. WT/MIN(01)/DEC/1, 20 November 2001; Ministerial declaration, adopted on 14 November 2001.

> ment should be interpreted and implemented in a manner supportive of the WTO members' right to protect public health and, in particular, to promote access to medicines for all.

Most importantly, the WTO patent rights provisions should be interpreted flexibly in accessing important medicines for developing countries. That is, WTO members have the right to grant compulsory licences and the freedom to determine the grounds for such licences. The members have the right to determine what constitutes a national emergency or other circumstances of extreme urgency, such as public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics that can represent a national emergency or other circumstances of extreme urgency. WTO members are free to establish their own regimes for the exhaustion of patent rights without challenge, subject to the MFN and national treatment provisions of Articles 3 and 4. For countries with insufficient or no manufacturing capacities in the pharmaceutical sector in making effective use of compulsory licensing under the TRIPS Agreement, WTO were to find a solution by end of 2002. The solution was generated in 'the 30 August decision'.

The WTO also encourages developed-country members to provide incentives to their enterprises and institutions to promote and encourage technology transfer to least-developed country members pursuant to Article 66.2, and that least-developed country members will not be obliged, with respect to pharmaceutical products, to implement or apply Sections 5 and 7 of Part II of the TRIPS Agreement, or to enforce patent rights, until 1 January 2016.

Taken as a whole, the Doha declaration provides flexibility for developing countries to access medicines in a more liberal framework. Developing countries can collaborate to improve pharmaceutical access to life-saving medicines if they can further improve this framework. This portends opportunities for developing countries, such as China, India and Brazil, which have pharmaceutical production capacities, as well as multinationals.

China's commitment in WTO and pharmaceutical regulation

China's accession to the WTO was a major concern for the global community. To prepare for entry to the WTO, China reached an understanding with the USA on critical issues, especially on intellectual property rights, in a memorandum (see BBC News, 15 November 1999). In 1993, China implemented a new patent law to protect medicines and reagents and promised administrative protection to foreign patented drugs not sold on the Chinese market between 1986 and 1992. Therefore, since 1993 it has been illegal for Chinese pharmaceutical companies to copy foreign patented drugs registered in China. As a rule, a party applies for a patent after it dis-

covers a molecule with a pharmacological function and, within a year, the party also needs to apply to other countries for patent protection. It usually takes 10–12 years to undergo the clinical trial process before a product reaches the marketing stage. The 1993 intellectual property rights agreement between China and the USA offers a 10-year protection for China's pharmaceutical companies.

The five major commitments by China related to pharmaceuticals are: the IPR of pharmaceutical inventions; removal of import tariffs; the discontinuation of administrative control of imported medical equipment; the opening of pharmaceutical sector from 1 January 2003; and the opening up of the health care services (*China Pharmaceuticals*, 13 August 2001).

Specifically:

(i) China had allowed more imports of pharmaceuticals. China's SFDA had allowed multinationals to invest, up to 70 per cent of the market share.
(ii) China allowed multinationals to enter domestic distribution and retail by 2003, but entry was limited to 11 November 2004 (*Chinapharm*, March 2002).
(iii) China allowed more intervention of the market in determining drug prices.
(iv) China promised to enforce pharmaceutical IPRs and allowed compensation of US$400 million – US$1 billion if pharmaceutical IPR was breached.
(v) A reduction of tariffs. After China's entry to the WTO, the average rate of tariffs for medicine and reagents was reduced from 9.6 per cent to 4.2 per cent. The price of medicines and preparations decreased to 4 per cent (Hong Kong Development Council, 15 July 2002). China also reduced its import tariffs from 8–15 per cent to 3–6 per cent by 2004 for pharmaceutical raw materials. A similar reduction was offered to imported Chinese herbs, such as ginseng (see also *China Pharma*, 21 June 2002).

For imported pharmaceuticals, the multinationals still have to comply with China's Pharmaceutical Regulation Law, effective since 28 February 2001, and its Imported Pharmaceutical Regulation Law and Pharmaceutical Pricing Law, also since 2001. According to Imported Pharmaceutical Regulations, an imported medicine has to obtain an imported medicine registration certificate before it gains market entry. The conditions for registration are:

(i) the imported medicine has to be approved by China's pharmaceutical manufacturing authority;
(ii) it has to meet the requirement of GMP regulation, which regulates the quality of pharmaceuticals;

(iii) it has to undergo clinical trial test procedures outlined by GCP regulations, which mandate that clinical trials have to be conducted within Chinese territories; and
(iv) pharmaceutical products from Taiwan, Hong Kong and Macao are required to follow the same rules as other imported medicines.

Imported medicines should be sold through business agents who have a Pharmaceutical *Sales Agent Permit*. These agents should also be legally registered with the Chinese pharmaceutical regulation authorities (Hong Kong Development Council, 15 July 2002).

The full impact of the WTO on China's pharmaceutical sector remains to be seen. Yet a positive outlook was postulated before and during the initial phase of China's accession. Many believed that the WTO would open up more markets for Chinese pharmaceutical producers. Chinese producers would be forced to update their innovations, technology and management resulting from competitive pressures. WTO membership would open the markets in prescriptions and OTC drugs for foreign producers.

These predictions have been largely true. Sales in all categories of the pharmaceutical sector have increased since China's entry to the WTO. It is estimated that prescription drugs will rise to US$6.5 billion by 2010 (*Chinapharm,* 2001). WTO membership has opened up government-approved pharmaceutical retailers. By 2001, China had 16,000 retailers, only 1,000 of which were large sellers. They accounted for 70 per cent of the market share, with an average profit rate of 12 per cent. After entry to the WTO, their market share has reduced, replaced by foreigner sellers or joint ventures (ibid.).

It is also important to note that China's WTO membership has inevitably posed a challenge to all stakeholders in the pharmaceutical sector. For example, it was noted that, prior to WTO entry, some widely used medicines produced by domestic manufacturers, mainly OTCs, was already experiencing excessive supply. This has intensified the price wars between domestic and foreign medicine. The foreign pharmaceutical companies were advised to avoid competition in this area and pursue their respective market niche (Hong Kong Development Council, 15 July 2002). These kinds of challenges will inevitably continue to intensify as China further opens up its pharmaceutical sector. This will be discussed later in this book.

China's developments in pharmaceutical regulation under the WTO framework

The major impact brought about by WTO entry is in the changes that the Chinese legal and regulatory system has had to make to comply with WTO requirements of non-discrimination and transparency. It is worth noting that China has made rapid improvements in legal and regulatory frame-

works in pharmaceutical-related issues, such as clinical trials, quality control and intellectual property rights, to accommodate WTO rules.

Historically, drug-related regulations were administered by the former Bureau of Drug Policy Administration (BDPA) within the Ministry of Public Health; drug production and distribution were regulated by the former State Pharmaceutical Administration (SPAC); and traditional Chinese medicine was supervised by the State Administration of Traditional Chinese Medicine (SATCM). The function of the BDPA was similar to that of the US FDA, in charge of enforcing Chinese pharmaceutical law in general. Specifically, it implemented China's Drug Administration Act in 1995, and regulated pharmaceutical manufacturing, distribution, sales and advertising. In addition, it approved domestic and imported drugs and biologics, and formulated and issued national drug standards. A major function of BDPA was pharmaceutical quality control through the National Institute for the Control of Pharmaceutical and Biological Products (NICPBP), the most important gate-keeper of pharmaceutical quality control. The other agency closely related to the function of the BDPA was the Centre for Drug Evaluation, whose main charge was pharmaceutical regulation, such as the technical review of applications, and technical and scientific guidelines for drug development. The SPAC, created in 1978 under the direct supervision of the Ministry of Public Health, supervised pharmaceutical R&D, manufacture, sales and distribution. As the state allowed more autonomy by private companies, SPAC's duties have been reduced to reviewing and approving the administrative protection of pharmaceutical products (Gross, 1998). This old structure was believed to have major problems: contradictory administrative behaviours and standards among different agencies, neglected areas that are not regulated by any agencies, and conflicts of interest (see Zhen, 2003).

The reforms starting from 1998 paved the way for today's pharmaceutical regulation system. In 1998, China founded the State Drug Administration (SDA), similar to the US FDA. In 1999, China reformed its health insurance system. In 2000, China established the system categorizing prescription from non-prescription drugs. This reform sharply increased the sale of non-prescription drugs. In 1999, the sale of non-prescription drugs was US$600 million and in 2000 US$1.5 billion, six times more than the volume in 1990. It was estimated that sales of non-prescription drugs in 2005 was worth more than US$7.3 billion (see also *China Pharma*, 21 June 2002).

The 1998 reform focused on the centralization of responsibilities and power. As a result, the State Drug Administration agency was created to combine the responsibilities of drug administration, production, distribution and traditional Chinese medicine by the SPAC and BDPA, and some responsibilities by the State Administration of Traditional Chinese Medicine (SATCM). The creation of the SDA has helped to streamline and centralize regulatory authority by replacing the SPAC and BDPA, and facili-

tating collaboration with SATCM for pharmaceutical regulation. As an entity, the SDA engaged in pharmaceutical regulation, the supervision of research, registration, production, market circulation/advertising, the use of chemical drugs and antibiotics, traditional Chinese medicine and preparations, biological products, radiopharmaceuticals, biochemical drugs, diagnostic products, medical devices and material, and medical packaging material. Under the SDA, the Department of Drug Registration closely supervised the technical operations of the registration of new drugs, biologics, generics and imported drugs (for example, narcotics and radiopharmaceuticals), conducted drug evaluation, and guided China's other drug control institutes through the Division of Chemical Drugs, Division of Traditional Chinese Medicine, Division of Biologics, and Division of Special Drugs. In this structure, pharmaceutical regulation was also controlled by the Department of Safety and Surveillance, Department of Market Supervision, Department of International Collaboration, and Department of Personnel and Education (Gross, 1998).

In March 2003, another administrative reform paved the way for the system currently used in China. In that reform, the SDA was reorganized into the State Food and Drug Administration (SFDA). Previously, the SFDA had only been in charge of food safety (Zhen, 2003). The major challenge since then has been to separate administration and execution. The 1998 Food and Health Law stipulates that the SFDA should be in charge of food control, but because of its limited staff members and equipment, its implementation ability is limited. As a result, food control is carried out by Epidemic Prevention Stations (ibid.).

Initially, the new system created confusion because of the uncertainty as to the responsibilities of each of the new departments. Reduction in the numbers of support staff has also caused some delays in reviewing some drug applications and clinical data. At the time, the restructuring of the local provincial and local pharmaceutical regulatory system was uncertain. Vertical integration was a challenge to the reform.

Now, the major Chinese agencies that regulate the pharmaceutical industries are the SFDA, the State Development and Reform Commission (SDRC), and the Provincial Administration for Industry and Commerce, which cooperates with the Provincial Food and Drug Administration to regulate drug advertisements. The SFDA takes charge of drug administration, while the SDRC oversees drug price administration (ibid.).

Specifically, the reformed SFDA has expanded its responsibilities beyond the 1998 regulations to include: pharmaceutical regulation; supervision of research; registration; production; market circulation/advertising; use of chemical drugs and antibiotics; traditional Chinese medicine and preparations; biological products; radiopharmaceuticals; biochemical drugs; diagnostic products; medical devices and materials, and medical packaging material; drug standards; the national essential drugs list; the control of

non-prescription drugs and traditional Chinese medicines; quality control of manufacturers and distributors; supervision of controlled drugs; bulk chemicals; standards for registration of pharmacy practitioners; and international collaboration and liaisons (Rui, 2001). The SFDA oversees eleven functional departments, includes seven departments covering drugs administration: General Office, Department of Drug Registration, Department of Medical Devices, Department of Drug Safety and Inspection, Department of Market Compliance, Department of Personnel and Training, and Department of International Co-operation. Since its reorganization, it has made progress in two major areas: (i) improving drug regulation. Since 1998 the SFDA has been given major responsibilities in the design and implementation of drug administration rules and regulations that address legislative gaps in harmonizing with international practices in medical devices regulation, pharmacist law, prescription and non-prescription drug administration systems, and a drug adverse reaction reporting system; and (ii) The SFDA has also abolished new drug administrative protection in the current Drug Registration Regulations and strengthened the punishment for the manufacture and distribution of adulterated or misbranded drugs under the current Drug Administration Law. These rules and regulations have effectively 'confronted, restrained, and decreased unhealthy or unlawful practices in the pharmaceutical industry'. The SFDA also reinforces the legal management of administrative staff (Zheng, 2003, p. 10).

The SFDA is also instrumental in fostering the growth of the pharmaceutical economy. For example, the SFDA has expedited environmental policy by harmonizing its laws and regulations to make them consistent with the WTO regulatory framework, and standardizing the rules and regulations governing the pharmaceutical industry. This was designed to encourage the sustainable growth of the pharmaceutical industry in China (Chinese Medicine and Commerce Association, 2003; see also Cheng, 2003).

Reimbursements

Pharmaceutical reimbursements are payments from the Chinese Government to public hospitals for prescriptions to patients. The pharmaceutical reimbursement system in China, based on the 1998 reform, shows the involvement of the public sector in pharmaceutical access in hospitals. The principles underlying pharmaceutical reimbursements were: clinical need, safety, efficacy, price comparisons, convenience, and a balance between Chinese herbs and biomedicine (see also *China Pharma*, 21 June 2002). Under this structure, pharmaceutical reimbursement schedules were maintained at both national and provincial levels. Around 1,400 pharmaceuticals received reimbursements from state-controlled insurance organizations. About 90 per cent of the drugs on this list were identical to those on local government reimbursement lists. Because of price controls, most of the reimbursed drugs were made by local manufacturers (ibid.).

Provincial and municipal governments were allowed a 10 per cent local readjustment to alter the national reimbursement list, but this system was criticized by foreign pharmaceuticals as inconsistent. The demand for low-priced drugs makes it hard for foreign companies to qualify. It was pointed out that the drugs on the list were not consistent with the regulations. The local adjustment was often found to be on a different system from that of the central government which encourages multinational participation. One solution that foreign pharmaceutical companies found to address this dilemma was to enter into joint ventures with local partners to facilitate their involvement in the regulatory process and to gain a greater market share. It was also pointed out that this reimbursement might have little effect on the competition for market share, since most of the population did not have health insurance. By 1998, national health insurance only covered some 10–15 per cent of the population, government insurance covered 7–8 per cent, and local labour insurance covered 13–20 per cent of the local population (Gross, 1998).

Classification of domestic drugs

The classification system derived from the 1998 system, which had the following framework:

Class I: new pharmaceuticals that have not been approved in any country (such as those reported in a foreign pharmacopoeia);
Class II: products currently in process of being approved by a major regulatory agency (FDA, EU, Japanese government) but not specified in a foreign pharmacopoeia;
Class III: preparations made of two or more compounds;
Class IV: synthetic products of natural compounds, approved drugs, and modified formulas that have long been approved and in use in international markets; and
Class V: adopted drugs with a new indication.

Foreign drugs belong to a separate class.

In the old system, the SDA regulated Class I, II, III and imported drugs, and provincial governments dealt with Class IV, and V. Now, the SFDA makes a distinction between OTC and prescription drugs.

Registration

The current system derives from the 1998 reform. In the 1998 reform, two separate processes existed for locally manufactured drugs and imported drugs. Both required the submission of a registration data package. This package required the following information: application form, technical data, chemistry, manufacturing, standard and analytic methods, stability,

quality control, non-clinical pharmacology and toxicology, local clinical data, labelling, and three samples testing.

In this system, Class I manufacturers may apply directly to the Centre for Drug Evaluation (CDE). Other manufacturers needed to submit an application to the provincial Department of Health, which then forwards it to the Centre for Drug Evaluation. A CDE advisory committee performs a full review of the drug, identifies possible deficiencies in the application, and sends queries to to the manufacturer for a response. After the CDE's review, the results are communicated to the BDPA. BDPA reviews an new drug under investigation, while MOPH (Ministry of Public Health) decides whether to approve of a new drug application (Gross, 1998).

On 28 February 2005, new Administrative Measures for Drug Registration were issued and implemented on 1 May 2005. These measures aim to further streamline the pharmaceutical regulatory processes. However, pharmaceutical registration and obtaining production and sales permits still involves the co-ordination and co-operation of numerous different central, provincial and local authorities, and this process can be cumbersome.

Approval of imported drugs

The current system retains the major elements of the 1998 framework. In the original regulations, the manufacturer first sent an application to the MOPH's International Co-operation Centre's pharmaceutical division, where the Imported Drug Evaluation department reviewed the application. The committee could request the manufacturer to conduct a local registration/clinical verification study. After reviewing the report submitted by the manufacturer, the BDPA would give its decision. Imported drugs were required to provide the following information:

1. Name of the drug, purpose, and proof.
2. Chemical composition.
3. Technological and manufacturing conditions.
4. Quality assessment.
4. Pharmacodynamic data and literature.
5. General pharmacological investigations.
6. Acute toxicity, long-term toxicity, and toxicity of a topical new drug.
7. Impact of each ingredient on the efficacy or toxicity of a compound preparation.
8. Mutagenicity tests.
9. Reproductive toxicity.
10. Carcinogenicity tests.
11. Drug dependency data.
12. Pharmacokinetic investigations on animals.

13. Preliminary stability tests on drug substances and their singular or compound preparations.
14. Quality standard of drug used for clinical investigation.
15. Drug sample, clinical investigation plan and preclinical review.
16. Clinical pharamcokinetic investigation.
17. Bioavailability or dissolution tests.
18. Stability test results and dates of expiration.
19. Protocol and remarks of production quality standards.
20. 3–5 sample batches produced in succession, with analytic reports.
21. Clinical reports and summary.
22. Samples of packaging material, labelling material and package inserts.

China has made attempts to harmonize its drug approval system with international standards. A new drug requires about five to eight years to be approved, shorter than the eight to ten years' average length in the USA. New drug approval requires:

(i) Investigational new drug application: besides the application materials, a sample of the drug is required to be submitted to the drug administration at the provincial level. Foreign biopharmaceutical manufacturers may apply direct to the SFDA.
(ii) Preclinical and clinical trials: China introduced its first GCP guidelines in 1998, as mentioned earlier; multiple designs, including single or double-blinded randomized controls are allowed.
(iii) Trials in China are generally not placebo-based. Instead, they compare the drug's performance with existing methods of treatment. In 2000, the SFDA issued new rules stipulating that at least 50 per cent of the work for Phase I–III clinical trials must be conducted by accredited National Clinical Trial Centres.
(iv) Quality testing: once clinical trials have been completed, the manufacturer should provide enough product samples, which have to be manufactured in three consecutive batches, for random tests.
(v) Certification: a registration certificate is issued once the quality test process has been completed successfully. Chinese provincial governments may require additional procedures to be carried out, which may not be transparent or consistent.
(vi) Post-market surveillance: the level and quality of post-market surveillance activity is increasing. All of the phase IV trials must be carried out at the same site as earlier trials (BGCG, 2005, p. 1).

Clinical trials

Drug approval is closely related to clinical trials. In the 1998 reform, clinical trials for domestic manufacturers were a separate process from that for foreign producers. The procedures for foreign producers were:

1. All foreign drugs need clinical trial data in China. China has gradually harmonized with the international clinical trial system since 1998 by the adoption of good clinical practice (GCP), which was compatible with international standards. These GCP standards were intended for drug-registration-related issues in clinical trials in China. After the clinical trials, all foreign drugs must undergo an initial two-year trial/review involving periodic comparative studies with locally manufactured products.
2. The study must be comparative, with randomized, double-blind parallel groups.
3. The minimum sample size is usually sixty samples per group.
4. Open-label studies must be evaluated on a case-by-case basis.
5. For ethical reasons, active controls over placebos are preferred for the control group.
6. Clinical and/or surrogate endpoints should be used for efficacy endpoints, depending on the drug (for example, blood pressure reduction, intraocular pressure reduction and so on)
7. Data concerning both clinical and laboratory adverse events should be collected at the safety endpoints (Gross, 1998).

This system was criticized because: (i) the uniform testing system did not take into account specific conditions of different diseases or specific population characteristics; (ii) it lacked statistical standards and specification of sample size; (iii) the hypothesis testing was not sufficient to detect population-level effects; and (iv) the standard was somewhat different for domestic producers. Domestic manufacturers have to submit one drug sample that is the exact product the company intends to manufacture; and drug stability data and the specification of OTC or prescription categories. (Gross, 1998).

Some modifications have been made and the clinical trials system in China is now more in line with international standards.

Now, under China's GCP, health authorities are responsible for approving new drugs by assigning clinical trials to investigational centres. It has been estimated that the Chinese government has given permission to 50–60 hospitals and medical centres for clinical trials. In addition, each study must be carried out at a minimum of three different sites, and of these, one must be in North China and one in South China. Furthermore, a foreign company may not conduct clinical trials itself; it must go through its Chinese counterpart. In addition, the determination of sample sizes varies on a case-by-case basis. In this system, the principal investigators of clinical trials play a significant part in determining the process of the clinical trials and the final reports for the review committee (*see* Pacific Bridge newsletter, 2005, and interview with Dr Wei Zhang, Assistant Professor, Bejing University, 20 January 2006).

Approval of non-prescription (OTC) products

The information (from the SFDA) relevant to manufacturers includes:

1. OTC drugs must be clearly identified on the labels and data insert sheets and must be conform to the National Catalogue of OTC Products list.
2. The SFDA is the authority to approve and regulate the use of OTCs.
3. Manufacturers can use a special OTC mark once it has received the Certificate of Examination and Registration for Non-prescription Drug Products.
4. Manufacturers should print this special mark on the product's label, data insert sheet, and interior and exterior packaging within 12 months of it obtaining the Certificate of Examination and Registration for Non-prescription Drug Products.
5. The red label is used for Class-A OTCs and green lake used for Class-B OTCs.
6. When using monochrome printing, the Chinese characters meaning Class A or Class B should be printed on the base of the products.
7. Penalties for violations have been regulated since 2001 by the Pharmaceutical Administration Law of the People's Republic of China.

Price controls

The Chinese government plays an active role in pharmaceutical price control. The basis of current price control is the 1999 reform, which had several stipulations: (i) the distinction was made between brands and generics, (ii) the criteria of price comparisons derived from developing countries are comparable to levels in China; (iii) a distinction was made between GMP-compatible and non-GMP compatible drugs; and (iv) a distinction was made between copies and innovative drugs. In this framework, the government did not allow any arbitrary reduction or increase in drug prices. It also mandated a special discount prices for autonomous regions. It granted high profit margins to more innovative drugs – 25–30 per cent for Class I drugs and decreasing profit levels for Class II, III and IV. It was criticized because this system excludes marketing expenses from profit calculations (Gross, 1998; see also *China Pharma*, 21 June 2002).

The regulatory mechanism for price controls was the State Development and Reform Commission (SDRC). In its scheme, only a small number of prices are regulated by the market (Guo *et al.*, 2003). This system is based on the following principles:

(i) prices are established by the SDRC. The SDRC plays a major role in regulating the drugs on the National Medical Insurance Drug List, and those manufactured or distributed by monopolies or restrictively (for example, patented drugs, Class I and II new drugs, narcotics, and cate-

gory A psychotropics. Price factors include average cost, supply and demand, and affordability for the general public;

(ii) prices are guided by the SDRC: the SDRC controls drug prices indirectly by implementing a policy of purchasing/selling price differences and profit margins. Price formulations are based on: setting an intermediate price that allows the drug price to increase; setting an intermediate price that allows the drug price to increase and decrease within a fixed range; setting a ceiling price below which the drug price can only decrease; and setting a threshold price above which a drug price can only increase. The drugs in the last category listed have more price elasticity than those established by the SDRC;

(iii) prices adjusted by the market: these include drugs that are of low value and small-yield products, such as tinctures, vulcanized fatty oils and syrups. For these drugs, the manufacturers, distributors and medical institutions must report to the SDRC the actual purchase and selling prices, as well as quantity, and establish prices according to the principles of impartiality, reasonableness, honesty, and the match between price and quality. This policy allows the supply of drugs at reasonable prices to consumers (*China Pharmaceuticals*, 2002).

The central government constantly monitors pharmaceutical prices and adjust these in response to public concerns. For example, in June 2004, the state lowered the prices of twenty-four antibiotics by 30–50 per cent. On average, pharmaceutical prices in hospital pharmacies were much higher than those of retail pharmacies, on average by 39.5 per cent. In an estimate of the most-used 100 pharmaceuticals, hospital pharmacies priced them at 1.85 per cent higher than the national average, while in contrast, retailers priced them at 16.15 per cent lower than the national average. (*Chinapharm*, 2004).

Advertising control authorities

The main agency regulating food and drug advertising is the Provincial Food and Drug Administration (PFDA), while the Provincial Administration for Industry and Commerce (PAIC) supervises all advertisements, including those for drugs. All drug advertisements must be regulated by the local Food and Drugs Administration to verify their authenticity and legitimacy consistent with the package labels approved by the SFDA (Shang, 2001). In this practice, review and supervision responsibilities are separate. To co-ordinate the possible loopholes caused by this gap, a law introduced in November 2000 stipulates that the local Food and Drug Administration has the authority to supervise and urge the PAIC to sanction unlawful drug advertisements. The revised law says that the Provincial Food and Drug Administration should monitor drug advertisements, report breaches to the PAIC and suggest penalties for those who disobey the law; or, and prosecute offenders after investigation (Cai, 2001).

Intellectual property rights

The prospects for China's pharmaceutical business are closely linked with the enforcement of intellectual property rights (IPR). IPR-related issues are critical to China's scientific and technology development as a whole. By 2004, it was estimated that China owned the IPR of only 0.3 per cent of the core technology; 99 per cent of enterprises have not applied for IPR protection; and 66 per cent do not have their own trade marks. But, since then, Chinese IPR capacity has improved and in most of the recent IPR law suits, the plaintiffs have won their cases (China State Intellectual Property Rights Office, 2005). The history of IPR regulation in China demonstrates the country's attempt to integrate with the international system since occassion to the WTO. In April 1985, China implemented the People's Republic of China Intellectual Property Rights Law; on 1 January 1993, this IPR regulation was extended to cover pharmaceuticals; the People's Republic of China Trademark Law was passed by the People's Congress and implemented on 1 January 1983. It was further amended in 1993 and 2001. The People's Republic of China Pharmaceutical Management Law was passed on 20 September 1984 and implemented on 1 December 2001. The Approving a New Drug Law and Regulations on the Protection of New Drug and Pharmaceutical Technology Transfer were implemented on 1 May 1999. On 12 December 1992 and 14 October 1992, the State Council passed the Regulations on Administrative Protection of Pharmaceuticals and Protection of Chinese Herbal Medicines Laws, which were implemented on 1 January 1993. On 2 September 1993, the People's Congress passed the People's Republic of China Anti-Illegal-Competition Law to further strengthen intellectual property rights protection. In this new climate, pharmaceutical patent applications have increased since 2000. On 2001, pharmaceutical-related and raw chemicals patents numbered 2,487, about a 14.4 per cent increase; in 2002, the total number was 3,050, about a 22.6 per cent increase; and in 2003, the number was 3,423, about a 12.2 per cent increase over the previous year. Across those three years, the average rate of increase was 16.4 per cent. Biomedicine-related patents during those three years were 1,806 applications (a 13.3 per cent increase) in 2001; 2,342 applications (a 29.7 per cent increase) in 2002; and 3,263 (a 39.3% increase over the previous year) in 2003. Biomedicine-related patents increased by an average rate of 27.4 per cent over 2001–3. Patent applications for Chinese herbal formulas were 3,247 in 2001 (a 63.9 per cent increase over the year 2000); 2,865 applications in 2002 (a 11.5 per cent increase over 2001); and 4,030 applications in 2003 (a 40.7 per cent increase over 2002). Chinese herbal patent applications have increased 31 per cent on average. Biotechnology patent applications were 884 in 2001, a 37.7 per cent increase over 2000; 1,075 in 2002, a 23.8 per cent increase over 2001; 1,476 in 2003, a 41.3 per cent increase over 2002. The average increase rate for biotechnology patents between 2001 and 2003 was

34.3 per cent. Patents for genetic engineering numbered 2,331 in 2001, a 47.1 per cent increase over the year 2000; 2,077 in 2002, an 11.9 per cent increase; and 2,144 in 2003, a 3.2 per cent increase over 2002. The average increase rate for patents for genetic engineering was 18.6 per cent between 2001 and 2003 (*Chinapharm*, 2004).

In terms of administrative structure, China's State Intellectual Property Rights Office (SIPO) was established in 2005 to strengthen the enforcement of intellectual property rights issues in China. This move derived mainly from the policy changes in 1980, when the State Council required the Patent Office of the People's Republic of China (CPO, the predecessor of SIPO) to 'protect intellectual property, encourage invention and creation, help popularize inventions and their exploitation, promote the progress and innovation in science and technology, and meet the needs of socialist modernization' (see China's SIPO website). A series of changes including those in 1985, 1992 and 2000 led to a more complete structure. In 1985, the Patent Law of the People's Republic of China was proposed and came into force during the same year. The patent law was further amended twice by the Standing Committee of the National People's Congress, on 12 March 1992 and 25 August 2000. In 1998, a reform in government agencies changed the CPO (China Patent Office) into the SIPO (State Intellectual Property Rights Office). Now the SIPO is under the direct control of the State Council and is the main government authority dealing with patent-related enforcement and foreign intellectual property rights issues with China.

The major responsibilities of SIPO are:

(i) to receive and examine patent applications of inventions, utility models and designs, granting patent rights to inventions and creations according to the patent law; and the examination and determination of requests for re-examination and invalidation;
(ii) to participate in the revision of the patent law and its implementation regulations;
(iii) to formulate an examination guide, working procedures and regulations;
(iv) to participate in the study of patent rights discretion and infringement determination; accept the entrustment of the people's court and patent administrative authorities to provide advice on the settlement of rights discretion and infringement;
(v) to join the organization of patent education and training and;
(vi) to manage patent documentation, provide a patent information service to the public, assist with patent documentation and patent information work in departments and local areas, and promote the dissemination of patent information at all levels of society (ibid.).

Administration offices that concern the pharmaceutical industry are the following:

(i) The Patent Affairs Administration Department deals mainly with the examination of patents, the formulation and implementation of patent procedures, laws and regulations, and the publication of patent applications.
(ii) The Preliminary Examination and Flow Management Department deals with initial procedural and examination matters related to patent applications, such as receiving patent applications and fees, patent-related inquiries and requests, the management of patent-related archives, issuing of patent certificates, etc.
(iii) Chemical Examination Department 1 processes the classification of patent applications in the fields of food engineering, medicine, biological engineering, chemical engineering, petroleum chemical engineering and metallurgy, and the substantive examination of patent applications.
(iv) Chemical Examination Department 2 processes the classification of patent applications in the fields of non-organic chemistry, organic chemistry, polymer chemistry, biochemistry, agricultural chemistry and electronic chemistry, and the substantive examination of patent applications.
(v) The Patent Re-examination Board of the SIPO deals with re-examining applicants who were not satisfied with decisions made by the patent office; examining invalidation requests; defending cases in court relating to patent litigation; participating in research into patent rights discretion and infringement determination; and accepting the decisions of the people's court and patent administrative authorities to provide advice on the settlement of patent infringement.
(vi) The Patent Documentation Department processes the collection and international exchange of patent documentation; establishes, prepares and manages search files for examination (including patent and non-patent documentation); manages the patent library, which provides a patent information service to the public; offers professional guidance to the national patent documentation network and information service; and is responsible for patent documentation research (ibid.).

It is important to note that China has made attempts to harmonize with the intellectual property rights requirements of the WTO and other major international conventions. A historical review of major events shows that China has made significant changes in intellectual-property-rights-related issues. For example, in the patent law implemented on 1 April 1985, pharmaceuticals or chemical derivatives were not allowed to be granted

patents. In July 1987, the Regulations on Pharmaceutical Protection and Technology Transfer changed this regulation by mandating that new pharmaceutical inventions would be protected by patents for ten years. On 2 January 1993, amendments to the patent law extended the protection of pharmaceutical inventions from ten to twenty years. In another regulation, Article 10 of the Anti-llegal-Competition Law stipulated the criminality of the violation of trade secrets, such as in counterfeiting Chinese herbal medicine formulae (*Chinapharm*, 2001)

China has also gradually harmonized its IPR practices with international norms (China SIPO 2005). For example, on 3 June 1980, China acceded to the Convention supported by the World Intellectual Property Organization. China is also a practising member of the Paris Convention for the Protection of Industrial Property, the Patent Co-operation Treaty (PCT), the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure, the Locarno Agreement Establishing an International Classification of Industrial Designs, and the Strasbourg Agreement Concerning International Patent Classification. On 1 January 1994, after becoming a member state of the PCT, the SIPO began to serve as a Receiving Office, International Searching Authority and International Preliminary Examining Authority. Chinese became one of the PCT working languages (ibid.).

In 2004, the National Copyright Administration (NCAC) participated in a WTO transition review of intellectual property protection in China, the APEC (Asia-Pacific Economic Cooperation) Experts' Conference, and the intellectual property negotiations between China and the EU. In March, the NCAC attended the bilateral consultations and negotiations between China and the USA at the working party level. NCAC provided opinions on copyright legislation, enforcement and policy for the Leading Workgroup on Commerce and Trade with the USA, and promoted the successful solution to the IPR problems between China and the USA.

The government's action to enforce intellectual property rights

Despite international criticism, the Chinese government has taken measures to comply fully with IPR protection in spite of the difficulty of implementing laws at the local level. In 2004, under the leadership of Vice-Premier Wu Yi, a Lead Group of IPR Protection of the State Council was set up. The Lead Group of IPR Protection comprised twelve related central authorities including the Supreme People's Court, the Supreme People's Procuratorate (SPP), the Ministry of Commerce (MOFCOM), the Ministry of Public Security (MPS), the State Administration for Industry and Commerce (SAIC), the National Copyright Administration (NCAC), the SIPO, and the General Administration for the Customs of China (GACC). The Lead Group aimed to direct and co-ordinate IPR protection issues at the national level,

and to resolve IPR cases. Under the aegis of this Lead Group, enforcement by multiple departments was established. This determination to enforce IPR issues at the national level has also trickled down to local levels. Similar IPR protection working groups to those at the national levels were set up in every provincial local government. This decision to enforce IPR protection was supported by Vice-Premier Wu, who said in a speech on 13 January at the National Patent Conference that IPR enforcement is crucial to the nation's economy (China SIPO, 2005).

On 26 August 2004, the General Office of the State Council issued an Action Plan for Special Operations of Intellectual Property Protection, which aimed to conduct a special IPR protection platform across the country to combat IPR (patent, trade mark, copyright) infringement, raise IPR protection awareness, promote innovation in science and technology, and educate the public about WTO-related issues. This message was re-inforced in a National IPR Protection Special Operation Teleconference on 27 August, presided over by the Lead Group of IPR Protection, the State Council. This was endorsed by the Committee for Education, Science, Culture and Health (CESCH) of the National People's Congress.

Legal enforcement

The legal framework of enforcement was emphasized by China's Supreme Court on 22 December 2004. The Supreme People's Court and SPP jointly issued the Interpretations on Several Issues on Application of the Law for the Trial of IPR Criminal Cases by the Supreme People's Court and the Supreme People's Procuratorate (or Judicial Interpretation), for the purpose of prosecuting criminal actions of IPR infringement, and maintaining the order of the socialist market economy. The penalty for IPR infringement was clearly defined by the Judicial Interpretation, with standards being stricter than before. For example, the penalty for counterfeiting a registered trademark, counterfeiting a registered trademark design and infringing copyright was 50,000 yuan (US$6,000). This development was an important step for the Chinese judicial system in reinforcing the legal framework to protect intellectual property rights 2005.

In 2004, the public security authorities across the country continued to take action against infringement and piracy. A total of 30,000 infringement and piracy cases were resolved; 21 assembly lines for illegal disc production; and 130 million infringement and piracy publications were seized (ibid.).

IPR judicial protection in China is enforced by civil, administrative and criminal judicial protection, where the civil system serves as the foundation of the entire system. The trials are usually conducted by People's Courts at each level of China to deal with IPR disputes and infringement. The mechanism of juridical organs handling IPR related cases is relatively complete in China. By the end of 2004, various divisions specializing in the trial of

IPR cases had been established. At higher levels, IPR cases are also tried by Higher People's Courts at the provincial level, Intermediate People's Courts in all provincial capital cities and some other large cities, and even in certain Primary People's Courts in small towns and cities. The IPR Trial Division in the Supreme People's Court was set up in October 1996, and later (in 2000) renamed the Third Civil Division (ibid.).

The jurisdiction over IPR cases in China is relatively centralized. In respect of cases involving patents, new plant varieties and layout designs of integrated circuits, a designated jurisdiction has been adopted. The Supreme People's Courts have appointed 49, 34 and 43 Intermediate People's Courts to try patents, varieties of new plant, and layout designs and integrated circuits, respectively. In general, civil cases involving other kinds of IPR are handled by Intermediate Courts, or courts above the level of People's Courts. In 2004, about 90.76 per cent of IPR cases were tried by Intermediate Courts or courts above the level of People's Courts.

Statistics on IPR prosecution reported by the Chinese government showed that, despite the challenging nature of the issue and the difficulties in implementation, it was determined to tackle the issue head-on. From 1985 to 2004, local People's Courts have accepted a total of 69,636 IPR civil cases in the first instance, and concluded 66,385 of these. Of all the accepted cases, 18,654 involved patents, 14,708 were copyright disputes, 6,629 were trademark cases, and 8,368 were other kinds of IPR cases (ibid.). The Chinese authorities reported that IP civil cases accepted by People's Courts have increased at a high rate. In 2004, People's Courts across the country accepted 12,205 IPR civil cases covering first instance, second instance and retrial proceedings, an increase of 31.65 per cent over the previous year. Most of these cases (about 11,113) were concluded with a total settlement of 2,980 million yuan (US$3,70 million). Most cases involved ownership and infringement of IPR: about 86.86 per cent. The foreign/unique territories involved were Hong Kong, Macau and Taiwan (ibid.).

For IPR criminal judicial protection, it was reported that a total of 387 IPR criminal cases were accepted by the People's Courts across the country in 2004, of which 385 were concluded, and 528 of the accused were found guilty. Most of the cases were trademark violations – about 82.94 of all cases in 2004. The IPR criminal cases shared the following characteristics: (i) there was a major involvement of private companies; (ii) most crimes were complex and clever; (iii) the crimes were repeated in several regions; and (iv) penalties involved prison terms (usually for less than five years), and fines. In addition to the IPR crimes, the Chinese authorities reported that 932 and 1,434 cases were related to counterfeiting of commodity or illegal business operations (ibid.). About 1,961 individuals were convicted for commodity IPR infringement; 2,526 were charged for illegal IPR businesses (ibid.).

IPR protection and increased innovation

The statistics on patent applications in general showed that China's improved patent system has resulted in increased numbers of applications for patents. For example, by 31 December 2004, a total of 2,284,925 patent applications had been accepted by the China Patent Office (CPO). Of these, 1,874,358 were from domestic applicants and 410,567 from overseas applicants, accounting respectively for 82 per cent and 18 per cent of the total (ibid.). By 31 December 2004, the total number of patents granted by the CPO were 1,255,499. Of those granted patents, 1,093,268 were from domestic applicants and 162,231 from overseas applicants, accounting respectively for 87.1 per cent and 12.9 per cent of the total number of patents granted (ibid.). The CPO received 518 requests for an international preliminary examination, and completed 534 international preliminary examination reports. By 17 March 2004, the CPO had already accepted 2 million patent applications. On 12 March 2004 the CPO formally inaugurated its Patent Application Electronic Filing System, and by 31 December 2004 a total of 4,239 electronic patent applications had been accepted by the CPO (ibid.).

The reports from China's CPO were important indicators of the inventors' participation in Chinese intellectual property rights' framework. It reported that: (i) the process for patent applications and approval had become less complex; and (ii) there had been an increase in invention patents, accounting for more than 20 per cent of the applications. The rate of increase was significant from domestic applicants and averaged more than 20 per cent over five years. The overall numbers and percentages of invention patents have increased, achieving a 32.9 per cent increase over the previous year. The review process has also been speeded up. The increase in numbers of invention patents, especially from the domestic sector, was a particularly positive sign, a possible indication that the Chinese IPR system has spurred innovation, and there was growing confidence among the public in the system to protect their inventions (ibid.).

In addition, (i) overall, applications in all categories of IPR have increased. In the first half of 2005, the CPO witnessed an 18 per cent increase in patent applications – 81.6 per cent (2,028,053) from domestic applicants and 18.4 per cent (456,764) from foreigners. Invention patents accounted for 31.5 per cent. Among the applications, 86.5 per cent and 13.5 per cent were awarded to domestic and foreign applicants, respectively (*Chinaip*, 2006; *Economy Daily News*, 2005); (ii) the number of foreign applications were greater than domestic applications; (iii) most of the invention patents (about 85.7 per cent) came from foreigners; and (iv) patents granted increased by 35 per cent in the first half of 2005, compared to the same period in 2004 (ibid.).

Overall, foreigners have played a major role as participants in the patent system. From 1 April 1985 to 28 February 2005, China awarded 193,843 invention patents, of which 123,948 (64 per cent) came from foreign appli-

cants, excluding those from multinationals, joint ventures or Chinese research institutes (*Chinaip*, 2006).

Requests for re-examination have also increased. For example, in 2004, a total of 2,768 requests for patent re-examination were accepted by the CO, 955 more than in 2003 (52.7 per cent increase), among which more than half (1,447) were settled. Most cases questioned rejection in the essential examination process and the decision in the invention patent revocation process. Most of the cases involved in patent dispute at the provincial level, and 1,215 out of 1,455 were settled.

The IPR protection for pharmaceutical business in China has important implications for all stakeholders. The IPR framework for pharmaceutical businesses evolved gradually. As mentioned earlier, in 1993, China's patent law extended its protection to pharmaceuticals. Prior to the 1993 patent law, chemicals and pharmaceuticals were only covered by 'process protection'. Now, China's patent law has been harmonized with the WTO's and patents are protected for twenty years. Patent protection is different from the administrative protection that was used sometimes in the old system, which grants exclusive marketing rights to pharmaceuticals.

The major specifications in the patent process are:

(i) Disclosure of drug information is necessary when applying for patents.
(ii) Local governments have the authority to issue manufacturing permits to medical factories and distributors. Gradually, this authority is being transferred to central government agencies, in order to offer stronger patent protection for high-tech pharmaceuticals.
(iii) The central government has mandated local governments' intellectual property law enforcement to crack down on illegal licensing practices or counterfeiting.
(iv) Registered product protection is another item on China's legal reform agenda. The 1993 Product Quality Law, for example, prohibits producers and sellers from counterfeiting products or falsely using others' trademarks, such as certification marks and famous brand marks or marks of excellence. It also prohibits producers and retailers from falsifying a product's origin, or using another factory's name and address. Violators face severe punishments and are liable for damages.
(v) China's State Intellectual Property Office (SIPO) is strengthening international property rights for new fields, such as microelectronic technology and biological engineering. The estimate from one Western investment analyst showed that SIPO expects to receive 100,000 applications each year and 150,000 patent applications every year until 2010 (Pacific Bridge Medical).

Despite all the improvements, intellectual property-rights-related issues will continue to challenge the Chinese government and society because of

conflicting cultural assumptions and a lack of enforcement power. These issues were at the centre of trade disputes between the USA and China in early 2006.

Positions of the stakeholders in the WTO framework

Multinationals

To multinationals or joint ventures, China remains a challenge with a major market potential. The following factors are likely to affect their position:

- The timing of investments. Early investors have fared much better than latecomers because: (a) early investors have developed brand loyalty among consumers and therefore have much lower costs for marketing and advertising; (b) they already know how to manage labour costs; and (c) the early arrivals are in a strong position to enlarge their market share.
- Scale of investment in the early stages. Early investment in capital equipment, facilities, technology and management tends to have a larger return later. It has been estimated that it takes 5–10 years to reap the returns of a given investment. Most of the successful arrivals have been in China for more than two decades (see also *China Pharma*, 21 June 2002).
- Models of local partnerships. After China's entry to the WTO, multinationals are entering the Chinese market through either joint ventures or by creating subsidiaries in China. The former model is believed to be a safe approach, because of the knowledge the multinationals need in terms of local consumer culture, needs, market and distribution channels, which is linked directly to a reduction in production costs. Before China's entry to the WTO, most multinationals chose to develop low-cost medicines – for example, by making copies or low-cost generics. GlaxoSmithKline and Pfizer used a combination of two approaches: making copies for general markets and producing high-priced brands for selective markets (see ibid.).
- Understanding of the local culture, and business and management environment. It is crucial that multinationals understand the cultural norms in health maintenance practices, the health needs of changing demographics, government policies, business practices in pharmaceutical sales, and the organizational structure in production, marketing and distribution. These factors have a direct or indirect impact on pharmaceutical consumption. Most pharmaceutical sales representatives deal directly with hospitals and retailers in China, and therefore pharmaceutical promotion has been focusing on these venues. It is also important for foreign distributors to balance a global, universal management style

with local unique needs; centralization versus decentralization; and developing formal distribution and informal channels. It was noted that adjustment to local factors is a more important consideration than lowering cost by centralized marketing and distribution. A centralized management and decentralized distribution network seems to be a better model for pharmaceutical management in China. A well-known case in point was the multi-domestic geographical structure used by Johnson & Johnson, where finances and accounting were controlled from the head office, and local branches (possibly with local partners) were in charge of retail and distribution (see ibid.).

The other culture-unique management model was the use of polycentric staffing policies: that is, using local personnel for field operations while retaining decision-making power in the hands of executive managers. It was noted that some management models in the globalization framework by multinationals have been quite successful. For example, the partner of Johnson & Johnson, Xian-Janssen, was lauded as the 'Janssen University' for pharmaceutical and related management training for Chinese personnel. The maturing of China's WTO membership has also provided multinationals with more opportunities in China. In 2005 there was a deepening of the global structure by the multinationals into Chinese society in terms of (i) establishing their subsidiaries in China; (ii) taking full advantage of the global localization management model; and (iii) using China as a global strategic base and for the global standardization of practices.

- Understanding the legal environment and procedures. China's laws and policies are changing rapidly. It is important that stakeholders are familiar with this environment as well as playing a constructive and active part in the legal, regulatory and policy processes by consulting and having a direct dialogue with the public authorities.
- Capitalizing on labour costs. China's labour costs are already among the lowest in the world. In addition, the tax incentives provided by the Chinese government make it more attractive for foreign companies to set up their facilities in remote provinces to further lower their production costs. Special tax breaks apply to investment in inland provinces. Smaller pharmas, especially some Western start-up biopharmaceutical businesses, also see opportunities in the Chinese markets because of the lower costs, which allow them to buy time to prove the viability of their drug prospects before seeking more stable funding commitments from Western venture capitalists. Venture capital is now considered to be an important investment instrument in Western support of portfolio companies, to take advantage of the pool of research talent in China as well as looking for investment opportunities in Chinese markets.
- Vertical and horizontal integration. A business strategy considered by some multinationals is to increase their partnerships with local com-

panies through mergers and joint ventures, as discussed earlier. A typical operation model is: The companies first establish their base, including their sales force and market share; next they they set up manufacturing facilities, and then increase their local partnerships. In 2004, mergers in pharmaceutical sectors reached a peak, and most of the mergers totalled more than US$6 million (*Chinapharm*, 2005). Novartis, which developed an innovative approach using mergers and collaborations, is a case in point (ibid.). It established its manufacturing base in Beijing in 1987 and has invested another US$15 million in expansion. Its sales increased by 49 per cent in 2004, the highest rate of increase among all its global subsidiaries. The brands that will expire in 2008 and that will become generics account for 18 per cent of Novartis's total sales (*Chinapharm,* 2005).

Novartis's strategy to deepen its involvement when Chinese manufacturers play a larger role in the generics market is a well-timed move. The major issues with such horizontal integration, such as mergers, are the hidden costs associated with changing and integrating the management system and the culture, as well as the costs associated with improving efficiency.

The multinationals are also increasing the R&D capabilities of their Chinese partners as their involvement in China deepens. Increasing local R&D can have potential benefits that go beyond cost savings; for example, GlaxoSmithKline was the first multinational pharma to establish an R&D centre in China, in 2002, after it observed that the Chinese market accounted for 7 per cent of its total global business (*China Health Sciences Newsletter*, 12 June 2002).

Roche invested US$11 million in their facilities, with the aim of building strong ties with the Chinese regulatory authorities. Roche's R&D centre is the fifth-largest in its global operation and supports the Chinese National Human Genome Centre in its work on diabetes and schizophrenia. This move is likely, in the long term, to strengthen Roche's operations as well as to explore new market opportunities in China (see Agres, 2006; see also *Chinapharm,* 2005).

Novartise is also partnering the Shanghai Institute for Materia Medica to identify compounds derived from traditional Chinese medicine. This partnership allows Novartis to develop new products. Other major pharmaceutical companies also have similar plans. For example, Pfizer, which has manufacturing facilities and a marketing operation in China, plans to establish a R&D clinical trials centre in Shanghai. GlaxoSmithKline, which has manufacturing facilities and joint ventures in China, has already established an OTC medicine R&D centre; developed a recombinatorial chemistry lab with the Shanghai Institute of Materia Medica; and has invested over US$100,000 per year to support long-term antibiotic sensitivity studies since 1990. Eli Lilly, which has a

manufacturing facility, has established a research lab in co-operation with its Chinese partner, Shanghai ChemExplorer. Merck and Company, which has manufacturing and joint development projects in China, has some joint research initiatives with leading domestic Chinese stakeholders, such as the Yangzi River Pharmacy Group. AstraZeneca has signed agreements with the School of Management at Beijing University, to invest US$37,500 to establish a research centre on pharmaceutical management and economics, focusing on pharmaceutical policies, hospital and pharmacy management, counselling and training that will provide feedback on the government's health care reforms, pharmaceutical pricing, health insurance and hospital management. A Chinese pharmaceutical manufacturer will also provide a further US$2.5 million research fund for similar projects (*Chinapharm*, 2003).

- Using China as a major centre for clinical trials. China has been approved by the US FDA to conduct clinical trials for US pharmaceutical companies. This is a business opportunity for both multinationals and their Chinese partners. AstraZeneca, for example, sees China as a critical component of its future global clinical trials because it allows possible access to data that include different ethnic populations and genetic variations. AstraZeneca has established a clinical trial operation and participated in a joint study with Shanghai Jiaotong University to identify the genes linked to schizophrenia. It has also agreed to fund a new centre for pharmaceoeconomics and outcomes research at Beijing University. The US pharmas are shifting their strategies from making traditional blockbusters to developing individually targeted drugs. The Chinese population offers access to a wide gene pool. The individually targeted drugs aimed at patients with specific genetic polymorphisms require a large pool of genetic data from diverse populations, which the Chinese population can offer. AstraZeneca claims to be the first international pharmaceutical company to locate its R&D centre in China with the hope of developing closer relations with Chinese health institutions and organizations (Santini, 2004).
- Finding unique niches for smaller pharmas. Smaller foreign drug manufacturers cannot compete with the big pharmas. They have to consider finding their niche and specialized markets, generating a diverse product portfolio, creating brand name awareness, partnering with local companies that have sales expertise, and exploring the vast untapped markets in rural areas or neglected satellite towns near big cities. The most important consideration for the smaller pharmas is to focus on a few innovative products. The greatest challenge for them is that they have to concentrate on the marketing and promotion of their products. For example, a joint venture between Dr Reddy's Laboratories, a company originating in India, and China's Kunshan Double-Crane Pharmaceutical Company was established at with total investment of nearly US$43 million to produce large volume of bulk formulations, tablets, capsules,

ointments, gels and other products across a limited range of 6–7 products, while in comparison, Dr Reddy's Laboratories in India produce 200 products. Companies have to choose between producing a wide range of products or focusing on fewer products in limited geographical regions. For this joint venture, 150 employees, out of a work force of 270, work in sales and marketing. The strategies that joint ventures usually employ are: building strong connections with health care professionals and providing professional seminars, medical education programmes and symposia for doctors. As mentioned earlier, hospital doctors are the major decision-makers about pharmaceutical recommendations, and in China some 85 per cent of pharmaceuticals are sold through hospitals, after going through a prolonged registration process that can take as long as 2–3 years. The registration process starts with the medical authorities in each province and, after their approval sales representatives apply for approval at the hospital level. In the case of KRRP (Kunshan Rotam Reddy Pharmaceuticals Ltd – a health care product company), its products are sold in eighteen provinces, through more than 100 distributors, which are accepted by 500 pharmacies, 800 hospitals and 5,500 doctors. The company's investment broke even and registered a turnover of US$9 million in 2004–5, the fifth year of its investment in China. A turnover of US$12 million is required before any profits are generated (*Business India*, 2005, p. 98).

Innovation remains the key to the competitiveness of the smaller pharmaceutical companies, and relying on only one or two products can be a risky undertaking. The story of Aurobindo Pharma, a major Indian pharmaceutical manufacturer and one of the largest of the small pharmaceutical ventures in China, is instructive. A major reason for its inability to make a profit is a fall in the price of Penicillin G, the mainstay of its production. The lesson learned in this case is that it is important not to rely on traditionally profitable pharmaceutical products but to diversify (ibid.).

- Using China as a re-export centre. The strategy of gaining a market share in China and using China as a manufacturing base to export to other countries is being used by some manufacturers. Indian companies have already learnt that they can use China as a manufacturing base and re-export to other middle-income or low-income developing countries (China Internet Information Centre, 2002). Other multinationals also find that China is a major hub for exporting to other BRIC countries: Brazil, Russia and India.

  Orchid Chemicals and Pharmceuticals, a joint venture between Indian and Chinese companies, uses China as a base for exports. It takes advantage of the low labour costs in China and targets the more regulated markets such as the USA and Europe with high-value generics that are out of patent. Orchid predicted that China would be a most competitive

exporter in the near future. The diversifying strategy that Orchid uses is informative: a wide spectrum of pharmaceutical products, including semi-synthetic antibiotics, vitamins, fermentation-based products, recombinant DNA products and formulations as well as traditional Chinese medicine, veterinary medicine and pesticides, and market sterile cephalosporin bulk actives and formulations. It also partners with locals who fit with its strategy of diversity. The strategy of integration from upstream to intermediary products also helps. The business is profit- and efficiency-driven and has become a globally positioned company that is also competitive in local markets (*Business India*, 10–23 October 2005, p. 99).

- Understanding the pharmaceutical consumption culture. According to a study conducted by the Chinese Medicine Regulation Bureau on the need and utilization rate for Chinese medicine, a third of respondents surveyed said they would prefer to go to a practitioner of Chinese medicine when health problems arose (Central Daily News Agency, 2003). Among the chronically ill, the rate was as high as 48 per cent. There was a higher utilization rate than the national average among those who suffer from high blood pressure, heart diseases and diabetes. The level of confidence in Chinese medicine practitioners among Beijing residents was also higher than in other regions. This survey also pointed out that residents who wished to receive Chinese medical treatment or a combination of Chinese and Western treatment was about 30 per cent, especially among those who sought treatment by internal medicine. It was estimated that Chinese medical practitioners supported a third of the volume of clinical care in Beijing City. According to this survey, as of 2003, 664 clinics in Beijing practised Chinese medicine, or a combination of Chinese and biomedicine or other forms of herbal medicine (ibid.). A creative partnership between biopharmas and herbal product makers might be the next step in sustaining a win–win situation.
- Imports of quality herbal medicines. Imports of foreign-manufactured Chinese medicines, especially those made in Japan and Southeast Asia, accounted for more than 20 per cent of the herbal medicine market in China by November 2004. More than 10,000 patents for Chinese herbal medicines were filed by foreign companies, while, in comparison, the patients filed by Chinese manufactures in foreign markets were about only 3,000 by 2004. A Japanese manufacturer who imported raw herbal materials from China and exported the final products back to China achieved a sales record of US$100 million in 2003, when total Chinese exports in herbal medicines were only US$700 million. The major exporters of finished Chinese herbal products to China were Japan, Korea, the Southeast Asian region and Western European countries. Chinese consumers' confidence in foreign-made Chinese medicines lies in the stability of quality and more advanced technology. These trends

> apparently point to the need for Chinese manufactures to use scientific processes in the production of Chinese medicines, to regain domestic consumers' confidence (*World Journal*, 21 November 2004).

Overall, the major challenge facing the multinationals is sustainable competitiveness. It was estimated that the attrition rate for foreign pharmas was about 30 per cent. Other challenges include: finding a more cost-effective way of developing new drugs; adapting to global as well as local markets; containing hidden costs, such as the costs and efficient returns from the promotion and marketing of products. In addition, understanding the local business environment and consumption culture remains a major barrier for newcomers to local pharmaceutical industries.

Research and development

As mentioned earlier, R&D is a challenge to all pharmaceutical manufacturers, and this is particularly true for local stakeholders: on average, multinationals invest a minimum of 10–15 per cent on R&D, while in comparison, Chinese manufacturers invest less than 2–5 per cent (*Chinapharm,* 2001). The existence of a large number of small-sized pharmas competing in a small generics market in China in the past was a major barrier for local pharmas to make larger profits. For example, it was noted that more than 100 pharmas were competing for the production of one antibiotic. The competition for a narrow list of generics leads to the fact that generics are often priced at a-tenth or a-twentieth of their brand's counterparts. In contrast, generics are priced at 7 per cent to 80 per cent of the prices of brands in Western markets, with fewer competitors for one drug (*Chinapharm,* 2005).

The key challenges to the local pharmaceutical industry as a whole are: innovations, IPR protection of their innovations, and how to market their innovations to the global community. On innovations, China needs to: (i) continue producing innovative products; (ii) strengthen training, recruiting, retaining and upgrading R&D talents; (iii) increase investment through various domestic and global financial mechanisms, such as through venture capital; (iv) commercialize innovative products; (v) upgrade R&D equipment and facilities; (vi) integrate R&D upstream and downstream development; and (vii) employ modern managerial skills in R&D. It was noted that before China's accession to the WTO, between 1991 and 1996, China approved 1,546 new drugs, most of which were Class II (copied drugs) and Class IV (changes of forms). Class I drugs (that is, new inventions) accounted for only 2.6 per cent of the total approved (*China Pharmaceuticals*, 13 August 2001). It was obvious that there was a general lack of invention or lack of registration for new pharmaceutical developments prior to China's entry into the WTO. Under the WTO, China's pharmaceutical companies can no longer copy foreign patented drugs. If this practice

does not change, it will mean a tremendous loss of profit for the majority of local pharmas. It was pointed out that the gross sale volume of all Chinese local pharmaceutical companies totalled US$40 billion, which was less than the US$45 billion sale volume of the US-based Pfizer Pharmaceutical Company (*World Journal*, 28 April 2006). R&D investment will be a major factor determining competitiveness for Chinese pharmas. It is crucial that the Chinese pharmaceutical industry increases major R&D spending on finding new products or partners among other global players for R&D collaboration. In the past, most new investment went to the purchase of equipment, the building of facilities or assembly lines, with companies vying for the production of the same drug. This trend became a vicious cycle for the local pharmas: increased competition among them led to decreased profit margins, which affected innovation. These together become restricting factors to their competitiveness in global markets (*see* some of the discussions in *China Pharmaceuticals*, 13 August 2001).

It will take some time for China's R&D to be at the same competitive level as the multinationals. Nevertheless, local pharmaceutical manufacturers should not be underestimated. Their competitive potential has gradually been realized. As mentioned earlier, the cost advantage can be an important determinant of Chinese competitiveness. A new drug typically costs more than US$800 million before it is allowed to be marketed in the West; in comparison, its cost is a-tenth of this or less in China. In addition, China's R&D capacity has already shown some potential. China's biotechnology expertise was recognized when an advanced cancer drug was approved in China. A cancer therapy that uses a virus to attack tumour cells but not healthy cells is the first to be approved in the world. This therapy, H101, a modified version of Onyx-015, which was tested in the USA in 2003, attacks only cells with the particular genetic defect that characterizies the cancer cells (Pollack, 17 November 2005).

Chinese investment in these kinds of US-abandoned drugs has proved to be rewarding. The anti-cancer drug H101 was originally developed by an American biotechnology company but was discontinued for a number of reasons. The Chinese company Shanghai Sunway Biotech continued the research, and developed the therapy after going through China's clinical trial process. China is also the only country that has approved gene therapy. The other example is the approval of Endostar in China. Endostar (based on the endostatin invented in the 1990s), similar to the FDA-approved Avastin, which was based on the theory of 'starving' the blood supply to malignant tumours, was first developed in the USA by Boston-based scientist Judah Folkman. Before Avastin was allowed to be commercialized by Genentech in February 2005, EntreMed already owned the patent rights of endostatin but abandoned the drug because of high production costs, and because it did not pass clinical trials in the USA. Dr Folkman then allowed a Chinese scientist, Professor Luo Yongzhang, to

have endostatin undergo clinical trials in China and it was approved by China's SFDA. The initial results from clinical trials were said to be encouraging in China but the drug's efficacy needs to be further proved by a larger scale of clinical trials and more rigorous studies published in internationally credible journals. Despite the fact that it might take Chinese manufacturers a long time to gain approval from the US FDA or from other countries, the drug itself already has a large market. In China, it has been estimated that more than 1.5 million individuals die of cancer every year, and the need for ground-breaking cancer treatment has never been greater (*World Journal*, 9 January 2006; see also *World Journal*, 23 December 2005). In addition, the recent discovery by Hong Kong scientists of a channel regulating the electric activities of stem cells, as in cell regeneration and multiplication, was considered a breakthrough in understanding the growth of tumours and possibly offering an effective cure. These developments in biotechnology among Chinese affiliates are conducive to the expansion of China's pharmaceutical sector if the public and private sectors continue their investment in these little-researched areas (*World Journal*, 4 December 2005).

Overall, these cases demonstrate that: (i) China's domestic pharmas should focus on niche areas in pharmaceutical innovation; (ii) they can increase their R&D capacity by acquiring smaller pharmas or drug research centres in other countries who are developing promising new drugs; (iii) they should build partnerships with already highly developed R&D sectors in Taiwan and Hong Kong, both of which have very close cultural, social and economic ties with China. Chinese pharmas should take advantage of the scientific expertise and infrastructure in both regions to grow China's domestic R&D; and (iv) domestic manufacturers should work jointly with multinationals to develop new drugs. Related to this approach is that a large number of Chinese scientists are already working in the pharmaceutical sector in the West. China should develop a framework to collaborate with these scientists in a mutually beneficial manner, and with the Western companies for, whom these scientists are working. (For example, collaboration with smaller, promising pharmaceuticals overseas, such as Tanox, could be a possible approach. Presided over by a Chinese scientist, Tanox is in the process of rolling out a new HIV drug, TNX-355, using amAb antibody that can be attached to CD4 cells and acts to prevent HIV from entering the lymph system. It has passed Clinical Trials stages I and II and is moving on to Clinical Trial stage III in 2006. This approach is a departure from the conceptual basis underlying all the existing anti-retrovirals.)

Retail pharmacy

The challenge to local pharmaceutical manufactures and distributors from 2006 onwards will be the volume of sales to retail pharmacies. The multinationals' entry into the retail market has already put immense pressure on

local retailers. It was noted that, by 2003, there were only eleven local retail businesses, accounting for only 15 per cent of total sales volume. In comparison, in the USA, the top ten retail pharmacy businesses owned more than 15,000 retail pharmacies and grossed more than 60 per cent (interviews with Dr Phil Gerbino, President of the University of the Sciences in Philadelphia, 17 March 2006; see also *China Pharmaceuticals*, 6 June 2003). The competition between hospital pharmacies and retailers can further complicate this picture: most profits derive from branded pharmaceuticals that only hospitals are allowed to sell, which makes it more difficult for local retailers to compete. It was noted that a hospital pharmacy could easily gross more than US$100,000 a day while, in contrast, a retailer's total sale volume is less than US$1,000 a day. The profit margins for brands in some cases are three times higher than for non-prescription drugs. Competitive strategies for local pharmacies would be: maintain a cost advantage and customer loyalty; upgrade their scale; improve their management style and collaboration framework; capitalize on their competitive advantages, such as familiarity with local health needs; and deepen their presence in remote areas (*Chinapharm*, 2006).

Generics

For now, the most promising area for local biomedical pharmaceutical manufacturers is the production of generics. The generics market bodes well for local pharmas because first, they account for 40–50 per cent of local sales. Second, a range of the most popular brands on the global market will expire between 2001 and 2005, and more between 2005 and 2009. It has been estimated that about fifty brands with leading sales records expired between 2000 and 2005, and each of these drugs grossed more than US$500 million in the past. This list includes Prilosec (Omeprazole) by AstraZeneca, which grossed more than US$6 billion in 1999 and 2000 (*Chinapharm*, 2 December 2001). In another estimate, a large number of brands expiry between 2004 and 2008 will be worth about US$6–10 billion to the market globally (*Chinapharm*, 12 February 2005). Third, half of the drugs sold by foreign pharmas on the Chinese market since the beginning of 2001 were generics. It was also noted that half of the US pharmas relied on the production of generics as their major source of profit (*Chinapharm*, 2001) Local pharmaceutical companies can expand their generics production by conducting an exhaustive survey of those brands that will be off patent in the near future; and acquiring the rights to produce the generic form of these drugs (*China Pharmaceuticals*, 13 August 2001).

OTC

China set up its regulatory framework for OTC drugs through the Regulations on Prescriptions and OTC Drugs, and published *A National*

Catalogue of OTC Drugs in January 2005. It was estimated that the OTC market had grown by more than 30 per cent and had reached some US$2 billion (*Chinapharm*, 2005). The OTC market is likely to be contested by all the stakeholders in China. This market can be a niche for local manufacturers if they can develop a more sophisticated mode of production and marketing for selling OTCs. It was noted that, in China, the most critical issues facing the consolidation of the OTC market are brand name recognition, credibility and customer loyalty (*China Pharmaceuticals*, 13 August 2001).

It was noted that OTC customers usually follow a process of decision-making that includes needs, previous information, price comparisons, proven efficacy of OTC products, and after-sales services. The efficacy of the core products and derivatives of core products are the two major factors in sustained customer loyalty. The major OTC drugs sold in China since early 2000 are antibiotics; medicines to relieve symptoms of influenza or colds, calcium deficiency, cardiovascular problems, respiratory infections, bronchitis, skin irritations, digestive problems and eye problems; and analgesics. The increase in demand for calcium supplements is worth noting, because it is closely related to demographic trends in China. According to China's fifth census (1 November 2000), the population aged over 60 years will number around 410 million by 2050, accounting for 27.4 per cent of China's total population. Calcium deficiency and osteoporosis-related issues are already a major health problem among this age group. As indicated in a survey in 2005, 16.1 per cent of men and 19.9 per cent of women aged over 40, and 15 per cent of men and 28.6 per cent of women aged over 60 are suffering from osteoporosis. Calcium supplements account for 16–18 per cent of the food supplement market in China (*Chinapharm*, 2001). Most OTCs are not likely to be distinguished by the efficacy of the core products, and competitive strategies will need to capitalize on their derivative services.

The derivatives of OTCs are likely to make a major difference in terms of brand loyalty. Derivatives of OTCs are a new concept in the marketing of OTCs, but are believed to be correlated with sustained brand loyalty. Derivatives include information on the OTC labels and after-sales services. After-sales service is rare but can be a competitive strategy, since most of the public in China lack health and pharmaceutical literacy. These derivatives can include: free or discounted physical examinations, free prevention services, information and referral services, home deliveries, or post-sales monitoring. Health literacy and education can include: personal hygiene and health maintenance, family health, nutrition, disease prevention, drug interactions, and reactions and side-effects. Monitoring and tracking side effects for customers, which is already being implemented in some Chinese pharmacies, can also offer a competitive advantage. Yet the ethical issues involved in offering derivative services must be monitored closely to avoid

fraudulent practices, such as the recommendation of unnecessary medicines to vulnerable patients. At the macro level, local pharmaceutical manufacturers need to expand their scale of operations by: (i) merging with multinationals; (ii) breaking geographical barriers by merging with other local retail chains; and (iii) expanding the internet retail market (*Sina Net*, 13 May 2001; see also *Sina Net*, 10 April 2001).

Pharmaceutical raw materials

China has been one of the largest producers of pharmaceuticals-related raw materials since 1997. By 2000, China was already exporting about US$2.25 billion in raw materials, more than sixty categories of which are globally competitive. China's potential has increased greatly since its entry to the WTO. China's major strengths in this area in the past have been: low production costs, including low labour costs; competitive labour skills; volume and scale of production; and global market share. The major weakness is quality control and competitiveness. As a whole, China's potential in this area is increasing, for a number of reasons. Because of its implications for pollution, most of the pharmaceutical producers in North America have relied more on imported raw materials than locally derived ones. In the early 2000s, this demand for raw materials was worth more than US$1.5 billion. Japanese producers were largely self-sufficient, but because of rising labour costs and the need for environmental protection, Japan has increasingly looked to foreign producers, especially China, for supplies. The EU countries are major producers and exporters of raw materials. In the early 2000s, the EU was exporting more than 80 per cent of its production of pharmaceuticals-related raw materials, with a value of more than US$3.6–4 billion, making it the top producer of pharmaceutical raw materials in the world. Indian pharmaceutical strengths are in formulations and generics, but India has always relied on foreign producers for raw materials. For example, India's antibiotics are a major export item but it has relied on China for most of the raw materials to produce these. Other potential competitors of China are the former USSR, Eastern European countries, Israel, South Africa and some Latin-American countries (*Chinapharm*, 2001).

Several global trends are conducive to China's competitiveness in this area:

(i) the low-cost raw materials suppliers account for a small proportion in the US/Western market. This is advantageous to Third-World producers;
(ii) because of environmental concerns and increasing quality control, the EU is planning to terminate the production of certain raw materials and move its production bases to developing countries;
(iii) the need for the raw materials for OTCs is increasing globally;

(iv) competition to obtain raw materials to produced generics from expired brands is growing and will improve the position of the suppliers in countries such as China and Brazil;
(v) profit margins are higher in pharmaceuticals-related raw materials than those in other chemical industries, such as petrochemicals and synthetic fibres. This trend will be a positive incentive for investors and producers in China (*Chinapharm,* 2001);
(vi) China's labour in this sector costs much less but is better-trained than in other countries;
(vii) at the time of writing China is only realizing about a third of its production potential;
(viii) production costs in this sector are much lower than in pharmaceutical production and as a result, profit margins are higher for Chinese producers; and
(ix) WTO membership has eliminate the tariff barrier and enlarges global market opportunities for Chinese producers.

Overall, the most promising markets for Chinese producers are in artemisinin and Vitamin C. In the early 2000s, China's artemisinin accounted for 30 per cent of the global market and production was increasing by 10 per cent annually. Vitamin C accounted for 30 per cent of the global market, and 90 per cent of Chinese production was for export. Production was concentrated in the hands of some five Chinese producers, and the average production cost was US$5 per 1,000 grams. Despite the fact that the international market for Vitamin C is saturated, the domestic market for this vitamin remains very large. On average, in the industrialized countries, the consumption of Vitamin C is 60–90 grams per capita, of which 55 per cent is in pharmaceuticals, 35 per cent in food and drinks, and 10 per cent in other areas. In contrast, in China, the per capita consumption is less than 4 grams, in which 90 per cent is used in pharmaceuticals and 10 per cent in food and drinks. There remains plenty of room for growth in China's domestic market (*Chinapharm,* 2001).

The major challenges for China's competitiveness in crude materials are:

(i) developing high-end, patent-protected products;
(ii) the need to diversify its global markets – at present, China is overly reliant on North American and EU markets;
(iii) the need to improve its distribution and marketing strategies in a global context;
(iv) the need to upgrade production technology in niche areas of raw materials, such as vitamins and proteins, and develop their derivatives; and
(v) the need to focus on low-pollution products.

Innovative products

Despite their lack of competitiveness in the conventional pharmaceutical market, Chinese producers have shown major potential with other innovative products, especially those in the biotech sector. As mentioned earlier, China has selected biotech as its key area of development in pharmaceutical sector since 1980, and is expected to own the patents of 10–15 biotech products in the coming years. The key areas of development are: upgrading technology in translation and molecular modification to improve the efficacy of antibiotics, vitamins and protein products to treat cancer, cardiovascular diseases, neurological problems, digestive problems and AIDS; diversifying the forms of vaccines, testing and screening devices, and therapeutics; using genetic and molecular engineering to increase the production of rare or nearly extinct herbal medicines; and developing new formulations through the use of biotechnology (*Chinapharm*, 2004).

The growth and profit-return rates in the biotech sector in China are worth noting, as discussed earlier. China has experienced rapid growth since the mid-1990s in infrastructure building in the biotech sector. For example, it has developed twenty-one genetically-engineered products and vaccines (*Chinapharm*, 2004). Among the top-ten best-selling genetically engineered products and vaccines, China is able to produce eight of them. China owns the patent of the recombinant p53 injection as a cancer cure and became the first in the world to approve it, as discussed earlier. China had more than seven genetically engineered products, to treat various intractable diseases, at the clinical trials stage in 2004. Vaccine development is also encouraging. New regulations by the SFDA in China mandates that vaccines and blood products cannot be re-processed overseas and be re-imported for domestic use. This ruling would increase the market share of domestic pharmas or foreign joint ventures of locally-needed vaccines (*Beijing Sina*, 29 November 2005).

The major challenges in China's biotech sector are: reorganizing its fragmented structure and integrating resources, recruiting top talents and searching for cutting-edge technology, capacity building, narrowing the gap between upstream and downstream production, building sustainable policy support, and capital investment from public and private sectors, and from domestic and international sources.

Capacity building

China has the potential to become a manufacturing centre for global pharmaceutical supplies and clinical trials, and Chinese domestic pharmaceuticals can be a direct beneficiary of this process. Certain steps taken by the government were important to moving in this direction, the most important being quality control. As discussed earlier, GMP, GLP and GCP were

important steps for standard-setting. Since 1 July 2005, China has required all manufacturers to be GMP certified. By February 2005, about 60 per cent were GMP certified, and they controlled 90 per cent of China's pharmaceutical production (*Chinapharm*, 2005). Enforcing rigorous standards is important for China's pharmaceutical development because the regulations filter out inefficient and uncompetitive manufacturers; they increase horizontal integration (such as mergers); they improve safety and efficacy; and are important in the battle against counterfeit or expired drugs. The other important improvement is that China has gained approval from the US FDA to conduct clinical trials for multinationals. Chinese pharmaceutical companies thus have the opportunity to be a major competitor in this field because of low labour costs. As stated earlier, the prospect of being a major centre for clinical trials needs to be closely regulated because of its implications for public health. A lack of monitoring of clinical trials can seriously hamper the prospects for Chinese operators in global markets. The standards set by the US FDA should be upheld and harmonized in China. Quality control should also be applied in the monitoring of traditional Chinese medicines.

Chinese herbal medicines

Chinese herbal medicines and their derivatives are the major strength of domestic pharmaceuticals producers, yet most of their potential is not realized in the global market. It has been estimated that the total sales volume is US$13 billion across the world, in which Japanese pharmaceuticals manufacturers account for 80 per cent; Korean pharmas account for 10 per cent and Chinese local pharmas accounted for only 2–3 per cent by 2005 (*World Journal*, 28 April 2006). The search of a cure for malaria shows that, if the Chinese local pharmas improve their competitive position, they can take a major lead in this area.

The case of malaria medicine is instructive for Chinese herbal medicine producers. The urgent need for the Chinese herb artemisinin to cure malaria shows the promise of the Chinese pharmaceutical industry. The increasing need for malaria medicine by forty developing countries has led to a threefold price rise. Malaria is the major cause of mortality for 1 million children globally. Since some populations in malaria-prevalent countries have developed resistance to existing therapeutics, major donors such as charities, non-governmental agencies and inter-governmental agencies in the West are convinced that artemisinin is the most effective and cost-effective drug against malaria.

The shortage of artemisinin has caused a major problem for the WHO and the Global Fund against HIV/AIDS, TB and malaria. This shortage has led to a major crisis among those infected in poor countries, for several reasons: other new drugs need to undergo a lengthy process of registration;

and medical professionals need to be informed about the pharmacotoxicity and side-effects of these new drugs. This trickle-down process in information transmission can be time-consuming and might well delay the efforts to save the lives of those infected. Artemisinin has been used as an effective therapy in Asia since ancient times. Chinese medical professionals who assisted the North Vietnamese during the Vietnam War proved that artemisinin could treat malaria. The natural plant containing artemisinin grows only in the hills of China and Vietnam. It is usually planted in January and is harvested in the autumn. A group of donors, including the Global Fund, the WHO, the World Bank, UNICEF and USAID recommended in April 2004 that those developing countries most affected by malaria should gradually replace chloroquine and sulfadoxine-pyrimethamine with antemether and artesunate.

Immediately after this announcement, a shortage of artemisinin was discovered. Before this announcement about the efficacy of artemisinin, about 30 tons of artemisinin, costing US$115 per pound, was consumed globally. Since April 2004, the price has risen rapidly, to US$180 per pound. When it was estimated that global demand for artemisinin was to rise to 220 tons, the unit price increased from US$365 to US$455. Now, it is not even a matter of price. The severe shortage of artemisinin is affecting all countries and has caused some tension between nations: for example, Ipca, an Indian pharmaceutical maker, has accused the Chinese producers of hoarding artemisinin.

According to *Chinapharm*, globally, by 2004, the market for Chinese herbal medicines grossed more than US$16 billion, in which Japanese products accounted for 80 per cent; Korea produced 10 per cent; and other countries, especially India and Singapore, accounted for 7 per cent (*Chinapharm*, 2004). In this slightly different picture, Chinese herbal manufacturers accounted for only 5 per cent of global production. The finished products were mainly in the form of food supplements. Interestingly, though, In 2004 China also imported more than US$100 million worth of herbal products from Japan, Korea, Southeast Asia and Western Europe (ibid.).

Most of the high-value-added herbal products were manufactured by foreign producers. For example, China produced an average of only 4,000 formulations annually, compared to 150,000 in the USA and 40,000 in Japan. The gap is even bigger for compounds (ibid.).

It was estimated by the Chinese Customs Bureau that, in 2005, exports of Chinese herbal medicines reached US$734 million, a 15.06 per cent increase over 2004, and it was estimated that the actual volume was worth more than US$1 billion. Raw herbal materials, totaling US$338 million, accounted for 46.05 per cent of total herbal exports, but was 3 per cent less than in 2004, while in contrast refined products and extracts continued to expand. Extracts totaling US$226 million accounted for 35.69 per cent of all herbal exports, 4 per cent higher than in 2004. The average unit price

per kilogram decreased from US$2,802 to US$2,726. Exports have increased to all regions, and the major market for Chinese medicines for 2005 was Asia, which imported 67.03 per cent of China's total herbal products, a 14.97 per cent increase over 2004. For other markets, exports have increased by 23.76 per cent in Europe, 5.06 per cent in North America, 33.85 per cent in Latin America, and 25.52 per cent in Africa (Liu, 2006).

Chinese herbal medicine derives from a comprehensive ethnomedical framework. Among the four major traditional systems, the Chinese ethnomedical system is the most widely used and practised. The clinical effects of Chinese herbal medicines have been well documented for more than 3,000 years in the medical literature. For example, currently, 12,870 types of herbal medicines are being used. By the end of the Ch'ing Dynasty early in the twentieth century, more than 100,000 prescriptions were issued. Since the mid-1990s, among the Chinese medicine formulae approved by the Chinese SFDA, more than 90 per cent have been derived from those ancient formulae (*China News Net*, 4 March 2005). The use of Chinese herbal medicine to control the symptoms of SARS in China demonstrated the need to find more innovative and scientific ways to realize the full potential of traditional Chinese medicine (*World Journal*, 13 November 2005). And, as mentioned earlier, the Chinese herbal derivative artemisinin has been found to be a most effective treatment for malaria.

Because of its potential for chronic diseases and possibly emerging infectious diseases, Chinese herbal medicine is arousing major interest in the West. For example, Novartis initiated a joint research programme with SIMM to develop natural herbal compounds in 2006. Bill and Melinda Gates Foundation granted US$42.6 million to three institutions to develop the malaria drug artemisinin. Artemisinin, despite being most effective as a treatment for malaria, is still unaffordable for most developing countries when produced in its natural form. The search for a synthetic counterpart for artemisinin is now under way. A recent project unites three partners in this undertaking: Amyris Biotechnologies Inc., a company focused on synthetic biology to make chemicals for drugs and other uses; One World Health, the first non-profit pharmaceutical firm in the USA; and UC-Berkeley. UC-Berkeley will conduct the research necessary to create a microbial factory for artemisinin. Amyris will develop the process for the industrial fermentation of the drug, and One World Health will provide drug development and regulatory support, hoping to prove bioequivalence of the synthetic drug with its existing natural counterpart.

The prospects of Chinese medicine are positive if their potential can be fully realized, with the following improvements:

(i) the trend of using high technology to purify and extract Chinese herbal medicine is conducive to the establishment of a standardized system and to enlarging the global market share;

(ii) new inventions specifically target difficult-to-treat chronic diseases, such as cancer, AIDS, malaria and hepatitis. These can offer competitive advantages for the Chinese herbal industry because these diseases prove hard to tackle in the existing Western biomedical framework;
(iii) new sources of medical treatments are being sought from plants, minerals and animal parts by researching the therapeutic effects of their active ingredients, such as ginseng. The Chinese herbal industry is also searching for substitutes for body parts of protected species, such as the polar bear, rhinoceros and hippopotamus;
(iv) preventive therapeutics is a promising area, which could be built on the abundant resources in the existing Chinese ethnomedical repertoire. The emphasis on prevention in Chinese ethnomedical knowledge can help to promote such products in food supplements and related health foods. The fact that the Shaolin Temple, an ancient centre of Chinese martial arts, is applying for a range of patents and trade marks for its martial arts and fitness knowledge is setting an encouraging precedent for local health product manufacturers.

The Chinese herbal industry is well positioned to enlarge its global market share given global regulatory trends and needs, both of which are favourable to this industry. For example, both the EU and the USA have relaxed their laws on the regulation of herbal medicines (*Chinapharm*, 2001). The global need for herbal medicine is also encouraging for Chinese manufacturers. Worldwide, the total volume of sales of herbal medicines has averaged more than US$60 billion since 2002, but Chinese herbal medicines only accounted for some 5 per cent of the market share. However, as mentioned earlier, it was noted that the profit margins for Chinese herbal producers were higher than for biomedical pharmaceutical makers in China (see *China Pharmaceuticals*, 6 March 2002).

The interest in herbal medicines has been growing rapidly in both the USA and the EU. In October 1994, the US Congress passed a law that allowed herbals to be included as 'food supplements'. This stipulation opened the door for Chinese herbal medicine on the US market, the US FDA has been studying the possibility of also registering herbal pharmaceuticals. The US market remains very attractive, for several reasons. There has been an increasing interest in natural herbals in the USA since the early 1990s, evidenced by the fact that sales of natural herbal products increased from US$6.5 billion in 1996 to US$12 billion in 2000, with an average yearly increase of 15–20 per cent, much higher than the 8 per cent increase in sales for biomedicine. In 2003, the herbal supplements market totalled more than US$400 billion in the USA (see *China Pharmaceuticals*, (6 March 2002).

In addition, the USA has also paid attention to the possibility of using the active ingredients of Chinese herbal medicines to cure chronic diseases.

By 2004, it was reported that more than 200 Chinese herbals had been permitted by the FDA to enter the clinical trials stage. More than half of the applications came from US domestic research institutions, and only ten came from Chinese research centres (*Chinapharm*, 2004).

The law relating to traditional medicine legislated by the European Union formally took effect on 30 April 2004. Before that, both Germany and Australia have approved the entry of some fifty Chinese herbals to their respective markets. The natural herbal market has been growing by 15 per cent a year in the EU.

This legislation significantly lowered the threshold for herbal medicine to enter the European Union. It recognizes the legitimacy of Chinese medicine and allows it to gain entry to the European market. Before this legislation, Chinese medicine could only be imported into the EU as food supplements or raw medical materials. The legislation allows for the broadening of pharmaceutical registration to include traditional herbal medicine, from active ingredients in a single herb, to vitamins and minerals and non-biomedical ingredients. It also allows for a change of wording in efficacy explanations: from 'its effectiveness has not been clinically proven' to 'its safety and effectiveness derive from information from long-term use and experience'. This will possibly lead to an increase of Chinese medicine on the EU market. This legislation mandates a transition period between May 2004 and April 2011, with strict conditions:

(i) exporters of Chinese herbals have to apply for a pharmaceutical sales permit;
(ii) their quality should meet EU standards;
(iii) individual EU members can mandate their pharmaceutical regulation authorities to conduct separate pharmaceutical quality testing;
(iv) exporters also need to generate a framework and mechanisms to trace the origin of poor products and record side-effects; and
(v) the exporters also need to provide facilities for recalling or recycling herbal medicines.

Serious challenges to Chinese herbals in global markets remain, however. For example, it was noted that the raw herbals and OTC herbals that were allowed into foreign markets were less than 10 per cent of the complete list (*Chinapharm*, 2001). The other issue is market share, as mentioned earlier. Chinese herbal products totalled more than 2,000 on the Chinese market, twice the number of biomedicine brands, but their share of the domestic market is only 20 per cent. Most producers are small-scale; products are repetitive; quality monitoring and control are lacking; and there is no organized management system (ibid.).

The EU framework poses major challenges and opportunities in quality testing for Chinese exporters. Because of the diverse kinds and production

processes of Chinese medicine, it is almost impossible to specify the active ingredients so the new EU requirement is likely to force the smaller, less well-equipped and less provisioned exporters out of the EU market. However, the advantage of the new legislation is: it provides a greater profit margin for Chinese herbal medicine producers because they can raise their prices. If Chinese herbal medicine passes the quality test and is allowed to be included in the EU's universal health care system, it will give the Chinese pharmaceutical industry a major boost (Zhih and Shao, 2004).

Overall, the major issues facing the Chinese herbal medicine industry are: the need to preserve effective formulations and to create new ones deriving from existing formulations; to modernize, standardize and modulize the production process; to enhance the quality and quantity of production; to preserve the environmental resources for Chinese herbal medicines standardize cultivation; and to upgrade processing and extraction methods and the commercialization process. Specifically, these concerns make it imperative for local producers to pay attention to the following issues.

Quality control

Quality control is a major challenge for Chinese herbal medicine. The major problems are lacking consistent quality, the difficulty in monitoring heavy metal and toxic residuals, and the need to upgrade extraction technology. The Chinese herbal medicine industry needs to demonstrate its quality by meeting rigorous standards: according to a sample quality testing of seventeen Chinese herbal medicines from specialized retailers in July 2003, more than 70 per cent did not pass the test.

Many factors affect the quality of traditional Chinese herbal medicines. According to the Chinese National Food and Pharmaceuticals Supervision and Management Bureau, the major issues with the Chinese herbal market are: disorganization, high turnover rate for specialists, uneven quality, counterfeits, and the lack of a clear boundary between Chinese herbal medicines and food supplements. Biomedical medicine, in contrast, had a pass mark of 97.9 per cent, when subjected to quality testing (*Sina News*, 31 July 2003).

Patent Application and Protection for Chinese Herbal Medicines

It was noted that Chinese government has made serious attempts to modernize IPR protection for Chinese herbal medicines. For example, in 1993, the State Council announced Chinese Herbal Medicine Protection Regulations to reinforce IPR protection of Chinese herbal medicines. The length of protection varies from 10, 20 and 30 years for Class I herbal medicines; and 7 years for Class II. Article 13 mandated that the ingredients and manufacturing methods are protected as trade secrets during the legal period of protection. By 1996, the Chinese patent authorities had accepted

981 applications, and authorized protection for 523 Chinese herbal formulations, 54.5 per cent of which were made by local producers (*China News Net*, 4 March 2005).

In general, Chinese domestic pharmas need to catch up in patent applications, and this is especially urgent for Chinese herbal producers. Among pharmaceutical patent applications, it was noted that foreign applicants tended to outnumber domestic ones, and there were very few applications from Chinese herbal medicine producers (*Chinapharm*, 2001).

The prevailing IPR problems facing the Chinese herbal industry are: ignoring patent protection for new drugs, a tendency to copy drugs, and little innovation and little motivation to innovate (ibid.). These IPR related issues expose other long-existing problems and affect the prospects of the herbal industry (ibid.). Most producers lack the knowledge of how to use IPR mechanisms to protect their formulations effectively. Some of the research published in international journals or conferences which could result in the development of effective therapeutics were attended by researchers in other countries and IPR-protected products were developed.

The need to improve the current situation has never been greater. Chinese producers need to:

(i) Establish a patent protection system for all related knowledge, procedures, equipment and devices, and derivatives in the modernized Chinese medicine framework. Lack of patent protection tends to lead to the duplication of formulae, which means that the original developer is often not the beneficiary of the market. In the past, once a formula, had been developed, it was easily copied by other manufacturers.

(ii) Increase IPR education for Chinese herbal manufacturers. Ignorance of patent mechanisms leads to the loss of valuable herbal knowledge to other competitors. Multinational competitors have often obtained valuable formulae from their joint-venture partners and then used IPR mechanisms to protect their acquisitions against local Chinese producers. The development of artemisinin was the most prominent example of this. Artemisinin was developed by the Chinese Herbal Medicine Institute after more than ten years of research. It was the first patent for a new Chinese herbal medicine granted by the Chinese patent authorities since the new patent law came into force in 1985. A more potent derivative of artemisinin was approved by the Ministry of Public Health and was ranked as one of the top ten new drugs in China. Yet, in neither case was global patent protection applied for, and this resulted in tremendous financial loss for its developers. Similar experiences were reported by producers of a certain Vitamin C derivatives technology. A foreign enterprise was

interested in buying the technology for US$5 million, but, because the Chinese originator had never applied for patent protection the deal fell through. The foreign business eventually obtained the technology from a published article for US$80. The story of Viagra was even more intriguing. Various perspectives were presented by different parties. Yet, in China, it was reported that more than ten Chinese enterprises had been studying the therapeutic effects of the active ingredients long before Pfizer applied for the Viagra patent in 1994 in China as well as in 111 other countries. The patent protection in 1994 for Pfizer prohibited Chinese domestic producers from benefiting from their research results. These instances show that Chinese manufacturers really need to catch up with the application of the new IPR mechanisms in the TRIPS framework, but the fact that applications by foreign producers for Chinese herbal formulae have been increasing was a positive sign for local producers (*Chinapharm*, 2001).

(iii) Form a collective force. From the perspective of fair competition, it is critical that Chinese herbal manufacturers form a collective force to use the IPR mechanisms to operate in the WTO environment to market their herbal products. It is equally important that their competitive position is not reduced by bilateral and trilateral agreements, which sometimes contradict TRIPS (ibid.).

(iv) Have a unified strategy towards the global market. The industry as a whole needs to decide its strategic position in global markets and generate effective solutions to meet challenges from global competitors. For example, to improve their weak infrastructure, a possible solution is horizontal or vertical integration via mergers among local small and medium-sized producers. Other strategies are: increasing collaboration between research institutes and industry; initiating international collaboration and patent applications in global communities; and creating their own named brands. They also need to participate actively in bargaining for IPR protection for their industry at international meetings.

(v) Increase technical capacity. There is an unwillingness or lack of the knowledge needed to apply for patents, or for re-application. It was estimated that 70 per cent of state-owned manufacturers and 95 per cent of small enterprises have never applied for a patent. Again, this is mainly because of the lack of IPR knowledge; lack of IPR expertise; or fear about the expense related to patent applications (ibid.). It has been noted that patents granted to Chinese herbal formulae are comparatively fewer than biomedical patents. One major explanation is that applicants were sometimes not familiar with IPR application procedures; some did not re-apply; others did not pay the renewal fees and then lost their patents; and others did not know

how to write the application to prove novelty and utility (*Sina Net*, 27 May 2005).

(vi) Create brand name awareness. The public and private sectors need to make a major commitment to invest in innovations in Chinese herbal products, and create global brand names for them. There needs to be a major change of traditional practices among Chinese herbal producers. For example, many effective formulae handed down for thousands of years were kept as family secrets by some experienced herbal practitioners and these would be lost if they did not apply for patent protection (*Chinapharm*, 2001).

(vii) China still needs to harmonize its IPR protection system with international standards in the existing legal and regulatory framework. Herbal formulas were kept secret in patent applications for fear of counterfeiting, and Chinese herbal producers were usually not required to list the full ingredients of the formulation on the labels. This practice is inconsistent with the labelling requirement of patent application regulations in an international framework, and herbal producers are usually penalized if this practice is discovered by the importing countries. And harmonizing Chinese herbal IPR is important for another reason: so that it can extend the protection not only to its domestic herbal industries but also to outside producers of Chinese herbal medicines, especially in Taiwan, Hong Kong and Southeast Asia.

(viii) China needs to speed capacity-building in supporting a comprehensive IPR framework for Chinese medicines. There needs to be IPR education and knowledge-sharing at all levels of the government, between state agencies, industries, communities and non-governmental organizations (NGOs), establishing free IPR services for herbal producers, and increasing the education and training of IPR experts for the industry. (*Chinapharm*, 2001)

A coherent management system

The modernization of Chinese herbal production requires a coherent and systematic framework. There is an urgent need to establish a coherent upstream and downstream Chinese herbal production and management system, including the cultivation of herbal plants; storage; identification of the therapeutic effects of active ingredients and compounds; and a standardized production system (and related issues in preservation, facilities management, efficient equipment, automation, disposal of residues, and the handling of pharmaceutical pollution); quality control (standard setting, monitoring and surveillance systems and equipment); establishing theoretical pharmacology models; clinical trials; establishing Chinese herbal informatics; and integrating Chinese herbal medicines with biomedicine (ibid.).

Standardization

Establishing a GMP process for Chinese herbal medicines is critical to the competitiveness of Chinese medicines in the global market. China, Korea and Japan are all major markets and producers of integrated Chinese medicines. The competition to set quality and production standards among these three entities will affect the leadership positions of these countries in global markets. Korea, which imported more than 80 per cent of Chinese raw herbal materials in 2005, has proposed a new law to regulate the standards of heavy metal content and pesticide residues in all Chinese herbal medicines. Similarly, Japan has proposed to extend such monitoring from an original list of three products to cover fourteen products, the major ingredients of more than 300 herbal formulae. The Chinese domestic herbal industry needs to take the initiative in regulating such issues to enable the industry to grow (Liu, 2006).

In conclusion, this chapter has offered a review of the way in which the WTO has had an impact on major stakeholders in China's pharmaceutical market. In this fiercely competitive environment, the multinationals can capitalize on their R&D position, quality standards, leadership in branded biomedical products and niche markets, their capital advantage, and management efficiency. Yet strategies might vary between multinationals and small pharmas in different areas. Chinese manufacturers are facing very severe challenges, but their potential cannot be underestimated. For example, they can capitalize on their familiarity with generics and OTCs, local marketing and distribution channels, the consumer culture, raw materials and Chinese herbal medicines. Their competitive position in biotechnology can also not be ignored. The WTO's regulatory framework can be a positive force for both domestic and multinational producers if they take full advantage of the market entry mechanisms and IPR framework. It can be a win–win situation if vertical and horizontal integration is facilitated among different stakeholders. In this regard, the potential of the Chinese pharmaceutical sector is unlimited in the WTO framework, and it also increases the dynamic momentum of global pharmaceutical interaction.