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China Pharmaceutical Guide

中国医药市场指南

13th Edition (2018)

Written by:

James J. Shen, MBA

Unrivaled China Healthcare Intelligenece Since 1991

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WiCON | China Pharmaceutical Guide is authored, edited and published by James J. Shen, a veteran of the Chinese healthcare industry and market, who has dedicated his entire 30-year career to pharmaceutical businesses in China.

James Shen has rich operational and senior level management experience on China's healthcare businesses in the capacities of a senior consultant to multinational pharmaceutical companies, a manager of joint venture projects and companies, a business development executive, an entrepreneur, and most recently a publisher.

James Shen started his career in the pharmaceutical industry in 1987 when he joined Beijing Ciba-Geigy Pharmaceutical Ltd. (now Beijing Novartis) as Assistant to the General Manager. While he studied MBA in England in various periods of 1980s, he worked as an editorial consultant for Scrip/PJB Publications, IQVIA and *Financial Times* Business Information on China's healthcare news.

In 1991, he founded W*i*CON International Group in the USA to provide strategic consulting and competitive intelligence to international healthcare companies in order to assist and facilitate their market entry into China. He has worked with many large and mid-size international pharmaceutical companies on a diverse range of projects including entry strategy development, strategic alliances and joint ventures, marketing and distribution agreements, product registration and clinical trials, licensing and technology transfer, API sourcing, and M&A due diligence.

As an entrepreneur, James Shen co-founded *Beijing Jicai Pharmaceutical Technologies Ltd.* in 1992, one of the first private pharmaceutical research institutions in China, and took over its management in 2001. He is also a co-founder of *Nanjing Zinox Pharmaceutical Co. Ltd.*, an emerging generic pharmaceutical company in China.

James Shen was the Managing Editor of the well-known *IQVIA China Update*, a monthly newsletter covering China's pharmaceutical market co-published by IQVIA and W*i*CON. He authored many China healthcare business publications in English throughout 1990s, including *Marketing Pharmaceuticals in China*, *Guide to Pharmaceutical Research Institutions in China*, and *Directory of Bulk Pharmaceutical Manufacturers & Products in China*.

In early 2006, following a restructure of WiCON's businesses, James Shen founded **W*i*CON | *Pharma China***, the highly-respected English media and business intelligence service on China's pharmaceutical industry and market which is subscribed by almost all multinational pharmaceutical companies, CROs, consulting companies and investment banking firms active in China.

James Shen was educated in China, Europe and the USA at university and postgraduate levels, and received an MBA from the University of Exeter (UK) in 1990.

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He is now based in Beijing with frequent visits to the U.S., Europe and Japan. He continues to be active in strategic consulting with multinational pharmaceutical companies at headquarter and regional head office levels, as well as selective entrepreneurial and VC/PE investment projects in the Chinese healthcare sector.

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PREFACE

Despite the enormous business opportunities and growth prospects offered by China's healthcare sector, I've witnessed and experienced countless regulatory and business environmental changes, which has frequently caused painful business difficulties, frustrations and downfalls, in my past 31 years of work in the sector as a consultant, manager and entrepreneur.

The ever-changing legal and market environments in China healthcare present the single biggest challenge to companies and executives operating in the sector. Naturally, many operational level issues and problems in the country also pose significant challenges to successful businesses.

In spite of these challenges and difficulties, the Chinese pharmaceutical industry and market have achieved remarkable growth in the past two decades. The sector is generally developing towards a positive direction in the sense that it continues to grow steadily, its regulatory regime has become increasingly compatible with international standards with improving transparency, once rampant corruption is being tackled, its ongoing consolidation will eventually help establish order and stability, and the country's new healthcare reform will ultimately led to a more stable and healthier market environment.

There are success stories from all categories of players, whether they are foreign or local, large or small, newcomer or established, private or state-owned. However, to be one of the success stories require a thorough understanding of the sector, ability to face and tackle challenges, flexibility to deal with changes, and skills to maneuver through complex situations.

It has been my wish to put my experience and observations in the past 31 years of operating in almost every aspect of China's pharmaceutical business into a publication, which will serve as a one-stop reference to anyone seeking to enter or operate in the Chinese pharmaceutical market. As of our 2007 edition, we have been adding a rising number of commentaries and contributions from many other leading pharma industry executives and experts.

Packed with hard-to-find current data and the author's expert knowledge from years of hard-earned experience in the industry, its comprehensiveness, practicality, insight, reliable data and analysis, and up-to-date information, are the features which set this the guide apart from other publications with similar titles.

This Guide is written based on my past experience, interviews with relevant industry experts and government officials, articles from Pharma China, information obtained from or published by Chinese government agencies, information obtained from or published by independent pharmaceutical industry associations, reliable data and released exclusively to WiCON for publication from various reputable market research and consulting firms, information from other trustworthy trade journals and newspapers, related information

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found on the internet, and a large in-house information collection by WiCON International Group accumulated since 1991.

About W*i*CON | *China Pharmaceutical Guide 2018 (13th Edition)*

The W*i*CON | *China Pharmaceutical Guide 2018 (13th Edition)* is organized into the following four volumes:

Volume I – *Overview of the Chinese Pharmaceutical & Healthcare Sectors* (covering update of China's business environment, history and structure of the Chinese pharmaceutical industry, Chinese health sector structure and statistics, health insurance sector structure and data, as well as disease and drug consumuption patterns);

Volume II – *Chinese Pharmaceutical IP and Regulatory Guide* (covering the Chinese drug regulatory system overview, summaries of major healthcare/pharmaceutical related laws and regulations, government agencies and industry associations and pharma IP strategies & legal issues);

Volume III – *Annual Review, Trends, Opportunities and Strategic Considerations* (including a complete review of latest data, business trends, regulatory & IP/legal developments and healthcare reform progress of the Chinese pharmaceutical industry and market in 2016/1H2017, and a large collection of feature articles from industry experts relating to competemporary trends, issues and strategic considerations as well as promising opportunities of the present and future); and

Volume IV – *Sales & Marketing, Entry Strategies and Case Studies* (covering orientation, models and strategies of pharmaceutical sales, marketing and distribution in China, marketing entry strategies and execution, case studies featuring success stories of MNCs and domestic players, R&D and outsourcing, human resource management and legal/IP issues), as well as appendices with full texts of important healthcare/pharmaceutical related policies, laws and regulations.

It is thoroughly updated with ample latest data from many reputable sources, abundant analysis by leading industry experts, new regulations and more case studies. Its coverage was renewed and expanded significantly in the following areas:

- ☞ Hundreds of pages of new data, information, analysis and case studies.
- ☞ Thorough summaries and analysis of the latest healthcare reform, drug pricing & reimbursement and hospital tender purchase policies.
- ☞ Comprehensive industry, market and foreign trade data as well as health statistics are updated with the 2017 (full year) and available figures for the first half of 2018.
- ☞ Expanded coverage on e-commerce and digital marketing opportunities, the primary healthcare sector, OTC and consumer healthcare sector, high growth market segments, regional hospital markets, and the pharma distribution sector,

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- ☞ Updated coverage of the Chinese biosimilars/biologics market prospects and regulatory outlook.
- ☞ Updated coverage of emerging legal issues (including latest Chinese government crackdown on corruption in healthcare, FCPA/compliance and liability issues) and drug-related IP and trademark concerns.
- ☞ Comprehensive top line data, research findings and observations from our collaborative partners such as IQVIA, Kantar Health, Nicholas Hall, ZS Associates, Rubicon Strategy Group and RDPAC, as well as other reputable sources including the Chinese Pharmaceutical Association, SMEI and Sinohealth.
- ☞ All regulatory changes in 2017/H12018 are updated to present a clear and most up-to-date picture of the Chinese drug regulatory framework with summaries and analysis of all pharmaceutical related regulations in effect by mid-2018.
- ☞ Focused coverage of China's ongoing efforts to revamp its drug regulatory regime through amendments of the *Drug Administration Law*, its latest proposal and preparations to overhaul the drug pricing mechanism, deepening reform of its drug registration and evaluation regime, new policies to support drug innovation and high clinical value generics, and its initiative to re-evaluate all generic drugs with bioequivalence studies.
- ☞ An updated section covering proposed new drug-related laws and regulations under drafting process with selective previews of the draft versions.
- ☞ Extensive review and analysis of China's drug registration applications and approvals as well as Chinese drug innovation trends in recent years.
- ☞ Comprehensive review of Sino-foreign M&A, joint venture, strategic alliance, licensing, research partnerships, co-marketing, and new drug research events in 2017 and H1/2018.
- ☞ Expanded coverage on MNC strategies in China with healthcare reform in the backdrop, intellectual property/patent law amendments, data exclusivity, patent litigation, drug regulations, pharma marketing and distribution strategies, drug consumption patterns, the Chinese R&D and outsourcing sector, clinical studies/practices, healthcare reform, community healthcare sector, essential drug policy, regional drug consumption patterns, and the vaccine and API sectors.
- ☞ Numerous new case studies are added.

I would like to take the opportunity to thank all those organizations and individuals who contributed to this publication and their continued cooperation is greatly appreciated.

James J. Shen

July 30, 2018

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TABLE OF ABBREVIATIONS

ADR – Adverse Drug Reaction

API – Active Pharmaceutical Ingredients

APP – Administrative Protection of Pharmaceuticals

AmCham – American Chamber of Commerce

CAGR (Compound Annual Growth Rate)

CCCIEMHP – China Chamber of Commerce for Import & Export of Medicines and Health Products

CAPC – China Association of Pharmaceutical Commerce

CFDA – China Food and Drug Administration (predecessor of NMPA)

NMPA – National Medical Products Administration, successor of CFDA

ChP – Chinese Pharmacopoeia

CMH – China Monitor Health

CNCM – China National Corporation of Medicines

CNY – Chinese Yuan

CPIIC – China Pharmaceutical Industry Information Center

CRO – Contract Research Organization

DRGs – Diagnosis Related Groups

ED – Erectile Dysfunction

FDA/USFDA – U.S. Food and Drug Administration

FDI – Foreign Direct Investment

FIEs – Foreign Invested Enterprises

GCP – Good Clinical Practices

GDP – Gross Domestic Products

GLP – Good Laboratory Practices

GMP – Good Manufacturing Practices

GSP – Good Supply Practices

IFPMA – International Federation of Pharmaceutical Manufacturer Associations

JV – Joint Venture

M&A – Merger and Acquisition

MIIT – Ministry of Industry and Information Technology

MOFCOM or MOC – Ministry of Commerce

MOF – Ministry of Finance

MOH – Ministry of Health

MoHRSS – Ministry of Human Resources and Social Security

MNCs – Multinational pharmaceutical companies (*in the context of this guide*)

MR – Medical Representative

NBS – National Bureau of Statistics

NCGHSR – National Coordination Group for Healthcare System Reform

NDRC – National Development and Reform Commission

NHC – National Health Commission, successor of NHFPC

NHFPC – National Health and Family Planning Commission, predecessor of NHC

NMPA – National Medical Products Administration (formerly CFDA)

OECD – Organization for Economic Co-operation and Development

OTC – Over the Counter

QA – Quality Assurance

QC – Quality Control

PRC –People's Republic of China

R&D – Research and Development

RDPAC – R&D-based Pharmaceutical Association Committee in China

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SATCM – State Administration of Traditional Chinese Medicine

SDA – State Drug Administration, predecessor of SFDA

SFDA – State Food and Drug Administration of China (predecessor of CFDA)

SAMR – State Administration for Market Regulation, governing body of NMPA

SIPO – State Intellectual Property Office

SMEI – Southern Medicine Economic Institute under the CFDA

SOE – State Owed Enterprise

SPAC – State Pharmaceutical Administration of China, predecessor of SDA

STD – Sexually Transmitted Disease

TC – Therapeutic Class

TCM – Traditional Chinese Medicine

USTR – US Trade Representative

VAT – Value Added Tax

VC – Venture Capital

WM – Western medicine

WHO – World Health Organization

WTO – World Trade Organization

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EXECUTIVE SUMMARY

The Chinese Horoscope 2018 predicts that the *Year of the Brown Earth Dog* is going to be a good year in all respects, but it will also be an exhausting year. From this perspective, President Donald Trump, being born in the year of the fire dog, is set to remain very influential of this year, which will bring both opportunities and tension.

Turning to the Chinese healthcare sector, the structural reform and anti-corruption campaign have now been expanded to all corners of the country. The "top level" design or reform blueprint is now near completion but it will take years before the medical system can digest the tasks and goals.

Meanwhile, the structural flaw of Chinese healthcare financing remains untackled. The central government continues to draw up grand plans with ambitious goals, while most of bills, however, need to be footed by local governments, which are already suffering from a chronic decline of fiscal revenues as housing market plummeted and debt escalated to an unsustainable level. Government healthcare budget increases have been limited at all levels and are not expected to be raised substantially in a stumbling economy. Achieving reform objectives set by top officials therefore rest mostly on savings from cost containments, which are doomed to hurt healthcare quality.

The pharmaceutical industry will be challenged during this unsettling period and it will be squeezed by both medical providers and the government. As drug regulatory standards go up following reform, the industry will be confronted by the growing pain to supply high quality products at low prices and secure the bottomline at the same time.

It's encouraging, however, to see the pharmaceutical industry in China, especially leading MNCs, are making considerable progress reshaping its business model to adapt with the fast changing marketplace and fast emerging opportunities in the area of innovative new medicines. What will be the name of the new game? The answer is no longer blowing in the wind anymore for MNCs.

China needs to make good on its own repeated calls to open up its markets, or face consequences, warned the European Union Chamber of Commerce in China. In recent years, China has publicly avowed to do so, with President XI Jinping making speeches on openness and globalization. But critics say China's many words have few actions behind them. It appears that in many areas, China is no longer opening up, but selectively closing up.

Recent moves of pharma MNCs to scale back and refocus their China businesses coincide with the growing discontent of foreign companies in China. The Chamber said in its latest whitepaper that their members are suffering from "promise fatigue" in Chinese pledges to open up markets. Foreign firms have long complained of an uneven playing field and an opaque regulatory environment.

As money rushes into China's fledgling biotechnology sector and reform of the country's drug registration and regulatory system to accelerate harmonization with international norms, some foreign drugmakers are scaling back, a *Bloomberg* feature article noted.

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Eli Lilly and GlaxoSmithKline announced plans in 2017 to cut research teams in China, after Novartis AG shuttered a biotech research unit there a year before. The high-profile cutbacks, part of a broader restructuring that pharmaceutical companies are undertaking, contrast with the Chinese government's push to speed the uptake of innovative drugs that's spurred a rush of money into the industry.

While drug discovery may have disappointed, pharma giants are doubling down on the development part of R&D in China. In Shanghai's Pudong Zhangjiang Hi-Tech Park, Glaxo is preparing for growth, the company said in August, when it announced it would narrow the range of global neuroscience research and development activities, including terminating some projects.

The *Bloomburg* article concluded with a quote from Zhang Fangning, a partner at McKinsey & Co. in Shanghai, who said "closing research sites in China doesn't diminish the importance of the market. Instead, it means multinational companies have alternative ways to gain access to innovation here."

Meanwhile, China has been introducing various policies since late 2017 to speed up review and approvals of foreign innovative medicines, as well as timely negotiations for and inclusion of such products for BMI reimbursement. Many MNC patent drugs, which had previously been held up in the registration matrix, have been unleashed in recent months, with MSD's newest HPV vaccine approved within nine days of submitting its NDA.

It all seems to be primed for a fast takeoff. InChina is too big to be neglected both in terms of its current market size and future potential, but MNCs should stay sober despite positive developments recently and remain realistic with goals.

Chinese pharmaceutical market growth fell to single digit in 2017

The Chinese pharma growth continued to slide in all terminal markets in 2017 as a result of intensified cost containment and deepening healthcare reform. The chronic falling trend is anticipated by most industry observers to continue in 2018.

The three major Chinese terminal drug markets, which include the public hospital market, the retail pharmacy market and the public primary healthcare market, rose 7.6% in 2017, reaching CNY 1,611.8 billion at retail level, according to a recent information release by SMEI. Adding the drug market of private hospitals and clinics as well as village clinics, the entire Chinese pharmaceutical market is estimated to be around CNY 1.9 trillion at retail level. The public hospital market, the retail pharmacy market and the public primary healthcare market rose 6.98%, 8.06% and 11.63% respectively in 2017, reaching CNY 1,095.5 billion, CNY 364.7 billion and CNY 151.7 billion, representing 68.0%, 22.6% and 9.4% of total value.

The Chinese Pharmaceutical Association (CPA) also released topline data of its latest hospital drug purchase audit, which are based on drug purchases of representative hospitals nationwide, including level 3 hospitals (69.0%) and level 2 & below hospitals (31%). National hospital drug consumption growth slowed further to only 3.3% in 2017, down from 9.0% in 2016. The growth of level 3 hospitals was in line with the broad

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market at 3.6%.

Nicholas Hall & Co. reported that OTC drug market size in China reached CNY 160,980 million in 2017, up 5.7%, a fraction below the 5.8% rise recorded in 2016. Growth failed to strengthen during the year owing to increased competition from the cross-border e-commerce channel (not tracked in the DB6 topline), the reverse switches of Ketoconazole (which affected the general antifungals and scalp treatments categories) and Xianling Gubao (joint health) as well as the initial impacts of the new two-invoice system on pricing and company operations. The company also forecasts that the annual Chinese OTC drug market size to grow 6% CAGR between 2017 and 2022 to reach US$33,406 million and surge at another 6% CAGR again between 2022 and 2027 to reach US$44,299 million at the end of their respective periods.

CFDA powers forward drug regulatory system reform as it boosts support of drug innovation

Two years into the drug regulatory reform, the CFDA made significant advancements in 2017 to overhaul the regime with numerous new regulations and draft documents released monthly. A number of progresses are made in the year.

At the beginning of 2017, CFDA Minister BI Jingquan outlined the direction of the agency's drug evaluation and approval system reform in 2017 before the end of last month. Bi said the agency will deepen reform in 2017 to resolve the backlog completely and further energize the pharmaceutical industry through the following seven measures: 1) accelerating the generic drug quality and efficacy evaluation; 2) encouraging drug innovation; 3) establishing the review-oriented drug and medical device evaluation and approval technical system; 4) facilitating the responsibilities of onsite inspections; 5) building drug product master files; 6) establishing and implementing the drug eCTD system this year for electronic application and review; and 7) expediting manufacturing process verification.

In late March 2017, the CFDA hosted the National Drug Registration Regulatory Conference. CFDA Vice Minister WU Zhen delivered a keynote speech at the conference. He admitted the current CFDA approval time for clinical trials is too long, therefore needing reform. He then outlined the following considerations for future reform in the clinical trial approval area: 1) Reform of drug clinical trial management model to accelerate approval; 2) Accelerating registration approvals of urgently needed; 3) Enhancing technical support capacity and level of drug evaluation; and 4) Strengthening IP protection and researching on the formulation of drug clinical trial data protection system to secure rights of drug patent holders.

The State Council's major reform policy covering full process of the pharmaceutical industry, *Certain Opinions for Further Reform and Improvement of Pharmaceutical Manufacturing, Distribution and Application (Guo Ban Fa 2017 #13)*, has been dissected into 58 specific reform tasks which have been assigned to different government departments with deadlines for implementation. Among all tasks, two are in the center, according to an official with the State Council's healthcare reform office at an industry hearing event. The two critical tasks are: 1) encouraging development of first-to-copy

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generic drugs; and 2) import drug price negotiation.

CFDA Minister BI Jingquan delivered a report to the National People's Congress in August 2017 over the progress of the Chinese drug evaluation and approval system reform. Besides progresses made on the fronts of prioritized review and approval of innovative drugs, generic drug quality and efficacy equivalence evaluation, MAH trial and clinical research quality, he said the CFDA has essentially eliminated the backlog of drug registration review and reduced the number of applications pending review to around 6,000 at present from 22,000 at a peak in 2015. All types of drug registration applications, including those for chemical drugs, vaccines and TCMs, are now up to speed with official timeline requirements.

Throughout the year, China persisted to toughen up its drug regulation and enforcement. In April 2017, the National People's Congress has set up a drug administration law enforcement inspection group which would focus its inspection on 13 areas including formulation of complementary rules and regulations of the DAL, infrastructural building of the drug regulatory regime, supply security of commonly-used and emergency aid medicines as well as orphan drugs, development and execution of policies relevant to encouragement of new drug R&D, top issues of drug R&D, and reform of drug evaluation and approval system.

The CFDA was also given more teeth to police pharmaceutical R&D with issuance of the Interpretations of the Supreme People's Court and the Supreme People's Procuratorate for Application of Criminal Laws over Cases Relating to Faking Drug and Medical Device Registration Data in August 2017.

Besides, the *PRC Law on Traditional Chinese Medicine* became effective in July 2017. It is well-known that the law aims to give traditional Chinese medicine (TCM) a bigger role in the healthcare system.

The CFDA published its 2018 legislation plan in February 2018. According to the plan, the agency plans to work on 36 legislation projects including three laws, three regulations and 31 rules in the year of 2018. The three laws to be worked on include: 1) continued amendment of the *Drug Administration Law of PRC*; 2) completion of the amendment draft of the *Drug Administration Law of PRC* for review by the State Council; and 3) continued proposal of the *National People's Congress Decision on Authorizing the Trial of Patent Link Compensation of Selected Drugs and Exploration of Drug Patent Link System*. Among the 31 rules to be worked on, 15 are related to reform of the drug and medical device evaluation and registration system.

In March 2018, after about five years as a standalone agency, the China Food and Drug Administration (CFDA) will merge into the gigantic State Market Supervision General Administration (SMSGA) and survive on as the National Medical Products Administration (NMPA) as a subordinate agency. Other than spinning off its food related responsibilities, the NMPA is almost identical to its predecessor CFDA in terms of drug registration and regulation.

The newly established National Medical Products Administration (NMPA) held its first

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meeting of officials in April 2018 following inauguration earlier in the month. The meeting outlined five focal areas of the agency's work in 2018, including continuing to deepen reform of drug and medical device evaluation and approval system, expanding regulation and enforcement of drugs, medical devices and cosmetics with boosted sample testing, and cracking down on violations with emphasis on production and online sales of fake medicines.

In April 2018, the State Council came out with a major new policy, *Opinions on Reform and Improvement of Generic Drug Supply Security and Application*, under which China will offer preferential tax rates to generic drugmakers, setting corporate income tax for qualified high-tech firms at 15%. The State Council also said it would draw up new incentives aimed at encouraging the development and production of generic drugs, which are expected to substitute expensive foreign originator medicines. To "balance the interests of patent holders with those of the general public", China will also aim to strengthen enforcement of intellectual property rights and establish early warning mechanisms to prevent generic drug producers from infringing patents. But at the same time, the document also provides for the first time a roadmap for compulsory licensing of patent drugs to improve access in time of catastrophic infectious disease outbreak, drug shortage for prevention and treatment of major diseases and other sudden public health events.

Another major development in the same month was the State Council's decision to remove tariffs on certain imported drugs. According to the *Announcement of the Customs Tariff Commission of the State Council on Reducing the Import Tariff of Drugs*, import tariffs on all general medicines including anticancers, alkaloid drugs with anticancer efficacy, and formulated TCMs with actual imports will be reduced to zero starting from May 1, 2018.

Thereafter the Ministry of Finance (MOF), the General Administration of Customs (SGAC), the State Administration of Taxation (SAT) and the NMPA issued a new policy, *Notice on Value-Added Tax Policy of Anticancers (Cai Shui 2018#47)*, to offer ordinary VAT tax payers engaging in production, sales, wholesale and retailing of anticancer drugs the simplified 3% VAT option and at the same time cuts the VAT rate of imported anticancers will be reduced to 3% (import portion only).

Besides the import tariff slash for anticancers, the State Council decision mentioned above also calls for research into substantially reducing prices of urgently needed anticancers, expedited launch of imported innovative new medicines, strengthened intellectual property protection with a maximum data protection period of six years to be set up for innovative chemical drugs and a maximum of five year patent term compensation for innovative medicines applying for marketing in China and overseas synchronically.

Most recently, the NMPA and NHC issued a joint document, *Announcement on Matters Concerning Optimization of Drug Registration Evaluation and Approval (2018#23)*, in May 2018. It became effective upon issuance. The move aims to prioritize review and approval of drugs which prevent and treat life threatening diseases currently without effective and orphan drugs for rare diseases. It is provided that domestic clinical trials can

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be waived for such drugs already marketed overseas.

Furthermore, NMPA Commissioner Jiao Hong pledged in June 2018 the following measures to speed up new drug approvals: 1) adjusting import chemical drug registration testing process, changing current pre-approval testing requirement to the new post marketing sampling provision; 2) implementing data protection and provide corresponding data protection periods during which no other same products will be approved; and 3) introducing patent link and patent term restoration mechanisms to allow reasonable profits to innovators and encourage drug innovation.

Healthcare reform deepens amid intensified cost containment

Chinese Premier LI Keqiang delivered his government working report at the National People's Congress in March 2017, spending considerable time healthcare reform. Later on March 28, the National Healthcare Reform Teleconference was held and Premier Li repeated the ten major healthcare reform tasks in 2017. Tasks most relevant to the pharma industry include:

- ☞ Deepening coordinated healthcare reforms of medical service, BMI and pharmaceutical industry;
- ☞ Advancing the development of medical consortiums and developing demand-oriented family doctor contract services;
- ☞ Achieving full elimination of hospital drug sales margins;
- ☞ Introduction of two invoice system;
- ☞ Advancing BMI payment system reform in all urban hospital reform and overall healthcare reform trial sites;
- ☞ Completing integration of urban and rural resident BMI schemes in six primary aspects; and
- ☞ Pushing forward infrastructural building of healthcare IT and accelerating connectivity across platforms and regions.

A month later, the State Council recently issued a policy document, *Opinions for Major Tasks of Deepening Economic Reform in 2017*, which calls for accelerated reform in select areas including healthcare. The government remains committed to its planned spending and investments into healthcare reform. Besides, the reform of medical service pricing will be advanced with emphasis on “full implementation of medical service and drug price reform in urban public hospitals.” Finally, the government will dedicate its full force into coordinated reform of medical service, BMI and pharmaceutical sectors.

The General Office of the State Council followed up one more official document, *Major Tasks of Deepening Healthcare System Reform in 2017*, on May 2. The document includes a total of 70 major tasks to be implemented this year. The first part of the document includes 14 new policies to be formulated and issued in 2017 by various central government agencies. The rest 56 major healthcare reform tasks are mostly provided in various earlier documents. For details of this comprehensive document with deadlines and

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responsible agencies for implementation of each reform task, please refer to our full coverage of this story in the latter part of this journal edition issue.

In July 2017, the Healthcare Reform Leaders Group under the State Council released a surveillance report of healthcare reform progress in 2016. According to the report, the healthcare reform expanded to 200 trial site cities in 2016 covering 2,335 public hospitals. 92.6% municipalities and prefectures revised their medical service fees. It claims that healthcare quality has risen and relevant resource allocation has improved with continuously falling medical expenditures following the reform. The share of drug expenditures in outpatient and inpatient expenditures of public hospitals in reform trial areas fell to 49.0% and 34.2% respectively in 2016, compared with 51.0% and 36.7% in 2015.

Into the New Year, the NHFPC celebrated the following major advances of Chinese healthcare reform in 2017 at the *2018 National Health and Family Planning Conference* in January 2018:

- ☞ Important phased reform victories have been won with all public hospitals abandoning drug sales margins and all provinces introducing plans for the “two invoice” system in pharmaceutical sales.
- ☞ The capacity of primary healthcare facilities has significantly improved.
- ☞ Fallen share of personal out-of-pocket expenses in China’s overall healthcare expenditures to 28.8%.
- ☞ Continued growth of healthcare facilities and professionals to new highs of 990,000 and over 1.2 million respectively.
- ☞ Increased life span of Chinese population to 76.5 years and dropped death rates of maternity women and new born babies.

Earlier in late 2017, Harvard researchers designed for and proposed to China a system that aligns financial incentives for physicians and hospitals with key measures of performance, hoping to improve health care for millions of patients in some of China's poorest regions. The initiative – called APPROACH, for Analysis of Provider Payment Reforms on Advancing China's Health – is being conducted in collaboration with provincial governments and with teams from Chinese universities. It seeks to alter a system whose incentives are "mal-aligned".

China's basic medical insurance system (BMI) now covers 1.35 billion people, according to the NHFPC in February 2018. The enrollment rate of the BMI has been steady and held at 95% of the population in 2017, said WANG Hesheng, Vice Minister of NHFPC, at a press conference in Feb 2018. Meanwhile, the critical illness insurance scheme covers 1.05 billion people, said Wang. Future medical reform will focus on promoting balanced development of medical services in different regions, said Wang.

More recently, after a State Council executive meeting chaired by Premier LI Keqiang decided in April 2018 to launch a major initiative to enhance China's public health services through development of Internet + Healthcare, the State Council issued its

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official document, *Opinions for Enhancing Development of Internet Plus Healthcare*, at the beginning of May 2018. This policy is expected to liberalize telemedicine and online pharmacy restrictions. Specifically, online filling of physician drug prescriptions for common and chronic diseases may be delivered by qualified third parties following pharmacist verifications. Additionally, real time mutual sharing of physician drug Rx information of medical facilities and sales information of drug retailers will be explored.

Last but not the least, LAI Shiqing, Inspector at the System Reform Department under the National Health Commission (NHC), revealed at a industry meeting in June 2018 that the national BMI payment standards may be released by the State Medical Insurance Administration (SMIA) before the end of 2018. Lai said that the primary task of the SMIA, at its infancy at least, is not cost containment as rumored on the Chinese press. Instead, the chief tasks of the new agency will be: 1) integrating BMI funds; 2) elevating the level of premium funding; 3) introducing the BMI payment standards; and 4) strategic purchasing of medical services and clinical drugs.

Pharma industry in the process of revamping its business model to fit with new business environment

The NDRC release issued its official statistics on performance of the Chinese pharmaceutical industry performance in 2017. The core business revenues of Chinese pharmaceutical manufacturers grew 12.2% in 2017, reaching CNY 2,982,600 million. The growth speeded up by 2.3 percentage points last year compared with that in 2016. Among all subsectors, TCM crude drug sub-industry and API sub-industry saw the highest growth, followed by pharmaceutical formulations sub-industry. The industry's net profit rose 16.6% in 2017, totaling CNY 351,970 million. The growth accelerated by 1.0 percentage point compared with that in 2016. Sub-industries with the highest profit growth last year were biologics and pharmaceutical formulations.

Things began to accelerate for Chinese pharma in 2018. According to latest official data from the MIIT, core revenues of the Chinese pharmaceutical industry rose 17.6%, while its net profits grew much faster at 35.5% in Q1/2018. The sharp growth in the quarter is stimulated by implementation of the new national reimbursement drug list (NRDL) and two invoice system, steady growth of leading chemical drug formulation players, and accelerating industry consolidation and M&As, according to industry experts.

21 MNC pharmaceutical companies had Chinese revenues totaling CNY 149.2 billion in 2017, up about 10%, according to "incomplete statistics" of E-Healthcare Executive journal. The pack was led by Pfizer with CNY 23.3 billion in Chinese sales last year, followed by AstraZeneca and Bayer with CNY 20.0 billion and CNY 17.0 billion respectively. Allergan led all MNC pharmaceutical companies by Chinese revenue growth in the same year at 22%, followed by Abbvie and Bayer. It is also notable that GSK China's growth rebounded to 18%. Besides, UCB and Lundbeck also witnessed impressive growth despite smaller revenue size at the moment. 11 of the pack saw revenue growth above 10% in 2017. Two companies, namely BMS and Takeda, experienced 40% and 19% Chinese revenue fall last year. The 40% revenue drop of BMS is 8% after deducting financial impacts of its OTC business spinoff.

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However, structural issues with the Chinese healthcare system continued to haunt the pharmaceutical industry in 2017. Notwithstanding the touted pharma industry ambitions of the Chinese government, slogans are nothing but pies in the sky when it comes to paying for better medicines. The healthcare reform has long been hijacked by cost containment and gone astray from the pledged path of improving efficiency and fixing structural flaws. The crashing course of reform is deeply rooted in the growing contradictions between wishful goals and budget reality, as well as among different government policies and their pursuits.

With tax and other revenues drying up and under increasing threat of BMI system deficit amid a slowing Chinese economy, local governments are pressured by both the central government and the public to do more for healthcare with less financial resources. As local governments assaulted the pharma industry above the table with wave after wave of cost containment measures, public hospitals also squeezed drug companies under the table for funds through a variety of schemes. Shortage of low cost but clinically essential medicines has become widespread, forcing the central government to step in and often intervene administratively.

Pushed to the corner, the Chinese pharmaceutical industry is now at the brink of business bottomlines. Under pressures of escalating anti-corruption campaigns, increasingly sophisticated cost containment measures as well as policy shifts in drug pricing and reimbursements, both domestic and multinational drug companies had no choice but to change so as to meet the new challenges of the Chinese healthcare business today.

Old IP flaws remained as new issues spring up amid regulatory reform and antimonopoly enforcements

The U.S. Trade Representative (USTR) recently issued its *2017 Report to Congress on China's Compliance with WTO*, which comprehensively reviews the magnitude of China's continuing compliance problems related to intellectual property rights and market access, including such issues related to the pharmaceutical sector.

On the basis of the USTR report primarily and drawing references from other foreign government/trade association reports, I have built the case for contemporary IP concerns in relation to the Chinese pharmaceutical sector.

<u>IP and market access related issues</u>

- ☞ *Patent application and related issues* – It is an area of serious concern of foreign pharmaceutical stakeholders. In particular, SIPO examination guidelines governing information disclosure requirements for pharmaceutical patent applications have been revised through a series of amendments making these guidelines more restrictive. Besides, amended patent examination guidelines that entered into force in April 2017 now require patent examiners to take into account supplemental test data submitted during the patent examination process. However, there are reports that China's patent examiners continue to deny applicants' requests to supplement their test data.
- ☞ *Patent infringement* - In its Economics and Trade Bulletin on January 8, 2018, the

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USDOC highlighted that, under Chinese law, companies are unable to bring patent infringement cases against a patent violator until the product has been launched to the market by the alleged violator.

- *Data exclusivity* - There has been persistent concern over the extent to which China provides effective protection against unfair commercial use of, and unauthorized disclosure of, undisclosed test or other data generated to obtain marketing approval for pharmaceutical products. China's law, and a commitment that it made in its WTO accession agreement, require China to ensure that no subsequent applicant may rely on the undisclosed test or other data submitted in support of an application for marketing approval of new pharmaceutical products for a period of at least six years from the date of marketing approval in China. However, Chinese law does not include an appropriate definition of the term "new chemical entity" for purposes of identifying test or other data entitled to protection. An additional area of concern in the pharmaceuticals sector involves the long delays in China's review of applications for permission to market new and innovative pharmaceutical products in China, and for these products to be placed on approved reimbursement lists. These concerns, along with analogous concerns relating to medical devices, have been the focus of various bilateral meetings with China.
- *Protectionist measures* - Another serious concern stems from China's proposals in the pharmaceuticals sector that seek to promote government-directed indigenous innovation and technology transfer through the provision of regulatory preferences.
- *Drug distribution* - China committed to allow foreign suppliers to distribute pharmaceuticals by December 11, 2004, and it began accepting applications from and issuing wholesale licenses to foreign pharmaceutical companies about six months after that deadline. At the same time, despite overall progress in this area, many other restrictions affecting the pharmaceuticals sector continue to make it difficult for foreign pharmaceutical companies to realize the full benefits of China's distribution commitments.
- *Price control* - In its WTO accession agreement, China agreed that it would not use price controls to restrict the level of imports of goods or services. China agreed that it would try to reduce the number of products and services on this list. In 2016, China continued to maintain price controls on several products and services including pharmaceuticals.

Antimonopoly and other legal issues

- *Counterfeit drugs and API/bulk drug regulation* - Despite years of sustained engagement, China still needs to improve its regulation of the manufacture of active pharmaceutical ingredients to prevent their use in counterfeit and substandard medications. In October 2017, China published limited draft revisions to the Drug Administration Law and stated that future proposed revisions to the remainder of this law would be forthcoming.

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- *Anti-monopoly Law enforcement* – Chinese regulatory authorities' implementation of China's Anti-monopoly Law poses multiple challenges. One key concern relates to how the *Anti-monopoly Law* will be applied to state-owned enterprises. While Chinese regulatory authorities have clarified that the Anti-monopoly Law does apply to state-owned enterprises, to date they have only brought enforcement actions against provincial government-level state-owned enterprises, not any central government-level state-owned enterprises under the supervision of SASAC. In addition, provisions in the *Anti-monopoly Law* protect the lawful operations of state-owned enterprises and government monopolies in industries deemed nationally important. Overall, many U.S. companies cite selective enforcement of the *Anti-monopoly Law* as a major concern to doing business in China, and they have highlighted the limited enforcement of this law against state-owned enterprises. Another concern relates to the procedural fairness of *Anti-monopoly Law* investigations. U.S. industry has expressed concern about insufficient predictability, fairness and transparency in the investigative processes of the NDRC, including NDRC pressure to "cooperate" in the face of unspecified allegations or face steep fines and actions by NDRC to discourage or prevent foreign companies from bringing counsel to meetings

More Challenges in the New Year, Despite Unchanged Long Term Prospects

In 2017, Chinese pharma continued to be overshadowed by many old flaws of the Chinese healthcare sector with no fixes as new challenges develop. The industry is expected to face mounting challenges in 2018 amid intensified cost containment flood the country.

With growing emphasis on reform of the BMI payment system, local governments are set to put more cost containment pressure on pharmaceutical companies, as they try to keep the public and central government happy and the books of BMI programs balanced in a time of fiscal crisis amid a slowing economy. On the other hand, the pharmaceutical industry will continue to be confronted by a host of other challenges including continued uncertainties of the broad Chinese economy, non-stop drug regulatory and healthcare reform turbulences, more stringent compliance requirements, and risks associated with constantly changing pharmaceutical business environment. The biggest hope for MNCs lies with the reform of drug evaluation and approval system, which appears to be opening a new door for innovative medicines in China.

Chinese pharmaceutical industry experts have predicted ten upcoming Chinese pharma industry and market trends in 2017 as follows:

- The Chinese biosimilar drug market is going to take off, led by monoclonal antibody drugs.
- As MAH system experiment deepens, the domestic contract manufacturing business will surge. The demand for integrated pilot and scaled production will increase sharply from 2018.
- The new provincial BMI reimbursement drug lists (developed on the basis of 2017 NRDL) will begin to have full impacts on the market this year with half of the

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provinces already initiating implementation in late 2017 and the rest expected to do so in the first quarter of 2018. In addition, the dynamic BMI reimbursement drug negotiation may provide opportunities to many recently approved innovative new drugs. These are expected to boost the overall Chinese pharmaceutical market.

- ☞ Drug evaluation and approval will be more efficient and accelerated after introduction of various reform measures and participation of the CFDA in ICH in 2017.
- ☞ Direct-To-Patient (DTP) Pharmacies will flourish and more hospital drug prescriptions will be filled by such pharmacies, especially innovative medicines and premium-priced chronic disease drugs. Many of the DTP pharmacies will be owned and operated by retail pharmacy chains.
- ☞ Support policies for generic drugs passing quality and efficacy equivalence studies are expected to be implemented this year. It is expected the first batch of such drugs will rip the benefits of higher market shares and profit margins.
- ☞ Import substitution of major off-patent originator drugs are expected to accelerate in 2018 as more generic drugs pass equivalence studies.
- ☞ The two-child family planning policy and regulatory liberalizations will give rise to a CNY 100 billion in-vitro fertilization (IVF) market. The market for reproductive assistance drugs will grow with accelerated import substitution.
- ☞ The in-vitro diagnostics (IVD) market will be reshuffled under intensified cost containment with only selected optimal channel distributors prevailing.
- ☞ Coronary DNA testing market is taking shape and will see explosive growth.

Meanwhile, new opportunities are also emerging for pharmaceutical companies, especially in the area of drug innovation, as China boosts support for new drug R&D, uplifts review and speed up approval process with increased harmonization with international standards and enhanced IP protection. In early 2018, the CFDA issued a new policy, *Opinions for Priority Review and Approval to Encourage Drug Innovation*, to accelerate the R&D and marketing of new drugs with clinical value and urgently needed generic drugs. The agency and the Ministry of Science and Technology (MOST) also issued a joint policy document, *Guidance Opinions for Promoting and Enhancement of Food and Drug Science and Technology Innovation*.

Although the sporadic reform of Chinese healthcare system and drug regulatory regime has created wide-ranging turbulences, the marketplace has nevertheless become cleaner for business with fallen sales and marketing expenditures.

The short and intermediate term outlook of Chinese pharmaceutical market remains to be tough and blurred, but long term prospects are hopeful and warrant patience of those with sustaining power. Conversely, let’s also remember that most Chinese pharma industry observers still agree that the Chinese healthcare market will keep on growing in the foreseeable future, albeit at a slower rate and with lower profitability.

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Has China done enough to keep itself attractive to pharma MNCs?

Regardless the challenges, we should still be thankful that the Chinese pharmaceutical market continued to grow at an impressive speed of around 8% by some estimates, albeit at further reduced speed than the previous year.

Looking ahead, the Chinese pharmaceutical market remains clouded by structural flaws, contradictions in government healthcare and industry policies, irrational cost containment, and irregular enforcements. Before these clouds and imbalances are contemplated and resolved, market growth is likely to be bottlenecked for an extended period of time despite the positive long term growth trend for healthcare demand in China.

In early 2017, CFDA Minister BI Jingquan told journalists at a press interview on the sidelines of the "Two Conferences" that there is a huge market potential for drug products and more foreign pharmaceutical companies should tap the sector. When asked about the delayed access to new drugs, Bi said his agency will streamline approval procedures for drugs, intensify protection of intellectual property rights, and increase the staff for drug approval.

The State Council and CFDA launched in the last quarter of 2017 new policies including the *Opinions on Deepening Reform of Evaluation and Approval System to Encourage Drug and Medical Device Innovation*, as well as proposals to amend the *Drug Administration Law of PRC* and the *Provisions for Registration of Drug Products* in order to help the country remain attractive to MNC innovators. Major policy incentives for research-based MNCs include a more streamlined drug evaluation and approval system which seeks to encourage innovation, renewed government promise to enhance reimbursement of new drugs, support of global clinical trials in China, removal of restrictions for phase I clinical trials of foreign new drugs, and conditional acceptance of overseas clinical data in support. Besides, the Chinese government has also made specific promises, though still somewhat vague, in these policies to introduce patent linkage & patent term restoration systems as well as enhanced data protection. As a concrete step to show its sincerity, the CFDA has hastened its approval of foreign innovative drugs recently.

These are all worth some serious applauses and it is indeed encouraging to see the Chinese government committed to harmonize its drug regulatory system with the world and to foster drug innovation. Nevertheless, readers are reminded to concentrate on the overall pie of Chinese healthcare/drug expenditures, which is what truly matters in the big picture and need to be watched at all times.

What will happen if that pie doesn't change much as new drug approvals speed up? How should research-based MNCs position themselves to maximize their slices in the Chinese healthcare matrix? What shall be the realistic healthcare policy goals for China?

These are the questions without straightforward answers. I encourage our readers to dig into in this comprehensive publication for references, clues and advice on which I hope effective solutions will be developed.

Most recently in April 2018, despite recent pledges of the Chinese government to open up

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the domestic market further and faster approvals of innovative medicines, MNCs should be alarmed by China's latest generic drug policy, *Opinions on Reform and Improvement of Generic Drug Supply Security and Application*, which is everything about raising the market share of domestic companies at the expense of foreign companies.

Under the new policy, China will openly offer preferential tax rates to domestic generic drugmakers, setting corporate income tax for qualified high-tech firms at 15%. The State Council also said it would draw up additional incentives aimed at encouraging the development and production of generic drugs. Besides, while the country said it would boost IP protection, as it also makes compulsory licensing easier than ever.

While recent positive policy moves undertaken by Beijing may improve market access of innovative drugs somewhat, but they are constrained by a host of other government policies for healthcare cost containment and import substitution. Without fundamental changes of Chinese mentality for self-reliance, industrial policies supporting domestic and state-owned enterprises, and relentless healthcare cost containment over-emphasizing on price competition, the bulk of demands for innovative and premium quality import drugs is likely to remain bottlenecked.

The root of the problem lies with the contradiction between reluctance of the Chinese government to pay for better healthcare of its people by sharply increase its healthcare spending budget and the public's expectation to receive mostly government funded healthcare as the last welfare of socialism, with or without Chinese characteristics. So far, central and local governments have done little to find consensus with the public to reconciliate this growing contradiction, other than resorting to cost containment as almost the only way to expand and upgrade BMI coverage.

The government's preoccupation with price competition of drug products and relentless healthcare cost containment has led to fallen healthcare quality broadly and will continue to bottleneck consumption of more expensive but premium quality and innovative import drugs.

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