

China policies to promote local production of pharmaceutical products and protect public health



IP
Intellectual
Property and Trade

R&D
Innovation

TT
Technology
Transfer

IA
Improving Access

FI
Financing

MR
Monitoring and
Reporting



European
Commission



World Health
Organization

China policies to promote local production of pharmaceutical products and protect public health



European
Commission



World Health
Organization

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Abbreviations and Acronyms

ANDA	abbreviated new drug application
API	active pharmaceutical ingredient
BMI	basic medical insurance
CDE	Center for Drug Evaluation
CDFA	China Food and Drug Administration
ChP	Chinese Pharmacopeia
CPC	Chinese Pharmacopeia Commission
CRO	contract research organization
EML	essential medicines list
EMA	European Medicines Agency
FDI	foreign direct investment
FPP	finished pharmaceutical product
GMP	good manufacturing practice
GSPA	Global Strategy and Plan of Action
HIC	high-income country
IP	intellectual property
MAH	marketing authorization holder
MNC	multinational corporation
MOFCOM	Ministry of Commerce of the People's Republic of China
NDA	new drug application
NDRC	National Development and Reform Commission
MPP	Medicines Patent Pool
MOH	Ministry of Health
NHFPC	National Health and Family Planning Commission
OTC	over-the-counter
PHI	Public Health, Innovation and Intellectual Property
PRC	People's Republic of China
R&D	research and development
SAIC	State Administration for Industry and Commerce
SIPO	State Intellectual Property Office
SOE	state-owned enterprise
SEZ	special economic zone

TCM	traditional Chinese medicine
UHC	universal health care
US FDA	United States Food and Drug Administration
US PTO	United States Patent and Trademark Office
USP	United States Pharmacopeia Convention
VAT	value-added tax
WHO	World Health Organization
WTO	World Trade Organization

CHINA REPORT

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Executive summary

As part of a series of studies and reports regarding local production and transfer of technology in the pharmaceutical sector, the Programme on Public Health, Innovation and Intellectual Property in the World Health Organization (WHO) Department of Essential Medicines and Health Products (EMP) commissioned this study with respect to the pharmaceutical sector in the People's Republic of China (China). This study involved desk research, interviews of relevant stakeholders in China, and follow-up review and comments by interviewees with respect to the report. The main objective of the report is to identify elements of the experience in China in terms of pharmaceutical sector development that may assist other WHO Member States, in particular developing countries, to foster development of their own pharmaceutical sectors.

From the WHO standpoint, the single most important aspect of China's current policy with respect to the pharmaceutical sector is its close linkage to the objective of universal health care (UHC). UHC is a key priority for the China Government, which has committed to providing access to medicines for its people. Pharmaceuticals account for a substantial part of the current China health care budget. To achieve and sustain UHC, pharmaceutical supply must be undertaken in a way that is affordable, notwithstanding the fairly substantial financial resources of China. China has a population of approximately 1.4 billion people, and it is a population that is rapidly aging. This will increase demand for pharmaceuticals, and place increasing burden on the health care budget and system as a whole.

China has a very substantial local pharmaceutical manufacturing sector and capacity. That manufacturing sector developed during a period of China's relative isolation from international trade, particularly with respect to high-income Western countries. The industry was state-owned and the Government provided significant incentives for development, including establishing special industrial zones that included provision for low-cost land purchase and infrastructure development. As China opened its economy in the late 1980s, and joined the World Trade Organization (WTO) in late 2001, it transitioned to a largely market-based economy. This transition witnessed a period of rapid economic growth, including for China's local pharmaceutical industry. That industry largely focused on production of basic chemicals and active pharmaceutical ingredients (APIs), and China has emerged as the leading supplier of APIs by volume to the global market. Although China's API manufacturers are major exporters, so far exports of finished pharmaceutical products (FPPs) are less significant. Currently about 97% of drugs sold by local Chinese manufacturers are generic. About 80% of the drugs sold on the Chinese domestic market are generic, with foreign-owned companies supplying almost all of the innovator (i.e. patent-protected) products. Traditional Chinese medicines (TCM) are a significant component of the Chinese domestic pharmaceutical market, and the Government is promoting TCM as an export opportunity.

The rapid growth of China's pharmaceutical manufacturing sector over the past 30 years was not accompanied by an equally robust development of the medicines regulatory framework. Recognizing this, China is today emphasizing the strengthening of that framework, both in terms of rule-making and addition of personnel. This process of regulatory strengthening necessarily takes some time. A number of smaller and medium-sized pharmaceutical companies may not be able to finance compliance with new rules requiring retrofitting and/or building new pharmaceutical manufacturing facilities.

Rapid growth of pharmaceutical manufacturing has led to environmental concerns that are being addressed through new regulation and enforcement. Some manufacturers are being shut down and/or required to move their facilities. One solution to achieving better environmental outcomes is location in industrial zones where common facilities for waste processing and disposal can be established.

The China Government is encouraging R&D in the pharmaceutical sector, with special attention to the biotechnology sector and the development of 'biosimilar' products capacity. In addition to government support, there is substantial foreign direct investment in R&D, which entails transfers of technology. Foreign originator companies appear more willing to license technologies to Chinese firms and research institutes than to local firms in other developing countries, presumably because of the size and dynamism of China's pharmaceuticals market.

China has in place intellectual property laws that are compliant with the WTO *Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)*, including implementation of available flexibilities. While some foreign governments and their industries have voiced concerns about China's enforcement of intellectual property (IP) rules, this does not appear to have had a significant effect on the flow of investment into China.

China is in the midst of a series of major reforms involving its health care sector. These include moving away from using public hospital mark-ups on pharmaceutical products as a source of hospital funding, to a 'fee-for-services' based funding mechanism. China has very recently eliminated price controls on virtually all pharmaceutical products, and is encouraging transparent bidding and procurement processes, as well as a certain level of centralization of procurement. Parts of China's pharmaceutical sector, especially those focusing on distribution, remain predominantly state-owned. The China Government has been negotiating lower prices for imported originator pharmaceutical products, as well as for locally-manufactured products. All of these activities are related to the objective of achieving UHC.

The precise model of pharmaceutical sector development followed in China is not one that is likely to be followed elsewhere. This model encouraged self-sufficiency. China's pharmaceutical manufacturing industry developed during a period of state control and relative isolation from international trade. State ownership and control of industry is not today the norm in developing countries, and few countries remain isolated from international trade. There are, however, important elements of development of the industry that may provide examples for development of the pharmaceutical sector in other developing countries and regions.

First, policy with respect to pharmaceutical industry development should be closely linked to the objective of providing access to medicines to the population, including measures to contain costs.

Second, it is important to establish a regulatory framework that can assure the quality and safety of medicines, preferably as a precondition to industrial development.

Third, environmental controls are an important element of pharmaceutical industry development, and should be a priority in government planning.

Fourth, financial, tax and related incentives are important elements of promoting pharmaceutical manufacturing, and the establishment of industrial zones where common infrastructure, environmental support, transport and other elements may be jointly used by manufacturers is likely to be a useful model for other settings.

Fifth, foreign direct investment may play a useful role in development of the local pharmaceutical sector, including through investments in R&D and transfer of technology.

Sixth, governments may promote areas of local advantage, such as strength in traditional medicines and their components, as an element of local production and export opportunity.

I. Overview

a. Global Strategy and Plan of Action

At the request of World Health Organization (WHO) Member States and in connection with implementation of the *Global Strategy and Plan of Action (GSPA)*, the Programme on Public Health, Innovation and Intellectual Property in WHO EMP has undertaken a series of studies and reports regarding local production of pharmaceutical products and related transfer of technology for developing countries.¹ A principal objective of these studies and reports is to assist other developing countries and regions – particularly in Africa – with promoting development of their local pharmaceutical sectors. This report is a part of that series.² It examines the policies and practices of the Government of the People’s Republic of China (China) that have been used to encourage the local production of pharmaceutical products,³ the situation with respect to the pharmaceutical sector, and perhaps most importantly, how that set of policies is linked to access to medicines by the Chinese population.⁴ While industrial policy objectives such as increasing employment opportunity and improving balance of payments are important to developing countries, WHO is primarily interested in local production and transfer of technology from the standpoint of how this may improve public health.⁵

b. China’s characteristics

There are various aspects of China and its development that distinguish it from other developing (or emerging market) countries. China is a country of almost 1.4 billion people,⁶ meaning that its public health requirements are on a scale vastly different than to nearly all other countries. India, with close to 1.2 billion people, is the only other country with a comparable population. In addition, from the late 1940s to early 1980s, China’s economy was not linked with the highly industrialized Western countries, and it largely followed an

- 1 WHO also has assisted with the development and implementation of a local production action plan in Ethiopia. Launch of Ethiopia’s National Strategy and Plan of Action for Pharmaceutical Manufacturing. Geneva: World Health Organization; 2015. (http://www.who.int/phi/news/ethiopia_nat-strat/en/), visited 15 July 2016, accessed 13 March 2017).
- 2 Local production for access to medical products. Geneva: World Health Organization; 2011. (http://www.who.int/phi/publications/local_production/en/), accessed 13 March 2017).
- 3 This report addresses “pharmaceutical products” as encompassing conventional small molecule drugs and biological drugs. It does not address vaccines and diagnostic products as these involve substantially different types of production processes and technologies.
- 4 This report is based on desk research, including Internet research, conducted prior to a WHO-led mission to Beijing in June 2016, as well as a mission to Shanghai in June 2015, which involved interviews and discussions with various stakeholders, including representatives of the domestic pharmaceutical industry, various government agencies, hospitals and foundations involved in promoting improved health care. A list of preliminary questions transmitted in advance to the interviewee organizations is attached as Appendix 1. A list of the interviewee organizations is attached as Appendix 2. A project concept note explaining the purpose and subject matter of the study is attached as Appendix 3.
- 5 Chinese laws and regulations, and governmental pronouncements, in the pharmaceutical sector are issued in the Chinese language. There is limited availability of such laws and regulations in the English language, particularly in view of the substantial number of regulations and announcements that have been made in the past year or two. For this reason, the principal researcher of this study largely relied on an external source, James Shen, *China Pharmaceutical Guide 2016*, vols. 1–4, 11th ed. (2016) [hereinafter “China Guide 2016”], as a source of information regarding regulatory provisions. *China Guide 2016*, and a related subscription service, Pharma China Online, provide detailed information concerning the China pharmaceutical sector, and are broadly relied upon by stakeholders in the pharmaceutical sector. (In a few cases, reference is made to the 10th edition (2015) of the *China Pharmaceutical Guide* [hereinafter “China Guide 2015”].)
- 6 China is the world’s second-largest national economy in nominal terms, as of 2015. Taken over the past three decades, China has been the fastest growing economy, with an average annual GDP growth rate of 10%, although having slowed recently. China is classified as a lower middle-income country, with GDP per capita approximately 7500 US\$ in 2014 (*China Guide 2016*).

industrial policy of self-sufficiency.⁷ It developed its domestic pharmaceutical production sector in order to meet the needs of its population through central government policy controls. This included establishment of industrial zones and infrastructure supporting the manufacturing sector. China's pharmaceutical manufacturing sector did not rely on exports as a significant source of revenue. China's regulatory infrastructure evolved according to local interests, and up until the past two decades or so was operating under different standards than high-income country regulatory frameworks.

During the past 30 years, China has undergone a sustained period of rapid economic development, combined with migration of labour from the countryside to large urban areas. This period of rapid economic development is largely coincident with China's transition beginning in the late 1980s away from a central government planning economic model to a more market-oriented model. This transition included accession to the World Trade Organization (WTO) in 2001, which involved accepting a number of commitments affecting the pharmaceutical sector. The transition included transformation of many state-owned enterprises (SOEs) into privately-owned and managed enterprises.⁸ The transition from SOEs to private ownership is reflected in the pharmaceutical sector, although some of the largest and most important pharmaceutical companies (including distribution companies) in China remain majority state-owned.⁹

The specific historical evolution of China's political and economic system, and the population and demographic characteristics of the country, suggest that while other developing countries may find elements of China's path to establishment of its pharmaceutical sector useful and important, it is not an evolution that can be replicated in the sense of a specific model. China's pharmaceutical manufacturing sector developed under a system of strong central government planning and control, and this model of industrial development is not prevalent among developing countries. China has gradually moved toward a more market-oriented model.

China is in the process of a dynamic transformation of its health care sector, with substantial focus on the pharmaceutical industry. New policies, rules and regulations are being adopted at a rapid pace.¹⁰

7 See generally, Arthur Daemrlich, *The political economy of health care reform in China: negotiating public and private*, SpringerPlus 2013, 2:448 (2013). (China Guide 2016). The rise of the Chinese Communist Party and problematic relations with the West led to self-reliance in development of pharmaceutical manufacturing capacity from late 1940s to early 1980s. By the late 1970s, China's pharmaceutical industry could produce almost all essential Western drugs. For a brief period of the 1980s, China had centralized almost all aspects of pharmaceutical regulation under the State Pharmaceutical Administration of China.

8 From 1978 to 2008, the share of employment by non-state enterprises (NSEs) in China has increased from 40% to 84%, shrinking state-owned employment to 16% (China Guide 2016).

9 Many of the largest domestic pharmaceutical companies in China are majority state-owned, but with shares listed on public securities exchanges, i.e. mixed public and private ownership.

10 More notably, however, the State Council released a new policy, *Guiding Opinions for Promoting Healthy Development of the Pharmaceutical Industry*, on 11 March 2016. The policy calls for the leading role of market force and guidance role of the Government to facilitate improved industrial policies and regulatory regime as well as fair competition environment. It sets main goals to be achieved by 2020 as follows: 1) significantly raised drug innovation capability and strengthened supply security; 2) generics are launched for at least 90% of drugs with expired patents and improved supply of shortage drug products; 3) green development of pharmaceutical industry with elevated quality control standards; 4) further optimized industrial structure with improved market environment; 5) expanded scale of pharmaceutical industry with at least 10% annual core business growth and leading industrial value-added growth among all Chinese industries. Besides, the document also wants to optimize industrial structure through cross-industry M&As, vertically-integrated strategic alliances, coordinated regional development, and consolidation of pharmaceutical enterprises at specialized industry parks. Shen. China Pushes Pharmaceutical Sector Reform from the Supply Side. *Pharma China*, 21 March 2016.

c. Commitment to universal health care and pharmaceuticals

Perhaps the most important single factor underlying China's current policies with respect to its pharmaceutical sector is the decision by the Government to assure universal health care (UHC) by 2020.¹¹ In light of the size of China's population, the distribution of population among rural and urban regions, and China's middle-income country level of GDP per person, the commitment to UHC represents a large-scale budgetary undertaking by the government.¹² In terms of the pharmaceutical sector, this has significant implications. Providing pharmaceutical coverage for 1.4 billion people requires close attention to controlling the cost of medicines, while providing extensive population coverage. In 2009, health expenditures in China were 12.1% of total Government expenditures. In 2015, China's health care expenditures represented 6% of annual GDP, which is below the global average of 8%.¹³

In connection with its UHC commitment, the Government is expanding attention to its essential medicines list (EML), which currently includes about 500 pharmaceutical products, including a substantial number of traditional Chinese medicines (TCM).¹⁴ Public hospitals are required to make essential medicines available at procurement cost,¹⁵ and the government-administered medical insurance scheme reimburses for those medicines.¹⁶

China's health care system is administered through a basic medical insurance (BMI) scheme that is funded by contributions from employers and individuals, but is supplemented by substantial government subsidies.¹⁷ The central and provincial governments work together in administering the health insurance programmes. Although its present role is minor, private insurance is envisaged as playing a complementary role to the public insurance system.¹⁸

Pharmaceuticals are generally dispensed by pharmacies that are part of public hospitals. The China health care model is different from that of most Western high-income countries

11 See Hao Yu, Universal health insurance coverage for 1.3 billion people: What accounts for China's success?, *Health Policy* (2015); 119: 1145–1152. By 2011, 95% of the Chinese population was insured, compared with less than 50% in 2005. Coverage is offered through three public insurance programmes: (1) New Rule Cooperative Medical Scheme (NRCMS); (2) Urban Resident Basic Medical Insurance (URBMI), and; (3) Urban Employee Basic Medical Insurance (UEBMI). See Meng Qingyue and Tang Shenglan. Universal Health Care Coverage in China: Challenges and Opportunities. *Procedia – Social and Behavioural Sciences* (2013); 77 330–340.

12 China is affected by important demographic shifts, including movement of workers from rural to urban areas, an aging population and declining birth rate. In addition, China has witnessed a sharp increase in the prevalence of certain noncommunicable diseases, including cancer. W. Chen, et al., *Cancer Statistics in China*. CA – A Cancer Journal for Clinicians (2016); 66:115–132. "Much of the rising burden is attributable to population growth and ageing and to sociodemographic changes."

13 China Guide 2016.

14 Regarding TCM, see infra at p. 21-22. Ultimately, over 2000 drugs could be covered by the public insurance packages. Interview with Dr Sun Yang, Deputy Director General, Department of Drug Policy and Essential Medicines (NHFPC), 14 June 2016.

15 Essential drugs must be provided in all primary health facilities, which are required to sell them at the purchase prices (China Guide 2016).

16 In 2009, the Government committed about 124 billion US\$ for five health care reform programmes, including expanded coverage, establishing national essential medicines list, improving primary care, promoting people access to public health services and piloting public hospital reform programme. Yu, supra note 11.

17 As of 2011, government subsidies accounted for between 75 and 85% of health insurance premiums. Through 2011, the percentage of insurance coverage for health services was about 35%, leaving the balance to individual responsibility. The Government set a target of reducing out-of-pocket payments to 30% of total health expenditures by 2018. This is a major financial challenge, particularly as the government seeks to reduce disparities between urban and rural provision of health care. Yu, supra note 11.

18 *Ibid.*

(HICs) where physicians are often private practitioners, or operate as part of health insurance provider networks. In China, the majority of physicians exclusively work within public hospitals.

Up until quite recently, China's public hospitals were largely funded by sales of pharmaceutical products at a mark-up over their procurement costs. This at least in part accounts for the fact that, until recently, 40% of Chinese health care costs were allocated to medicines.¹⁹ Prescription sales are reimbursed by Government-administered insurance, and otherwise by individual co-pays. The consequence of this arrangement was to encourage prescription and sale of pharmaceutical products since this paid for physician salaries, hospital budgets, etc. The practice may have encouraged the inflation of pharmaceutical prices.

Recognizing these drawbacks, the Government has recently shifted the model so that hospitals may no longer mark up pharmaceutical product prices, but are instead to be funded by fees-for-services.²⁰ In theory, this should reduce incentives for pharmaceutical prescription and sales, and result in overall cost savings for the government insurance system.²¹ However, given the recent adoption of this shift in funding model, it is too early to say whether pharmaceutical prescribing and sales volume will differ significantly. Almost certainly prices will go down since the hospitals should no longer charge a mark up.

The main point, from a WHO perspective, is that China's pharmaceutical production and distribution system is now directly linked to universal access to medicines for the population. The goal of policy in the pharmaceutical sector is to meet this objective. This system will certainly have an impact on pharmaceutical producers, who are confronting a variety of government cost-containment measures, in addition to strengthened commitment to quality and safety.

19 The shift in hospital financing model is so recent that data regarding percentage of overall health care expenditures on pharmaceuticals is not yet available. The fact that public hospitals heavily relied on over-prescribing drugs and diagnostic tests in order to fund their operations was a known phenomenon. *Ibid.*

20 This requires that the Government also closely monitor the way that the new fee-for-services model is administered, the 'value for money' equation.

21 In both cases, the spending largely comes from reimbursement by the basic medical insurance scheme administered by the Government (based on employer contributions, etc.). So, in principle the flow of funds from the insurance schemes to the hospitals is not dramatically altered. But, the encouragement of pharmaceutical prescribing and higher prices should be curtailed.

II. Regulatory reform

a. Background

China's pharmaceutical industry developed when the country was relatively isolated from international trade. China's pharmaceutical manufacturing sector supplied the needs of the country's population. As the nation's economy transitioned from centrally-planned to market-based, the pharmaceutical manufacturing sector grew rapidly, encouraged by the Government through use of special industrial or economic zones, and other incentives. But, China's regulatory framework for the pharmaceutical sector did not keep up with the rapid pace of industry expansion.²²

As China's pharmaceutical manufacturing sector began to play an increasingly large role in global market supply, particularly in relation to active pharmaceutical ingredients (APIs), problems in the regulatory framework surfaced. These problems were not isolated to international markets. A number of issues also arose in terms of quality and safety in the domestic market.²³ The China Government reacted by making reform of the regulatory framework in the pharmaceutical sector a major priority. At a Politburo meeting in May 2015, President Xi demanded that the Government implement the "toughest drug regulation" by setting the highest standards, exercising the most stringent regulation, imposing the stiffest penalties for violations and instituting the most serious accountability.²⁴

22 Haona Li, He Sun & Frances J. Richmond, *The Historical Evolution of China's Drug Regulatory System*, International Center for Regulatory Science International Center for Regulatory Science (ICRS), 2014 (hereinafter "Li, Sun & Richmond").

"The early period of the reform was not without positive results. From 1981 to 1985, the gross production of medical and pharmaceutical industry grew by 15% per year. From 1986 to 1990, the gross sales of drugs increased at a rate of 18.4% per year. By the end of the 1990s, the growth rates were much higher than other sectors of China's industry. The early period of the reform caused intense competition, disorder and substandard or even counterfeit drug production. In 1995, the number of pharmaceutical factories reached 5300. There were more than 17 000 wholesale companies and 80 000 retail companies. Most of these factories and companies were very small. During this period, the number of new drug applications increased substantially (only 10 in 1985 and 1700 in 1997), but very few were truly innovative. The quality of drugs was also declining.

The call for strengthening drug regulatory system appeared in the Government work report of 1995 and 1996. In 1997, the State Council of China decided to establish an independent drug regulatory system. In 1998, the State Drug Administration (SDA), an agency directly affiliated to the State Council, was established, and the relationship between the regulatory agency and the regulated enterprises underwent great change. SDA was no longer responsible for promoting the development of the state-owned pharmaceutical enterprises, which was the main mission of former Pharmaceutical Administration (PA). The newly established SDA was not allowed to take part in any profit-making activities. This reform marked the end of the unification of the regulator and the regulated. An independent drug regulatory system was established for the first time at least on paper. SDA later changed its name to the State Food and Drug Administration (SFDA), and more recently adopted the new name of China Food and Drug Administration (CFDA) with an ongoing core mission to protect public health.

The capture of regulation by the pharmaceutical industry was a serious problem, as illustrated by the serious corruption scandal that led to the execution of Zheng Xiao-yu, the former leader of SFDA. In spite of these challenges, China's new system is widely thought to have brought remarkable improvement to the regulation of drugs. Looking back over the past 10 years, a series of guidelines, such as on GMP, GSP, GLP and GCP, and many important regulations, such as the Reporting System of Adverse Drug Reactions and the Drug Recall System, were all introduced during this period. The quality of personnel and regulatory facilities of the agency have greatly improved. The quality of the drugs has also been improving. The percentages of qualified drugs in National Drug Evaluation Testing continued to rise (Figure 2)." *Ibid.*

23 It must be noted that corruption has been a problem with respect to the drug regulatory authority, leading ultimately to the execution of the former head of the then-SFDA. See Former SFDA chief executed for corruption. ChinaDaily.com.cn, 10 July 2007.

24 China Guide 2016.

The need for regulatory reform is mentioned early on in this report because it may be instructive for other developing countries. That is, prioritizing rapid industrial development may create longer-term problems that need to be addressed. Addressing these problems may require substantial investment, for example in requiring that manufacturers upgrade plant and equipment, and in some cases shut down operations. If an appropriate regulatory structure is incorporated in planning from the outset, this may avoid potential threats to public health, as well as reduce the need for expenditures “down the road”.

b. Institutional framework

Institutional coordination is a key feature of the China approach to health care. Under the China Government system, it is possible to engage in coordination of policy under a unified direction, with various relevant agencies having input into the process.²⁵ There may be more than 20 central government agencies involved in formulating health policy.²⁶ Major decisions are made and coordinated by a Steering Group formed by the State Council.

In 2013, the structure of administrative agencies in China was reformed by the State Council, and in the health care sector the National Health and Family Planning Commission (NHFPC) was established combining the Ministry of Health (MOH) and the National Family Planning Commission (NFPC).²⁷ The China Food and Drug Administration (CFDA) became (again) a cabinet level agency of the Government.²⁸

The central law governing the pharmaceutical industry and market in China is the *Drug Administration Law*, the most recent version of which became effective on 1 December 2001.²⁹ In accordance with the *Drug Administration Law* the State Council may issue ‘Regulations for Implementation’, authority for which may be delegated to the CFDA.³⁰ A wide range of regulations has been issued by the CFDA concerning pharmaceutical sector regulation.³¹

Notwithstanding the strong role of the central government in Chinese economic policy, there is a division of responsibilities for regulation of the pharmaceutical sector between the central and provincial governments. The provincial governments are predominantly responsible for certifying manufacturing facilities for compliance with good manufacturing practice (GMP) standards, even while those standards are adopted at the central government level. Although inspections with respect to several categories of sensitive

25 Interview with Dr Sun Yang, NHFPC, 14 June 2016.

26 e.g. adoption in late August 2016 of *National Action Plan to Contain Antimicrobial Resistance (2016–2020)*, that involved coordinated planning by 14 government departments, including the NHFPC and NDRC. See NHFPC, *National Action Plan to Contain Antimicrobial Resistance (2016–2020)*, 26 August 2016, available at en.nhfpc.gov.cn, and; Shan Juan & Wang Xiaodong. Plan targets antimicrobial resistance. *ChinaDaily.com.cn*, 28 August 2016.

27 The State Administration of Traditional Chinese Medicine remains under the Administration of the NHFPC (China Guide 2016).

28 *Ibid.* In 2008 this agency lost its status of reporting directly to the State Council and became a part of the Ministry of Health but it regained this privilege in 2013. Li, Sun & Richmond, *supra* note 22.

29 *Ibid.* This law was most recently amended on 24 April 2015 (the seventh amendment). One of the objectives of this latest amendment was to facilitate the removal of price controls, which the government subsequently did.

30 *Ibid.*

31 *Ibid.* The National Development and Reform Commission in 2011 issued a document setting out areas of pharmaceutical and health care that are encouraged, restricted, eliminated and out of date. China Guide 2016 at 76–79.

products are carried out directly by the CDFA,³² inspections of manufacturing facilities are carried out principally at the provincial level.

c. Good manufacturing practice

China first introduced GMP in 1988, and the latest GMP regulations are the 2010 revised edition of *Good Manufacturing Practice for Pharmaceutical Products* (with effect from 1 March 2011). It was widely anticipated that these strengthened GMP regulations would raise costs of compliance to the point where smaller and less well-capitalized manufacturers would cease doing business.³³ Separate regulations govern excipients, packaging and labelling. In addition, there is a regulatory regime covering pharmaceutical distribution, and a regulatory regime covering conduct of clinical trials.

The State Council issued a *12th Five-Year Plan for Drug Safety (2011–2015)* that emphasized raising the standards and quality of drug products in order to reach the advanced international level.

In accordance with an official reorganization plan of the CFDA from May 2013, provincial level agencies have the authority for GMP certification of drugs and medical devices, and approval of contract manufacturing.³⁴ For injectable medicines, radioactive pharmaceuticals and biologic products, the inspections and approvals are conducted by CFDA. Thus, while CFDA is responsible for developing regulations and standards for GMP, it is mainly provincial and local authorities that are responsible for inspection and certification. Foreign companies require CFDA marketing approval for specific drug products in order to manufacture and distribute.³⁵ Registration of imported drugs may be made on the basis of marketing authorizations in the country or region where production is located. Imported drugs may require clinical trials to be conducted in China. Contract manufacturing has its own set of regulations for approval.

The CFDA works in cooperation with the United States Food and Drug Administration (US FDA) and the European Medicines Agency (EMA) for certain inspections, and in relation to training programmes. In December 2007, CFDA and US FDA reached agreement to

32 See text at pg. 9.

33 "On 25 April 2011, the SFDA issued final notice on mandatory Good Manufacturing Practice (GMP) inspections for all pharmaceutical companies doing business in China, whether with manufacturing operations in China or abroad. The SFDA and the PFDA will administer the rules. Manufacturing costs will rise somewhat, pushing out some smaller manufacturers. Foreign pharmaceutical companies must comply, and see to it that their China-based subsidiaries, JVs, and potential M&A targets are also in compliance." Deloitte (2011). *The Next Phase: Opportunities in China's pharmaceuticals market* (hereinafter "Deloitte 2011"). Pharma China estimates that over 1000 Chinese pharmaceutical companies will be pushed out of business by more stringent GMP standards that require substantial investments. Chinese experts predicted that compliance with the 2011 standards would raise the cost of drug products by 30% (China Guide 2016).

34 This raises issues of training and oversight, inter alia, because of the interests of the provinces in maintaining production to foster employment, support the tax base, etc.

35 In order to manufacture in China, a manufacturer must receive a Drug Manufacturing Certificate, which is granted by the relevant provincial or local authority, following the guidance provided by the Good Manufacturing Practice (GMP) legislation at the Central level. As matters currently stand, there is some arguably problematic overlap between GMP manufacturing certifications and the drug approval process, as GMP certification is product specific, but cannot be granted without a drug approval, which can only be given with a drug manufacturing license. There is a three-step process: a new facility must be approved after passing facility inspections, whereupon it will receive a drug manufacturer license: then, it can initiate the drug registration approval process lasting at least nine months, whereupon it may receive a provisional approval; after that, there must be application for and approval of GMP certification. There is presently a lag between a year and 18 months after completing construction of a new manufacturing facility and placing a good on the market (China Guide 2016).

participate in each other's inspections and investigations against counterfeits and sub-standard drugs.³⁶ In November 2014, CFDA and US FDA signed an implementing agreement between the two agencies regarding cooperation among regulatory staff. In March 2008, the US Pharmacopeia Convention (USP) and Chinese Pharmacopeia Commission (CPC) signed a memorandum of understanding with the purpose of working together to strengthen the quality of medicines in both the United States and China.³⁷ This included planning for joint scientific symposia to facilitate information exchange. Some foreign regulatory authorities (i.e. in addition to the US FDA and EU EMA) perform inspections of pharmaceutical plants in China.³⁸ For example, one company mentioned, and the CFDA confirmed, that Colombia's Invima had performed inspections within China, and granted certain approval certifications. Although CFDA may prefer that foreign inspector groups provide information regarding their activities, it is not a requirement of Chinese law that CFDA be notified of foreign agency inspections.

CFDA is understaffed given the large number of pharmaceutical plants, and new drug applications, for which it is responsible. The CFDA is in the process of hiring a number of additional inspectors, and staff for evaluation of new drug applications. There are some difficulties associated with this. First, staff must be trained.³⁹ Second, the CFDA competes in terms of salaries with the private sector, and this makes it difficult to retain staff, particularly those with experience. Such individuals are courted by industry.

CFDA considers that it is a strict regulatory authority.⁴⁰ China has only 18 drugs included on the WHO list of prequalified drugs, compared to 355, for example, from India.⁴¹

d. New drug approvals

Applications for marketing approval of drugs are administered by the CFDA's Center for Drug Evaluation (CDE). The CDE analyses data and reviews chemical drugs, TCM and biological products. It employs approximately 100 reviewers. As of the end of 2015 there were approximately 17 000 drug registration applications pending review.⁴² Of the approximately 8800 drug registration applications received by CDE in 2014, about 340 involved new drug applications (NDAs), and 2590 involved abbreviated new drug applications (ANDAs) for generics.⁴³

36 *Ibid.*

37 *Ibid.*

38 It is unclear where the financing for the inspections by foreign regulatory authorities comes from, but visits might be financed by local Chinese companies in order to facilitate penetration of foreign markets.

39 The CFDA in June 2016 laid out a five-year nationwide training programme for staff. See Nick Paul Taylor. Asia Regulatory Roundup: CFDA Outlines Five-Year Training Program Following Government Criticism (14 June 2016), Regulatory Affairs Professional Society (RAPS), 16 June 2014. (<http://www.raps.org/Regulatory-Focus/News/2016/06/14/25128/Asia-Regulatory-Roundup-CFDA-Outlines-Five-Year-Training-Program-Following-Government-Criticism-14-June-2016/#sthash.PrODB6Qq.dpuf>, accessed 13 March 2017).

40 CFDA so far has not been admitted to the PICS network. CFDA attributes this to "political issues".

41 China Guide 2016.

42 *Ibid.*

43 A 2011 report on the drug registration process by Deloitte indicated: "Drug registration in China is a complicated and time-consuming process, involving a number of regulatory bodies at various levels of government, and at various regional levels. Drug approval applications could be sent directly to the central SFDA prior to 2002, but the applications are now initially reviewed by provincial and municipal authorities, and then passed to the SFDA for approval. The entire approval procedure generally takes between 18 and 26 months. Domestic clinical trials are mandatory for all drugs which are new to the Chinese market required by the Good Clinical Practice (GCP) guidelines. If a drug has not been approved in China or anywhere else, permission for the trial must be granted by the SFDA and the MOH, and it normally takes 12 months for the trial process."

Effective May 2016, the State Council authorized the initiation of trials of a new drug marketing authorization holder (MAH) system in 10 provinces and central municipalities. This trial allows all pharmaceutical research institutions or individual researchers in these geographically-defined trial areas to submit drug clinical trial and marketing applications as drug registration applicants, allowing them to become marketing authorization holders. MAHs with relevant production authorizations (including through licensed pharmaceutical manufacturers) can produce on their own or through a contract manufacturer for their approved products.⁴⁴ This new system is intended to spur R&D by small- and medium-sized research institutes (and individual scientists) and businesses, by providing a direct route to earning financial return.

Throughout 2016, the CFDA has been issuing a series of new regulations to accelerate the approval of significant new drug applications, and to tighten the requirements for approval of generic drugs.⁴⁵

Biosimilars are subject to the *Technical Guidelines for Development and Evaluation of Biosimilars (Interim)*, dated 3 March 2015, which was based on WHO and international guidelines. In general, biosimilars follow the registration path of new drugs. Reference drugs used in clinical research should be approved in China.⁴⁶

The *Chinese Pharmacopoeia* (ChP), compiled by the National Pharmacopoeia Commission under the CFDA, is an official compendium of national drug standards covering traditional Chinese and Western medicines. It provides official guidelines on standards of purity, description, test, dosage, precaution, storage and the strength for each drug, and is recognized by WHO as the official pharmacopoeia of China.⁴⁷

CFDA now accepts foreign preclinical data in support of domestic drug registrations. Also, the CFDA began overseas inspections of pharmaceutical manufacturing facilities of those exporting to China in late 2011.⁴⁸

Once the clinical trials have been completed, the product must undergo a quality test. The manufacturer should provide enough product samples to conduct three complete tests. Manufacturers should be prepared for unexpected questions and test results; a large number of Chinese test laboratories are not rigorously controlled. The quality test should take around three months." Deloitte 2011.

According to a recent report from Pharma China:

"The Center for Drug Evaluation (CDE) under the CFDA is reported to have accepted a total of 1,331 drug registration applications (excluding reconsideration applications) in the first quarter of 2016, down from 2,191 and 4,428 in the 3rd and 4th quarters of 2015, according to data released recently by the China National Pharmaceutical Industry Information Center (CPIIC). Among the newly submitted registration applications, most are for chemical drugs and 40% are for new drugs.

The CFDA issued a related new rule, CFDA Working Procedures for Drug Clinical Trial Data Inspection (Interim), in a move to secure quality and efficiency of such inspections. The document requires the Center for Drug Evaluation (CDE) and the Center for Food and Drug Inspection (CFDI) set up a communication and coordination mechanism for products to be inspected. Thereafter, the agency issued the No.1 Announcement of its Onsite Drug Clinical Data Inspection Plan. The announcement sets out a plan to conduct clinical data inspections of 16 drug products which are under registration. Under the above working procedures, relevant applicants are deemed to accept such inspections if they do not withdraw relevant applications within ten days." Shen, *Repercussions of Irrational Cost Containment Surface as Premier Calls for More Drug Price Cut*, 6 May 2016. See also for new regulations, Shen, *China Pushes Pharmaceutical Sector Reform from the Supply Side*, 21 March 2016.

44 State Council Issues Notice for Trial Plan of Drug MAH System. *Pharma China*, July 2016.

45 See, e.g. CFDA Issues More Policies and Rules for Equivalence Study of Generic Drugs, *Pharma China*, July 2016.

46 China Guide 2016.

47 *Ibid.*

48 *Ibid.*

The fees associated with registering a new locally-made drug increased dramatically in 2015, rising from approximately 6000 US\$ to over 100 000 US\$ (a nearly 20 times increment). The cost of registering a new imported drug is now over 150 000 US\$. These fee increases are designed to assist CFDA with meeting its increased regulatory burdens.⁴⁹

e. Market surveillance

Part of the Government's 12th Five Year Plan for the pharmaceutical sector involved combatting the production and sale of counterfeit drugs.⁵⁰

CFDA has authority to penalize drug advertising violations,⁵¹ to investigate drug-related complaints, and to bring actions against illegal drugs, including making referrals for criminal prosecution.⁵²

f. Elimination of price controls

The China Government has recently decided to eliminate direct price controls on pharmaceutical products, including products on the government's essential medicines list (EML).⁵³ The EML plays an important role in the Chinese pharmaceutical system because

49 *Ibid.*

50 "China has a thriving counterfeit medicine industry – a big headache for western drug makers and public health authorities around the world. In the second half of 2008, the SFDA launched an electronic tracking network pilot programme. Starting in 2009, all pharmaceuticals and biologics sold in China will eventually be marked with its barcode tags. The new tracking system will lay the groundwork for a rapid response to any adverse events triggered by drugs or devices and help crack on poorly made or counterfeit products." Janet Bumpas & Ekkehard Betsch, *Exploratory Study on Active Pharmaceutical Ingredient Manufacturing for Essential Medicines*, World Bank Health, Nutrition and Population (HNP) Discussion Paper, Sept. 2009 (hereinafter "Bumpas & Betsch").

51 "[T]he National People's Congress has passed on 24 April 2015 an amendment to the 20-year-old Advertisement Law of PRC, which sets more stringent provisions on drug and medical device advertisements. The bill reflects serious concern and determination of the government to combat against widespread and out-of-control illegal drug and other health care related advertisements nationwide and across all media types. It heightens requirements for such advertising and sharply raises penalties for violations. Newly approved amendments to China's Advertising Law will become effective on 1 September 2015. Articles 15 thru 19 of the revised law address drug and medical related advertisements specifically." Shen, *NDRC Abandons Government Pricing Setting, By No Means Letting Go of Control*, 22 May 2015.

52 China Guide 2016.

53 "*Price reform*. In May 2015, in a joint policy-reform programme for drug pricing, multiple government agencies, including the powerful National Development and Reform Commission and the National Population and Family Planning Commission (China's main health regulator), eliminated government-set prices for virtually all drugs. At the same time, the government is trying to implement a pricing-reform initiative that would eliminate price markups imposed by hospitals. These reforms are intended to reduce health care costs, promote greater market competition in drug pricing, and curtail side payments, over-prescription by physicians, and corruption." Joseph Wong and Xiaoru Fei, *Life Science Innovation in China, in The Rise of Chinese Innovation in the Life Sciences*, NBR Special Report No. 6, Apr. 2016, at 19 (hereinafter "Wong & Fei").

See also China Guide 2016: "The NDRC, along with the NHFPC and the MOHRSS, introduced on 4 May the *Opinions for Advancing Drug Price Reform*, which officially withdraws government price setting of all drug products except narcotics and class 1 psychoactive. The structure of drug price regime in China is provided as follows: 1) for drugs reimbursable by the BMI, BMI agencies should, in association of relevant departments, develop procedures, basis, methods and other rules for setting BMI payment standards and explore/build mechanisms for rational formation of market prices; 2) for patented drugs and exclusively produced drugs, a transparent negotiation mechanism for price formation with participation from multiple stakeholders should be established; 3) for blood products outside the BMI reimbursement lists as well as preventative immunization drugs, free antiviral drugs for AIDS and contraceptive drugs/devices uniformly purchased by the government, prices should be formed through purchase tenders or negotiation; 4) for class 1 psychoactive and narcotic drugs, (government set) maximum ex manufacturer and retail prices will remain in force for the interim; and 5) for other drugs, prices should be freely set by manufacturers according to their production and business costs as well as market supply and demand situations.

Along with introduction of the *Opinions for Advancing Drug Price Reform*, the NDRC also issued a circular, *Notice*

hospitals are required to make medicines on the list available, and because the Government undertakes to reimburse for those medicines. (The insurance scheme reimburses other medicines, but not under the same automatic coverage system as essential medicines.) As it removes price controls, the Government is taking steps to strengthen the monitoring of drug prices.

The reasons for shifting away from direct price control are complex. Pharmaceutical manufacturers generally do not favour direct price controls because they limit margins, and may discourage investment in plant and equipment improvements. However, in China the move away from price controls in part addresses difficulties associated with administration of the price control system, including some significant incidents involving corrupt practices. The Government is instead encouraging improved bidding and procurement practices. And, the central government has been negotiating prices with foreign pharmaceutical originator companies. That said, the situation regarding procurement in China is not straightforward because much procurement is done at the provincial or hospital level, and not through a central authority.

All of these changes are having an effect on the local manufacturing sector. First, the tightening of regulatory standards, including GMP rules, means that costs of regulatory compliance are increasing. For smaller, less well-capitalized, companies it may not be feasible to bring plant and equipment into compliance. Even for well-capitalized established companies, regulatory costs are increasing. Second, the movement away from financing hospitals through pharmaceutical mark-ups may mean reduced sales (although the impact is not yet clear). Third, growing emphasis on cost containment in connection with meeting UHC targets should affect procurement and yield lower unit prices.

While price controls have been removed, pursuant to a recently adopted Government policy, a 10% price premium may be charged by manufacturers providing drugs of higher quality.⁵⁴ This is to encourage procurement based on quality. As would be expected, innovative and originator drugs are sold at higher prices than generic drugs.⁵⁵ The Government has

on Termination of Drug Price Documents, on 4 May to terminate 166 prior government price documents.

While the new reform policy pledges to minimize government intervention and allow future drug prices to be formed by market competition, it also outlined a framework under which drug prices will continue to be controlled through a matrix of cost containment measures of the basic medical insurance system (BMI) in order to “promote fair market competition and guide rational formation of drug prices”: 1) improving drug purchase mechanisms; 2) boosting the role of BMI cost containment; 3) stepping up regulation of medical practices; and 4) strengthening regulation of pricing practices.

At the same time of launching the policy, NDRC also issued a document, *Notice on Strengthening Supervision of Drug Market Price Activities*, in an attempt to maintain order of drug market prices following the latest reform package” Shen, NDRC Abandons Government Pricing Setting, By No Means Letting Go of Control, *Pharma China*, 22 May 2015.

“Shortly after, the General Office of State Council issued a new document, *Major Tasks of 2016 for Deepening Pharmaceutical and Health System Reform*, on 26 April. Those on top of the agenda are outline as follows: 1) Expanding the trial site cities of urban public hospital overall reform experiment to 200 cities this year; 2) Tiered medical service trial will be conducted in 70% of Chinese prefectures and municipalities, and clinical pathways will be implemented in all level 3 hospitals and 80% level 2 and above medical institutions; 3) Hospital financing mechanisms will be improved with all newly added urban hospital reform trial sites eliminating drug sales markups and controlling irrational medical examination costs. Critical illness (major medical) coverage will be universally implemented within this year; 4) Centralized public hospital drug purchase will be fully implemented with drug ex-manufacturer price tracking mechanism established and two-invoice system adopted. Patients are allowed to purchase drugs at hospital or retail pharmacies; and 5) Common shortage drug reserve system will be established, free supply of special drugs like AIDS drugs will be increased and regulation of medical service and drug quality will be stepped up.” (Shen, Repercussions of Irrational Cost Containment Surface as Premier Calls for More Drug Price Cut, *Pharma China*, 6 May 2016)

54 Interview with officials of Fosun Pharma, 16 June, 2016. See China Guide 2016.

55 Interview with Dr Sun Yang, NHFPC, 14 June 2016.

recently undertaken well-publicized negotiations with foreign originator companies that have secured substantially lower prices on a number of important treatments.⁵⁶

It is widely recognized that the system of decentralized drug procurement, in which drug prices are negotiated by hospitals, was inefficient and costly.⁵⁷ This is leading central government efforts to standardized procurement processes.

g. Environmental concerns

Another important element of change involves addressing the environment in China. Pharmaceutical manufacturing, and especially active pharmaceutical ingredients (API) production, creates hazardous waste that must be processed and disposed of safely.⁵⁸ The location of API production plants near urban areas in China has led to substantial environmental problems, including water contamination. The Government is shutting down API production in areas that may pose a risk, and is pressing API producers to move toward industrial zones where pollution can be dealt with through common facilities.⁵⁹ Increased environmental compliance costs are affecting the API industry and in part account for the shift toward FPP production.⁶⁰

Pharmaceutical manufacturers are subject to *Water Pollutant Discharge Standards for the Pharmaceutical Industry*, which came into effect on 1 January 2008. These regulations were expected to boost production costs of API manufacturing significantly.⁶¹

56 See e.g., *Bloomberg News*, China's Drug-Price Cuts Are Hitting Big Pharma Where It Hurts, 8 March 2016.

57 China Guide 2016.

58 Industrial pollution is a significant problem in China, and existing API plants are a material source of air and water supply contamination. See e.g., Hepeng Jia. Pharma pollution is out of control in China. Royal Society of Chemistry, *Chemistry World*, 24 June 2011 (<http://www.rsc.org/chemistryworld/News/2011/June/24061103.asp>, accessed 13 March 2017); Rick Mullin. China's Priority Changes Impact Pharmaceutical Chemicals, *Chemical & Engineering News*, 7 October 2013 (<http://cen.acs.org/articles/91/i40/Chinas-Priority-Changes-Impact-Pharmaceutical.html>, accessed 13 March 2017); Jun Wang & Xiamin Hu. Ecopharmacovigilance: Current state, challenges, and opportunities in China. *Indian Journal of Pharmacology*. 2014 Jan–Feb; 46(1): 13–17.

59 "China has historically been criticized for lax environmental protection. For example, a November 2003 New York Times article entitled "Toxins Are Part of Cost of Boom in China's Exports" documented major violations of toxic waste regulations at Zhejiang Hisun, an FDA-approved manufacturer in Taizhou, which resulted in the death of employees and illness among the local population. Increasingly, China is toughening environmental protection." Bumpas & Betsch, *supra* note 50. For information regarding shutdown of API that is Zhejiang province, see China Guide 2016.

60 Recently adopted Chinese environmental standards are strict, but it is not clear that there is widespread compliance with these standards to date. China Guide 2016.

61 *Ibid.*

III. China's Pharmaceutical Sector

a. Industry direction

Chinese pharmaceutical manufacturers have until recently concentrated on the production of basic chemicals, intermediates and APIs. In a relatively short period of time, China has become the leading global supplier of APIs in terms of volume. In order to accomplish this, as well as to improve the quality and safety of medicines supplied within China, the API manufacturing sector has been adapting to conform to strict regulatory standards. This has required, and is requiring, a major build-up of regulatory resources within the country.

More recently, Chinese manufacturers are increasingly focused on development and production of finished pharmaceutical products (FPPs), primarily so far for the domestic market, but with increasing attention to export markets. This transition is consistent with the Government's interest in supply of low-cost generic products for the domestic public health system. Typically, FPPs have higher profit margins than APIs, and this accounts for increased industry attention. Regulatory reform has also been an important element is encouraging the transition toward FPP production and distribution. These reforms include, as previously discussed, the adoption and implementation of more stringent environmental controls on API producers.

Notwithstanding its well-developed and successful domestic pharmaceutical manufacturing sector, China is a major importer of foreign-developed originator pharmaceutical products. And, as is typical among developing countries, because of the substantially higher prices of patent-protected originator products than generic products, China spends a substantial part of its medicines budget on imported products.

Total revenues from sales of pharmaceuticals in China are substantially in excess of 100 billion US\$, making China the second-largest pharmaceutical market in the world, with annual growth of over 10%.⁶² Approximately 80% of the market is in generic drugs, and 20% is in patented drugs.⁶³ The overall revenue growth rate of the Chinese pharmaceutical market has been slowing somewhat in the past year or two, mainly as a consequence of the Government's efforts to reduce pharmaceutical prices.⁶⁴ There is no consensus as to projected longer-term trends.

The number of pharmaceutical manufacturers in China has dramatically increased since introduction of reform policy by the China Government in 1978, up to 5056 API, FPP, biologic and formulated TCM producers in 2015.⁶⁵ These companies are substantial taxpayers. Reducing their number has impact both on employment and on tax revenues.

⁶² *Ibid.*

⁶³ *Ibid.* (data from Bain & Co.).

⁶⁴ "The total output of medicines exceeded 5.8mn tons in 2012, almost a double increase from 3bn tons in 2007. Growth in output has been driven by a higher disposable income and expenditure for health care services and medicines, as well as by fast development of the industrial bases of domestic medicine manufacturers. Foreign demand has also contributed to the sector's growth during the 2000s. China is a large exporter of pharmaceutical products. Its exports accounted for around 33% of the total output in 2011, which makes the country vulnerable to external demand. Exports of pharmaceutical goods reached 756,000 tons in 2011. The share of exports in total production output has been decreasing during the economic recession of the past few years, although the nominal export value has retained a slow growth year-on-year." Emerging Markets Insight, *Pharmaceuticals Manufacturing Sector China*, 2014.

⁶⁵ China Guide 2016.

For this reason, it is difficult to pursue a policy of consolidating the industry.⁶⁶ Provincial governments, represented at the national level assemblies, try to preserve the position of their local industries.

b. APIs

China is the world's leading producer and exporter of active pharmaceutical ingredients (APIs) by volume, accounting for 20% of total global API output.⁶⁷ China produces over 2000 API drug products, with annual production capacity exceeding 2 million tons.⁶⁸ It appears to have displaced India as the largest API exporter, and Chinese API producers supply a good part of the Indian market.⁶⁹ However, just as with India, Chinese manufacturers are moving away from reliance on API production toward FPPs, in part because of generally low profit margins associated with APIs.⁷⁰ (Note, however, that 'complex' APIs may enjoy higher profit margins). China is also a substantial importer of APIs used in domestic formulation.⁷¹ In 2014, the United States was the largest source of imported APIs to China.⁷²

It has become more common for API plants in China to be forced to shut down temporarily because of environmental concerns.⁷³ API manufacturing facilities have been previously located in suburban areas, but the Government will no longer allow this, and these plants will need to be either moved and/or shut down.⁷⁴

Some Chinese API manufacturers, confronted with new environmental and regulatory restrictions, are considering whether it may be economically sensible to move some production activities outside China, such as to low labour-cost environments in South East Asia. This shift has not yet taken place.

Language barriers affect the capacity of Chinese API producers to participate in high income country export markets, such as the United States, where filing of Drug Master Files requires strong English language skills.⁷⁵ As Chinese producers gain experience with export

66 Interview with Dr Sun Yang, NHFPC, 14 June 2016.

67 China Guide 2016. "... In 2009, the number of chemical pharmaceutical manufacturers reached 2434, up 7.5% year-on-year. As of August 2010, China had roughly 1200 API manufacturers capable of producing more than 1500 categories of APIs. China is ranked first in the world in output of penicillin, vitamins, antipyretics, and analgesics. These ingredients accounted for 80% of China's total pharmaceutical export value in 2009. The government is said to be drawing up a plan that would invest \$761 million in API manufacturers with the goal of raising the country's export value of products by \$4 billion annually." Bumpas & Betsch, supra note 50.

68 China Guide 2016.

69 "China is now a provider of raw materials and fine chemicals to India and further partnerships in API trade, which would combine China's position in APIs with the finished drug-product manufacturing base in India, was one area of further collaboration discussed at the conference." Patricia Van Arnum, Tracking Pharmaceutical and API Growth in China, *PharmTech.com*, 12 July 2011.

70 *Ibid.* "The Chinese API industry is small-scale and fragmented even though each of the top 20 exported APIs has more than 50% global market share. For example, in 2006, only two manufacturers were among the top 500 national Chinese enterprises and pharmaceutical firm sales were less than 25% of the average sales of the top 500 Chinese companies and less than 1% of Pfizer's sales. While the top 10 global pharmaceutical firms contributed 44% of the global sales in 2006, the top 10 Chinese pharmaceutical firms contributed only 14% of China sales in 2006. However, the industry is rapidly consolidating. For example, the number of API manufacturers has decreased by 50% since 1999 due to industry consolidation and firms leaving as they were unable to meet increasingly strict quality and environmental standards."

71 China Guide 2016.

72 *Ibid.*

73 Interview with officials of Fosun Pharma, 13 June 2016.

74 Interview with Dr Sun Yang, NHFPC, 14 June 2016.

75 China Guide 2016.

markets, it may be that foreign language skills become a more important employment criterion, even as overseas companies doing business in China will further appreciate the importance of developing capacity to work in the Chinese language.

c. FPPs

The Chinese manufacturing industry has long produced FPPs, often referred to as ‘formulations’ in China. Local industry has served as the predominant supplier of pharmaceutical products for the national market. APIs (and their precursors) are not ‘end-user’ products used by patients. They are a manufacturing input that is used to create the finished product.⁷⁶

From a technical standpoint, the manufacture of FPPs is typically less complex than the manufacture of APIs. Making an FPP involves combining an API or APIs (i.e. a chemical compound) with excipients (e.g. a sugar) and placing those in some form of delivery mechanisms (e.g. a tablet, capsule, or liquid used as a syrup or injectable). There are FPPs that are quite technically difficult to manufacture, including some combination tablets. Injectable medicines are considered highly sensitive because of their direct entry into the bloodstream, as compared to tablets or capsules that operate through the digestive system.⁷⁷ The formulation of pharmaceutical products must be done under strictly controlled conditions as the chemicals involved may be quite sensitive to environmental changes (e.g. heat and humidity), and because the purity of the resulting products is important to their safety.⁷⁸ Close attention must be paid to tracking the movement of inputs during the production process. This can be challenging when different products are made in proximity to each other.

GMP standards regulate all aspects of the FPP manufacturing process, including the manner in which pharmaceutical manufacturing facilities are constructed, their environmental control systems, how water supplies are brought in and filtered, how waste discharge is processed, how employees maintain sanitary conditions, how products are tested at different stages in the production process, how tracking systems operate, how records are kept, and so forth.

Manufacturing and selling FPPs is typically more profitable than manufacturing and selling APIs, and this at least in part accounts for a relatively recent shift among Chinese pharmaceutical manufacturers from producing APIs to producing FPPs. There are other factors, however, including environmental issues connected with API production. But, until now, China’s FPP manufacturers have largely focused on the domestic Chinese market, and not on potential export opportunities. There are a number of reasons for this. In order to sell products in foreign markets, those products must be registered/approved for sale in those markets. Particularly in ‘high value’ markets such as the United States, Europe and Japan, registering an FPP for sale can be challenging, not least because the manufacturing facility for export (e.g. in China) must be inspected and approved by importing country authorities. In addition, language can be a substantial barrier. Many Chinese manufacturers do not have staff with sufficiently strong English language skills, and English is the first

⁷⁶ That is, a medicine that is ingested, injected or that otherwise enters the human body.

⁷⁷ Thus, for example, there is very little tolerance regarding the purity of water (or other liquids) used in manufacturing injectables.

⁷⁸ Different types of medicines have different sensitivities to environmental conditions, and to the tolerance with respect to impurities.

or second language in most high-value markets. India's generic FPP producers pioneered entry into the high-value markets, such as the United States, with the distinct advantage of English as a principal language. Although high-value export markets present an obvious target of opportunity for Chinese FPP manufacturers,⁷⁹ these companies recognize that the US, EU and Japanese markets are already highly competitive.

Perhaps just as important, the Chinese market for FPPs is large and expanding, with the main constraint being the Government's focus on cost containment. And, the global market is by no means limited to the high-value markets. Chinese API producers have become the leading global supplier by competing on price, and presumably Chinese FPP manufacturers will be able to likewise offer price-advantages to middle- and low-income markets.

In 2015, pharmaceutical formulations (or FPPs) represented 26.51% of Chinese pharmaceutical industry revenues, showing annual FPP revenue growth of 10.23%. Sales of FPPs in 2015 amounted to 695 billion yuan, or just over 100 billion US\$.⁸⁰ Net profit growth in 2014 for formulations was 16.07%, the highest among the three main categories (APIs, biologicals and FPPs). The value of Chinese exports of FPPs in 2014 was approximately 3 billion US\$, while API exports amounted to approximately 26 billion US\$.⁸¹ China imported approximately 12.8 billion US\$ in FPPs, the high value mainly accounted for by patented foreign originator products.⁸² Also in 2015, China imported 8.5 billion US\$ in APIs, and 4.9 billion US\$ in biochemicals. Total Western medicines imports were valued at 26.2 billion US\$.

Pharmaceutical formulation companies in China that manufacture drugs to treat HIV/AIDS expressed interest and concern in the policies of international procurement agencies – such as the US President's Emergency Plan for AIDS Relief (PEPFAR) – in particular finding it unclear whether approval by the WHO prequalification process is sufficient to allow procurement by such programmes.

There are approximately 400 manufacturers of excipients in China, about a quarter of which specialize in the production of pharmaceutical excipients.⁸³

d. Biologics

One major focus of investment, both in terms of R&D and production, is in the biological drugs segment. The China Government and industry view the emerging biosimilars market, both domestically and internationally, as a major opportunity. From a public health standpoint, cancer is a major cause of morbidity and mortality in China, and an increasing problem.⁸⁴ As many of the new cancer therapies are biologic products, the focus on biosimilars addresses a public health need of growing importance. Foreign investors are participating actively in the biologics R&D and production sector, through joint ventures and direct investment.

79 China Guide 2016. While China has been a major exporter of APIs, so far its exports of FPPs have been comparatively modest. Companies, with government support, are seeking to change this and increase export sales, including to high income markets.

80 *Ibid*; data from SMEI.

81 China Guide 2015 (10th ed.); data from CCCIEMHP.

82 *Ibid*.

83 China Guide 2016.

84 See Chen, et al., note 12, supra.

There are more than 500 biological product/biopharmaceutical companies in China.⁸⁵ Most of those involved in R&D were established by returnees from abroad or by Western/joint venture companies.⁸⁶ “Although estimates vary widely, analysts believe that the Chinese government spends more than 600 US million dollars annually on biotech R&D through its funding initiatives. China’s national and local governments also pour money into quasi-venture capital companies that invest in technology enterprises.”⁸⁷ “... The creation of high-tech zones has helped put important infrastructure and tax incentives in place.”⁸⁸ The revenues of China’s biopharmaceutical sector in 2014 were 275 billion yuan, or about 40 billion US\$.⁸⁹

The Chin Government recognizes that its R&D in biological products is currently behind that of Western countries such as the United States and Switzerland. However, China is placing a strong emphasis on development of capacity for biologic drugs, and in the near-to medium-term sees the introduction of biosimilar drugs as a major domestic and global market opportunity.⁹⁰

Provincial and national biotechnology parks and clusters in China evidence government support and commitment to this sector.⁹¹ China has issued guidelines for the registration of biosimilar products.⁹²

85 China Guide 2016.

86 *Ibid.*

87 *Ibid.*

88 *Ibid.*

89 *Ibid.*

90 “In 2013, there were 855 above-scale (i.e., large-scale, revenue-generating) biopharmaceutical firms in China, a 14% increase from 2012. Revenues generated from sales of biomedical products grew at an annual rate of over 20% between 2003 and 2013.” Wong & Fei, citing Zero Power Intelligence, *2014–2018 China Biopharmaceutical Industry Park Market Analysis and Trend Report*, 2014.

“Though the country’s pharmaceutical market is already huge – at around 98 billion US\$ in sales in 2013, or nearly 10% of total global sales – biological drugs (as opposed to conventional chemistry-based drugs) accounted for just 5.4% of the drug market, compared with 11.7% globally. To be sure, of the one hundred largest pharmaceutical and drug firms in China, only seven are biologics producers.” Wong & Fei.

“The Five-Year Plan provisions specifically related to biotechnology applications in the life sciences industry are expected to take effect shortly. It has been reported that China’s government will invest RMB10 billion to support major new drug innovation, with RMB5–10 million in funding for each project on average from 2011 through 2015. Genetic drugs, protein drugs, monoclonal antibody clone drugs, therapeutic vaccines, and small molecule drugs are the main development focus. Furthermore, 20 biotech zones have been set up nationwide, including zones at Beijing, Shanghai, Tianjin, Guangzhou, and Shenzhen, to improve independent innovation capability.” Deloitte 2011, *supra* note 31.

“China central government has put biopharma industry as one of the seven strategic emerging sectors in the China’s ‘12th Five-year’ Plan and commits 10 billion yuan for new drug innovation during the period of 2010–2015. Adding on the private sector’s counterpart funding to Government-funded projects, it will make total funding to new drug R&D up to 40 billion yuan. However, when the fund is divided up by hundreds of projects, available funding to each projects is estimated between 5 million to 25 million yuan, which is very modest comparing to the average cost of new drug R&D worldwide.” Canadian Trade Commissioner Service, *Pharmaceutical Sector Profile – China* – December 2013.

91 “In the life science field specifically, there are currently estimated to be at least four hundred provincial and national biotechnology parks and clusters in China, many of which are located around the Shanghai-Suzhou area, Beijing, and Guangzhou. Suzhou’s BioBay, nested within the Singapore-Suzhou industrial park, for example, is one of China’s most promising bio-nanotech incubators. BioBay currently hosts around 400 companies, of which 105 are engaged in drug discovery and 34 in contract research. Since the industrial park opened in 2007, BioBay-based labs and firms have submitted 58 applications for clinical trials; the CFDA has approved 18 of them, 2 of which qualify as novel Class 1.1 drugs (i.e., drugs that have not been approved and marketed in any other country).” Wong & Fei, at 11, citing Suzhou Industrial Park Administrative Committee, promotional displays at the BioBay Exhibition Center, 26 June 2015.

“Suzhou’s Innovent Biologics recently entered a 450 billion US\$ partnership with Eli Lilly to collaborate on R&D and potentially commercialize three new cancer treatments. BeiGene, located in Beijing’s Zhongguancun Life Science Park, licensed out two drug candidates to Merck in 2013.” Wong & Fei.

92 China Guide 2016.

There is substantial foreign investment and participation in China's biologics sector.⁹³ This includes investments by most of the world's leading biopharmaceutical companies.

e. Traditional Chinese medicines (TCM)

One important feature of China's public health system is its reliance upon TCM. TCM are an important part of ongoing government policy development, both in terms of medicinal products and in terms of hospital/physician practice. China has a long history of innovation in the medicines arena, tracing back millennia to the use of medicinal herbs and traditional medical practice. TCMs play a large role in the current Chinese health care system, and are expected to play a large role in the future. The public in China has confidence in these products and practices.⁹⁴ China is not, however, merely relying on a belief system in terms of development of its TCM health infrastructure. It is promoting R&D on the substances used in TCM, such as natural plant materials, to determine their clinical efficacy, as well as to isolate active ingredients and develop methods for creating 'modern' formulated products based on TCM materials. In the Chinese health care system, TCM products are not used in isolation from physician practice. There is a network of TCM hospitals that are visited by large numbers of Chinese patients, where treatments such as acupuncture are administered in addition to supply of TCM products. A number of these hospitals combine Western medical practice and TCM practice in a single facility.

In 2012, sales of formulated TCMs in China reached 800 billion yuan, or about 119 billion US\$, accounting for one third of China's pharmaceutical market, according to IMS data.⁹⁵ In 2014, hospital sales of TCMs reached 121.15 billion yuan.⁹⁶ Formulated TCM drugs were the top category of all pharmaceutical product sales by Chinese hospitals in 2015.⁹⁷ The Chinese formulated TCM market segment has consistently outperformed Western medical sales since 2008 in terms of growth rate. Formulated TCMs are about 44% of the pharmaceutical retail market segment, while only 20% of the hospital segment.⁹⁸ As of 2014, formulated TCMs represented 23.8% of Chinese pharmaceutical industry revenues.⁹⁹ As of the end of 2013, 504 TCM products were under administrative protection granted by the CFDA.¹⁰⁰

China's State Council has adopted a TCM development plan for 2016–2034, approaching this area as a vertically integrated one that includes agriculture, cultivation, distribution and provision of related services. The China Government is promoting the development of TCM as an export industry, including with the potential for the establishment of overseas

93 *Ibid.*

94 Arthur Daemrlich, *The political economy of health care reform in China: negotiating public and private*, SpringerPlus 2013, 2:448 (2013).

95 China Guide 2016.

96 *Ibid.*

97 *Ibid.*

98 *Ibid.*

99 *Ibid.*

100 *Ibid.*

TCM hospitals modelled on those operating in China.¹⁰¹ The prospective export of China's TCM model is part of the "one belt, one road" programme.¹⁰²

TCM is covered by China's health reimbursement system, including doctor's visits. Of the 520 essential medicines in China, 203 are TCM products. There are approximately 2000 TCM companies producing plant-based and synthetic therapeutics.¹⁰³

There are several patents pending (six or seven) at the US Patent and Trademark Office (PTO) for specific TCM products.

A visit to one of Beijing's prominent TCM hospitals – that combines TCM and Western medical practice – illustrated the advanced state of China's TCM system. There is a modern TCM prescription dispensing facility, complete with computerization and barcoding of package products, and product-tracking IT systems. The TCM product formulation facility is similar to a traditional Western pharmaceutical formulation facility, albeit with somewhat different characteristics.

Chinese foreign direct investment (FDI) regulations have recently been updated to include removal of joint-venture requirements for cultivation of herbs for TCM production.¹⁰⁴

f. Contract manufacturing and research¹⁰⁵

There are an increasing number of Chinese R&D and clinical trial research organizations, many of them founded by Chinese scientists returning from overseas.¹⁰⁶ In 2014, there were approximately 500 contract research organization (CROs) in China, although the level of development of these institutions varied significantly.

101 "China will develop traditional Chinese medicine (TCM) into a pillar industry, according to another government blueprint, Strategic Planning Guideline for TCM Development (2016–2020), released by the State Council on 26 February. The plan proposes universal access to TCM care by 2020. By 2030, TCM should make a notably greater contribution to social and economic development." Shen, China Pushes Pharmaceutical Sector Reform from the Supply Side, *Pharma China*, 21 March 2016.

102 See e.g., Bert Hofman, *China's One Belt One Road Initiative: What we know thus far*. World Bank, East Asia and the Pacific Blog Posting, 4 December 2015.

103 Daemmrich, *supra* note 94.

104 China Guide 2016.

105 "For example, the central government recently announced a slate of policies to encourage the development of China's technology services industry and growth of contract research organizations (CRO) to meet the demands of global innovation firms, such as big pharma. Projected to grow at almost 25% per year, China's large CRO industry is expected to more than double its market revenues to 40 billion renminbi (6.4 billion US\$) by 2017. In the life science sector specifically, local industry reports estimate that three of China's leading health technology firms account for nearly 15% of the total market value among domestic CROs. Local governments have also been proactive in encouraging local firms to plug into the global innovation landscape. Shanghai's municipal administration, for instance, has put together a multiyear CRO plan that aims to achieve 30 billion renminbi (4.8 billion US\$) in revenue by 2017. As a result, the CRO sector in Shanghai tripled revenue from 5 billion renminbi (800 million US\$) to 15 billion renminbi (2.4 billion US\$) between 2008 and 2012. Wong & Fei.

"A market survey by JTMed Inc. indicated there are 250 professional service providers, 50 multinational service providers, 150 traditional Chinese pharmaceutical companies, and 20 Chinese biotechnology companies operating in the CRO industry. Local CRO alliances have also been set up to promote the industry such as the Alliance of Bio-Box Outsourcing (ABO) in Beijing and Contract Research Organization Service Alliance (CROSA) in Shanghai. In 2009, the ABO had over 20,000 transactions with a value of USD 700 million. The CRO industry is growing rapidly in China and is attracting international CROs to join the local alliances or set up their own presence in China such as PPD, MDSPharma, and Covance." Canadian Trade Commissioner Service, *supra* note 90.

106 China guide 2016.

Multinational CROs are major players in China's clinical trial and preclinical research sector.¹⁰⁷

g. Information technologies

The China Government is looking to information technologies (IT), including 'big data', to improve efficiencies and the security of its pharmaceutical distribution system.¹⁰⁸ A point-to-point tracking system for pharmaceutical products, which will allow users to determine the location and expiration date of drugs, is being created. The Chinese e-commerce company 'Alibaba' is among the major companies investing in the pharmaceutical IT infrastructure.

E-commerce distribution of drugs is a relatively new and untested arena. Nevertheless, interest among patients/consumers is growing, and the Government is turning attention to whether digital sales may help to facilitate its efforts at cost-containment. Experience outside China with Internet sales of pharmaceuticals suggests that measures to avoid facilitating access to medicines without prescription, and to avoid the introduction of sub-standard products by unethical operators, should be among those considered.

h. Financing and incentives

While much of the domestic pharmaceutical industry is state-owned, it nonetheless operates largely on a market basis.¹⁰⁹ A number of the largest state-owned pharmaceutical companies have portions of their ownership listed on securities markets, including on the Hong Kong,¹¹⁰ Shanghai¹¹¹ and Shenzhen¹¹² securities markets. While there are offsetting benefits to being a China-based pharmaceutical enterprise in terms of facilitated participation in the procurement market, the general rules regarding essential medicines, price controls, reimbursement, etc. apply to state-owned pharmaceutical companies, just as much as to private companies. A state-owned pharmaceutical company pays taxes in the same manner as a private company.

107 *Ibid.*

108 "In a separate development, CFDA announced in late February its decision to suspend implementation of the drug electronic regulatory system and an unnamed CFDA official told Caixin magazine that the agency has withdrawn operational rights of the drug electronic regulatory network by Alibaba Health and it will begin a public tender procedure to search for a third party, which will only provide IT services. Besides, the CFDA released a drafted revision to the Quality Control Standards for Pharmaceutical Distribution (GSP). Under the draft revision, all existing GSP provisions for the "electronic drug regulatory network" are replaced by those for the 'drug tracing system'. The requirements for compulsory scanning of electronic regulatory codes and data uploading are withdrawn." Shen, China Pushes Pharmaceutical Sector Reform from the Supply Side, *Pharma China*, 21 March 2016.

109 Chinese firms continue to move away from the traditional SOE (state-owned enterprise) focus on volume sales towards private firms focused on profit. In 2006, 36% of the firms were government owned, 35% privately owned and 29% foreign-funded. This transition provides challenges for production decisions. In the past, a planned economy meant the government dictated what factories produced and where their products were sold, and subsidized operations. But as the economy shifts to a market economy, subsidies have been reduced or withdrawn, leaving manufacturers responsible for portfolio management and production decisions. Without accurate market information or a culture of making production decisions based on market realities, firms often duplicate production. For example, in a consolidating market, the SFDA has approved 1,600 generics in 2002, 6,100 in 2003, and more than 8,000 in 2004/5. For levofloxacin hydrochloride injection, there were 145 approvals alone. Bumpas & Betsch, *supra* note 50.

110 See: <http://www.hkex.com.hk/eng/index.htm>

111 See: <http://english.sse.com.cn/>

112 See: <http://www.szse.cn/main/en/>

China has a long history of using special economic or industrial zones to foster business development. Such zones typically offer low land prices, infrastructure support, and may involve preferential supply of basic utilities. To the extent that a pharmaceutical company manufactures for export, there may be exemptions from domestic tax payments, and preferences on import duties for materials incorporated in exported products.¹¹³

As discussed elsewhere in this report, environmental concerns regarding pharmaceutical production facilities, and in particular API facilities, has risen to the top of the Government's concerns. The Government and industry view the expansion of the industrial park concept to include joint facilities for waste processing and disposal appears to be one element of addressing environmental concerns.

At this stage in China's industrial development, the special industrial or economic zones may play a less significant role for the small-molecule chemical industry than during the early development phase. However, in the biotech sector, biotechnology innovation parks and clusters are a major feature of national and provincial government efforts.¹¹⁴

i. Foreign direct investment and taxation

China has encouraged FDI in the pharmaceutical sector, both in terms of production facilities and R&D. China permits wholly-owned foreign investment in the pharmaceutical sector, but foreign enterprises commonly find that successful participation in the Chinese market is facilitated by partnering with domestic investors/enterprises. Multinational originator companies have made very sizable investments in China, and are undertaking significant R&D within the country. This shows a level of optimism regarding the technological capacity of China and its scientists. This also involves transfer of technology into China, including with respect to training of personnel.

Although there have been, and continue to be, complaints from foreign enterprises and governments regarding protection of intellectual property (IP) in China, adverse 'effect-in-fact' of allegedly weak IP protection is not readily apparent from the levels of FDI in the pharmaceutical sector. Recent slowdowns, if any, in levels of FDI appear to have more to do with changes in Government approaches toward pharmaceutical pricing than with respect to IP policy.

China's large and rapidly growing health care market has been an obvious target of opportunity for major multinational pharmaceutical companies, and these companies are among the largest revenue earners in the Chinese pharmaceutical market. Until the past year or two, these companies have enjoyed virtually unconstrained pricing power. However, the Government has been taking active steps to reduce originator pharmaceutical prices, including through aggressive negotiation and initiation of competition law actions. The

113 Benxi is the location of an industrial zone where pharmaceutical API and finish pharmaceutical product manufacturers are located. Benefits in the zone include lower tax rates, educational opportunities, water supply and roads. Interview with officials of Northeast Pharm, 13 June 2016. Interview with officials of China Meheco Corporation, 13 June 2016. Hainan Province Industrial Zone is another location for the pharmaceutical sector. Advantages include electric and water supply, special waste disposal system, and some tax benefits. However, industry representatives indicated that the benefits of locating in the zone are not very significant. See Hainan Province Industrial Zone, < <https://en.wikipedia.org/wiki/Hainan>>; "Hainan Province is the largest Special Economic Zone established by Chinese leader Deng Xiaoping in the late 1980s." (https://en.wikipedia.org/wiki/Special_Economic_Zones_of_China, accessed 13 March 2017).

114 See note 91, supra.

level of profitability for the multinational originators may be going down, but the size of China's market and the overall dynamism means that they continue to invest.

All of the world's leading 20 pharmaceutical companies now have manufacturing facilities in China and many have also established R&D centres in the country. Notwithstanding the attractiveness of the China market, revenues from the country remain a relatively small part of income for the major originator companies, at approximately 4% in 2012.¹¹⁵

A notable feature of FDI in China is that a significant part is directed toward R&D. All foreign investments into China require some form of Government approval or screening. China has been increasingly relaxing its restrictions on FDI, and foreign companies are increasingly free to invest with limited entry clearance and reporting for investments in non-sensitive areas.¹¹⁶ Foreign investment in an 'encouraged' industry sector may be eligible for Government support, for example in the form of a lower tax rates, and duty-free importation of production equipment, etc. Foreign investments may be subject to anti-monopoly (depending on the level of industry concentration) and/or national security review. Cross-border financing, payments and remittances, and all currency conversions in China, are subject to Government oversight.¹¹⁷

China's tax code has been revised in 2008 to eliminate preferences in favour of foreign investors, establishing a unified income tax rate of 25% for domestic and foreign companies. The 2008 law also eliminated certain tax holidays in favour of foreign investors.

China imposes both enterprise income taxes, and various turnover or value-added taxes (VAT). A VAT is levied on the increased value of commodities at different stages of production or circulation.

Foreign investment in the pharmaceutical sector may take a variety of forms, including through wholly-owned subsidiaries, equity joint ventures with no restriction on percentage of foreign ownership, equity joint ventures with percentage of foreign ownership restrictions, collaborative projects or ventures, licensing or technology transfer projects, acquisition of Chinese private or state-owned companies, representative offices and venture capital, as well as private equity investment.¹¹⁸ Although previously restricted, foreign investment may now be allowed in the pharmaceutical distribution sector with joint venture interest not exceeding 49%.

The *2015 Foreign Investment Industrial Guidance Catalogue* includes production of new chemical compounds or APIs as encouraged investment areas, as well as a variety of other pharmaceutical related production activities.¹¹⁹

115 For some companies, the percentage is substantially higher, reaching 8–10%. China Guide 2016.

116 The principal directive is Foreign Investment Industrial Guidance Catalog (revised in 2015), as well as various Chinese laws on equity joint ventures, cooperative joint ventures, wholly-owned foreign enterprises, and various rules and regulations. There are special rules with respect to mergers and acquisitions by foreign investors of domestic non-public companies, and public companies. Main responsibility for review and approval of foreign direct investment resides with the National Development and Reform Commission (NDRC) and the Ministry of Foreign Commerce (MOFCOM). *Ibid.*

117 *Ibid.*

118 *Ibid.*

119 *Ibid.*

j. Industry consolidation

China has more than 5000 pharmaceutical manufacturers, and the Government is strongly promoting consolidation of the pharmaceutical industry,¹²⁰ especially to reduce the number of smaller companies that do not have the financial capacity to meet newly demanding regulatory standards.¹²¹

There are several very large-scale state-owned pharmaceutical companies, including SinoPharm, China Resources Pharmaceuticals (CRPG) and Shanghai Pharmaceutical Group. These state-owned companies are nevertheless public companies, and raise capital in the public securities markets, allowing them to make acquisitions and investments. In 2015, there were a total of 202 domestically-listed pharmaceutical companies accounting for about 29% of broad pharmaceutical industry revenue for that year.¹²² The number of major merger and acquisition deals in China among domestic companies grew substantially in 2014, and deals between Chinese and foreign companies increased slightly.

China-based companies have been investing in overseas companies, including in the United States and Israel.¹²³

A Government policy openly sets the goal of having the top 20 domestic manufacturers of essential drugs control at least 80% of the China market for such drugs.¹²⁴

120 There were fewer than 1400 pharmaceutical manufacturing companies in China in 1985, but by 2014 there were close to 5000 in spite of intensive consolidation. *Ibid.*

121 "The industry's consolidation started in the second half of the 2000s, and intensified after the government issued a directive for the sector's development in 2009. In 2010, there were 46 announced mergers and acquisitions of pharmaceutical manufacturing companies on the two stock exchanges in China, and 32 only in the first half of 2012. Mergers and acquisitions resulted in constantly decreasing numbers of enterprises, and growth of the group companies and their market shares. With recent policy changes favouring domestic manufacturers, many foreign pharmaceutical suppliers are pushed to establish joint ventures with local players in order to guarantee their positions and development in the market, which results in additional M&A activity." *Emerging Markets Insight*, supra note 64.

122 China Guide 2016.

123 *Ibid.*

124 *Ibid.*

IV. Distribution

The pharmaceutical distribution system in China is complex. Generally speaking, drugs are prescribed and supplied by “hospitals”, where patients visit physicians. This is different from the private medical practice concept often employed in Western countries. As noted previously, the hospitals and physicians were largely funded by the mark-up on pharmaceutical products, although the Government has recently decided to change this model and move towards a fee-for-services model. A major reason for this change is to discourage over-prescription and consumption of medicines.

Hospitals are typically owned and operated by provincial or local governments, which are responsible for the procurement of medicines. Most procurement is done through some form of tendering and bidding system, although these vary among the provincial and local governments. This makes it difficult for individual pharmaceutical companies to operate on a national level, since this involves familiarity with the various procurement processes, and participation across the range of consumers. Nonetheless, this gap is at least partly filled by several large Chinese distribution companies such as SinoPharm. SinoPharm is responsible for 20% of China’s total medicines distribution, operating in 31 provinces and 268 cities. It has 57 manufacturing plants. SinoPharm has total annual revenues of approximately 40 billion US\$, 80% of which are from distribution, and 20% from manufacturing.¹²⁵

Foreign companies doing business in China partner with or engage the services of SinoPharm, allowing them to participate in effectively national scale distribution. SinoPharm is a state-owned company, but it is publicly listed on the Hong Kong Stock Exchange. It has two or three major competitors in China in terms of its distribution model. SinoPharm is 30% owned by Shanghai Fosun Pharmaceutical Development Co (Fosun Pharma), which itself is a partially state-owned publicly-traded company.

Typically, the procurement process managed by provincial and local governments involves submitting information regarding the company and its product(s). The procurement agency selects “approved bidders”, who may then submit quotations for prices. Where there are multiple bidders, more than one may be selected. Price is not the only criterion; quality and reliability are also factors. ‘Winning’ a bid typically means having the chance to negotiate a contract with the hospital or other procurement authority.¹²⁶

Overall the distribution of pharmaceutical products in China is dominated by state-owned enterprises, including state-controlled enterprises with public shareholders. Foreign owned and private companies play a small role in the distribution of pharmaceutical products in China.¹²⁷ E-commerce is playing an increasing role in Chinese pharmaceutical distribution.¹²⁸

SinoPharm and Fosun have agreed to establish a 40–60 joint venture to build a national pharmaceutical logistics network, which when completed will have 20 provincial

125 Less than 5% of its revenues are directed towards R&D.

126 Interview with officials of Fosun Pharma, 13 June 2016.

127 China Guide 2015.

128 *Ibid.*

pharmaceutical distribution centres and 30 provincial level delivery facilities, with planned investment of 5–10 billion US\$.¹²⁹

In 2015, China's foreign trade in medicines and health products reached 98 billion US\$, with exports at 55 billion US\$ and imports at 43 billion US\$.¹³⁰ In 2014, Western medicine exports (including APIs) grew to 31.4 billion US\$, with formulations accounting for 2.94 billion US\$ of that total. Export of plant extracts was 1.8 billion US\$. Imports of Western medicines was 26.2 billion US\$ in 2014. Medical devices accounted for the remainder of the trade, with 20 billion US\$ in exports and 15.8 billion US\$ in imports.¹³¹

Since joining the WTO, China's tariffs on imports of pharmaceutical products has declined substantially, with drug import customs duties between 5.5% and 6.5%. In addition, China imposes a 17% VAT on all imported goods, in addition to customs duties.¹³²

In 2015, 16 of the top 20 drug suppliers (by sales) to Chinese urban hospitals were domestically-based pharmaceutical companies, while four of the top 20 drug suppliers were foreign multinationals.¹³³ The top two drug suppliers, however, were foreign multinationals (Pfizer and AstraZeneca). Oncology drugs have experienced a major growth in sales over the past decade, as rates of cancer prevalence (or its detection) have dramatically increased.

As is common throughout much of the world, multinational originator companies dominate the market in China for new drug products, while domestic companies dominate the supply quantity of generic, including essential drugs.¹³⁴

China is actively engaged in implementing the China Drug Electronic Regulation Network that will track the movement of drugs throughout the distribution process, including at the provincial, local and hospital levels.¹³⁵

Until very recently, China had not generally distinguished between prescription and non-prescription medicines, and most 'ethical' drugs were sold in retail pharmacies without doctor's prescription. Pharmacies of medical institutions, including hospitals and clinics, represent around 80% of China medicines sales. There is a growing interest among pharmaceutical companies in the over-the-counter market (OTC), particularly as cost containment measures affect originator and generic prescription products. Locally-owned Chinese companies currently dominate the OTC market, but foreign multinationals are taking a greater interest.¹³⁶

129 CPhi.cn, *Fosun Joining Hands with Sinopharm to Establish Nationwide Pharmaceutical Logistics Network*, EN-CPhi.CN, 9 June 2014.

130 China Guide 2016.

131 China Guide 2015 (2014 data latest published).

132 China Guide 2016.

133 *Ibid.*

134 *Ibid.*

135 *Ibid.*

136 "Nicholas Hall, a leading global OTC drug market research firm, also released its topline data on the Chinese OTC drug market in 2015 to Pharma China. The company estimates the Chinese OTC drug market (OTC drug sales in all retail channels, prescription sales of OTC-registered brands-plus packaged herbal medicines including branded TCMs) to be US\$21,657.54 million in 2015, up 6.9% year on year. The growth rate of the Chinese OTC drug market was held steady at 6.9% in 2015 compared with the previously. The growth rate rebounded in the past two years from 6.4% in 2013, but was still lower than 8.2% in 2011 and 7.6% in 2012." Shen, *Repercussions of Irrational Cost Containment Surface as Premier Calls for More Drug Price Cut*, *Pharma China*, 6 May 2016.

V. Innovation and technology transfer

China's pharmaceutical R&D institutions were exclusively state-owned prior to 1990, and technologies developed by those institutions were freely available to all pharmaceutical manufacturers.¹³⁷ Today, most large- and medium-sized pharmaceutical companies in China have their own R&D departments or research institutes. There are a substantial number of central and local government-sponsored research institutes, universities and manufacturer-affiliated research institutes. Although a substantial number of Chinese pharmaceutical companies are state-owned, the R&D sector is principally market-based and profit-oriented. The China Government is targeting the domestic pharmaceutical industry to invest 5% of revenues in R&D, but that target is not yet reached.¹³⁸

Historically, R&D by local Chinese companies has been directed toward development of generic drugs, including copies of new drugs developed outside China, as well as drugs based on TCM. This direction has expanded to include R&D on biosimilars. Until recently, Chinese companies have not invested substantially in the development of new drugs because of the high cost and failure rate. The entry of China into the WTO, and granting of patent protection to foreign innovator companies has substantially reduced the space for local companies to copy foreign innovator products, which in part motivates a trend towards investment in new drug R&D.

Currently, 97% of the medicines sold by local, Chinese-owned companies on the domestic market are generic drugs or copies of originator drugs.¹³⁹ However, the number of new drug applications to the CFDA has been expanding dramatically, with 388 new drug applications submitted in 2014 (up from about 50 in 2009). Among the top Chinese companies, R&D investments as a percentage of total revenues has increased to almost 5%, with investment by 26 companies having exceeded 5%. The highest percentage of R&D expenditure is in the biologics sector.¹⁴⁰

The China Government is strongly encouraging R&D in the pharmaceutical sector,¹⁴¹ including with respect to new biologic products.¹⁴² It is aware that pricing premiums are associated with new originator products, and is seeking to move domestic Chinese industry from a focus on lower-cost generic products to newer high-value products.

137 China Guide 2016.

138 *Ibid.*

139 *Ibid.*

140 According to China Guide 2016, the measures taken by the Chinese pharmaceutical industry and central/local governments to enhance new drug R&D include:

1. Increased central and local government funding into the R&D of new drug;
2. Incentives and preferential policies for organizations or businesses carrying out new drug R&D;
3. R&D alliances between state research institutes and manufacturers or among manufacturers themselves;
4. Encouragement from the government for mergers and acquisitions to form large research based pharmaceutical groups;
5. Three fast track approval processes with early stage-involvement roadmap for new drugs established by the CFDA, and;
6. Preferential policy for reimbursement of indigenously-developed new drugs. *Ibid.*

141 Over the past several years, Chinese spending on R&D in general has increased an average of 12% annually. *Ibid.*

142 See China Guide 2016; references to Guiding Catalogue for Adjustment of Industry Structure (2011), and the 12th Five-Year Plan for the Chinese Pharmaceutical Industry Development (2011–2015), Ministry of Industry and Information Technology (MIIT).

Between 2011 and 2015, the China Government invested a total of 1.6 billion US\$ in new drug development.¹⁴³

China is training a large number of PhD scientists in order to facilitate R&D and production capabilities. China has encouraged scientists with training in these areas to return from abroad, and this encouragement appears to be successful in attracting returnees. This is an important form of transfer of technology from other countries.

Foreign-based multinational corporations (MNCs) have invested heavily in R&D ventures in China.¹⁴⁴ In recent years, some major MNCs have relocated key R&D functions to China. Also, foreign-based companies have invested in research based on TCMs. In addition to the large domestic market, lower costs are a factor in driving this move. Typically, foreign companies investing in Chinese R&D facilities prefer to partner with local Chinese companies as a way of navigating the domestic environment. According to the foreign research-based originator industry, it is investing about 1.2 billion US\$ per year in R&D activities in China, accounting for more than 50% of China's large and mid-size pharmaceutical industry R&D spending.¹⁴⁵

There are a substantial number of strategic joint ventures between foreign companies and non-commercial enterprises, both to undertake research projects (including construction of facilities) and to develop, test and market pharmaceutical products.¹⁴⁶ There are major alliances between multinational biotechnology firms and Chinese universities, cancer research partnerships and company-to-company deals.¹⁴⁷

According to *China Guide 2016*, foreign-to-China licensing and R&D partnerships were a major source of activity in 2015, with transfer of technology and partnership deals rising, with foreign parties of these deals mostly small- and medium-size drug development companies. There were 45 foreign-to-China licensing deals recorded in 2015, and 18 contract research/collaborative R&D deals.¹⁴⁸ These transactions include rights to market patented and non-patented products, and product development transactions in which local Chinese firms work on developing products with commercial potential from earlier stage research.¹⁴⁹ These transactions have recently included licenses from organizations such as the TB Alliance, to commercialize TB regimens in China.¹⁵⁰ Through the Medicines Patent Pool (MPP), Gilead has authorized sub-licensing of treatments for HIV and hepatitis B to Chinese companies for manufacture and distribution in low- and (some) middle-income countries.¹⁵¹

143 China Guide 2016.

144 "Most of the top 20 multinational pharmaceutical companies have been expanding their footprint and are setting up more R&D facilities through various enterprise structures. For example, in November 2010, it was reported that Novo Nordisk planned to invest US\$100.0 million to expand its R&D centre in Beijing. In March 2011, Pfizer announced that it will close its R&D facility in Groton, Connecticut and move its anti-bacterial research operations to Shanghai. GlaxoSmithKline is setting up one of its largest research centres in Shanghai, and has charted plans to recruit between 50 and 100 top international scientists and employ more than 1,000 researchers at the new facility by 2017." Deloitte 2011.

145 China Guide 2016.

146 *Ibid.*

147 *Ibid.*

148 *Ibid.*

149 *Ibid.*

150 China Guide 2015. Noting 2014 exclusive license from TB Alliance to Fosun Pharma to develop and commercialize regimens to treat both drug-sensitive TB and multi-drug-resistant TB.

151 *Ibid.*

There are a number of 'innovation parks' in China, including in the Shanghai area.¹⁵²

The Government is promoting acquisition or establishment of overseas R&D facilities to facilitate expansion.¹⁵³

One bottleneck to new drug development in China is slow regulatory approval. This is at least partially accounted for by a small number of reviewers at CFDA. While the US FDA employs 2000 individuals to review drug registration applications, CFDA employs only 120 (although that number is increasing).¹⁵⁴ In addition, new drugs approved in China by the CFDA must also find acceptance in the provincial markets, which may add substantial delay to distribution.

With respect to drug technology transfer, the CFDA issued *Provisions for Registration of Drug Technology Transfer* with effect from 19 August 2009.¹⁵⁵ Under the regulations, transferees of drug technologies must be licensed pharmaceutical manufacturers with authorized production scope for the product under transfer. Foreign companies are able to transfer production technologies for approved import drugs to local manufacturers. Such transfers must be approved by the CFDA or relevant provincial authorities.

The willingness of foreign multinationals and other foreign companies to enter into licensing and joint venture arrangements with Chinese local companies distinguishes China from almost all other developing country markets. Multinational originator companies have traditionally avoided licensing their valuable technology assets in foreign markets, preferring to control their technology and distribution. Presumably, the situation is different in China because of the very large-scale of the Chinese market, causing the multinational companies to accept risks that they might not take for smaller potential rewards. In this regard, the situation for pharmaceuticals is similar to that for other industry sectors where the attractiveness of the large and growing China market has induced companies to enter into transfer of technology arrangements that are outside the "norm".¹⁵⁶

152 "Global life science firms, especially in the biomedical field, have set up their own R&D centres in China since 2004. Shanghai, for instance, is home to R&D centres for all the major global drug companies, including Roche, Pfizer, GlaxoSmithKline, AstraZeneca, Novartis, and Eli Lilly. In 2014, Johnson & Johnson recently opened its Asia Pacific Innovation Center in Shanghai, with the company citing China's growing capacity in biotech innovation as a key motivation for its decision to base its Asian operations there. To date, the innovation centre has established three R&D partnerships with Chinese universities (China Pharmaceutical University, Beijing University, and Zhejiang University), a partnering office in Suzhou's BioBay life science industry park, and a commercial deal with WuXi AppTec, China's largest domestic CRO, to internationally source and advance promising new drugs." Wong & Fei, at 15, citing "J&J Is On the Hunt for Chinese Innovation," *Forbes*, 18 November 2014 (<http://www.forbes.com/sites/medidata/2014/11/18/jj-is-on-the-hunt-for-chinese-innovation>, accessed 13 March 2017).

"Johnson & Johnson Innovation Launches Asia Pacific Innovation Center and Announces New Alliances," Johnson & Johnson, 28 October 2014 (<http://www.jnj.com/news/all/Johnson-Johnson-Innovation-Launches-Asia-Pacific-Innovation-Center-and-Announces-New-Alliances>); and "New Collaboration Model Gives Entrepreneurs and Transformational Asset Owners an Edge," Johnson & Johnson, 11 June 2015 (<https://talk.jnjinnovation.com/article/new-collaboration-model-gives-entrepreneurs-and-transformational-asset-owners-edge>).

"Administrative streamlining. Although the government continues to fund its many S&T programmes, such as the 863, 973, and Technology Support Programmes, government agencies will no longer manage and evaluate specific S&T projects. Currently more than a hundred national S&T programmes are administered by over 40 government agencies. In line with President Xi Jinping's efforts to streamline government functions and improve overall efficiency within the state apparatus, management of specific S&T programmes will be delegated to professional project management institutions. This move is accompanied by Xi's recent efforts to foster specialized advisory bodies that can provide independent policy analysis and consultation services." Wong & Fei.

153 China Guide 2016.

154 *Ibid.*

155 *Ibid.*

156 See discussion in Frederick M Abbott, *The Enduring Enigma of TRIPS: A Challenge for the World Economic*

VI. The Role of Intellectual Property

From the founding of the People's Republic of China (PRC) in 1949 until 1978, all inventions in China were considered state property, and could not be monopolized.¹⁵⁷ All enterprises were free to make use of them. China introduced its first patent law in 1984, and has since amended that law several times. China joined the Paris Convention in 1985.¹⁵⁸ China's patent law and administrative processes were largely modelled on the German patent system. Following a Memorandum of Understanding reached with the United States in 1992,¹⁵⁹ China amended its patent law to provide protection for chemical inventions, including pharmaceuticals and related processes.¹⁶⁰

When China joined the WTO in 2001, it became party to the TRIPS Agreement and its corresponding obligations to grant and protect pharmaceutical product patents.¹⁶¹ China also committed to providing six years of market exclusivity as a form of regulatory data protection.¹⁶² In connection with WTO accession, China amended its patent law to establish TRIPS consistency.

China's *Drug Administration Law* and *Drug Administration Regulation* establish a six-year period of protection against unfair commercial use for test data of products containing a new chemical ingredient, although foreign industry sources suggest it is not clear how these rules are implemented by the CFDA. Some foreign companies have complained that generic versions of their drugs are approved prior to expiration of an exclusivity period.¹⁶³

China again amended its patent law in 2008, at which time it liberalized its compulsory licensing rules, expressly allowed parallel imports of patented products, and introduced a regulatory review exception.¹⁶⁴ As permitted under WTO rules, China does not provide a period of patent term extension in connection with its regulatory review exception. In 2012, the State Intellectual Property Office (SIPO) introduced revised *Measures for Compulsory Licensing of Patent Implementation* that eliminates several impediments to the granting

System (1 January 1998). *Journal of International Economic Law* (1998). Vol. 1, Issue 4: 497–521. Available at SSRN: <http://ssrn.com/abstract=915040> and Frederick M. Abbott, *Reflection Paper on China in the World Trading System: Defining the Principles of Engagement* (1 July 1997), in *China in The World Trading System: Defining the Principles of Engagement*. F.M. Abbott, ed., Kluwer Law International 1998. (<http://ssrn.com/abstract=1919486>, accessed 13 March 2017).

157 Wei Zhang, Evolution of the Patent System in China, in *Emerging Markets and the World Patent Order* (F.M. Abbott, C. Correa, and P. Drahos eds., Elgar 2013).

158 *Ibid.*

159 See documents in F. Abbott, T. Cottier & F. Gurry. *The International Intellectual Property System: Commentary and Materials, Part Two* (Kluwer Law Int'l 1999).

160 Zhang, *supra* note 157.

161 WTO, Working Party on the Accession of China, Report of the Working Party, WT/ACC/CHN/49, 1 October 2001, See also Frederick M. Abbott and Carlos M. Correa, *World Trade Organization Accession Agreements: Intellectual Property Issues*, QUNO Global Economic Issues Publication (May 2007).

162 WTO, Working Party on the Accession of China, Report of the Working Party, WT/ACC/CHN/49, 1 October 2001:

"This protection would include introduction and enactment of laws and regulations to make sure that no person, other than the person who submitted such data, could, without the permission of the person who submitted the data, rely on such data in support of an application for product approval for a period of at least six years from the date on which China granted marketing approval to the person submitting the data. During this period, any second applicant for market authorization would only be granted market authorization if he submits his own data. This protection of data would be available to all pharmaceutical and agricultural products which utilize new chemical entities, irrespective of whether they were patent-protected or not."

163 China Guide 2016.

164 Zhang, *supra* note 157.

of compulsory licenses, including elimination of rules relating to pharmaceuticals (and pharmaceutical exports), that were not required by WTO rules.¹⁶⁵ However, notwithstanding this additional flexibility and some hints that they would do so, Chinese authorities have yet to issue a compulsory license with respect to a pharmaceutical product.¹⁶⁶

As of late 2015, China was considering an amendment to the patent law that might facilitate private patenting/ownership, or return of income, from government-sponsored research (i.e. a Bayh-Dole type system).¹⁶⁷

Pursuant to the 2008 amendments to China's patent law, an applicant for an invention patent based on genetic resources must disclose the direct and original source of the genetic resources. 2010 Implementation Rules define genetic resources as "the materials of actual or potential value which are obtained from human bodies, animals, plants and microorganisms and contain functional units of heredity." Failure to comply with these obligations may result in the rejection of an application or invalidation of a patent.¹⁶⁸

The China Government has encouraged the filing of patent applications by domestic inventors, and this has led to a very high level of patent filings.¹⁶⁹ Until now, the quality of these applications has been questioned. But, as the Chinese public and inventors become more familiar with what is expected from the filing of a patent application, it is reasonable to anticipate an improvement in patent quality.

Western pharmaceutical companies and their supporting governments have questioned whether the Chinese patent system is sufficiently robust to support new R&D efforts for which substantial sums are being expended.¹⁷⁰ Notwithstanding this uncertainty, major Western originator companies have continued to invest substantial sums in R&D facilities in China.

165 *Ibid.*

166 *Ibid.*

167 "The government has proposed amendments to the Patent Law and the Law on Promoting the Transformation of Scientific and Technological Achievements, with the former still pending approval and the latter passed by the National People's Congress in August 2015. The revisions clarify the ownership of IP and the distribution of returns from commercialized IP for inventions generated under programmes receiving government funds. In addition, rather than being subjected to lengthy government approval processes, universities and public research institutes will have the autonomy to commercially exploit such IP as they see fit. These reforms are intended to address low rates of technology transfer inside Chinese institutions and firms."

"Encouraging entrepreneurialism. The State Council created a policy in May 2015 to allow researchers at universities and public research institutes to retain their academic positions for up to three years upon starting their own venture firms. This policy intends to reduce the risk of entry for would-be entrepreneurs among publicly employed researchers with potentially commercializable IP. Prior to this reform, publicly employed researchers were reluctant to create start-ups for fear they would lose their positions." Wong & Fei.

168 Zhang, *supra* note 157.

169 *Ibid.* China Guide 2016.

170 See, e.g., "Although Chinese companies are becoming better informed about intellectual property issues and expectations, most Chinese firms do not have a legal staff devoted to patent searches. There appears to be little understanding of the official IP policy and IP enforcement is weak. While China's central government has largely followed through on its WTO (World Trade Organization) IP commitments, the local levels often lack the will and ability to enforce the policy." Bumpas & Betsch, *supra* note 50.

VII. Competition Law

In Western high-income countries, such as those of the EU and the United States, competition law plays an important role in balancing the exclusive rights established by patents and other forms of exclusivity with the broader public health interest.¹⁷¹ For example, the EU Competition Commission undertook a detailed investigation of the pharmaceutical sector and determined that patent owners were abusing patents and the patent system to delay the introduction of generic products, and has since undertaken a number of enforcement actions against such practices. In the United States, the Federal Trade Commission has actively challenged so-called 'pay for delay' arrangements in which patent owners pay generic challengers to drop litigation that would otherwise accelerate entry of generic products onto the market. The US Supreme Court recently affirmed that holding a patent does not insulate its owner from legal challenges under the antitrust (or competition) laws.

China's *Antimonopoly Law* of 2007 provides its enforcement authorities – the Ministry of Commerce (MOFCOM), the National Development and Reform Commission (NDRC) and the State Administration for Industry and Commerce (SAIC) – with the legal basis for taking action against anti-competitive practices involving the pharmaceutical industry, including those based on abuse of intellectual property rights.¹⁷² Chinese authorities have begun looking into the pharmaceutical sector, although no formal actions appear to have been taken so far.¹⁷³ It is reasonable to infer that the initiation of this investigation is part of China's overall efforts at making sure pharmaceutical pricing is consistent with the national objective of achieving universal health care.

171 See generally UNDP: *Using Competition Law to Promote Access to Health Technologies: A Guidebook for Low- and Middle-Income Countries* (19 May 2014). United Nations Development Program (ed. F. M. Abbott) (2014). (<http://ssrn.com/abstract=2439416>, accessed 13 March 2017).

172 See Frederick M Abbott. Competition Law in Emerging Markets: the Virtue of Regulatory Diversity, in *International Economic Law and Governance: Essays in Honour of Mitsuo Matsushita* 216 (eds. J. Chaisse & T-Y Lin), Oxford University Press 2016.

173 Pillsbury Winthrop Shaw Pittman LLP, *China Competition Authority Initiates Drug Pricing Investigation*, Lexology, 3 June 2016 (<http://www.lexology.com/library/detail.aspx?g=9da2ed27-e437-4b05-9afc-eb87151ae01e>, accessed 13 March 2017; King & Wood Mallesons, *NDRC Targets Price-related Illegal Conducts in the Pharmaceutical Sector*, China Law Insight, 8 June 2015.

VIII. Modelling for local production and transfer of technology

Measures adopted by China

As indicated in this report, the Government of China has adopted and implemented a variety of specific measures intended to promote the local production of pharmaceuticals and technology transfer. These include:

- The establishment of special economic zones (SEZs) to provide economic and/or infrastructure-related benefits to China-based manufacturers. The benefits may include lower-than-market prices for land acquisition; facilitated and/or discounted access to electricity, water and other utilities; access to common waste processing and/or disposal facilities; relief from import duties with respect to materials and/or equipment used for export-related activities; preferential tax rates; subsidies; access to low-cost employee housing, and/or; facilitated access to transport services. There are a variety of different approaches to the specific benefits of the SEZs, which change from time to time.
- The establishment of R&D 'parks' that provide economic and/or infrastructure-related benefits to research-oriented entities located within the R&D parks. These R&D parks may be established at the provincial and/or local level, and the benefits vary. These may include making available low-cost facilities; R&D grants or subsidies; facilitated access to loans; tax benefits, and/or; organization of conferences.
- Measures to facilitate the repatriation of scientists of Chinese origin from abroad, as well as measures to facilitate other hiring of foreign scientists. In addition, a national educational focus on training of PhD scientists with interest in the pharmaceutical sector.
- Administrative encouragement of mergers and acquisitions in the domestic pharmaceutical sector.
- Gradual relaxation of laws and regulations imposing restrictions on FDI, with particular emphasis on 'encouraged' sectors, which generally includes the pharmaceutical sector (including biotechnology).
- Reform and build-up of pharmaceutical sector regulatory capacity to strengthen oversight of compliance with GMP standards, to accelerate processing of new drug applications and applications for approval of generic products (including biosimilars), and to generally assure the quality and safety of locally-produced products.
- Adoption of TRIPS-compliant IP laws and regulations, as well as build-up of administrative capacity in IP offices, *inter alia*, in order to accelerate review of patent applications. Reform of IP laws to take advantage of TRIPS flexibilities.
- Establishment of essential medicines list (EML) and national health scheme commitment to providing access to all citizens of medicines on EML as part of UHC programme.
- Elimination of direct price controls along with strengthening of administrative oversight of prices.
- Improvements in transparency of central and provincial procurement processes.
- Introduction of electronic tracking system for pharmaceutical products.
- Increased regulatory attention to distribution of pharmaceuticals through electronic commerce.

- Regulatory emphasis on strict environmental controls to reduce potential for air and water contamination, with particular focus on API sector.
- Substantial attention to use of TCM as part of national health care scheme, including administrative encouragement of TCM-related R&D, administrative protection of TCMs, and promotion of TCM as export-oriented industry.

Observations

The fact that China has a population of close to 1.4 billion people means that the Government faces a challenge that other countries, with the exception of India, do not face. The industrialization of the China pharmaceutical sector took place during a period of relative isolation from international trade, particularly with Western high-income countries, encouraging China to pursue a path of self-sufficiency in the supply of essential pharmaceutical products. While, in principle, self-sufficiency in the supply of important public health goods may appear to be a worthwhile objective, in today's global economy there are limits for most countries regarding the feasibility or desirability of meeting such an objective.

This study of the Chinese pharmaceutical sector and the health care system as it relates to that sector suggests a number of observations regarding elements that may be useful for other countries, especially developing countries.

1. Industrial policy can be used to establish a pharmaceutical manufacturing sector capable of meeting the basic pharmaceutical needs of a national population given the necessary resources. The necessary resources include financial capital, basic natural resources (or access to basic resources), sufficiently trained/educated human resources, and a local population sufficient to establish demand at a scale that is adequate to support production. Such industrial policy may be undertaken through central planning.
2. China developed a successful local manufacturing sector adequate to support the basic needs of the population through industrial policy that included state ownership of the means of production, government capital, industrial policy incentives such as the establishment of special industrial or economic zones that offered infrastructure support, financial incentives, tax incentives and reduced land prices, and otherwise supported local producers located outside special economic zones.
3. China's regulatory framework development did not keep pace with the rapid pace of industrial expansion, particularly after its economy began to transition to a more market-based approach. This gap is currently being addressed through strong government measures designed to build up the regulatory infrastructure to the highest international standards. Such measures will necessarily require some time to implement as technical staff with adequate training must be integrated into the regulatory structure, and as regulatory agencies compete with the private sector for trained personnel.
4. The strengthening of regulatory controls requires, in many cases, that manufacturers upgrade plant and equipment, or build new facilities, and train additional personnel to assure regulatory compliance. Retrofitting and/or rebuilding plant and equipment can be a costly undertaking, and in China's case it is anticipated that a significant number of smaller manufacturers will not be able to meet the economic challenge.

5. From the standpoint of developing countries establishing industrial policy measures for encouraging local production of pharmaceutical products, the experience of China suggests that attention should be paid to putting in place the appropriate regulations and rules for assuring quality and safety of products prior to authorizing construction and operation of facilities. In other words, a strong regulatory structure should be a pre-condition to implementation of policies designed to bolster local production.
6. Because of the nature of 'divided government' – such as between central and provincial authorities – it may be considered important to allocate responsibilities among agencies at different levels or geographies. However, divided regulatory responsibilities present rule-making and enforcement challenges. China is not alone among countries where regulatory responsibility for matters such as GMP inspection is allocated among different levels of government. Because of the complex nature of pharmaceutical regulation and the training required for regulatory personnel, dividing regulatory responsibility presents challenges. At the least, such allocation demands close attention to over-arching coordination mechanisms.
7. The China Government designs and implements laws and regulations addressing the health sector, including the pharmaceutical sector, through active inter-institutional/agency coordination. In a positive sense, this inter-institutional coordination is intended to assure that the optimal policies are designed and implemented. In a precautionary sense, this inter-institutional coordination is intended to assure that the policies adopted to promote a particular public health and/or industrial policy objective do not generate adverse consequences that might not be foreseen if a single government agency was acting in isolation.
8. China's current attention to environmental reform suggests that other developing countries seeking to encourage local production should pay close attention to how manufacturing facilities will interact with the environment. There are some fairly straightforward policy suggestions, such as to avoid locating facilities where groundwater contamination is more likely to occur. It may be useful/important to consider the establishment of industrial zones where common environmental control infrastructure is created as a means to control costs as well as protect the environment.
9. Pharmaceutical procurement and pricing systems that entail direct government controls raise certain risks. Because manufacturers are highly dependent upon the prices paid for their products, there is an incentive for seeking to induce government employees to authorize higher prices and payments. For this reason, pricing systems that entail transparency and competitive bidding may be important to government budgetary control and avoiding distortions in the pricing system.
10. China's system of funding hospitals through mark ups on sales of medicines is being eliminated. A direct linkage between hospital funding, including funding of employee salaries, through prescription sales appears to have encouraged over-prescribing (and corollary irrational use of medicines), and to have increased overall public health expenditures in China. This suggests that other countries might avoid medicines prescribing and dispensing systems that link the income of the prescriber with revenues from the sale of medicines.
11. The development of new pharmaceutical products requires investment in R&D. Such R&D may entail various degrees of risk. The development of new process technologies and/or minor modifications to existing pharmaceutical products may entail modest

risk, while development of entirely new therapeutic areas, or novel biological products, may involve high risk. Without investment in production R&D, the pharmaceutical manufacturers of a country are likely to become inefficient. Without investment in new product development, a country will be dependent on importing new products from outside the country, or will require exercise of alternative means to acquire new technologies to satisfy the needs of the local population.

12. The China Government is providing substantial support in the form of subsidies, tax incentives and establishment of special R&D parks to encourage the development of new products and processes in the pharmaceutical sector. It has recently begun trial programmes involving market authorization holder certificates that allow individual and small enterprise (including academic) inventors to obtain marketing authorization for new drugs, and to monetize that authorization through production agreements and/or sales to firms with manufacturing capability. China has adopted patent laws that are consistent with its WTO TRIPS Agreement obligations, and offers pharmaceutical patents to inventors in the pharmaceutical sector. China has encouraged foreign direct investment in facilities and projects relating to R&D, and foreign enterprises are investing substantially in R&D in China. There are a substantial number of transfer of technology projects involving technologies developed outside China, including licensing of R&D for further development within China. This combination of approaches reflects traditional perspectives regarding useful mechanisms for encouraging R&D.
13. China pharmaceutical expenditures include substantial amounts for imported originator products protected by patents and regulatory exclusivity. Chinese authorities have recently negotiated price reductions for certain originator import products, and have opened competition law inquiries into the pricing of pharmaceutical products. Because China faces major budgetary challenges in connection with providing UHC, controlling pharmaceutical costs is an important element of meeting that objective. As part of its patent law, China has included necessary legal flexibility for issuing compulsory licenses if it is unable to achieve appropriate pricing with holders of patents. Chinese authorities have referred to the possibility of compulsory licensing, but so far have not issued any. The option of compulsory licensing is an important component of pharmaceutical price negotiation. It provides a background of alternative government action.
14. China ascribes an important role in its health care system to TCM, and TCM is a major part of its pharmaceutical sector. China is investing in R&D on TCM products, and products derived from TCM products, including the science underlying the efficacy of such products. There are other countries and regions where traditional medicines can and will play a significant role, such as the African region and elsewhere in Asia Pacific. There appears to be substantial room for cooperation between China and the African region in terms of developing traditional medicinal resources, and establishing facilities for traditional medicinal services.
15. China Government authorities and stakeholders expressed interest in the development of the pharmaceutical sector in the African region. It was noted that the Chinese Development Bank is undertaking studies and projects in the region, and that some Chinese manufacturers have initiated operations within China, albeit of a limited nature. Several specific concerns were expressed, including with respect to the state of infrastructure development in some African countries, concerns regarding preferences that may be given to locally-based suppliers in procurement processes, and concerns

with political stability. These concerns did not preclude further involvement of Chinese stakeholders in African pharmaceutical manufacturing projects, but suggested an approach that may rely initially on pilot projects.

16. The single most important aspect of China's pharmaceutical sector policy is the linkage with the objective of UHC. The objective is critical because it places the health needs of China's people as the top priority, and views the development of the pharmaceutical sector in terms of its contribution to meeting the UHC objective. China's population is aging, and the pharmaceutical needs of its population will only increase. A system of UHC and an aging population mean that budgetary pressures regarding pharmaceuticals are likely to grow. This is one reason why the Government is actively addressing cost containment. There are, of course, many other factors and elements at play in the Chinese local production and transfer of technology arena with respect to pharmaceuticals. From the WHO public health perspective, the main point is that China Government policy is focused on providing UHC and how pharmaceutical sector policy can aid in achieving that goal.

Appendix 1: Questions for interviewees in China regarding country models for the promotion of the pharmaceutical production sector (Long form)

5 April 2016

General questions

1. What is the balance between private and public sector production in China? This is relevant because the Government would typically provide much of the investment funding for public sector enterprises, and investment incentive programmes would be of less relevance than for the private sector. Among domestically-based private sector pharmaceutical companies, how many have equity shares traded on public securities markets? This is relevant to understanding the mechanisms by which capital for research and development (R&D) and production facilities is raised.
2. Assuming that there are government/public production facilities, are these concentrated in a particular part of medicines and/or vaccines production? For example, are government facilities producing 'essential medicines', or some group of medicines directed to particular disease categories?
3. What investment incentives are provided to the pharmaceutical production sector? These may include: (1) tax credits or related tax incentives; (2) availability of special financing; (3) provision of infrastructure benefits, such as special industrial zones; (4) supply of utilities, such as electricity and water; (5) government assistance with environmental controls, including assistance with waste disposal.
4. China has witnessed phenomenal growth of its active pharmaceutical ingredient (API) production sector over the past decade, appearing to have surpassed India as the major producer of bulk drugs. Assuming that this growth was based at least in part on Government policy preference, why did China elect to pursue manufacturing of APIs as a key element of its pharmaceutical sector development? What incentives did the Government provide to encourage API production?
5. Innovation and transfer of technology are major issues for the pharmaceutical industry. China appears to be investing heavily in pharmaceutical R&D, including in cooperation with major foreign originator companies investing in the country, such as Novartis. What policy instruments is China using to encourage (1) product innovation, and (2) process innovation? Does China have specific innovation policies directed toward API production? Does a focus on new drug R&D potentially signal a shift away from promoting API production?
6. How does China view the relationship between its internal market and external/export markets from the standpoint of its pharmaceutical manufacturing sector? Does it apply the same regulatory standards for both market segments? There is probably a distinction between pharmaceutical manufacturing plants meeting FDA/EMA GMP standards, and those that do not. Is there a plan to bring all plants into compliance with the standards of so-called strict regulatory authorities, or will China retain an internal/external distinction?
7. There is an ongoing debate at the international level whether 'local production' of pharmaceuticals makes an important contribution to national health care systems.

Some argue that the key issues are price and quality, and that if imports of high-quality low-price drugs are available, there is no justification for investing in local production. How does China view the role of local production in contributing to the national health care system?

8. In many countries, government responsibility for assuring adequate health care is divided between central/national and state/subnational/regional authorities. Similarly, budgets and incentive policies (e.g. tax incentives) may be divided between central and state authorities. How is responsibility for providing adequate health care allocated in China generally? Does this pose particular problems with respect to promoting local production of pharmaceuticals? For example, do state/regional authorities compete with each other to attract producers by offering more generous terms? If such incentive competition exists, is there a risk that state/regional authorities will offer less rigorous regulatory control as an incentive? How might this be addressed?
9. Does China view foreign ownership of pharmaceutical product patents within the country as an impediment to local production? Have any Chinese companies secured licenses for new pharmaceutical products from foreign companies that have allowed the Chinese companies to manufacture and sell the products within China (or for export)?
10. How does China view its relationship with the pharmaceutical industry of India? The two countries appear to be cooperating through investments and joint ventures in some areas, and to be in strong competition in others. Are there particular areas where relations could be improved in a way that would provide benefits to the public?
11. The price of pharmaceuticals is a central concern for all health systems around the world. Some countries, e.g. the United States, do not generally control prices through national government mandates. Most countries, however, have some form of price controls for pharmaceutical products. How does China control pharmaceutical product prices in the public and/or private sectors?
12. What impact do price controls (if any) have on the pharmaceutical manufacturing sector? Typically, pharmaceutical manufacturers do not support price controls because they limit profits. Manufacturers argue that “cost-plus” price controls discourage investment in new plant and equipment because there is little incentive to improve efficiencies under cost-plus price control systems. Does China use cost-plus price controls? How does China address these concerns?
13. Biological products have become a major source of revenue for the pharmaceutical originator industry, particularly for companies based in the United States and Europe. What steps is China taking to build up its capacity for innovation with respect to biological products? Are Chinese companies manufacturing biosimilar products today? If so, for local consumption and/or export? Does China view the rules of the Transpacific Partnership Agreement (not yet in force) on biologics market exclusivity to be a potential problem for its biological drug manufacturers?
14. It appears there is considerable interest in China in encouraging production of traditional medicines, including pharmaceutical-grade medicines derived from traditional plant matter. What policies is the China Government using to encourage investment in the traditional medicines production sector? What government agencies are responsible for overseeing such policies?

15. One aspect of this WHO project is to provide support for countries in Africa seeking to build up their pharmaceutical manufacturing sectors. What types of projects or programmes does China have that may be supporting African local production? What types of projects or programmes might be considered for the future?
16. Pharmaceutical plants use chemicals and other substances that may pose problems for the environment. Costs of safe disposal of chemicals can be a substantial part of manufacturing costs. Does the China Government have programmes, including financing programmes, designed to assist pharmaceutical manufacturers with good environmental practices?

Questions for the China Food and Drug Administration

1. Many countries face a challenge in regulating local production of pharmaceuticals because the local industry is divided between companies that are seeking to meet strict international regulatory standards of GMP, on one hand, and companies that are satisfied with meeting local requirements which may be less stringent, on the other. We know that it is expensive to bring pharmaceutical manufacturing facilities into compliance with strict GMP standards, and that local companies often do not have the financial resources to redesign and reconstruct their manufacturing facilities. Does China have programmes designed to help local companies improve their level of GMP compliance, whether or not that is up to the levels of FDA/EMA-type strict standards? Does the China Government provide financing for such activity? What about technical expertise?
2. On-site inspection of pharmaceutical manufacturing facilities is essential to assuring compliance with GMP. How many inspectors does CFDA employ for this purpose, or is inspection the responsibility of another agency or instrumentality? Are GMP inspections the responsibility of the national government (CFDA), or is that responsibility shared (or exclusively with) the state governments? In India, for example, shared responsibility between the Central and State governments regarding GMP inspections has been a difficult issue.
3. Does the same agency in China handle regulatory matters with respect to small-chemical drugs and biologics? If not, how is authority divided?
4. As major exporters to the United States and Europe, some of China's pharmaceutical companies must meet US FDA and EMA GMP requirements. What type of cooperation arrangements does the CFDA have with the US FDA and EMA in terms of inspections and/or staff training regarding GMP?
5. China is a substantial importer of pharmaceutical products from other countries. What types of quality and/or inspection controls does China employ with respect to imported pharmaceuticals? Does the CDFA perform GMP inspections of foreign plants that export to China?

Questions for private sector companies in China

1. What government policies have been important to the success of your company in building up local production? These might include tax incentives, subsidies, government purchase commitments, pricing preferences in favour of local companies, benefits from special industrial zones, and so forth.

2. Does your company invest in manufacturing facilities in foreign countries? In developed or developing countries? What factors make a country attractive to you in terms of investment in manufacturing facilities? What are potential obstacles or negative factors that impact on decisions whether to invest?
3. Are there particular government policies that make it more difficult to operate profitably, such as price control systems? What changes would make it easier to operate your business successfully?
4. Do you have access to the technology necessary to manufacture for local consumption and/or export? If not, what types of measures do you think the government might use to make that technology available to you?
5. Does your company invest in the development of new products or processes? Is your company more heavily involved in biotechnology products or small-molecule chemical products? Does your company apply for and/or own any patents in the pharmaceutical area?
6. Do your facilities meet FDA/EMA strict regulatory GMP standards so that you may export to the United States and/or Europe? If not, are you interested in upgrading your facilities to meet those standards? Do you require special government financing to undertake that?
7. Do you manufacture your own APIs, or do you purchase them from other companies? If you purchase from other companies, are these companies located in China, or do you import from abroad? If you import APIs from abroad, how do you assure that those APIs are of adequate quality?
8. If you are involved in the production of biological pharmaceutical products, are you presently manufacturing and selling biosimilar products for the local and/or export markets? Are you concerned that new international rules, such as those incorporated in the Transpacific Partnership Agreement may restrict your access to foreign markets?

Questions for interviewees in China regarding country models for the promotion of the pharmaceutical production sector (Short form)

13 April 2016

1. What is the balance between private and public sector pharmaceutical production in China? Among domestically-based private sector pharmaceutical companies, how many have equity shares traded on public securities markets?
2. Are government/public production facilities concentrated in a particular part of medicines and/or vaccines production?
3. What investment incentives are provided to the pharmaceutical production sector? These may include: (1) tax credits or related tax incentives; (2) availability of special financing; (3) provision of infrastructure benefits, such as special industrial zones; (4) supply of utilities, such as electricity and water; (5) government assistance with environmental controls, including assistance with waste disposal.
4. Why did China elect to pursue manufacturing of APIs as a key element of its pharmaceutical sector development? What incentives did the government provide to encourage API production?

5. What policy instruments is China using to encourage (1) pharmaceutical product R&D, and (2) process innovation? Does China have specific innovation policies directed toward API production?
6. Does China apply the same regulatory standards for its internal market and external/export markets from the standpoint of its pharmaceutical manufacturing sector? Is there a plan to bring all plants into compliance with the standards of so-called strict regulatory authorities (e.g., FDA/EMA GMP), or will China retain an internal/external distinction?
7. How does China view the role of local production in contributing to the national health care system?
8. How is responsibility for providing adequate health care allocated in China between central/national and state/subnational/regional authorities? Does this pose particular problems with respect to promoting local production of pharmaceuticals?
9. Does China view foreign ownership of pharmaceutical product patents within the country as an impediment to local production?
10. How does China view its relationship with the pharmaceutical industry of India?
11. How does China control pharmaceutical product prices in the public and/or private sectors? What impact do price controls (if any) have on the pharmaceutical manufacturing sector? Does China use cost-plus price controls?
12. What steps is China taking to build up its capacity for innovation with respect to biological products? Does China view the rules of the Transpacific Partnership Agreement (not yet in force) on biologics market exclusivity to be a potential problem for its biological drug manufacturers?
13. What policies is the Chinese government using to encourage investment in the traditional medicines production sector?
14. What types of projects or programmes does China have that may be supporting African local production?
15. Does the China Government have programmes, including financing programmes, designed to assist pharmaceutical manufacturers with good environmental practices?
16. Does China have programmes designed to help local companies improve their level of GMP compliance, whether or not that is up to the levels of FDA/EMA-type strict standards? Does the China Government provide financing for such activity? What about technical expertise?
17. How many on-site inspectors does CFDA employ, or is inspection the responsibility of another agency or instrumentality (including state/regional authorities)?
18. Does the same agency in China handle regulatory matters with respect to small-chemical drugs and biologics?
19. What type of cooperation arrangements does the CFDA have with the US FDA and EMA in terms of inspections and/or staff training regarding GMP?
20. What types of quality and/or inspection controls does China employ with respect to imported pharmaceuticals? Does the CFDA perform GMP inspections of foreign plants that export to China?

Appendix 2: List of interviewee organizations

Business representative organization

China Chamber of Commerce for Import & Export of Medicines and Health Products (CCCMHPIE)

Enterprise

Beijing Ton Ren Tang Chinese Medicine Co., Ltd.

China Meheco Co., Ltd.

China National Pharmaceutical Group Corporation (Sinopharm)

CSPC Zhongnuo Pharmaceutical Co., Ltd.

Northeast Pharmaceutical Group Co., Ltd. (Northeast Pharm)

Shanghai Fosun Pharmaceutical Development Co., Ltd. (FosunPharma)

Zhejiang Jiangbei Pharmaceutical Co., Ltd. (Jiangbei)

Government

China Food and Drug Administration

State Administration of Traditional Chinese Medicine

National Health and Family Planning Commission

Hospital

Xiyuan Hospital of China Academy of Chinese Medical Sciences

Appendix 3: Project Concept Note

Proposed study regarding Chinese policies intended to promote local manufacturing of pharmaceutical products and the protection of public health

Programme on Public Health, Innovation and Intellectual Property in WHO EMP on the local production for access to medical products – *Concept Note* – 6 October 2015

I. Statement of objective

In response to request by member states, WHO is preparing guidance documents to assist developing countries to improve their capacity to develop, manufacture and distribute pharmaceutical products. Several large “emerging economy” countries have established or are in the process of establishing dynamic pharmaceutical sectors (development and production) to address public health and industrial topics. As other developing countries pursue similar objectives, it will be important for their policymakers to have reference to the models or systems that have been put in place in countries where those models have evidenced success. To this end, WHO PHI proposes to undertake a study of the pharmaceutical sector of China with a view toward identifying policy options and what may be “best” or “better” practices that might be employed elsewhere. In addition to examining the policies specifically aimed at improving the performance of the pharmaceutical production sector, this study will examine links between the local pharmaceutical production sector and the domestic situation with respect to access to medicines.

The selection of China as subject of this study is based on a number of factors. Chinese companies produce a substantial volume of active pharmaceutical ingredients (APIs), and China is a major supplier of APIs to the global market. Chinese companies are rapidly increasing their capacity to produce high-quality finished pharmaceutical products (FPPs). The Chinese pharmaceutical manufacturing sector is moving toward comprehensive compliance with strict regulatory controls based on newly adopted government policies. China is focusing substantial resources on development of advanced research and development (R&D) capacity for new pharmaceutical products, including biologicals and plant-based products. China’s strategy appears to include encouraging cooperation with foreign-based multinational originator companies investing in the establishment of research facilities.

From the WHO standpoint, the key objective of improving capacity for manufacture of quality-assured pharmaceuticals is to improve access to medicines within the country at affordable prices. An important element of the proposed study will be to examine the link between improvements in domestic manufacturing capacity and availability of medicines for the population of China.

Following an initial review of publicly-available literature, the proposed next step is an information-gathering visit to China – the principal subject of this Concept Note. In areas characterized by dynamic industry development and progressive changes in government policy, it is useful to gather information (including available documentation) from those directly involved. On this visit, the researchers would be seeking information regarding the incentives and regulation that successfully promoted the rapid development of China’s API manufacturing capacity, the government policies that are encouraging investment in

FPP formulation facilities (including for upgrading to meet strict regulatory standards), the government policies and incentives designed to stimulate domestic R&D capacity, the government policies and programmes for educating and training research scientists, and information regarding how the government seeks to link the successful development of China's domestic pharmaceutical industry with the public health needs of China's citizens. It would, in addition, be useful to explore how foreign investments and technology transfer are expected to be integrated into domestic industry development. Each of these subjects are of interest to developing country governments outside China as they look for models on which to base their pharmaceutical industry development programmes.

A similar study is underway with respect to India. The Indian pharmaceutical sector up until now has played an important role in the supply of pharmaceutical products to the developing world.

While the main objective of this proposed study is to identify best or better practices that may be implemented by developing countries with respect to local production of pharmaceuticals and related R&D, the results also may be useful for stakeholders in the Chinese pharmaceutical sector. For example, the study could suggest areas where improved coordination mechanisms among government regulatory authorities would improve the implementation of policy.

II. Research methodology

Preparation of this study is proposed to be conducted using the following approach. Regarding this initial visit to China: (1) discussions with individuals having expert knowledge regarding the way the Chinese pharmaceutical sector is regulated and incentivized, including with members of the Chinese government, executives and employees of private sector companies, and government officials and health care providers responsible for procurement and distribution of medicines to the public; (2) obtaining, when available, relevant documents regarding the regulatory and incentive programmes. Attached as Annex 1 is a List of Government Departments of Interest that may assist in identifying the appropriate departments or agencies for visit and discussion.

The next steps following the visit will be: (3) compiling and synthesizing information from the discussions in light of government documents and policy announcements, as well as available data; (4) preparing and distributing a draft of the study to the discussants and other stakeholders for suggestions, comments and corrections; (5) organizing a workshop with stakeholders in China to discuss the draft study; (6) circulating a revised draft of the study for suggestions, comments and corrections, and; (7) finalizing the study.

III. Principal researchers

The proposed researchers and authors of the study are:

Professor Frederick Abbott, WHO Consultant: he has prepared a number of studies on behalf of governments and international organizations regarding transfer of technology and pharmaceutical industry development. He is the author of books regarding pharmaceutical regulation and international intellectual property law (as well as editing a book on China in the World Trading System). Several of his books are available in the Chinese language. As a consultant to the World Bank, he previously prepared studies for the government of

China on the subjects of protection of biological diversity, and on geographical indications. Professor Abbott has worked with PHI since the inception of its project on transfer of technology and local production of pharmaceuticals. He is researcher and author of the related study with respect to India.

Dr Jicui Dong, Programme Manager for Local Production, EMP, WHO. Dr Dong is leading and managing the local production work within WHO.

Dr Zafar Mirza, Director of Health Systems Development, WHO EMRO (former Coordinator of the Programme on Public Health, Innovation and Intellectual Property, EMP, WHO)

Annex 1 – List of Government Departments/ Agencies of Interest

1. Department concerned with developing and implementing fiscal and tax incentives for investment in pharmaceutical manufacturing, as well as promotion of export. This may include special economic zones designed for pharmaceutical (including API) producers. It may also include department concerned with managing import controls (e.g. tariffs) with respect to inputs for pharmaceutical manufacturing.
2. Department concerned with developing and implementing rules regarding good manufacturing practices (GMP), including inspection programmes. Programmes designed to promote upgrading of manufacturing facilities, which may be linked to fiscal and tax incentives (see 1 above), are relevant.
3. Department concerned with developing and implementing programmes intended to promote innovation in the pharmaceutical sector and/or the biological drug sector. Intellectual property (e.g. patents) with respect to pharmaceutical products and processes are relevant, but also programmes involving subsidies, incentives to university inventors, startup business incubators, etc.
4. Department concerned with foreign investment in the pharmaceutical sector, including incentives intended to promote technology transfer;
5. Department concerned with procurement (public and/or private) of medicines from local producers intended for domestic consumption. Interest is in potential links between local production and assuring affordable access to medicines.

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