Cross-Border Life Sciences Collaborations in China (Part 2)

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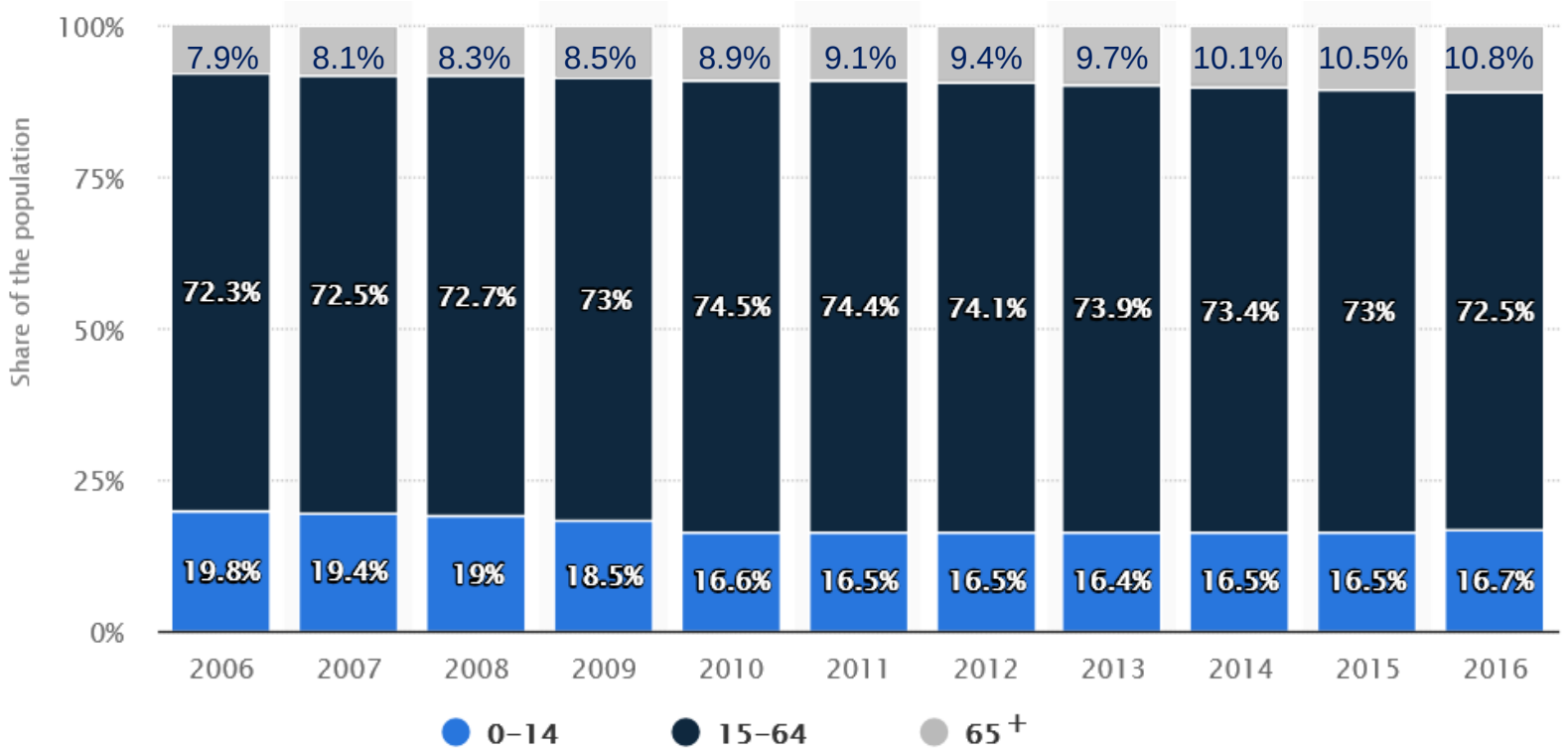
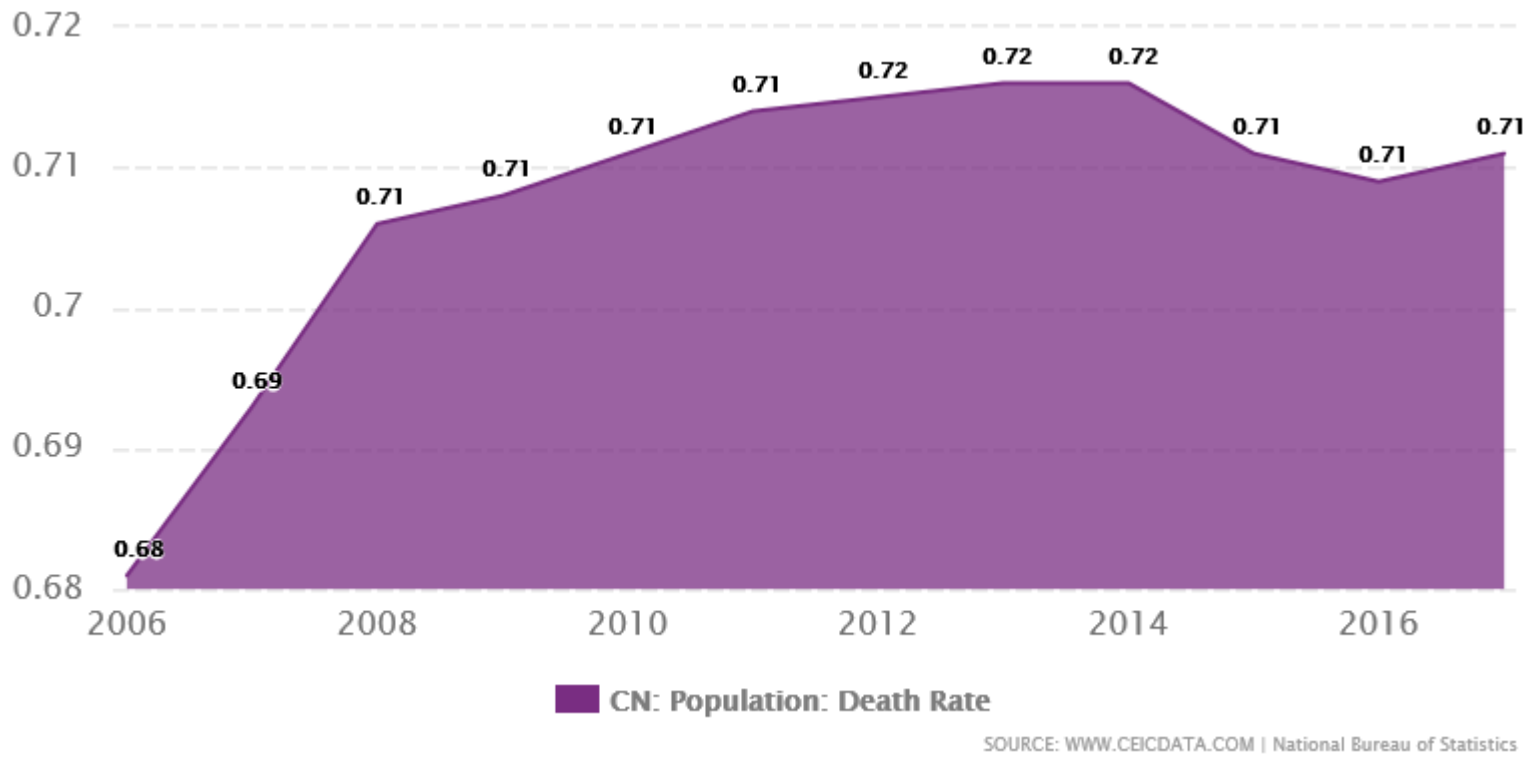
Longitudinal Demographic Profile in China (2006 – 2016)



Source: Statista 2018 (https://www.statista.com/statistics/270163/age-distribution-in-china/)

The 65+ age cohort rose by one-third to 10.6% between 2006 and 2016 and is projected to rise to 15% in years to come in response to improved health, legacy birth control measures, and lifestyle changes, increasing the need for healthcare to address medical needs of the elderly.

Longitudinal Mortality Profile in China



The crude mortality rate has gradually risen from 0.68 to 0.71 per 1000 persons between 2006 and 2017.

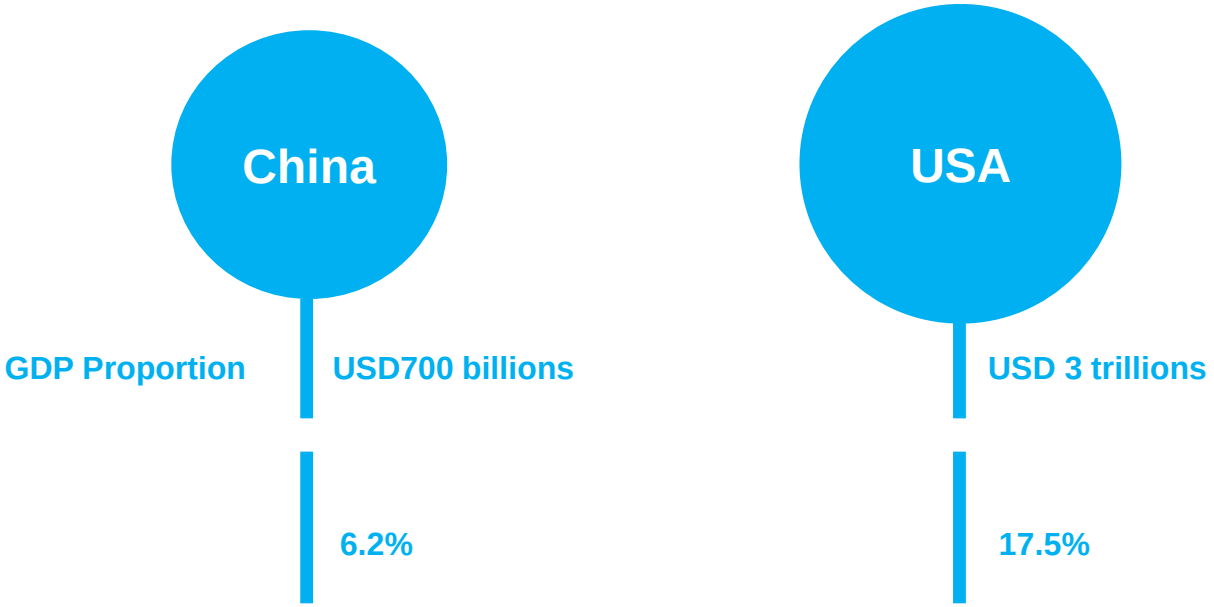
Longitudinal Cancer Incidence and Mortality Profile in China

- About 3,804,000 new cancer cases (2,114,000 male cases; 1,690,000 female cases) were diagnosed in 2014
- The crude incidence rate was 278.07/100,000 (301.67/10,000 in males; 253.29/100,000 in females) in 2014
- The crude mortality rate was 167.89/100,000 (207.24/100,000 in males; 26.54/100,000 in females)

Source: Vol 30, No 1 (February 2018): Chinese Journal of Cancer Research (http://www.cjcrcn.org/issue/418.html)

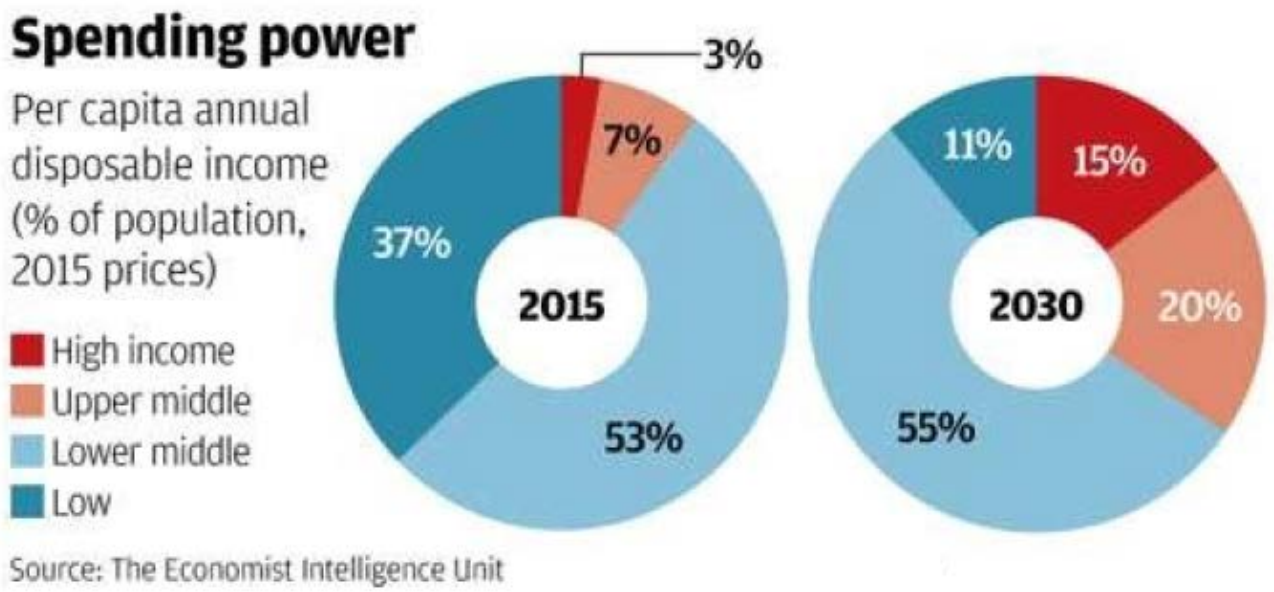
2016 Healthcare Expenses

US v. China

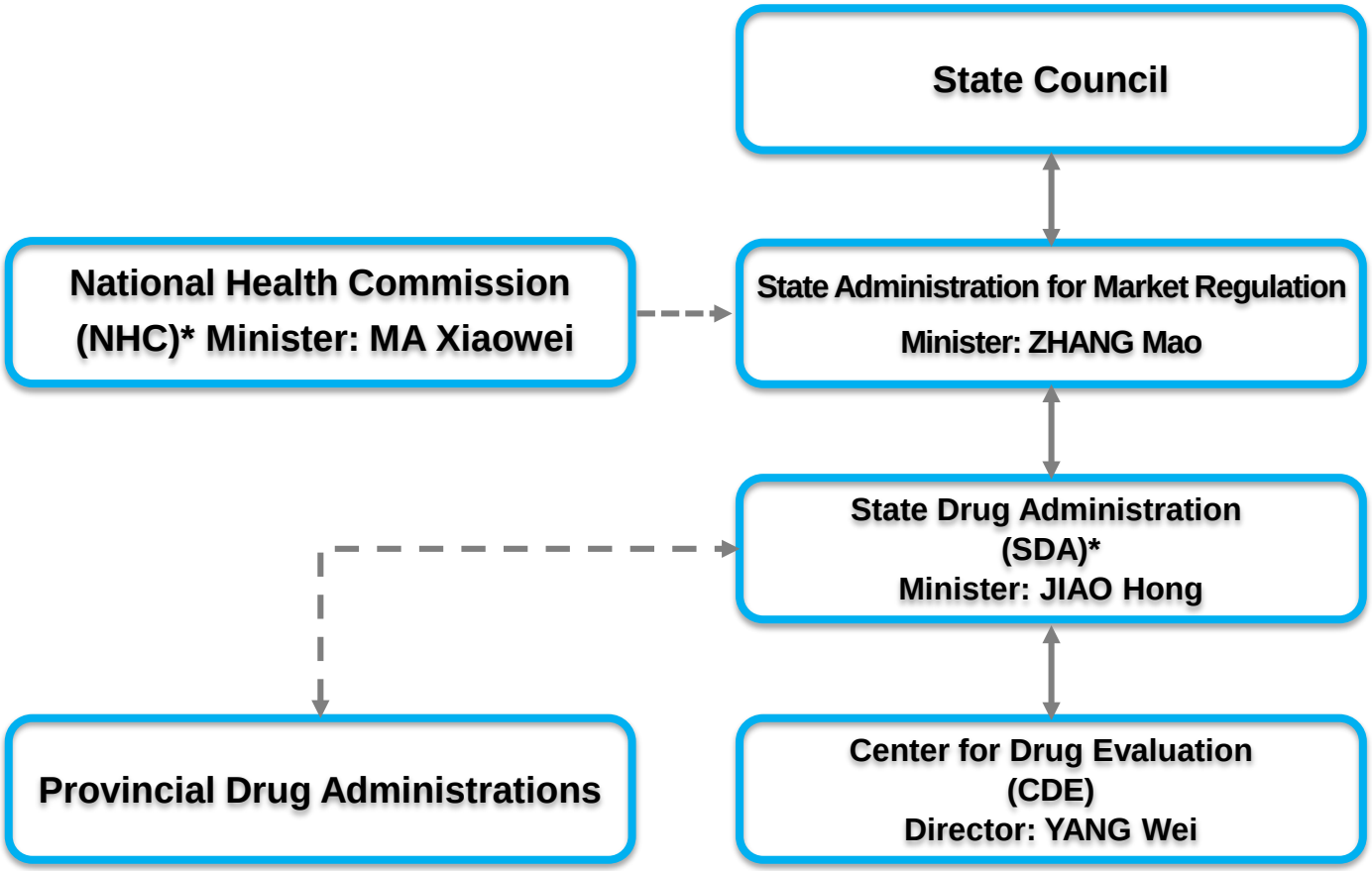


Source: http://www.rdpac.org/UpLoad/UpLoadFileDir/201802/03/201802032252341998.pdf

Growth of the Middle Class in China



Reorganized Organization Structure



*NHC and SDA – Previously known respectively as the National Health and Family Planning Commission and China Food and Drug Administration ("CFDA") before the State Council's institutional reform in March 2018.

Major Laws and Regulations

1. Drug Administration Law (药品管理法, amended April 24, 2015)

2. Regulations for Implementation of Drug Administration Law (药品管理法实施条例, amended February 6, 2016)

3. Measures on the Administration of Drug Registration (药品注册管理办法, amended October 1, 2007)

Key Legislative and Regulatory Developments 2015 – 2018

China has been engaged in comprehensive regulatory reform of drugs and medical devices policy since 2015. Regulatory reforms have been introduced to encourage innovation while reducing costs and regulatory burdens on life sciences companies

1. **Opinions on the Reform of Review and Approval System for Drugs and Medical Devices (关于改革药品医疗器械审评审批制度的意见, State Council August 2015, http://www.sda.gov.cn/WS01/CL0056/126821.html)**

   - initiated the comprehensive and fundamental regulatory reform of drugs and medical devices policy, particularly with respect to registration

2. **Opinions on Resolving the Backlog of Drug Registration Applications and Implementing the Priority Review and Approval Procedure (总局关于解决药品注册申请积压实行优先审评审批的意见, former CFDA February 2016, http://www.sda.gov.cn/WS01/CL0844/145260.html)**

   - announced a new priority review procedure to ease the registration backlog affecting drugs and medical devices
   - encourage innovation in new domestic and international drugs to meet unmet medical needs
   - encourage overseas manufacturers to plan and perform clinical developments in China in parallel with the US, EU and other jurisdictions

Key Legislative and Regulatory Developments 2015 – 2018 (cont'd)

3. Work Plan for Reforming the Chemical Drugs Registration Classification System (former CFDA March 4, 2016, the "New Classification") (化学药品注册分类改革工作方案), an important component of the general reform of the drug and device approval system initiated in the 2015 State Council Opinions:

- redefines "new drugs" and "generics", changing the current chemical drug classification system
- "new drug" eligibility is limited to those drugs that have not been marketed anywhere in the world, as opposed to "not marketed in China" in the previous definition
- This change may incentivize multinational companies wishing to bring innovative drugs to China to start their product development in China earlier than before in order to realize marketing advantages

Key Legislative and Regulatory Developments 2015 – 2018 (cont'd)

Party General Secretary Xi Jinping at the August 2016 National Health Conference called for:

- Promoting healthy lifestyle
- Strengthened health delivery services
- Improved health protection
- Healthier environment
- Development of research-based health industries
- Expanding healthcare delivery capacity at the grassroots level
- Mobilizing societal as well as governmental investment
- Curbing excessive drug prescription and lowering medical costs
- Lowering barriers to foreign investment and expert foreign personnel

Key Legislative and Regulatory Developments 2015 – 2018 (cont'd)

4. Four draft reform policies (former CFDA May 2017):

- 关于鼓励药品医疗器械创新加快新药医疗器械上市审评审批的相关政策 (http://www.sda.gov.cn/WS01/CL0087/172567.html) Circular 52 - to expedite the review and approval of new drug registration applications
- 关于鼓励药品医疗器械创新改革临床试验管理的相关政策 (http://www.sda.gov.cn/WS01/CL0778/172568.html) Circular 53 - to deregulate the conduct of clinical trials to encourage innovation
- 关于鼓励药品医疗器械创新实施药品医疗器械全生命周期管理的相关政策 (http://www.sda.gov.cn/WS01/CL0778/172569.html) Circular 54 – to enhance post-market supervision throughout a product's entire life cycle
- 关于鼓励药品医疗器械创新保护创新者权益的相关政策 (http://www.sda.gov.cn/WS01/CL0087/172606.html) Circular 55 – to protect the rights of drug innovators

Key Legislative and Regulatory Developments 2015 – 2018 (cont'd)

5. Opinions on Deepening the Reform of the Review and Approval System and Inspiring Innovation of Drugs and Medical Devices (General Office of the Communist Party Central Committee and General Office of the State Council, October 8, 2017, "Innovation Opinions") (关于深化审评审批制度改革鼓励药品医疗器械创新的意见, http://www.gov.cn/xinwen/2017-10/08/content_5230105.htm), which adopted CFDA's four draft reform policies and covered all important regulatory matters relating to drugs and medical devices:

- encouraging innovation of drugs and medical devices
- accelerating drug registration approval process
- improving and simplifying clinical trial management
- strengthening intellectual property protection for innovators
- promoting production of generic drugs
- establishing the Marketing Authorization Holder ("MAH") system

6. Decisions to Adjust Relevant Items in the Registration of Imported Drugs (former CFDA October 10, 2017, "Imported Drug Decision") (国家食品药品监督管理总局关于调整进口药品注册管理有关事项的决定, http://www.sda.gov.cn/WS01/CL0053/178363.html)

- Implementing changes to facilitate the review and approval process for imported drugs, particularly for innovative imported drugs

Key Legislative and Regulatory Developments 2015 – 2018 (cont'd)

7. **Draft Amendments to the Drug Administration Law (former CFDA October 23, 2017) (中华人民共和国药品管理法修正案 (草案征求意见稿), http://www.sda.gov.cn/WS01/CL0050/178902.html)**

   - most of the proposed amendments focus on full implementation of the marketing authorization regime, an important item in the Innovation Opinions

8. **Draft Amendments to the Measures on the Administration of Drug Registration (药品注册管理办法 (修订稿), http://www.sda.gov.cn/WS01/CL0778/178900.html)**

   - would amend the regulatory review and approval process relating to clinical trials, marketing authorization and approval

9. **Notice Concerning Publication of the China Marketed Drugs Catalogue (former CFDA December 28, 2017, "Drug Catalogue Notice") (总局关于发布《中国上市药品目录集》的公告 (2017年第172号), http://www.sda.gov.cn/WS01/CL1757/220786.html)**

   - similar to the "Orange Book" in the U.S.
   - formulated to encourage drug R&D and innovation in China

Key Legislative and Regulatory Developments 2015 – 2018 (cont'd)

10. State Council Opinions on Promoting Internet Plus Medical Treatment and Healthcare (关于促进"互联网+医疗健康"发展的意见, April 25, 2018)

- Medical institutions are encouraged to use Internet to expand the space and content of healthcare service;
  - It allows the development of online hospitals based on physical medical institutions
- Healthcare institutions also are encouraged to cooperate with internet companies to enhance the integration of regional healthcare information
- Construction and utilization of the information platform will be accelerated so that patients can sign up online with a family doctor
  - Online evaluation and reward mechanism will be explored to improve the services of family doctors
  - Ping An Healthcare and Technology Co Ltd. which operates China's largest online healthcare platform (Ping An Good Doctor Online Platform) has raised $1.12 billion in its IPO on Hong Kong Exchange at the end of April
- Interconnection of prescription information of healthcare institutions and medicine retail information will be further explored
  - This may help promote the development of online medicine sales and the logistics of medical supplies
- The integration of medical insurance information will be accelerated, and online payments will be gradually expanded to provide more convenient service for insured people

Priority Review Procedure for Innovative Drugs

- Pursuant to the Opinions on Resolving the Backlog of Drug Registration Applications and Implementing the Priority Review and Approval Procedure (总局关于解决药品注册申请积压实行优先审评审批的意见, http://www.sda.gov.cn/WS01/CL0844/145260.html), a new priority review procedure has been promulgated to:

  1. encourage innovation in domestic and international drugs to meet unmet medical needs
  2. encourage overseas manufacturers to plan and perform clinical developments in China in parallel with the US, EU and other jurisdictions

- Priority review status may be requested based on the following criteria:

  1. Registration applications for drugs with apparent clinical value including:
     - innovative drugs not marketed anywhere else in the world
     - innovative drugs for which manufacturing is transferred to China
     - drugs with advanced formulation technologies, innovative treatment methods and apparent treatment advantages
  2. Parallel clinical trial applications for new drugs approved for clinical trials in the U.S. or the EU
  3. Parallel registration applications for drugs with the same production line and which have passed on-site inspections in the U.S. or the EU
  4. Registration applications for drugs to prevent or treat HIV, tuberculosis, viral hepatitis, rare diseases, malignant tumors, pediatric drugs and drugs for diseases of the elderly

Conditional/Accelerated Marketing Approval

Pursuant to the Innovation Opinions:

1. Drugs that offer new solutions for treating life-threatening diseases or address critical unmet medical needs may be eligible for conditional approval before completion of Phase III confirmatory trials, so long as early and mid-stage study data indicates their efficacy and predicts their clinical value

2. Companies receiving conditional approvals must develop a risk management plan and initiate confirmatory post-approval study as per the requirements in the conditional approvals. Innovative drugs sponsored by the National Science and Technology Major Project may also be eligible for priority review and approval

3. Similar approval will be given to treatments for rare diseases if such therapy has already been approved elsewhere, under the condition that post-approval commitment studies are required

Reform of Registration Procedure for Imported Drugs

Former CFDA on October 10, 2017 promulgated the Decisions to Adjust Relevant Items in the Administration of Registration of Imported Drugs (国家食品药品监督管理总局关于调整进口药品注册管理有关事项的决定, the "Decisions", http://www.sda.gov.cn/WS01/CL0053/178363.html). Fundamental changes to the existing imported drug registration system include:

1. Opening of Full Clinical Development

- Previously, an imported drug must await completion of a Phase II or Phase III clinical study or be a recipient of marketing authorization abroad before beginning an international multi-center trial ("IMCT") in China. Under the Decisions, such requirement has been eliminated which substantially reduces development delays for many foreign companies
- Except for biological products for preventive use, the Decisions opened the Phase I trial to global development which means that foreign applicants for new chemical drugs and new therapeutic biological products can conduct a full clinical development plan inside China in parallel with the global development program

2. Simplified Clinical Trial Procedure

- Previously, imported drug manufacturers applying to conduct an international multi-center trial ("IMCT") in China were required to submit three applications:
  - i. multinational clinical trial (MNCT) application to request global Phase II or III trials in China
  - ii. after the drug has been approved and the certificate of pharmaceutical product is available from the US or EU (or any other jurisdiction), application to SDA to request clinical trial waiver (requesting exemption from need to conduct additional local trials)
  - iii. new drug registration application ("NDA") to SDA for approval of marketing authorization application ("MAA")

Reform of Registration Procedure for Imported Drugs (cont'd)

2. Simplified Clinical Trial Procedure (cont'd)

- Under the Decisions, for Clinical Trial Applications (CTA) or NDA for imported new chemical drugs and innovative biological products for therapeutic use, there is no need for the second application (i.e., application to SDA to request a clinical trial waiver) which allows the applicant for an imported drug to apply directly for MAA upon completion of its IMCT in China before the product has been approved in its home jurisdiction
- This simplified procedure is expected to shorten the entire approval process by at least one year

3. Simplified Requirement for Evidence Documents

- The Decisions eliminate the requirement that an imported drug be approved outside China before China grants marketing authorization in the case of an "imported new chemical drug or innovative therapeutic biologic"
- For an imported drug in which the IMCT has already been conducted in China, the applicant may apply directly for marketing approval with the SDA after the multi-center trial has been completed

4. Shortened Review and Approval Timeline for Imported Drugs

- 19 imported cancer drugs approved in 2017, up from 7 in 2014;
- The average approval time for imported cancer drugs has been cut from 420 days to 111 days; and the average time for approval of cancer drug clinical trials has been cut from 243 days to 114 days

Reform of Registration Procedure for Imported Drugs (cont'd)

Imported drugs that offer new treatment for life-threatening diseases or address critical unmet medical needs may be eligible for priority review process and conditional marketing approval by SDA

- On April 28, Merck received the conditional marketing approval by SDA for its nine-valent HPV vaccine (GARDASIL 9) for which SDA took only nine days to approve
  - April 20 - SDA's Center for Drug Evaluation ("CDE") received the application
  - April 23 – application was put in the priority review process
  - April 27 – dosage forms passed the technical review by CDE
  - April 28 – SDA issued the conditional marketing approval to Merck
- The fast-track approval process recognized the urgent demand for the vaccine to prevent cervical cancer
  - more than 28% of the world's cervical cancer patients are in China
  - 98,900 new cases and 30,500 deaths per year due to cervical cancer
- The priority review/conditional approval by SDA based on:
  - GARDASIL data that previously led to the quadrivalent HPV vaccine approved by SDA May 2017
  - foreign clinical trial data specifically on GARDASIL 9
- The conditional approval initially in the Hainan Boao Lecheng International Medical Tourism Pilot Zone comes with requirements for additional studies and post-marketing supervision

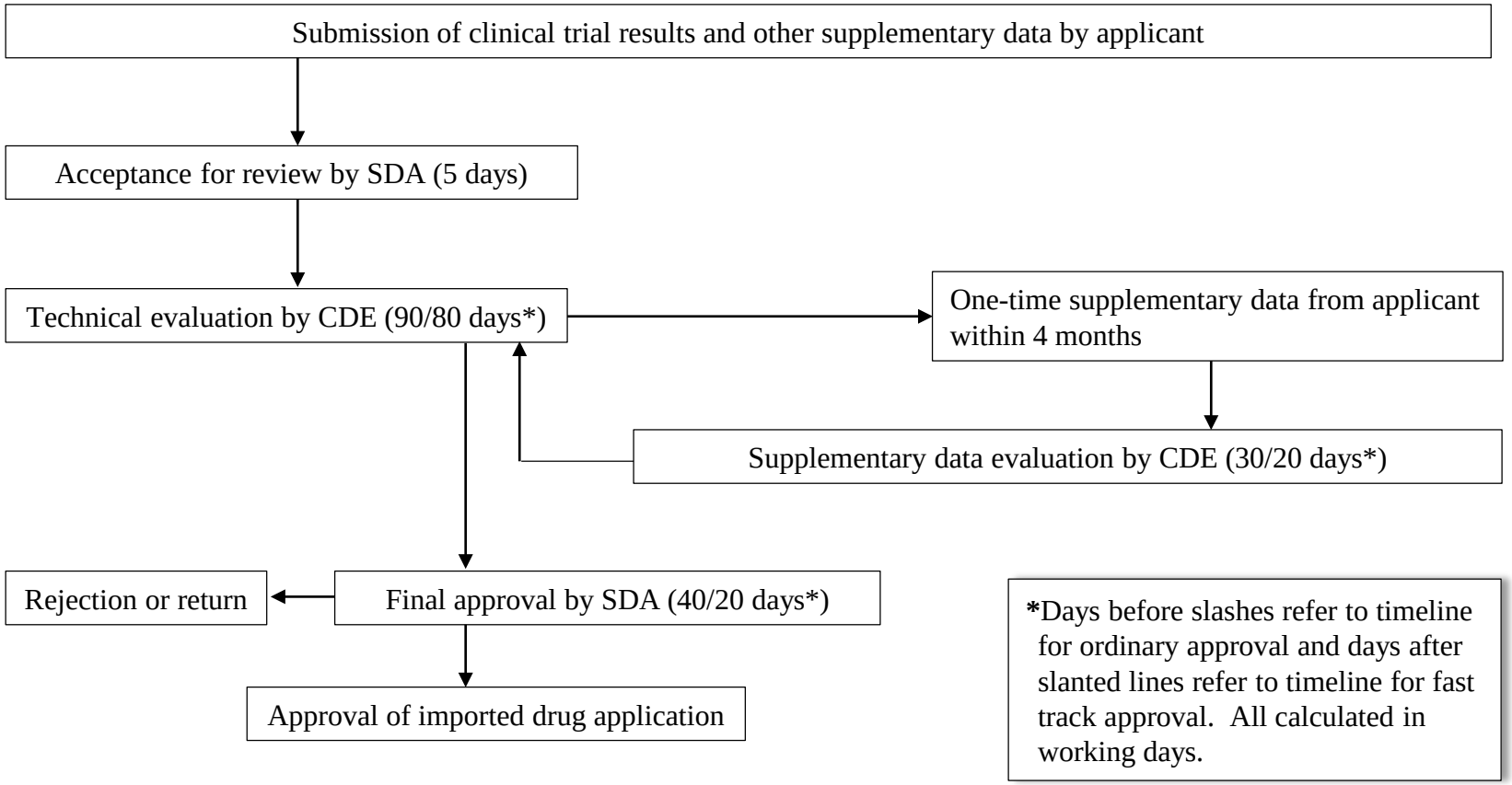
Tariff Reductions and Other Market Liberalization Measures for Imported Anticancer Drugs

1. The Standing Committee of the State Council decided on April 12 to reduce tariffs on imported anticancer drugs as of May 1:

   - 5-6% import tariff for anticancer drugs and alkaloid drugs with anticancer efficacy will be zeroed-out
     - Imports of anticancer drug total RMB 40 billion per year so the elimination of tariffs will reduce the cost of such drugs by at least RMB 2 billion
   - 17% import VAT will be substantially reduced as well but it remains to be seen by how much

2. The Medical Insurance Department of the Ministry of Human Resources and Social Security has initiated work plans for negotiation of reimbursement of anti-cancer drugs that were not covered by medical insurance

China Marketing Authorization Approval Procedure for Imported Drugs



Encouragement of Development and Production of Generic Drugs

Following up to the Innovation Opinions, the State Council on April 3, 2018 promulgated the Opinion on Reforming and Improving Supply and Use of Generic Drugs" (国务院办公厅关于改革完善仿制药供应保障及使用政策的意见, http://www.gov.cn/zhengce/content/2018-04/03/content_5279546.htm) to further promote China's generic pharmaceutical industry:

1. A generic drug list will be formulated by the NHC and SDA to encourage production of generic drugs
   Encouraging production of generic drugs for rare diseases, major infectious diseases and pediatric treatments, as well as important drugs that are short in supply
   - Encouraging production of drugs with the underlying patent to be expired in one year but yet to apply for drug registration with CNDA
   - Generic drugs which have passed the quality and efficacy evaluation will be also included in Catalogue of Marketed Drugs in China 2. Research and development of generic drug technology will be strengthened
   - Key technologies for generic chemical and biosimilar in the generic drug list will be included in the national related science and technology program

3. Improve IP protection to encourage innovation of originator drugs and R&D of generic drugs
   - An "early warning" mechanism will be established to reduce the risk of patent infringement by the generic drug manufacturers

4. Qualified generics manufacturers are entitled to be designated as High and New Technology Enterprises (HNTE) with preferential income tax reductions (15%)

Strengthening Intellectual Property Protection for Innovators

To strengthen intellectual property protection for innovators, broaden protection of innovator's data and facilitate market access for innovative drugs, detailed steps have been contemplated under the Innovation Opinions and former CFDA's Circular 55. Key highlights include:

1. Drug Patent Linkage

(1) Practice under Current Drug Registrations

- Did not clearly provide whether the innovators/patent holders of the underlying drug can bring a patent infringement action in court against generic manufacturers' pre-market infringement
- Generic manufacturers can file a drug registration application with the SDA within two years prior to the expiry of such drug patent which makes it impractical for innovators/patent holders to initiate such patent lawsuits under the current legal schemes

(2) Compared with the current legal schemes, the Innovation Opinions and Circular 55 have made significant progress on the patent linkage system:

- Outlines the patent linkage system for the first time, i.e., innovators can bring infringement actions prior to the SDA's grant of marketing approval for the generic drug products in the first place
- Patent linkage is provided between pharmaceutical regulatory approvals and patent infringement, whereby regulatory approval is denied until the underlying patent has expired or is determined to be invalid or not infringed
- The patent linkage system would provide greater stability in patent enforcement for both innovators and generics in China, by assuring innovators that their innovation is amply protected, and generic companies are afforded opportunities to seek regulatory approval based on proof that a patent that might otherwise prevent their entry into the market is invalid or not infringed by the generic company's product

Strengthening Intellectual Property Protection for Innovators (cont'd)

1. Drug Patent Linkage (cont'd)

(3) Patent linkage contemplated under Circular 55

- Upon the filing of an application for drug registration, the applicant must submit a statement regarding the relevant patent rights of which the applicant is aware. Where the applicant seeks to challenge a patent, the applicant is to declare non-infringement of the relevant patent and notify the patent owner within 20 days of filing
- Where infringement is alleged, the patent owner is to file an action within 20 days of receiving notification from the applicant and notify the SDA. Once the infringement action is accepted by the court, the SDA shall stay the grant of approval for up to 24 months ("Stay Period"), during which the assessment of the application will continue
- In the event the parties reach a settlement or a decision is issued by the court during the Stay Period, the SDA shall take such settlement or decision into consideration in its approval process. However, if no infringement ruling is rendered within the 24-month Stay Period, the SDA may grant marketing authorization with respect to the pending application
- If the applicant did not file a non-infringement declaration but a patent holder has initiated a patent infringement action, the SDA may also implement a Stay Period

(4) Issues remain unclear

- The Patent Law (2008) needs to be amended to provide that marketing approval applications for generic drug products covered by innovator's patents may constitute infringement
- Which courts have jurisdiction over such matters
- Whether administrative and/or civil remedies are available for the various obligations proposed by these policies

Strengthening Intellectual Property Protection for Innovators (cont'd)

2. Improved Drug Data Exclusivity

- The Innovation Opinions also provides that drug registration applicants are entitled to data exclusivity when filing drug registration applications with SDA
- The data would be restricted to clinical trial data and other data developed by applicants of innovative drugs, drugs for rare diseases, pediatric drugs, innovative therapeutic biologics, and applicants for generic drugs that succeeded in patent challenges
- The data protection scope is much broadened compared to the Regulations for Implementation of the Drug Administration Law (February 6, 2016) under which only a developer of a new drug containing a new chemical entity is entitled to data exclusivity
- The data exclusivity period starts from the date of marketing authorization and lasts for:
  - 6 years for new innovative drugs
  - 10 years for innovative pediatric drugs and innovative drugs for rare diseases
  - 10 years for innovative biologic products
  - 3 years for improved new drugs for rare diseases and children
  - 1.5 years for generic drugs which (a) have successfully invalidated a patent or (b) are the first generic drug to be approved locally based on an originator which has been marketed abroad

Strengthening Intellectual Property Protection for Innovators (cont'd)

3. Chinese version of the "Orange Book"

Catalogue of Marketed Drugs in China (中国上市药品目录集, comparable to the "Orange Book" in the United States) is further proposed under Circular 55 to encourage R&D and innovation of new drugs, foster access to medicine and lower drug costs:

- Each approved drug will be classified as an innovative drug, improved new drug or generic drug that has passed the review for equivalency in quality and efficacy
- Besides scientific information on the drug's use (API, dosage, specification) and the market approval holder's information, the record may also include such intellectual property information as lists of relevant patents and the data protection and drug monitoring period
- Includes a list of originator drugs and their generic substitutes which have passed the quality and efficacy evaluation
- First iteration currently includes 131 drugs and will be updated as new drugs are approved
- Among the 131 drugs on the list, 13 are generic drugs that have met China's recently introduced quality and efficacy equivalency standards compared with originator reference products
- Some 39 multinational pharmaceutical companies have products on the list
- Provide a full record of all newly listed drugs, including details such as API, dosage form, specification, registration/approval number, registration/approval date, the market authorization holder name, manufacturer's name and links to other databases with more information about the drugs and related patents

Market Authorization Holder Program

Since 2016, an initiative known as the market authorization holder (MAH) program has been piloted in 10 provinces with the goal of reforming the licensing process for drugs

1. **Ease the restrictions on who can be an MAH:**
   - Under the current regulatory regime, life sciences companies or individuals seeking marketing authorization for their product are required to have their own manufacturing facilities
   - The MAH program eliminates this requirement by allowing such companies to contract third-party manufacturers (CMOs) to produce their product
   - R&D organizations and academic research institutions can qualify to be an MAH even if they do not possess manufacturing capability
2. **License holders are still largely responsible for many legal liabilities associated with pre- and post-marketing regulations**
   - Companies wishing to contract third-party manufacturers must ensure the facilities are GMP-compliant
   - MAH also remains responsible for promptly reporting any adverse drug reactions to the SDA following product launch
3. **MAH program benefits**
   - small and mid-sized life sciences companies that do not have the capital to build and maintain a costly manufacturing base
   - multinational firms apprehensive about entering the Chinese market
4. **The MAH program is expected to incentivize innovation by R&D organizations and academic research institutions which are frequent drivers of pre-clinical studies and clinical studies**

Cross-Border Transfer of Clinical Data

1. **Laws/Regulations/Guidelines (collectively, "Guidelines") governing cross-border data transfer include:**

   - Cybersecurity Law (2015)
   - Information Security Technology - Personal Information Security Standard (信息安全技术 - 个人信息安全规范, December 29, 2017, https://www.tc260.org.cn/upload/2018-01-24/1516799764389090333.pdf)
   - Information Security Technology – Guidelines for Data Cross-Border Transfer Security Assessment (Draft) (信息安全技术 数据出境安全评估指南 (征求意见稿), August 25, 2017, https://www.tc260.org.cn/ueditor/jsp/upload/20170527/87491495878030102.pdf)
   - Measures for the Security Assessment of Outbound Transmission of Personal Information and Important Data (Draft) (个人信息和重要数据出境安全评估办法 (征求意见稿), April 11, 2017, http://www.cac.gov.cn/2017-04/11/c_1120785691.htm)

2. **The cross-border transfer of clinical data may be subject to a security assessment by Network Operators before transmission**

   - Network Operators are broadly defined as the owners and operators of networks as well as providers of services to networks, including foreign-invested enterprises and providers of services to networks

Cross-Border Transfer of Clinical Data (cont'd)

3. For clinical data involving any Personal Information or Important Data generated in China which needs to be transferred outside China, a security assessment will have to be conducted by the Network Operator before transmission regardless of whether clinical data are from global studies that are sponsored by foreign drug manufacturers in China or from studies sponsored by the China licensee in China:

- **<u>Personal Information</u>**:

  i. any information, recorded in electronic form or otherwise, which can be used, solely or together with other information, to determine the identity of a natural person, including but not limited to name, date of birth, ID card number, personal biometric information, and address and telephone number

  ii. ethnicity, political opinion, religion, genetic information and fingerprints

  iii. for personal information to cross borders, the consent of the owner of such information is required

- **<u>Important Data</u>** is broadly defined under the Guidelines as data closely related to national security, economic development, and social and public interests

Cross-Border Transfer of Clinical Data (cont'd)

4. **In the following circumstances, Network Operators will be required to apply to the Cyberspace Administration of China ("CAC") or its local counterpart to conduct a security assessment before transfer:**
   - outbound data transfers involving Personal Information of over 500,000 individuals
   - data size over 1,000 GB
   - transfers involving data relating to nuclear facilities, chemistry and biology, national defense and the military, population health, megaprojects, the marine environment or sensitive geographic information
   - transfers involving data relating to information about the cybersecurity of Critical Information Infrastructure, such as system vulnerabilities and security protection
   - outbound transfers of Personal Information and Important Data conducted by an operator of Critical Information Infrastructure
   - outbound data transfers that may affect the national security or the public interest

5. **Clinical data which includes Personal Information and/or Important Data may not be transmitted outside of China if, after performance of a security assessment, either the Network Operator or the CAC determines that the outbound transfer**
   - was not approved by the owner of Personal Information or may jeopardize personal interests;
   - may cause security risks to the nation's politics, economy, technology or defense, or
   - may result in damage to national security or the public interest

Rules for Drug Pricing effective June 1, 2015

Beginning June 1, 2015, drug prices were required to follow the new rules pursuant to the Circular Concerning Opinions on Promotion of the Drug Pricing Reform (关于印发《推进药品价格改革意见》的通知, NDRC and former CFDA May 2015, the "2015 NDRC Opinions"), http://www.ndrc.gov.cn/zcfb/zcfbtz/201505/t20150505_690664.html):

- For drugs reimbursed by government medical insurance funds, the newly-organized National Health Insurance Bureau (国家医疗保障局) will determine drug reimbursement rates or standards which were previously under the jurisdiction of the Ministry of Human Resources and Social Security (MOHRSS), National Development and Reform Commission (NDRC) and NHC
- For patented drugs or drugs produced exclusively by one manufacturer, the price is to be set through a transparent negotiation mechanism involving multiple parties, including hospitals (most of which are public medical institutions), provincial governments and other stakeholders
- Prior to the reform, hospitals and their pharmacies purchased drugs through bidding processes or procurement programs that were determined and run by local government authorities (provincial-level and below). Now, for blood products not included in the National Reimbursement Drug List (NRDL), vaccines subject to the government's system of centralized procurement, government-provided HIV treatment drugs, and contraceptive drugs and devices, the price is to be determined through a bidding process or procurement negotiations between pharmaceutical manufacturers (or their distributors) and hospitals
- For narcotic and certain psychotropic drugs, although the Opinions do not expressly state the rules for those products, the government will likely still set a Maximum Retail price (MRP) on the basis of a formula that combines a restricted set of reportable costs (ex-factory prices) and a permitted profit margin
- For all other drugs (including off-patent drugs), the price may be set freely by the manufacturer or importer, provided that it accurately reflects their costs and the balance between supply and demand

Drug Price re: Patented Drugs v. Off-patent Drugs

- Previously, patented drugs and off-patent originators (i.e., drugs with expired patents) were able to command a large price premium over locally produced generics
- Policy changes under the 2015 NDRC Opinions regarding implementation of the drug pricing reform:
  - Patented Drugs (including exclusively-produced drugs)
    - prices to be determined through a transparent negotiation mechanism involving multiple parties, including hospitals (most of which are public institutions), provincial governments and other stakeholders
    - NDRC has implemented international reference pricing with respect to patented drugs since 2012 under which multinational pharmaceutical companies have been asked to provide drug prices in the home country as well as prices in such major international markets as the United States, the United Kingdom, France, Germany, Russia, Japan, Korea, India, Hong Kong and Taiwan, etc.
    - NHFPC together with other 16 government agencies have initiated price negotiations with respect to patented drugs or exclusively-produced drugs since November 2016
    - all of which has led to significant price cuts for patented drugs
  - Off-Patent Drugs
    - generally, the price may be set freely by the manufacturer or importer, provided that it accurately reflects their costs and the balance between supply and demand
    - the special pricing premium previously enjoyed by off-patent originators appears to have been eliminated under the new pricing scheme

Current Drug Pricing Procedure

- Register the drug with SDA to receive approval and market authorization
- After approval, drugs may be listed on the NRDL or applicable Provincial reimbursement Drug List (PRDL) reimbursement lists
- Tendering for off-patent drugs or direct negotiations for patent drugs, with the NHC's provincial-level counterparts in the lead:
  - Tendering is the primary mechanism by which provinces procure drugs listed in the NRDL or PRDL
  - Pharmaceutical manufacturers must win tenders to sell their drugs within a province and the government generally requires that health care institutions (including hospitals) purchase a majority of their drugs (around 80% by value) from tender winner lists
  - Tendering has reportedly lowered drug prices by 25% on average, but history is very short
  - Most provinces tender off-patent originators separately from generic drug manufacturers under the assumption that the originators are of higher quality. Previously, off-patent originators were able to command a large price premium over locally produced generics. However, under the 2015 drug pricing reform, the further implementation of international reference pricing (not to exceed the sales price in the producing country or comparable country in China's region, e.g., the United States, the United Kingdom, France, Germany, Russia, Japan, Korea, India, Hong Kong and Taiwan, etc.) (NDRC Notice on Intensifying Supervision of Price Conduct in the Pharmaceuticals Market, May 4, 2015) may lead to significant price cuts for off-patent drugs
  - Hospitals play a more crucial and authoritative role in bidding, and a smaller proportion of the process is determined by the government

Current Drug Pricing Procedure (cont'd)

- After tender winners are announced, hospitals engage with individual manufacturers in a process known as secondary negotiation. During this process, actual drug volumes are specified and hospitals obtain a price that is often below the listed tender price
- Finally, hospitals sell drugs directly to patients and can charge a 15% markup above the price paid to the distributor
  - Note that public hospitals were required to abolish all markups on pharmaceuticals since September 30, 2017 pursuant to the Notice on the Introduction of Comprehensive Reform in Public Hospitals Nationwide (Ministry of Finance and former NHFPC, jointly with five other ministries, April 24, 2017)

Import of Technology to China

1. Under the 2001 Technology Import and Export Regulation ("TIER") and relevant regulations, technologies imported to China are classified into three categories (Ministry of Commerce (MOFCOM) Catalogue for Prohibited and Restricted Imported Technologies http://www.mofcom.gov.cn/aarticle/b/g/200712/20071205295018.html):
   - prohibited (technologies that cannot be imported in China)
   - restricted (technologies that can be imported in China only after obtaining an import license from MOFCOM or local commerce commission following substantive review and approval)
   - permitted (technologies that can be freely imported in China without an import license but subject only to a recordation process, i.e., without a requirement for substantive approval)
2. The majority of technologies imported to China fall under the "permitted" category and therefore are subject only to a straightforward recordation process by MOFCOM or local commerce commission
3. Import process for a permitted technology:
   - The parties sign the License Agreement which is effective on the execution date (MOFCOM approval or registration is not a pre-condition for effectiveness of the Agreement)
   - The domestic licensee submits a copy of the signed License Agreement together with other application documentation to the local commerce commission for filing which takes from a few days to several weeks
   - Upon completion of the filing, the licensee receives an Import Technology Contract Registration Certificate from the local commerce commission. The Certificate together with its ancillary documents set out the payment terms with respect to license fee, royalties and other fees (i.e., a "quota" for foreign exchange settlement)
   - When the licensee needs to make a payment, the Certificate, the license agreement, tax withholding receipt together with other related documents shall be submitted the local bank to convert RMB into US$ for remittance abroad
   - The bank will approve the payments so long as such payments are within its foreign exchange "quota"

Assignment of Improvements to Products to Licensors Outside China

1. Under TIER and relevant regulations, technologies exported from China are subject to regulation under the comparable three categories (link to the Export Technologies Catalogue http://www.mofcom.gov.cn/article/b/c/200809/20080905801122.shtml):

- prohibited (technologies that cannot be exported outside China)
- restricted and permitted (technologies that can be exported outside China only after obtaining an export license from MOFCOM or local commerce commission following substantive review and approval)
- Xi Jinping in his keynote address at last month's Boao Forum notably confined China's commitment not to force technology transfer to "patented" technology
- permitted (technologies that can be freely exported outside China without an export license but subject only to a recordation process, i.e., without a requirement for substantive approval)

2. Although TIER provides that the party which makes improvements shall own the improvements, there is no clear restriction on the improvement owner's right to dispose of such improvements by means of license or transfer

3. The transaction may constitute a "technology export" transaction assuming the Chinese party is the owner of the improvements. The technology export will be subject to the export registration and licensing process pursuant to the Export Catalogue

4. In practice, there may be some difficulty for the Chinese party to assign patents to a foreign party, but that is unlikely to apply to know-how that has yet to be patented

5. If the improvement is deemed a restricted technology, the prospective transferor must first submit to a state secrets assessment under the Measures on the Administration of the Prohibition and Restriction of the Export of Technology (禁止出口限制出口技术管理办法, effective May 20, 2009), http://www.mofcom.gov.cn/article/b/e/200904/20090406212733.shtml) and the Provisional Measures of Transfer of Intellectual Property Rights to Overseas (知识产权对外转让有关工作办法(试行), March 29, 2018, http://www.gov.cn/zhengce/content/2018-03/29/content_5278276.htm)

- TIER and overlapping Joint Venture Regulations are now likely to be challenged at the WTO if China does not make substantial amendments to provide stronger protection to imported IP

Measures to Control Drug Expenses

- Full implementation of Two-Invoice System by the end of 2018
  - drug manufacturers are permitted to issue only one invoice to one distributor followed by the same distributor issuing a second invoice to the end customer (hospitals)
  - Only one distributor is permitted to distribute drug products between the manufacturer and the hospital
- End of 15% drug price markup
  - All public hospitals abolished markups on drugs as of September 30, 2017
  - Significant increases in either direct government subsidies or revenue generated from the provision of medical services
- Implementation of a multi-tier treatment system from the end of 2015
  - Multi-tier treatment system built with appropriate referral mechanisms to optimize the distribution of medical resources among different tiers of medical institutions
  - Community-level medical institutions shall provide basic medical services to patients, and higher-tier hospitals shall give priority to those patients referred by community-level medical institutions

Measures to Control Drug Expenses (cont'd)

- Promoting production of generic drugs
  - A preferential 15% corporate income tax may be enjoyed by the generic pharmaceuticals which are accredited as high- and new-tech enterprises
- Encouragement to develop online healthcare services to reduce the burden on public hospitals and deliver services more efficiently
  - Promotion of basic medical services like appointment scheduling, OTC drug referral, and drug prescription
  - Accelerate construction of the information platform so that patients can sign up online with a family doctor
    - Ping An Healthcare and Technology Co Ltd. which operates China's largest online healthcare platform (Ping An Good Doctor Online Platform) has raised $1.12 billion on the IPO in Hong Kong Exchange at the end of April
  - Promote the development of online medicine sales and the logistics of medical supplies

Continuation of Opening Up of Healthcare Market in China

1. Faster opening up of China's medical and pharmaceutical market to attract more foreign medical practitioners and foreign medical institutions to China

   - 60 Chinese-foreign joint venture medical institutions were registered in China by January 2018;

   - More pharmaceutical multinationals like Eli Lilly have set up R&D centers in China to better meet Chinese market demand

2. Foreign investors are said to feel more optimistic about the growth of and lowering of investment barriers in China's pharmaceutical, medical device and healthcare markets

Questions

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