
REGULATIONS

PRC LAWS AND REGULATIONS

Regulations on Company Establishment and Foreign Investment

The establishment, operation and management of corporate entities in China are governed by the Company Law of PRC (《中華人民共和國公司法》), the “**PRC Company Law**”), which was promulgated by the Standing Committee of the NPC in December 1993 and further amended in December 1999, August 2004, October 2005, December 2013 and October 2018, respectively. According to the PRC Company Law, companies are generally classified into two categories: limited liability companies and companies limited by shares. The PRC Company Law also applies to foreign-invested limited liability companies. According to the PRC Company Law, where laws on foreign investment have other stipulations, such stipulations shall prevail.

Investment activities in the PRC by foreign investors are governed by the Guiding Foreign Investment Direction (《指導外商投資方向規定》), which was promulgated by the State Council in February 2002 and came into effect in April 2002, and the Special Administrative Measures for the Access of Foreign Investment (Negative List) (《外商投資准入特別管理措施(負面清單)(2019年版)》), the “**Negative List**”), which was promulgated by the MOFCOM and NDRC in June 2019 and came into effect in July 2019. The Negative List set out the restrictive measures in a unified manner, such as the requirements on shareholding percentages and management, for the access of foreign investments, and the industries that are prohibited for foreign investment. The Negative List covers 13 industries, and any field not falling in the Negative List shall be administered under the principle of equal treatment to domestic and foreign investment.

Foreign Investment Law of the PRC (《中華人民共和國外商投資法》) (the “**Foreign Investment Law**”) was promulgated by the NPC in March 2019 and came into effect in January 2020. After the Foreign Investment Law came into effect, the Law on Wholly Foreign-owned Enterprises of the PRC (《中華人民共和國外資企業法》), the Law on Sino-foreign Equity Joint Ventures of the PRC (《中華人民共和國中外合資經營企業法》) and the Law on Sino-foreign Cooperative Joint Ventures of the PRC (《中華人民共和國中外合作經營企業法》) have been repealed simultaneously. The investment activities of foreign natural persons, enterprises or other organizations (hereinafter referred to as “foreign investors”) directly or indirectly within the territory of China shall comply with and be governed by the Foreign Investment Law, including: 1) establishing by foreign investors of foreign-invested enterprises in China alone or jointly with other investors; 2) acquiring by foreign investors of shares, equity, property shares, or other similar interests of Chinese domestic enterprises; 3) investing by foreign investors in new projects in China alone or jointly with other investors; and 4) other forms of investment prescribed by laws, administrative regulations or the State Council.

REGULATIONS

In December 2019, the State Council promulgated the Regulations on Implementing the Foreign Investment Law of the PRC (《中華人民共和國外商投資法實施條例》), which came into effect in January 2020. After the Regulations on Implementing the Foreign Investment Law of the PRC came into effect, the Regulation on Implementing the Sino-Foreign Equity Joint Venture Enterprise Law of the PRC (《中華人民共和國中外合資經營企業法實施條例》), Provisional Regulations on the Duration of Sino-Foreign Equity Joint Venture Enterprise (《中外合資經營企業合營期限暫行規定》), the Regulations on Implementing the Wholly Foreign-Invested Enterprise Law of the PRC (《中華人民共和國外資企業法實施細則》) and the Regulations on Implementing the Sino-Foreign Cooperative Joint Venture Enterprise Law of the PRC (《中華人民共和國中外合作經營企業法實施細則》) have been repealed simultaneously.

In December 2019, the MOFCOM and the SAMR promulgated the Measures on Reporting of Foreign Investment Information (《外商投資信息報告辦法》), which came into effect in January 2020. After the Measures on Reporting of Foreign Investment Information came into effect, the Interim Measures for the Administration of Filing for Establishment and Changes in Foreign Investment Enterprises (《外商投資企業設立及變更備案管理暫行辦法》) have been repealed simultaneously. Since January 1, 2020, for foreign investors carrying out investment activities directly or indirectly in China, the foreign investors or foreign-invested enterprises shall submit investment information to the relevant commerce administrative authorities according to the Measure on Reporting of Foreign Investment Information.

Regulation on Pharmaceutical Product Development, Approval and Registration

Drug Regulatory Regime

The Drug Administration Law of the PRC (《中華人民共和國藥品管理法》) (the “**Drug Administration Law**”) was promulgated by the Standing Committee of the NPC, in September 1984. The last two amendments to the Drug Administration Law were the amendment promulgated in April 2015 and in August 2019. The Regulations for the Implementation of the Drug Administration Law (《藥品管理法實施條例》) was promulgated by the State Council in August 2002, and was last amended in March 2019. The Drug Administration Law and the Regulations for the Implementation of the Drug Administration Law have jointly established the legal framework for the administration of pharmaceutical products in China, including the research, development and manufacturing of new drugs. The Drug Administration Law applies to entities and individuals engaged in the development, production, trade, application, supervision and administration of pharmaceutical products, which regulates and provides for a framework for the administration of pharmaceutical manufacturers, pharmaceutical trading companies and medicinal preparations of medical institutions, and the development, research, manufacturing, distribution, packaging, pricing and advertisements of pharmaceutical products. The Regulations for the Implementation of the Drug Administration Law, at the same time, provide the detailed implementation regulations for the Drug Administration Law.

REGULATIONS

In 2017, the drug regulatory system entered a new and significant period of reform. The General Office of the State Council and the General Committee of China Communist Party jointly issued an Opinions on Deepening the Reform of the Evaluation and Approval Systems and Encouraging Innovation on Drugs and Medical Devices (《關於深化審評審批制度改革鼓勵藥品醫療器械創新的意見》) (the “**Innovation Opinions**”). The expedited programs, the record-filing system, the prioritized review mechanism, the acceptance of foreign clinical data under the Innovation Opinions and other recent reforms encourage drug manufacturers to seek marketing approval in China first in order to develop drugs in highly prioritized therapeutical areas, such as oncology or rare disease areas.

To implement the regulatory reform introduced by Innovation Opinions, the Standing Committee of the NPC, the NMPA, a newly formed government authority as well as other authorities, are currently responsible for revising the laws, regulations and rules regulating the pharmaceutical products and the industry.

In August 2019, the Standing Committee of the NPC promulgated the new Drug Administration Law (the “**2019 Amendment**”), which came into effect in December 2019. The 2019 Amendment contains many of the major reform initiatives implemented by the Chinese government since 2015, including but not limited to the MAH system, conditional approvals of drugs, traceability system of drugs, and the cancellation of relevant certification according to the GMP and the Good Supply Practice.

Regulatory Authorities

Pharmaceutical products, medical devices and equipment in China are monitored and supervised on a national scale by the NMPA. The local provincial medical products administrative authorities are responsible for supervision and administration of drugs within their respective administrative regions. The NMPA was newly formed under the SAMR. The NMPA’s predecessor, the State Drug Administration (the “**SDA**”), was replaced by the SFDA, which was later reorganized into the CFDA as part of the institutional reforms implemented by the State Council.

The primary responsibilities of the NMPA include:

- monitoring and supervising the administration of pharmaceutical products, medical appliances and equipment as well as cosmetics in the PRC;
- formulating administrative rules and policies concerning the supervision and administration of the pharmaceutical, medical devices, and cosmetics industry;
- evaluating, registering and approving of new drugs, generic drugs, imported drugs and traditional Chinese medicine;

REGULATIONS

- approving and issuing permits for the manufacture and export/import of pharmaceutical products, medical appliances and equipment;
- approving the establishment of enterprises to be engaged in the manufacture and distribution of pharmaceutical products;
- examining and evaluating the safety of pharmaceutical products, medical devices, and cosmetics; and
- managing the significant accidents involving the pharmaceutical products, medical devices and cosmetics.

In 2013, the Ministry of Health (the “**MOH**”) and the National Population and Family Planning Commission were integrated into the National Health and Family Planning Commission of the PRC (the “**NHFPC**”). In March 2018, the First Session of the Thirteenth NPC approved the State Council Institutional Reform Proposal (《國務院機構改革方案》), according to which, the responsibilities of NHFPC and certain other governmental authorities are consolidated into the National Health Commission (the “**NHC**”), and the NHFPC shall no longer be reserved. The responsibilities of the NHC include organizing the formulation of national drug policies, the national essential medicine system and the National Essential Medicines List and drafting the administrative rules for the procurement, distribution and use of national essential medicines.

According to the Decision of the CFDA on Adjusting the Approval Procedures under the Administrative Approval Items for Certain Drugs (《國家食品藥品監督管理總局關於調整部分藥品行政審批事項審批程序的決定》), promulgated by the CFDA in March 2017 and came into effect in May 2017, the IND approval should be issued by the CDE in the name of the CFDA.

Regulations on the Clinical Trials and Registration of Drugs

Administrative Measures for Drug Registration

In July 2007, the SFDA promulgated the amended version of the Administrative Measures for Drug Registration (《藥品註冊管理辦法》) (“**Registration Measures**”), which became effective in October 2007. The Registration Measures mainly cover: (1) definitions of drug registration applications and regulatory responsibilities of the drug administration; (2) general requirements for drug registration, including application for registration of new drugs, generic drugs, imported drugs and the supplemental application, as well as the application for re-registration; (3) clinical trials; (4) application, examination and approval of new drugs, generic drugs and imported drugs; (5) supplemental applications and re-registrations of drugs; (6) inspections; (7) registration standards and specifications; (8) time limit; (9) re-examination; and (10) liabilities and other supplementary provisions.

REGULATIONS

According to the Registration Measures, drug registration applications are divided into three different types, namely Domestic New Drug Application, Domestic Generic Drug Application and Imported Drug Application. Drugs which fall into one of three general types are divided according to the drug's working mechanism, namely whether the drug is classified as a chemical medicine, a biological product, a traditional Chinese medicine or a natural medicine. A NDA refers to an application for registration of a drug that has not yet been marketed for sale in China. In addition, the registration of drugs that change the dosage form of the marketed drugs, change the route of administration and increase the new indications shall be reported in accordance with the application procedures for new drugs. Under the Registration Measures, a Category 1 drug refers to a new drug that has never been marketed in any country, and such drug is eligible for special review or fast track approval by the NMPA.

In January 2020, the SAMR released the amended Administrative Measures for Drug Registration, or the Amended Registration Measures, which will come into effect in July 2020. As compared to the current effective version, the Amended Registration Measures provides detailed procedural and substantive requirements for the key regulatory concepts established by the Drug Administration Law, confirms a number of reform actions that have been taken in the past years, including but not limited to: (i) the full implementation of MAH System and implied approval of the commencement of clinical trial; (ii) implementing associated review of drugs, excipients and packaging materials; and (iii) introducing four procedures for expedited registration of drugs, which are procedures for ground-breaking therapeutic drugs, procedures for conditional approval, procedures for prioritized reviews and approval, and procedures for special examination and approval. Detailed implementing rules for drug classification and requirements for corresponding application materials will be promulgated by the NMPA.

In March 2016, the CFDA issued the Reform Plan for Registration Category of Chemical Medicine (《化學藥品註冊分類改革工作方案》), which outlined the reclassifications of drug applications under the Registration Measures. According to the Reform Plan for Registration Category of Chemical Medicine, Category 1 drugs refer to innovative new drugs that have not been marketed anywhere in the world. Improved new drugs that are not marketed anywhere in the world fall into Category 2 drugs. Generic drugs, that have equivalent quality and efficacy to the originator's drugs have been marketed abroad but not yet in China, can be classified as Category 3 drugs. Generic drugs, that have equivalent quality and efficacy to the originator's drugs and have been marketed in China, fall into Category 4 drugs. Category 5 drugs are drugs which have already been marketed abroad, but are not yet approved in China. Category 1 drugs and Category 5 drugs can be registered through the Domestic New Drug Application and the Imported Drug Application Procedures under the Registration Measures, respectively.

The SFDA promulgated the Special Examination and Approval of Registration of New Drugs (《新藥註冊特殊審批管理規定》) in January 2009, according to which, the SFDA conducts special examination and approval for new drug registration applications when: (1) the effective constituent of drug extracted from plants, animals, minerals, etc., as well as the preparations thereof have never been marketed in China, and the material medicines and the preparations thereof are newly discovered; (2) the chemical raw material medicines as well as the preparations thereof and the biological product have not been approved for marketing home

REGULATIONS

and abroad; (3) the new drugs with obvious clinical treatment advantages for such diseases as AIDS, malignant tumors and orphan diseases, etc. or (4) the new drugs for treating diseases currently with no effective methods of treatment.

The Special Examination and Approval of Registration of New Drugs provides that the applicant may file for special examination and approval at the clinical trial application stage if the drug candidate falls within items (1) or (2). The provisions provide that for drug candidates that fall within items (3) or (4), the application for special examination and approval cannot be made until filing for production.

Accelerated Approval for Clinical Trial and Registration

The Innovation Opinions established a framework for reforming the evaluation and approval system for drugs, medical devices and equipment. The Innovation Opinions indicated enhancing the standard of approval for drug registration and accelerating the evaluation and approval process for innovative drugs as well as improving the approval of drug clinical trials.

The CFDA released the Circular Concerning Several Policies on Drug Registration Review and Approval (《關於藥品註冊審評審批若干政策的公告》) in November 2015, which further clarified the measures and policies regarding simplifying and accelerating the approval process of clinical trials:

- a one-time umbrella approval procedure allowing the overall approval of all phases of a new drug's clinical trials, replacing the current phase-by-phase application and approval procedure, will be adopted for new drugs' clinical trial applications; and
- a fast track drug registration or clinical trial approval pathway for the following applications: (1) registration of innovative new drugs for treating HIV, cancer, serious infectious diseases and orphan diseases, etc.; (2) registration of pediatric drugs; (3) registration of geriatric drugs and drugs treating PRC-prevalent diseases in elders; (4) registration of drugs listed in national major science and technology projects or national key research and development plan; (5) registration of clinical urgently needed drugs using advanced technology, using innovative treatment methods, or having distinctive clinical benefits; (6) registration of foreign innovative drugs to be manufactured locally in China; (7) concurrent applications for new drug clinical trials which are already approved in the United States or EU or concurrent drug registration applications for drugs which have applied to the competent drug approval authorities for marketing authorization and passed such authorities' onsite inspections in the United States or EU and are manufactured using the same production line in China; and (8) clinical trial applications for drugs with urgent clinical need and patent expiry within three years, and manufacturing authorization applications for drugs with urgent clinical need and patent expiry within one year.

REGULATIONS

The CFDA promulgated the Opinions on Encouraging the Priority Review and Approval for Drug Innovations (《關於鼓勵藥品創新實行優先審評審批的意見》) in December 2017, which further clarified that a fast track clinical trial approval or drug registration pathway will be available to innovative drugs.

The NMPA released the Circular on Adjusting Evaluation and Approval procedures for Clinical Trials for Drugs (《關於調整藥物臨床試驗審評審批程序的公告》) in July 2018, according to which, within 60 days after the acceptance of and the fees paid for the IND application, the applicant may conduct the clinical trials for the drug in accordance with the clinical trial protocol submitted, if the applicant has not received any negative or questioning opinion from the CDE. Such approval process has been further enacted into the 2019 Amendment.

Trial Exemptions and Acceptance of Foreign Data

The NMPA issued the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data (《接受藥品境外臨床試驗數據的技術指導原則》) in July 2018, as one of the implementing rules for the Innovation Opinions, which provides that overseas clinical data can be submitted for the drug registration applications in China. Such applications can be in the form of waivers to China-based clinical trials, bridging trials and direct NDAs. According to the Technical Guidance Principles on Accepting Foreign Drug Clinical Trial Data, sponsors may use the data of foreign clinical trials to support drug registration in China, provided that sponsors must ensure the authenticity, completeness, accuracy and traceability of foreign clinical trial data and such data must be obtained consistent with the relevant requirements under the Good Clinical Trial Practice of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). Sponsors must also comply with other relevant sections of the Registration Measures when applying for drug registrations in China using foreign clinical trial data.

The NMPA now officially permits, and its predecessor agencies have permitted on a case-by-case basis in the past, drugs approved outside of China to be approved in China on a conditional basis without pre-approval clinical trials being conducted in China. Specifically, the NMPA and the NHC released the Procedures for Reviewing and Approval of Clinical Urgently Needed Overseas New Drugs (《關於臨床急需境外新藥審評審批相關事宜的公告》) in October 2018, permitting drugs that have been approved within the last ten years in the United States, the EU or Japan and that prevent or treat orphan diseases or prevent, or treat serious life-threatening illnesses for which there is either no effective therapy in China, or for which the foreign-approved drug would have clear clinical advantages. Applicants will be required to establish a risk mitigation plan and may be required to complete trials in China after the drug has been marketed. The CDE has developed a list of qualifying drugs that meet the foregoing criteria.

REGULATIONS

Clinical Trial Process and Good Clinical Practices

According to the Registration Measures, a clinical trial consists of Phases I, II, III and IV. Phase I refers to the initial clinical pharmacology and safety evaluation studies in humans. Phase II refers to the preliminary evaluation of a drug candidate’s therapeutic effectiveness and safety for particular indications in patients, to provide evidence and support for the design of Phase III clinical trials and to settle the administrative dose regimen. Phase III refers clinical trials undertaken to confirm the therapeutic effectiveness and safety on patients with target indications, to evaluate the overall benefit-risk relationships of the drug, and ultimately to provide sufficient evidence for the review of drug registration application. Phase IV refers to a new drug’s post-marketing study to assess therapeutic effectiveness and adverse reactions when the drug is widely used, to evaluate the overall benefit-risk relationships of the drug when used among the general population or specific groups and to adjust the administration dose.

To improve the quality of clinical trials, the SFDA promulgated the Good Clinical Trial Practice for Drugs (《藥物臨床試驗質量管理規範》) in August 2003, or the GCP Rules. According to the Administration of Quality of Drug Clinical Practice, clinical trial means systematical investigation of drugs conducted on human subjects (patients or healthy volunteers) to prove or reveal the function, adverse reactions and/or absorption, distribution, metabolism and excretion of the drug being investigated. The purpose of a clinical trial is to determine the therapeutic efficacy and safety of the drug.

In April 2020, the NMPA and the NHC promulgated the revised Good Clinical Trial Practice for Drugs (《藥物臨床試驗質量管理規範》), or the Revised GCP Rules, which will come into effective in July 2020, in order to further ensure the quality of clinical trials and the safety of human subjects. As compared to the current effective version, the Revised GCP Rules provides comprehensive and substantive requirements on the design and conduct of clinical trials in China. In particular, the Revised GCP Rules enhances the protection for study subjects and tightens the control over bio-samples collected under clinical trials.

The Revised GCP Rules also set out the qualifications and requirements for the investigators and centers participating in clinical trial, including: (i) professional certification at a clinical trial center, professional knowledge, training experience and capability of clinical trial, and being able to provide the latest resume and relevant qualification documents per request; (ii) being familiar with the trial protocol, investigator’s brochure and relevant information of the trial drug provided by the applicant; (iii) being familiar with and comply with the Revised GCP Rules and relevant laws and regulations relating to clinical trials; (iv) keeping a copy of the authorization form on work allocation signed by investigators; (v) investigators and clinical trial centers shall accept supervision and inspection organized by the applicant and inspection by the drug regulatory authorities; and (vi) in the case of investigators and clinical trial centers authorizing other individual or institution to undertake certain responsibilities and functions relating to clinical trial, they shall ensure such individual or institution are qualified and establish complete procedures to ensure the responsibilities and functions are fully performed and generate reliable data.

REGULATIONS

Communication with the CDE

According to the Circular on Adjusting Evaluation and Approval Procedures for Clinical Trials for Drugs, where the application for clinical trial of new investigational drug has been approved, upon the completion of Phases I and II clinical trials and prior to Phase III clinical trial, the applicant shall submit the application for Communication Session to CDE to discuss with CDE the key technical questions including the design of Phase III clinical trial protocol. Within 60 days after the acceptance of and the fees paid for the IND application, the applicant may conduct the clinical trials for the drug in accordance with the clinical trial protocol submitted, if the applicant has not received any negative or questioning opinion from the CDE.

The NMPA promulgated the Administrative Measures for Communication on the Research, Development and Technical Evaluation of Drugs (《藥物研發與技術審評溝通交流管理辦法》) in September 2018, during the research and development periods and in the registration applications of, among others, the innovative new drugs, the applicants may propose to conduct communication meetings with the CDE. The communication meetings can be classified into three types. Type I meetings are convened to address key safety issues in clinical trials of drugs and key technical issues in the research and development of breakthrough therapeutic drugs. Type II meetings are held during the key research and development periods of drugs, mainly including meetings before the IND application, meetings upon the completion of Phase II trials and before the commencement of Phase III trials, meetings before submitting a marketing application for a new drug, and meetings for risk evaluation and control. Type III meetings refer to meetings not classified as Type I or Type II.

Drug Clinical Trial Registration

According to the Registration Measures, upon obtaining the approval of its IND applications and before conducting a clinical trial, an applicant shall file a registration form with the SFDA containing various details, including the clinical study protocol, the name of the principal researcher of the leading institution, names of participating institutions and researchers, an approval letter from the ethics committee, and a sample of the Informed Consent Form, with a copy sent to the competent provincial administration departments where the trial institutions will be located. The CFDA released the Announcement on Drug Clinical Trial Information Platform (《關於藥物臨床試驗信息平臺的公告》) in September 2013, according to which, instead of the aforementioned registration field with the CFDA, all clinical trials approved by the CFDA and conducted in China shall complete a clinical trial registration and publish trial information through the Drug Clinical Trial Information Platform. The applicant shall complete the trial pre-registration within one month after obtaining the approval of the clinical trial approval in order to obtain the trial's unique registration number and complete registration of certain follow-up information before the first subject's enrollment in the trial. If the registration is not completed within one year after the approval of the IND applications, the applicant shall submit an explanation, and if the first submission is not completed within three years, the approval of the IND applications shall automatically expire.

REGULATIONS

New Drug Application

According to the Registration Measures, drug registration applications include domestic NDA, domestic generic drug application and imported drug application. Drugs are classified as chemical drugs, biological products and traditional Chinese medicine or natural drugs. When Phases I, II and III clinical trials have been completed, the applicant may apply to the SFDA for approval of NDA. The SFDA then determines whether to approve the application according to the comprehensive evaluation opinion provided by the CDE.

According to the Opinions on Implementing Priority Review and Approval to Encourage Drug Innovation, for new drugs which are developed for severe, life-threatening diseases currently lacking effective treatment and have great significance for meeting clinical needs, if, based on early-stage clinical trial data, the clinical benefits of such drugs can be reasonably predicted or decided and such drugs have distinctive advantages comparing with existing treatments, such new drugs may obtain a conditional approval for marketing before the completion of Phase III clinical trials undertaken to confirm its therapeutic effectiveness.

Pilot Plan for the Marketing Authorization Holder System

The Innovation Opinions provides a pilot plan for the MAH system.

Under the authorization of the Standing Committee of the NPC, the General Office of the State Council issued the Pilot Plan for the Drug Marketing Authorization Holder Mechanism (《藥品上市許可持有人制度試點方案》) in May 2016, according to which, a detailed pilot plan for the MAH system, for drugs in 10 provinces in China. Under the MAH system, domestic drug research and development institutions and individuals in the pilot regions are eligible to be holders of drug registrations without having to become drug manufacturers. The marketing authorization holders may engage contract manufacturers for manufacturing, provided that the contract manufacturers are licensed, and are also located within the pilot regions. Drugs that qualify for the MAH System are: (1) new drugs (including but not limited to drugs under category I to category IV of chemical drugs, and targeted preparation, sustained release preparation, controlled release preparation under category V of chemical drugs, biological products approved as category I and VII drugs and biosimilars under the Registration Measures) approved after the implementation of the MAH System; (2) generic drugs approved as category III or IV drugs under the Reform Plan for Registration Category of Chemical Medicine; (3) previously approved generics that have passed equivalence assessments against original drugs; and (4) previously approved drugs whose licenses were held by drug manufacturers originally located within the pilot regions, but which have moved out of the pilot regions due to corporate mergers or other reasons.

The CFDA promulgated the Circular on the Matters Relating to Promotion of the Pilot Program for the Drug Marketing Authorization Holder System (《關於推進藥品上市許可持有人制度試點工作有關事項的通知》) in August 2017, which clarified the legal liability of the MAH, who is responsible for managing the whole manufacturing and marketing chain and the whole life cycle of drugs and assumes the full legal liability for preclinical drug study, clinical

REGULATIONS

trials, manufacturing, marketing and distribution and adverse drug reaction monitoring. According to the Circular on the Matters Relating to Promotion of the Pilot Program for the Drug Marketing Authorization Holder System, the MAH shall submit a report of drug manufacturing, marketing, prescription, techniques, pharmacovigilance, quality control measures and other situations to the CFDA within 20 working days after the end of each year.

According to the Pilot Plan for the Drug Marketing Authorization Holder Mechanism, the pilot plan was originally set for a three-year period and was scheduled to expire in November 2018. The Standing Committee of the NPC promulgated the Decision of Extending the Pilot Period of Authorizing the State Council to Carry out the Pilot Plan for the Drug Marketing Authorization Holder Mechanism in Certain Places (《關於延長授權國務院在部分地方開展藥品上市許可持有人制度試點期限的決定》) in October 2018, which extended the term of the MAH system to November 4, 2019.

According to the 2019 Amendment, which came into effect on December 1, 2019, the MAH system will be applicable throughout the country and the legal representative and the key person-in-charge of a drug MAH shall be fully responsible for the quality of drugs.

Administrative Protection and Monitoring Periods for New Drugs

According to the Registration Measures, the Implementing Regulations of the Drug Administration Law and the Reform Plan for Registration Category of Chemical Medicine, the NMPA may, for the purpose of protecting public health, provide for an administrative monitoring period of not more than five years for Category 1 new drugs approved to be manufactured, commencing from the date of approval, to continually monitor the safety of those new drugs.

During the monitoring period of a new drug, the NMPA will not accept other applications for new drugs containing the same active ingredient. This renders an actual five-year exclusivity protection for Category 1 new drugs. The only exception is that the NMPA will continue to handle any application if, prior to the commencement of the monitoring period, the NMPA has already approved the applicant’s clinical trial for a similar new drug. If such application conforms to the relevant provisions, the NMPA may approve such applicant to manufacture or import the similar new drug during the remainder of the monitoring period.

The Amended Registration Measures, which will come into effect in July 2020, omits the provisions that provide for such administrative monitoring period.

International Multi-Center Clinical Trials

The International Multi-Center Clinical Trial Guidelines (Trial) (《國際多中心藥物臨床試驗指南(試行)》) (the “**Multi-Center Clinical Trial Guidelines**”), promulgated by the CFDA in January 2015 and came into effect in March 2015, provided guidance on the implementation of multi-regional clinical trials, or MRCTs, in China. According to the Multi-Center Clinical Trial Guidelines, international multi-center clinical trial applicants may

REGULATIONS

simultaneously perform clinical trials in different centers using the same clinical trial protocol. Where the applicants plan to implement the International Multi-Center clinical trials in the PRC, the applicants shall comply with relevant laws and regulations, such as the Drug Administration Law, the Implementing Regulations of the Drug Administration Law and the Registration Measures, execute the GCP Rules, make reference to universal international principles such as the ICH-GCP, and comply with the laws and regulations of the countries involved in the international multi-center clinical trials. Where the applicants plan to use the data derived from the international multi-center clinical trials for approval of a drug registration in the PRC, it shall involve at least two countries, including China, and shall satisfy the requirements for clinical trials set forth in the Multi-Center Clinical Trial Guidelines, Registration Measures and other related laws and regulations.

In April 2020, the NMPA and the NHC promulgated the Revised GCP Rules, which will come into effect in July 2020. The Revised GCP Rules summarizes the requirements for initiating a MRCT, that is, before initiating a MRCT: (i) the applicant shall ensure that all the centers participating in the clinical trial will comply with the trial protocol; (ii) the applicant shall provide each center with the same trial protocol, and each center shall comply with the same unified evaluation criterion for clinical trial and laboratory data and the same guidance for case report form; (iii) each center shall use the same case report form to record the data of each human subject obtained during the trial; (iv) before the initiating of a clinical trial, a written document is required to specify the responsibilities of the investigators of each center; and (v) the applicant shall ensure the communication among the investigators of each center.

Data derived from international multi-center clinical trials can be used for the new drug applications with the NMPA. When using international multi-center clinical trial data to support new drug applications in China, applicants shall submit the completed global clinical trial report, statistical analysis report and database, along with relevant supporting data in accordance with ICH-CTD (International Conference on Harmonization-Common Technical Document) content and format requirements; subgroup research results summary and comparative analysis shall also be conducted concurrently. Leveraging the clinical trial data derived from international multi-center clinical trials conducted by our partners, we may avoid unnecessary repetitive clinical trials and thus further accelerate the NDA process in China.

The CFDA released the Decision on Adjusting Items concerning the Administration of Imported Drug Registration (《國家食品藥品監督管理總局關於調整進口藥品註冊管理有關事項的決定》) in October 2017, which includes the following key points:

- If the International Multicenter Clinical Trial, or IMCCT, of a drug is conducted in China, Phase I clinical trial of the drug is allowed simultaneously. And the IMCCT drug does not need to be approved or entered into either a Phase II or III clinical trial in a foreign country, except for preventive biological products.;

REGULATIONS

- If the IMCCT is conducted in China, the application for drug marketing authorization can be submitted directly after the completion of the IMCCT. The Registration Measures and relevant laws and regulations shall be complied with for registration application;
- With respect to applications for imported innovative chemical drugs and therapeutic biological products, the marketing authorization in the country or region where the foreign drug manufacturer is located will not be required; and
- With respect to drug applications that have been accepted before the release of this Decision, if relevant requirements are met, importation permission can be granted if such applications request exemption of clinical trials for the imported drugs based on the data generated from IMCCT.

Approval of Human Genetic Resources

The Interim Administrative Measures on Human Genetic Resources (《人類遺傳資源管理暫行辦法》), promulgated by the Ministry of Science and Technology and the MOH in June 1998, aimed at protecting and fair utilizing human genetic resources in the PRC. The Ministry of Science and Technology promulgated the Service Guide for Administrative Licensing Items concerning Examination and Approval of Sampling, Collecting, Trading or Exporting Human Genetic Resources, or Taking Such Resources out of the PRC (《人類遺傳資源採集、收集、買賣、出口、出境審批行政許可事項服務指南》) in July 2015, according to which, the sampling, collection or research activities of human genetic resources by a foreign-invested sponsor fall within the scope of international cooperation, and the cooperating organization of China shall apply for approval of the China Human Genetic Resources Management Office through the online system. The Ministry of Science and Technology further promulgated the Circular on Optimizing the Administrative Examination and Approval of Human Genetic Resources (《關於優化人類遺傳資源行政審批流程的通知》) in October 2017, which became effective in December 2017 and simplified the approval of sampling and collecting human genetic resources for the purpose of listing a drug in the PRC.

The Regulations of the PRC on the Administration of Human Genetic Resources (《中華人民共和國人類遺傳資源管理條例》), promulgated by the State Council in May 2019 and came into effect in July 2019, further stipulates that in order to obtain marketing authorization for relevant drugs and medical devices in China, no approval is required in international clinical trial cooperation using China's human genetic resources at clinical institutions without export of human genetic resource materials. However, the type, quantity and usage of the human genetic resource to be used shall be filed with the administrative department of science and technology under the State Council before clinical trials.

REGULATIONS

Regulations on Import of Urgently Needed Drug in Boao Pilot Zone

According to the Drug Administration Law, based on urgent medical need by medical institution of certain drug that is not yet registered domestically (the “**Urgently Needed Drug**”), subject to the approval of NMPA or competent provincial government, a small amount of such Urgently Needed Drug may be imported but shall be solely applied for specific medical purpose at the designated medical institution.

The State Council issued the Official Reply of the State Council to Approve the Establishment of Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (《國務院關於同意設立海南博鳌樂城國際醫療旅遊先行區的批復》) in February 2013, according to which, Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (the “**Boao Pilot Zone**”) shall be established as a pilot zone where accelerated approval of the import of Urgently Needed Drug is available. The State Council further issued the Decision on Temporarily Adjusting the Implementation of the Relevant Provisions of the Implementing Measures of the Drug Administration Law in the Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (《國務院關於在海南博鳌樂城國際醫療旅遊先行區暫時調整實施<中華人民共和國藥品管理法實施條例>有關規定的決定》) in December 2018, according to which, the State Council empowers the People’s Government of Hainan Province (the “**Hainan Government**”) to approve the import of Urgently Needed Drug (excluding vaccines).

The Hainan Government promulgated the Interim Provisions on the Administration of Imported Drugs of Urgent Need in Boao Lecheng International Medical Tourism Pilot Zone of Hainan Province (《海南博鳌樂城國際醫療旅遊先行區臨床急需進口藥品管理暫行規定》) in April 2019, according to which, a qualified medical institution in the Boao Pilot Zone may apply for the import of Urgently Needed Drug (excluding vaccines and other drugs under special management) and apply to patient on case by case basis. Such application shall be subject to the evaluation and approval of Hainan Provincial Health Commission and the Medical Products Administration of Hainan Province, as well as the customs formalities with Haikou Customs.

Real-World Data

The NMPA published the Guidelines on Using Real-world Evidence to Support Research, Development and Review of Drugs (Trial) (《真實世界證據支持藥物研發與審評的指導原則(試行)》) on January 3, 2020. Real-world data (the “**RWD**”) refers to a variety of data collected on a daily basis related to patients’ health conditions and/or diagnosis, treatment and healthcare. Among others, the data collected in the application of Urgent Needed Drug that imported for special medical purpose, like the data collected under the Boao Pilot Program, can be admitted as RWD. Subject to relevance and reliability test, the RWD may be used to form real-world evidence which may be used as a basis for consideration in the NDA approval in the PRC.

REGULATIONS

The reliability test refers to the evaluation of the following four aspects of the RWD, namely, the completeness, accuracy, transparency and quality guarantee of the RWD. In this regard, under the Boao Pilot Program, the RWD collected for OT-401 and to be collected for OT-502 must satisfy the evaluation of completeness, accuracy, transparency and quality guarantee of the relevant RWD, to be formed as real-world evidence which may be admitted as a basis for consideration in the NDA approval in the PRC.

Regulations on Drug Manufacturing and Distribution

Drug Manufacturing

According to the Drug Administration Law and the Implementing Regulations of the Drug Administration Law, a drug manufacturing enterprise is required to obtain a drug manufacturing license from the relevant provincial drug administration authority of the PRC. The grant of such license is subject to an inspection of the manufacturing facilities, and an inspection to determine whether the sanitary condition, quality assurance systems, management structure and equipment meet the required standards. According to the Regulations of Implementation of the Drug Administration Law and the Measures on the Supervision and Administration of the Manufacture of Drugs (《藥品生產監督管理辦法》), promulgated in August 2004 and amended in November 2017, the drug manufacturing license is valid for five years and shall be renewed at least six months prior to its expiration date upon a re-examination by the relevant authority. In addition, the name, legal representative, registered address and type of the enterprise specified in the drug manufacturing certificate shall be identical to that set forth in the business license as approved and issued by the industrial and commercial administrative department.

In January 2020, the SAMR promulgated the revised Measures on the Supervision and Administration of the Manufacture of Drugs, which will come into effect in July 2020. According to such revised measures, to the extent the MAH does not manufacture the drug but through CMO, the MAH shall apply for drug manufacturing license with the provincial counterpart of the NMPA, subject itself to inspections and other regulatory oversight by the agency.

The Good Manufacturing Practice for Drugs (《藥品生產質量管理規範》) was promulgated in March 1988 and was amended in June 1999 and January 2011. The Good Manufacturing Practice for Drugs comprises a set of detailed standard guidelines governing the manufacture of drugs, which includes institution and staff qualifications, production premises and facilities, equipment, hygiene conditions, production management, quality controls, product operation, raw material management, maintenance of sales records and management of customer complaints and adverse event reports.

REGULATIONS

Drug Distribution

According to the Drug Administration Law and its implementing regulations and the Measures for the Supervision and Administration of Circulation of Pharmaceuticals (《藥品流通監督管理辦法》), which was promulgated by the SFDA in January 2007 and came into effect in May 2007, pharmaceutical enterprise shall be responsible for the quality of pharmaceuticals they manufacture, operate or use, purchase, sale, transportation, storage.

According to the Measures for the Administration of Pharmaceutical Operation Certificate (《藥品經營許可證管理辦法》) which was promulgated in February 2004 and amended in November 2017 by the CFDA, a Medicine Operation Certificate is valid for five years. Each holder of the Medicine Operation Certificate must apply for an extension of its permit six months prior to expiration. The establishment of a wholesale pharmaceutical distribution company requires the approval of the provincial medicine administrative authorities. Upon approval, the authority will grant a Medicine Operation Certificate in respect of the wholesale pharmaceutical product distribution company. The establishment of a retail pharmacy store requires the approval of the local medicine administrative authorities at or above the county level. Upon approval, the authority will grant a Medicine Operation Certificate in respect of the retail pharmacy store.

Regulations on Healthcare System Reform

The PRC government recently promulgated several healthcare reform policies and regulations. In March 2009, the Central Committee of the PRC Communist Party and the State Council jointly issued the Guidelines on Strengthening the Reform of Healthcare System (《關於深化醫藥衛生體制改革的意見》). In December 2016, the State Council issued the Notice on the Issuance of the 13th Five-year Plan on Strengthening the Reform of Healthcare System (《關於印發“十三五”深化醫藥衛生體制改革規劃的通知》). In April 2017, the General Office of the State Council issued the Main Tasks of Healthcare System Reform in 2017 (《深化醫藥衛生體制改革2017年重點工作任務》). Highlights of these healthcare reform policies and regulations include (1) establishing a basic healthcare system to cover both urban and rural residents and providing the Chinese people with safe, effective, convenient and affordable healthcare services, (2) improving the healthcare system through the reform and development of a graded hierarchical healthcare system, modern hospital management, basic medical insurance, drug supply support and comprehensive supervision, and (3) improving the efficiency and quality of the healthcare system to meet the various medical needs of the Chinese population.

In May 2019, the General Office of the State Council issued the Main Tasks of Healthcare System Reform in 2019 (《深化醫藥衛生體制改革2019年重點工作任務》), highlighting the following policies and regulations (1) reinforcing the degree of cancer prevention and treatment, accelerating the registration and approval of anti-cancer new drugs at home and abroad and remaining the temporary channel of imperative anti-cancer drugs importation open, (2) consolidating and improving the basic medicine system and establishing an inventive and

REGULATIONS

restrictive mechanism for preferential use. Improving the dynamic adjusting mechanism of the NRDL and incorporating the eligible therapeutic drugs listing in the National Essential Drug List into the NRDL first in accordance with the procedure.

In December 2019, the Standing Committee of the NPC promulgated the Law of the People's Republic of China on Promotion of Basic Medical and Health Care (《中華人民共和國基本醫療衛生與健康促進法》), which will come into effect in June 2020. Such law established the legal framework for the administration of basic medical and health services for citizens in China, including the administration of basic medical care services, medical care institutions, medical staff, guarantee of drug supply, health promotion and guarantee of medical funds.

In February 2020, the Central Committee of the PRC Communist Party and the State Council jointly promulgated the Opinions on Deepening the Reform of the Healthcare Security System (《中共中央、國務院關於深化醫療保障制度改革的意見》), which envisages that a higher level healthcare system should be established by 2030, which centers on basic medical insurance, is underpinned by medical aid and pursues the common development of supplementary medical insurance, commercial health insurance, charitable donations and medical mutual assistance. To this end, such opinions map out tasks in several respects, including making the mechanism of medical insurance benefits guarantee more impartial and appropriate, improving the robust and sustainable operating mechanism for funds raised, establishing more effective and efficient healthcare payment mechanism and enhancing the supervision and administration on medical security fund and etc.

Regulations on Coverage and Reimbursement

Reimbursement under the National Medical Insurance Program

The State Council promulgated the Decision of the State Council on the Establishment of the Urban Employee Basic Medical Insurance Program (《國務院關於建立城鎮職工基本醫療保險制度的決定》) in December 1998, according to which, all employers in urban cities are required to enroll their employees in the basic medical insurance program and the insurance premium is jointly contributed by the employers and employees. The State Council promulgated the Guiding Opinions of the State Council about the Pilot Urban Resident Basic Medical Insurance (《國務院關於開展城鎮居民基本醫療保險試點的指導意見》) in July 2007, according to which, urban residents of the pilot district, rather than urban employees, may voluntarily join Urban Resident Basic Medical Insurance. According to the Social Insurance Law of Peoples' Republic of China (《中華人民共和國社會保險法》) which was promulgated by the Standing Committee of the NPC in October 2010 and amended in December 2018, all employees are required to enroll in the basic medical insurance program and the insurance premium is jointly contributed by the employers and employees as required by the state.

REGULATIONS

Several authorities including the Ministry of Labor and Social Security and the Ministry of Finance of the PRC, among others, jointly promulgated the Notice Regarding the Tentative Measures for the Administration of the Scope of Medical Insurance Coverage for Pharmaceutical Products for Urban Employee (《關於印發城鎮職工基本醫療保險用藥範圍管理暫行辦法的通知》) in May 1999, which provides that a pharmaceutical product listed in the Medical Insurance Catalog must be clinically needed, safe, effective, reasonably priced, easy to use, available in sufficient quantity, and must meet the following requirements:

- it is set forth in the Pharmacopeia (the prevailing version) of the PRC;
- it meets the standards promulgated by the NMPA; and
- if imported, it is approved by the NMPA for import.

Medical Insurance Catalogue

According to the Notice Regarding the Tentative Measures for the Administration of the Scope of Medical Insurance Coverage for Pharmaceutical Products for Urban Employee issued by the PRC Ministry of Labor and Social Security, together with other government authorities, a drug product listed in the medical insurance catalogue must be clinically necessary, safe, effective, reasonably priced, easy to use and available in sufficient quantity. Besides, the above mentioned authorities have the power to determine the medicines included in the NRDL, which is divided into two parts, Part A and Part B. Patients purchasing medicines included in Part A of the Medical Insurance Catalog are entitled to reimbursement in accordance with the regulations in respect of basic medical insurance. Patients purchasing medicines included in Part B of the Medical Insurance Catalog are required to pay a certain percentage of the purchase price and the remainder of the purchase price shall be reimbursed in accordance with the regulations in respect of basic medical insurance.

According to the Notice of the Ministry of Human Resources and Social Security on Issuing the National Drug Catalogue for Basic Medical Insurance, Work-Related Injury Insurance and Maternity Insurance (《關於印發國家基本醫療保險、工傷保險和生育保險藥品目錄(2017年版)的通知》) (the “**2017 NRDL**”) which was promulgated in February 2017, the competent social insurance departments of the provinces (autonomous regions and municipalities directly under the Central Government) shall make adjustments to the drugs of Part B in strict accordance with the current laws, regulations, and documents. The quantity adjusted by each province (autonomous region or municipality directly under the Central Government) (including those drugs to be included in or removed from the NRDL and those within the scope of limited payment) shall not exceed 15% of the quantity of national drugs of Part B.

REGULATIONS

According to the Notice of the National Healthcare Security Administration and Ministry of Human Resources and Social Security on Issuing the National Drug Catalogue for Basic Medical Insurance, Work-Related Injury Insurance and Maternity Insurance (《關於印發國家基本醫療保險、工傷保險和生育保險藥品目錄的通知》) (the “2019 NRDL”) which was promulgated in August 2019 and came into effect in January 2020, all places shall implement the 2019 NRDL in a strict manner, and shall not have the discretion to formulate the catalogue or increase the drugs of Part B in any form, or adjust the scope of limited payment. For those drugs that were already added to Part B of the provincial catalogue in accordance with the 2017 NRDL, the drugs shall be gradually removed within 3 years. Priority shall be given to adjusting the scope of payment for the drugs that were listed in the First Batch of National Key Monitored Drugs for Rational Use (chemical and biological products) (《第一批國家重點監控合理用藥藥品目錄(化藥及生物製品)》), which was issued and came into effect in June 2019.

Medical Insurance Reimbursement Standards

The State Council promulgated the Opinions on Integrating the Basic Medical Insurance Systems for Urban and Rural Residents (《國務院關於整合城鄉居民基本醫療保險制度的意見》) in January 2016, which required the integration of the urban resident basic medical insurance and the new rural cooperative medical care system and the establishment of a unified basic medical insurance system, which will cover all urban and rural residents other than rural migrant workers and persons in flexible employment arrangements who participate in the basic medical insurance for urban employees.

The General Office of the State Council further released the Guidance On Further Deepening the Reform of the Payment Method of Basic Medical Insurance (《關於進一步深化基本醫療保險支付方式改革的指導意見》) in June 2017. The main objectives are to implement a diversified reimbursement mechanism including diagnosis related groups, per-capita caps, and per-bed-day caps. These new reimbursement methods will be rolled out nationwide by 2020 to replace the current reimbursement method that is based on service category and product price. Local administration of healthcare security will introduce a total budget control for their jurisdictions and decide the amount of reimbursement to public hospitals based on hospitals’ performance and the spending targets of individual basic medical insurance funds.

Commercial Insurance

The State Council and the Communist Party of China jointly issued the Plan for Healthy China 2030 (《“健康中國2030”規劃綱要》), or the Plan, in October 2016, according to which, the country would establish a multi-level medical security system built around basic medical insurance, with other forms of insurance supplementing the basic medical insurance, including serious illness insurance for urban and rural residents, commercial health insurance and medical assistance. Furthermore, the Plan encourages enterprises and individuals to participate in commercial health insurance and various forms of supplementary insurance. The evolving

REGULATIONS

medical insurance system makes innovative drugs more affordable and universally available to the Chinese population, which renders greater opportunities to drug manufacturers that focus on the research and development of innovative drugs, such as high-cost cancer therapeutics.

Price Controls

Instead of direct price controls which were historically used in the PRC, the government regulates prices mainly by establishing a consolidated procurement mechanism, revising medical insurance reimbursement standards and strengthening regulation of medical and pricing practices.

The Guiding Opinions of Economic Restructuring Office of the State Council, State Planning Commission and the State Economic and Trade Commission concerning the Urban Pharmaceutical and Healthcare System Reform (《國務院體改辦、國家計委、國家經貿委關於城鎮醫藥衛生體制改革的指導意見》), promulgated in February 2000, aims to regulate the purchasing process of pharmaceutical products by medical institution. The MOH and other relevant government authorities have promulgated a series of regulations and releases in order to implement the tender requirements. According to the Notice on Issuing Certain Regulations on the Trial Implementation of Centralised Tender Procurement of Drugs by Medical Institutions (《醫療機構藥品集中招標採購試點工作若干規定》) promulgated in July 2000 and the Notice of the State Drug Administration on Further Improvement on the Implementation of Centralised Tender Procurement of Drugs by Medical Institutions (《國家藥品監督管理局關於進一步做好醫療機構藥品集中招標採購工作的通知》) promulgated in August 2001, non-profit medical institutions established by county or higher level government are required to implement centralised tender procurement of drugs. The Working Regulations of Medical Institutions for Procurement of Drugs by Centralised Tender and Price Negotiations (for Trial Implementation) (《醫療機構藥品集中招標採購和集中議價採購工作規範(試行)》), promulgated in March 2002, provides rules for the tender process and negotiations of the prices of drugs, operational procedures, a code of conduct and standards or measures of evaluating bids and negotiating prices. The Notice of the Financial Planning Department of Ministry of Health on Issue of Opinions on Further Regulating Centralised Procurement of Drugs by Medical Institutions (《衛生部財務規劃司關於印發<進一步規範醫療機構藥品集中採購工作的意見>的通知》) was promulgated in January 2009, according to which, non-profit medical institutions owned by the government at the county level or higher or owned by state-owned enterprises (including state-controlled enterprises) shall purchase pharmaceutical products by online centralised procurement. Each provincial government shall formulate its catalogue of drugs subject to centralised procurement. Except for drugs in the National Essential Drug List (the procurement of which shall comply with the relevant rules on National Essential Drug List), certain pharmaceutical products which are under the national government's special control, such as toxic, radioactive and narcotic drugs and traditional Chinese medicines, in principle, all drugs used by non-profit medical institutions shall be covered by the catalogue of drugs subject to centralised procurement. The Notice on Printing and Distributing the Working Regulations of Medical Institutions for Centralised Procurement of Drugs (《關於印發醫療機構藥品集中採購工作規範的通知》) was promulgated in July 2010, which further regulates the centralised procurement of drugs and clarify the code of conduct of the parties in

REGULATIONS

centralized drug procurement. The Guiding Opinions of the General Office of the State Council on Improvement of Centralised Procurement of Drugs of Public Hospitals (《國務院辦公廳關於完善公立醫院藥品集中採購工作的指導意見》) promulgated in February 2015 by the General Office of the State Council further clarifies seven specific instructions on the centralised procurement of drugs. The Notice on Centralised Procurement of Drugs Negotiated by the State (《關於做好國家談判藥品集中採購的通知》) was promulgated in April 2016, which further improves the mechanism of price negotiation of the drug. The Opinions of the General Office of the State Council on Improvement of the Policy of Production, Circulation and Use of Drugs (《國務院辦公廳關於進一步改革完善藥品生產流通使用政策的若干意見》) promulgated in January 2017 by the General Office of the State Council aims to deepen the reform of medicine health system, improve the quality of the drug and regulate the circulation and use of the drug. The Notice of the General Office of the State Council on Issuing Pilot Plan of Centralised Procurement and Use of the Drug Organised by the State (《國務院辦公廳關於印發國家組織藥品集中採購和使用試點方案的通知》) promulgated in January 2019 aims to improve the pricing mechanism of the drug, which also further regulates the scope and mode of centralised procurement. The Circular of the National Healthcare Security Administration on Issuing the Opinions on Effectively Carrying out Drug Price Administration at Present (《國家醫療保障局關於印發〈關於做好當前藥品價格管理工作的意見〉的通知》) was promulgated by National Healthcare Security Administration in November 2019, which expounds on works in four aspects, including getting aligned with and improving the existing drug price policies, establishing and improving a normalization mechanism of drug price regulation, effectively carrying out price tendering and procurement related to safeguarding the supply and stabilizing the prices of drugs in short supply, as well as strengthening the organization of regulatory authorities and enhancing their administration.

The centralised tender process takes the form of public tender operated and organised by provincial or municipal government agencies. The centralised tender process is in principle conducted once every year in the relevant province or city in PRC. The bids are assessed by a committee composed of pharmaceutical and medical experts who will be randomly selected from a database of experts approved by the relevant government authorities. The committee members assess the bids based on a number of factors, including but not limited to, bid price, product quality, clinical effectiveness, product safety, qualifications and reputation of the manufacturer, after-sale services and innovation. Only pharmaceuticals that have won in the centralised tender process may be purchased by public medical institutions funded by the governmental or state-owned enterprise (including state-controlled enterprises) in the relevant region.

REGULATIONS

OTHER PRC GOVERNMENT REGULATIONS

Regulations on Intellectual Property Rights

In terms of international conventions, China has entered into (including but not limited to) the Agreement on Trade-Related Aspects of Intellectual Property Rights (《與貿易有關的知識產權協定》), the Paris Convention for the Protection of Industrial Property (《保護工業產權巴黎公約》), the Madrid Agreement Concerning the International Registration of Marks (《商標國際註冊馬德里協定》) and the Patent Cooperation Treaty (《專利合作條約》).

Patents

According to the Patent Law of the PRC (《中華人民共和國專利法》) promulgated by the Standing Committee of the NPC in March 1984, as amended in September 1992, August 2000 and December 2008, and came into effect in October 2009, and the Implementation Rules of the Patent Law of the PRC (《中華人民共和國專利法實施細則》), promulgated by the State Council in June 2001 and as amended in December 2002 and January 2010, there are three types of patents in the PRC: invention patents, utility model patents and design patents. The protection period is 20 years for an invention patent and 10 years for a utility model patent and a design patent, commencing from their respective application dates. Any individual or entity that utilizes a patent or conducts any other activity in infringement of a patent without prior authorization of the patent holder shall pay compensation to the patent holder and is subject to a fine imposed by relevant administrative authorities and, if constituting a crime, shall be held criminally liable in accordance with the law. According to the Patent Law of the PRC, for public health purposes, the State Intellectual Property Office of the PRC may grant a compulsory license for manufacturing patented drugs and exporting them to countries or regions covered under relevant international treaties to which PRC has acceded. In addition, according to the Patent Law of the PRC, any organization or individual that applies for a patent in a foreign country for an invention or utility model patent established in China is required to report to the State Intellectual Property Office for confidentiality examination.

Patent Enforcement

Unauthorized use of patents without consent from owners of patents, forgery of the patents belonging to other persons, or engagement in other patent infringement acts, will subject the infringers to infringement liability. Serious offences such as forgery of patents may be subject to criminal penalties.

REGULATIONS

A patent owner, or an interested party who believes the patent is being infringed, may either file a civil legal suit or file an administrative complaint with the relevant patent administration authority. A PRC court may issue a preliminary injunction upon the patent holder’s or an interested party’s request before instituting any legal proceedings or during the proceedings. Damages for infringement are calculated as the loss suffered by the patent holder arising from the infringement or the benefit gained by the infringer from the infringement. If it is difficult to ascertain damages in this manner, damages may be determined by using a reasonable multiple of the license fee under a contractual license. Statutory damages may be awarded in the circumstances where the damages cannot be determined by the above-mentioned calculation standards. The damage calculation methods shall be applied in the aforementioned order.

Trade Secrets

According to the PRC Anti-Unfair Competition Law (《中華人民共和國反不正當競爭法》), promulgated by the Standing Committee of the NPC in September 1993, and amended in November 2017 and April 2019 respectively, the term “trade secrets” refers to technical and business information that is unknown to the public, has utility, may create business interests or profits for its legal owners or holders, and is maintained as a secret by its legal owners or holders. Under the PRC Anti-Unfair Competition Law, business persons are prohibited from infringing others’ trade secrets by: (1) obtaining the trade secrets from the legal owners or holders by any unfair methods such as theft, bribery, fraud, coercion, electronic intrusion, or any other illicit means; (2) disclosing, using or permitting others to use the trade secrets obtained illegally under item (1) above; (3) disclosing, using or permitting others to use the trade secrets, in violation of any contractual agreements or any requirements of the legal owners or holders to keep such trade secrets in confidence; or (4) instigating, inducing or assisting others to violate confidentiality obligation or to violate a rights holder’s requirements on keeping confidentiality of trade secrets, disclosing, using or permitting others to use the trade secrets of the rights holder. If a third party knows or should have known of the above-mentioned illegal conduct but nevertheless obtains, uses or discloses trade secrets of others, the third party may be deemed to have committed a misappropriation of the others’ trade secrets. The parties whose trade secrets are being misappropriated may petition for administrative corrections, and regulatory authorities may stop any illegal activities and fine infringing parties.

REGULATIONS

Trademarks

According to the Trademark Law of the PRC (《中華人民共和國商標法》) promulgated by the Standing Committee of the NPC in August 1982, and amended in February 1993, October 2001, August 2013 and April 2019 respectively, the period of validity for a registered trademark is ten years, commencing from the date of registration. The registrant shall go through the formalities for renewal within twelve months prior to the expiry date of the trademark if continued use is intended. Where the registrant fails to do so, a grace period of six months may be granted. The validity period for each renewal of registration is ten years, commencing from the day immediately after the expiry of the preceding period of validity for the trademark. In the absence of a renewal upon expiry, the registered trademark shall be cancelled. Industrial and commercial administrative authorities have the authority to investigate any behavior in infringement of the exclusive right under a registered trademark in accordance with the law. In case of a suspected criminal offense, the case shall be timely referred to a judicial authority and decided according to the law.

Domain Names

Domain names are protected under the Administrative Measures on the Internet Domain Names (《互聯網域名管理辦法》) promulgated by the Ministry of Industry and Information Technology in August 2017, and the Implementing Rules on Registration of Domain Names (《中國互聯網絡信息中心域名註冊實施細則》) promulgated by China Internet Network Information Center in September 2002, which came into effect in December 2002 and was lastly amended in May 2012. The Ministry of Industry and Information Technology is the main regulatory body responsible for the administration of PRC internet domain names. Domain name registrations are handled through domain name service agencies established under the relevant regulations, and the applicants become domain name holders upon successful registration.

Regulations on Product Liability

In addition to the strict new drug approval process, certain PRC laws have been promulgated to protect the rights of consumers and to strengthen the control of medical products in the PRC. Under current PRC law, manufacturers and vendors of defective products in the PRC may incur liability for loss and injury caused by such products. According to the General Principles of the Civil Law of the PRC (《中華人民共和國民法通則》) (the “**PRC Civil Law**”), promulgated in April 1986 and amended in August 2009, a defective product which causes property damage or physical injury to any person may subject the manufacturer or vendor of such product to civil liability for such damage or injury.

In February 1993, the Product Quality Law of the PRC (《中華人民共和國產品質量法》) (the “**Product Quality Law**”) was promulgated to supplement the PRC Civil Law aiming to protect the legitimate rights and interests of the end-users and consumers and to strengthen the supervision and control of the quality of products. The Product Quality Law was last revised in December 2018. According to the revised Product Quality Law, manufacturers who produce defective products may be subject to civil or criminal liability and have their business licenses revoked.

REGULATIONS

The Law of the PRC on the Protection of the Rights and Interests of Consumers (《中華人民共和國消費者權益保護法》) was promulgated in October 1993 and amended in October 2013 to protect consumers’ rights when they purchase or use goods and accept services. According to which, all business operators must comply with this law when they manufacture or sell goods and/or provide services to customers. Under the latest amendment, all business operators shall pay high attention to protect the customers’ privacy and strictly keep it confidential any consumer information they obtain during the business operation. In addition, in extreme situations, pharmaceutical product manufacturers and operators may be subject to criminal liability if their goods or services lead to the death or injuries of customers or other third parties.

Regulations on Tort

According to the Tort Law (《中華人民共和國侵權責任法》) of the PRC promulgated by the Standing Committee of the NPC in December 2009, if damages to other persons are caused by defective products due to the fault of a third party, such as the parties providing transportation or warehousing, the producers and the sellers of the products have the right to recover their respective losses from such third parties. If defective products are identified after they have been put into circulation, the producers or the sellers shall take remedial measures such as issuance of a warning, recall of products, etc. in a timely manner. The producers or the sellers shall be liable under tort if they fail to take remedial measures in a timely manner or have not made efforts to take remedial measures, thus causing damages. If the products are produced or sold with known defects, causing deaths or severe adverse health issues, the infringed party has the right to claim punitive damages in addition to compensatory damages.

Regulations on Commercial Briberies in Pharmaceutical Industry

According to the Regulations on the Establishment of Adverse Records with Respect to Commercial Briberies in the Medicine Purchase and Sales Industry (《關於建立醫藥購銷領域商業賄賂不良記錄的規定》), promulgated in January 2007 and amended in December 2013, where a manufacturer of drugs, medical devices and medical disposables, an enterprise, an agency or an individual offers staff of a medical institution any items of value or other benefits, the enterprise should be listed in the adverse records with respect to commercial bribery in the event of the following circumstances: (1) where the act has constituted a crime of bribery as determined by the ruling of a people’s court, or where the circumstance of crime is not serious enough for the imposition of criminal punishment and criminal punishment is exempted as decided by the people’s court in accordance with the Criminal Law; (2) where the circumstance of the crime of bribery is minor and the relevant people’s procuratorate has decided not to lodge a prosecution; (3) where a discipline inspection and supervision authority has initiated a case of bribery and conducted investigation, and punishment has been imposed in accordance with the law; (4) where administrative penalties against the act of bribery have been imposed by, *inter alia*, the finance administration, the SAMR, the NMPA; (5) any other circumstances specified by laws, regulations and rules. If medical production and operation enterprises be listed into the Adverse Records of Commercial Briberies for the first time, their products shall not be purchased by public medical institutions, and medical and health institutions receiving

REGULATIONS

financial subsidies in local province for two years since publication of the record, and public medical institution, and medical and health institutions receiving financial subsidies in other province shall lower their rating in bidding or purchasing process. If medical production and operation enterprises be listed into the Adverse Records of Commercial Bribery more than once in five years, their products shall not be purchased by public medical institutions, and medical and health institutions receiving financial subsidies nationwide for two years since publication of the record.

Regulations on Foreign Exchange and the Dividend Distribution

Foreign Exchange Control

According to the PRC Regulation for the Foreign Exchange (《中華人民共和國外匯管理條例》) promulgated by the State Council in January 1996, which was amended in January 1997 and August 2008, and the Regulation on the Administration of the Foreign Exchange Settlement, Sales and Payment (《結匯、售匯及付匯管理規定》) promulgated by the People's Bank of China in June 1996, foreign exchanges required for distribution of profits and payment of dividends may be purchased from designated foreign exchange banks in the PRC upon presentation of a board resolution authorizing distribution of profits or payment of dividends.

According to the Circular of SAFE on Further Improving and Adjusting the Foreign Exchange Policies on Direct Investment (《國家外匯管理局關於進一步改進和調整直接投資外匯管理政策的通知》) and its appendix promulgated in November 2012 and amended in May 2015, October 2018 and December 2019 by the SAFE, (1) the opening of and payment into foreign exchange accounts under direct investment accounts are no longer subject to approval by the SAFE; (2) reinvestment with legal income of foreign investors in China is no longer subject to approval by SAFE; (3) the procedures for capital verification and confirmation that foreign-funded enterprises need to go through are simplified; (4) purchase and external payment of foreign exchange under direct investment accounts are no longer subject to approval by SAFE; (5) domestic transfer of foreign exchange under direct investment account is no longer subject to approval by SAFE; and (6) the administration over the conversion of foreign exchange capital of foreign-invested enterprises is improved. Later, the SAFE promulgated the Circular on Further Simplifying and Improving Foreign Exchange Administration Policies in Respect of Direct Investment (《關於進一步簡化和改進直接投資外匯管理政策的通知》) in February 2015, which was further amended in December 2019 and prescribed that the bank instead of SAFE can directly handle the foreign exchange registration and approval under foreign direct investment while SAFE and its branches indirectly supervise the foreign exchange registration and approval under foreign direct investment through the bank.

The Provisions on the Administration of Foreign Exchange in Foreign Direct Investments by Foreign Investors (《外國投資者境內直接投資外匯管理規定》), which were promulgated by the SAFE in May 2013 and amended in October 2018 and December 2019, regulate and clarify the administration over foreign exchange administration in foreign direct investments.

REGULATIONS

According to the Circular on the Reform of the Management Method for the Settlement of Foreign Exchange Capital of Foreign-invested Enterprises (《國家外匯管理局關於改革外商投資企業外匯資金結匯管理方式的通知》) promulgated by the SAFE in March 2015 and amended in December 2019, and the Circular on the Reform and Standardization of the Management Policy of the Settlement of Capital Projects (《國家外匯管理局關於改革和規範資本項目結匯管理政策的通知》) promulgated by the SAFE in June 2016, the settlement of foreign exchange by foreign invested enterprises shall be governed by the policy of foreign exchange settlement on a discretionary basis. However, the settlement of foreign exchange shall only be used for its own operation purposes within the business scope of the foreign invested enterprises and following the principles of authenticity.

Dividend Distribution

The SAFE promulgated the Notice on Improving the Check of Authenticity and Compliance to Further Promote Foreign Exchange Control (《國家外匯管理局關於進一步推進外匯管理改革完善真實合規性審核的通知》) in January 2017, which stipulates several capital control measures with respect to outbound remittance of profits from domestic entities to offshore entities, including the following: (1) under the principle of genuine transaction, banks shall check board resolutions regarding profit distribution, the original version of tax filing records and audited financial statements; and (2) domestic entities shall hold income to account for previous years' losses before remitting the profits. Moreover, domestic entities shall make detailed explanations of sources of capital and utilization arrangements, and provide board resolutions, contracts and other proof when completing the registration procedures in connection with an outbound investment.

Foreign Exchange Registration of Offshore Investment by PRC Residents

The SAFE promulgated the SAFE Circular 37 in July 2014. The SAFE Circular 37 requires PRC residents (including PRC institutions and individuals) must register with local branches of SAFE in connection with their direct or indirect offshore investment in an overseas special purpose vehicle (the “SPV”) directly established or indirectly controlled by PRC residents for the purposes of offshore investment and financing with their legally owned assets or interests in domestic enterprises, or their legally owned offshore assets or interests. Such PRC residents are also required to amend their registrations with SAFE when there is a change to the basic information of the SPV, such as changes of a PRC resident individual shareholder, the name or operating period of the SPV, or when there is a significant change to the SPV, such as changes of the PRC individual resident's increase or decrease of its capital contribution in the SPV, or any share transfer or exchange, merger, division of the SPV.

Failure to comply with the registration procedures set forth in the SAFE Circular 37 may result in restrictions being imposed on the foreign exchange activities of the relevant onshore company, including the payment of dividends and other distributions to its offshore parent or affiliate, the capital inflow from the offshore entities and settlement of foreign exchange capital, and may also subject relevant onshore company or PRC residents to penalties under PRC foreign exchange administration regulations.

REGULATIONS

Employee Stock Incentive Plan

According to the Notices on Issues Concerning the Foreign Exchange Administration for Domestic Individuals Participating in Stock Incentive Plans of Overseas Publicly Listed Companies (《國家外匯管理局關於境內個人參與境外上市公司股權激勵計畫外匯管理有關問題的通知》) which was promulgated by SAFE in February 2012, PRC citizens or non-PRC citizens residing in China for a continuous period of no less than one year (except for foreign diplomatic personnel in China and representatives of international organizations in China) who participate in any stock incentive plan of an overseas publicly listed company shall, through the domestic company to which the said company is affiliated, collectively entrust a domestic agency (may be the Chinese affiliate of the overseas publicly listed company which participates in stock incentive plan, or other domestic institutions qualified for asset trust business lawfully designated by such company) to handle foreign exchange registration, and entrust an overseas institution to handle issues like exercise of options, purchase and sale of corresponding stocks or equity, and transfer of corresponding funds. In addition, the domestic agency is required to amend the SAFE registration with respect to the stock incentive plan if there is any material change to the stock incentive plan. Moreover, the SAFE Circular 37 provides that PRC residents who participate in a share incentive plan of an overseas unlisted special purpose company may register with local branches of SAFE before exercising rights.

Regulations on Labor

Labor Law and Labor Contract Law

According to the PRC Labor Law (《中華人民共和國勞動法》), which was promulgated by the Standing Committee of the NPC in July 1994 and amended in August 2009 and December 2018 respectively, the PRC Labor Contract Law (《中華人民共和國勞動合同法》), which was promulgated by the Standing Committee of the NPC in June 2007 and amended in December 2012 and came into effect July 2013, and the Implementing Regulations of the Employment Contracts Law of the PRC (《中華人民共和國勞動合同法實施條例》), which was promulgated by the State Council in September 2008, labor contracts in written form shall be executed to establish labor relationships between employers and employees. In addition, wages cannot be lower than local minimum wage. The employers must establish a system for labor safety and sanitation, strictly abide by State rules and standards, provide education regarding labor safety and sanitation to its employees, provide employees with labor safety and sanitation conditions and necessary protection materials in compliance with State rules, and carry out regular health examinations for employees engaged in work involving occupational hazards.

REGULATIONS

Social Insurance and Housing Provident Funds

According to the Social Insurance Law of PRC (《中華人民共和國社會保險法》), which was promulgated by the Standing Committee of the NPC in October 2010 and came into effect in July 2011, and further amended in December 2018, and the Interim Regulations on the Collection and Payment of Social Security Funds (《社會保險費徵繳暫行條例》), which was promulgated by the State Council in January 1999 and amended in March 2019, and the Regulations on the Administration of Housing Provident Funds (《住房公積金管理條例》), which was promulgated by the State Council in April 1999 and amended in March 2002 and March 2019, employers are required to contribute, on behalf of their employees, to a number of social security funds, including funds for basic pension insurance, unemployment insurance, basic medical insurance, occupational injury insurance, maternity insurance and to housing provident funds. Any employer who fails to contribute may be fined and ordered to make good the deficit within a stipulated time limit.

Regulations on Enterprise Income Tax

According to the EIT Law promulgated by the NPC in March 2007 and amended in February 2017 and December 2018, and the Implementation Rules of the Enterprise Income Tax Law of the PRC (《中華人民共和國企業所得稅法實施條例》) promulgated by the State Council in December 2007 and amended in April 2019, other than a few exceptions, the income tax rate for both domestic enterprises and foreign-invested enterprises is 25%. Enterprises are classified as either “resident enterprises” or “non-resident enterprises”. Besides enterprises established within the PRC, enterprises established outside China whose “de facto management bodies” are located in China are considered “resident enterprises” and subject to the uniform 25% enterprise income tax rate for their global income. A non-resident enterprise refers to an entity established under foreign law whose “de facto management bodies” are not within the PRC but which have an establishment or place of business in the PRC, or which do not have an establishment or place of business in the PRC but have income sourced within the PRC. An income tax rate of 10% will normally be applicable to dividends declared to non-PRC resident enterprise investors that do not have an establishment or place of business in the PRC, or that have such establishment or place of business but the relevant income is not effectively connected with the establishment or place of business, to the extent such dividends are derived from sources within the PRC.

According to the Arrangement Between the Mainland of China and the Hong Kong Special Administrative Region for the Avoidance of Double Taxation and Prevention of Fiscal Evasion with Respect to Taxes on Income (《內地和香港特別行政區關於對所得避免雙重徵稅和防止偷漏稅的安排》) (the “**Double Tax Avoidance Arrangement**”) promulgated and came into effect in August 2006, and other applicable PRC laws, if a Hong Kong resident enterprise is determined by the competent PRC tax authority to have satisfied the relevant conditions and requirements under such Double Tax Avoidance Arrangement and other applicable laws, the 10% withholding tax on the dividends the Hong Kong resident enterprise receives from a PRC resident enterprise may be reduced to 5%. However, based on the Circular on Certain Issues with Respect to the Enforcement of Dividend Provisions in Tax Treaties (《關於執行稅收協定

REGULATIONS

股息條款有關問題的通知》) which was promulgated by the STA in February 2009, if the relevant PRC tax authorities determine, in their discretion, that a company benefits from such reduced income tax rate due to a structure or arrangement that is primarily tax-driven, such PRC tax authorities may adjust the preferential tax treatment; and based on the Announcement on Certain Issues with Respect to the “Beneficial Owner” in Tax Treaties (《國家稅務總局關於稅收協定中“受益所有人”有關問題的公告》) which was promulgated by the STA in February 2018 and came into effect in April 2018, if an applicant’s business activities do not constitute substantive business activities, it could result in the negative determination of the applicant’s status as a “beneficial owner”, and consequently, the applicant could be precluded from enjoying the above-mentioned reduced income tax rate of 5% under the Double Tax Avoidance Arrangement.

Other PRC National and Provincial-Level Laws and Regulations

We are subject to changing regulations under many other laws and regulations administered by governmental authorities at the national, provincial and municipal levels, some of which are or may become applicable to our business. For example, regulations control the confidentiality of patients’ medical information and the circumstances under which patient medical information may be released for inclusion in our databases, or released by us to third parties. These laws and regulations governing both the disclosure and the use of confidential patient medical information may become more restrictive in the future.

We also comply with numerous additional national and provincial laws relating to matters such as safe working conditions, manufacturing practices, environmental protection and fire hazard control. We believe that we are currently in compliance with these laws and regulations; however, we may be required to incur significant costs to comply with these laws and regulations in the future. Unanticipated changes in existing regulatory requirements or adoption of new requirements could therefore have a material adverse effect on our business, results of operations and financial condition.