OVERVIEW OF PRC LAWS, REGULATIONS AND REGULATORY DEPARTMENTS

Core Regulatory Authorities

Authority	Core Responsibilities
National Medical Products Administration ("NMPA") . .	Drawing up the laws and regulations related to pharmaceuticals and medical devices, making policy planning, formulating departmental regulations, organizing the development and issuance of pharmaceutical and medical device standards, classification and management systems, such as national formulary, and supervising the implementation.
Center for Drug Evaluation of NMPA ("CDE").	The technical evaluation unit for drug registration under NMPA. It is mainly responsible for conducting technical evaluation on the drugs applying for registration and verifying the relevant drug registrations.
National Health Commission ("NHC")	Drafting national health policies, supervising and regulating public health, healthcare services and health emergency systems, coordinating the reform of medical and health system, organizing the formulation of national drug policies and national essential medicine system, launching an early warning mechanism for the monitoring of the use and clinical comprehensive evaluation of medicine as well as the drug shortage, giving suggestions on the pricing policy of national essential medicine, and regulating the operation of medical institutions and practicing of medical personnel.
National Institutes for Food and Drug Control ("NIFDC")	It is responsible for the approval and registration inspection, import inspection, supervision and inspection, safety evaluation of drugs, biological products, medical devices, foods, dietary supplements, cosmetics, laboratory animals and package materials and the batch release of biological products, the research, distribution and management of the national drug and medical device reference materials and bacterial and viral strains for production verification, as well as the relevant technical research.
National Development and Reform Commission ("NDRC").	participating in the formulation of health development policies, the establishment of technical reform investment projects, the macro guidance and management of the economic operation of pharmaceutical enterprises, and the supervision of the implementation of relevant policies and regulations.
National Healthcare Security Administration ("NHSA") . .	formulating and organizing the implementation of policies, plans and standards for medical insurance, maternity insurance, medical aid and other medical security systems, organizing the formulation and adjustment of prices and charging standards for drugs and medical services, and formulating and supervising the implementation of the bidding and procurement policies for drugs and medical consumables.

Regulations on the Research and Development and Manufacturing Services of Drugs

Research and Development of Drugs

Research and Development of New Drugs

According to the Drug Administration Law of the PRC (《中華人民共和國藥品管理法》) (the "**Drug Administration Law**") and the Drug Administration Law of the PRC (《中華人民共和國藥品管理法實施條例》) (the "**Implementation Regulations**"), the PRC encourages the research and development of new drugs, and protects the legal rights and interests in the research and development of new drugs. The developer and clinical trial applicant of any new drug shall truthfully submit the new drug's manufacturing method, quality specifications, results of pharmacological and toxicological tests and the related data, documents and samples to the NMPA for approval before any clinical trial is conducted.

Non-clinical Research

The NMPA requires preclinical data to support registration applications for imported and domestic drugs. According to the Administrative Measures for Drug Registration (《藥品註冊管理辦法》), non-clinical safety research shall be carried out in an institution that has passed the certification of the Good Laboratory Practice of Non-clinical Laboratory and comply with the Administrative Measures for Good Laboratories Practice of Non-clinical Laboratory (《藥物非臨床研究質量管理規範》) (the "**GLP**"). The GLP has been promulgated to improve the quality of non-clinical safety evaluation and research. Pursuant to the Administrative Measures for Certification of Good Laboratory Practice for Non-clinical Laboratory (2023 Amendments) (《藥物非臨床研究質量管理規範認證管理辦法》(2023年修訂)), the NMPA is responsible for the certification of non-clinical safety evaluation and research institutions nationwide and local provincial drug administrative department is in charge of the daily supervision of non-clinical safety evaluation and research institution.

Animal Testing

According to the Administrative Measures on Good Practice of Experimental Animals (《實驗動物質量管理辦法》), performing experimentation on animals requires a certificate for use of laboratory animals.

Application for Clinical Trial

According to the Decision on Adjusting the Approval Procedures of Certain Administrative Approval Items for Drugs (《關於調整部分藥品行政審批事項審批程序的決定》), drug clinical trials shall be divided into Phase I clinical trial, Phase II clinical trial, Phase III clinical trial, Phase IV clinical trial, and bioequivalence trial.

In accordance with the Administrative Measures for Drug Registration and the Announcement 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》), where an application is filed for carrying out clinical trials, if an applicant does not receive any negative or questioned opinions from the CDE within 60 days after the date when the trial application is accepted and the fees are paid, the applicant can proceed with the clinical trial in accordance with the trial protocol submitted to the CDE.

Conducting Clinical Trial

After obtaining clinical trial approval, the applicant shall conduct clinical trials at qualified clinical trial institutions. The qualified clinical trial institution refers to institutions that have the conditions to conduct clinical trials in accordance with the requirements and technical guidelines set forth in the Regulations for the Administration of Drug Clinical Trial Institutions (《藥物臨床試驗機構管理規定》). Such clinical trial institutions shall be subject to filing requirements, with the exception of institutions that only engage in analysis of biological samples related to drug clinical trials, which shall not be subject to such filing requirements. Clinical trials must be conducted in accordance with the Good Clinical Practice for Drug Trials (《藥物臨床試驗質量管理規範》).

According to the Announcement 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》), 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 meetings to CDE to discuss with CDE the key technical questions including the design of Phase III clinical trial protocol.

According to 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》), 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.

Overseas Clinical Trial

On January 30, 2015, the NMPA promulgated the Guidelines for International Multi-Center Clinical Trials of Drugs (for Trial Implementation) (《國際多中心藥物臨床試驗指南(試行)》) to guide the application, implementation and administration of international multi-center drug clinical trials in China. When the data of international multi-center drug clinical trials are used to support the drug registration applications in China, a further trend analysis concerning clinical trial data in China and Asia shall be conducted after an overall review of global clinical trial data, during which the consistency of characteristics between subjects in the study and subjects in China shall be considered. The sample size of Chinese subjects shall be sufficient to evaluate and infer the safety and effectiveness and meet the requirements of statistics and relevant laws and regulations. Also, both domestic and overseas centers involved in the international multi-center clinical trial are subject to on site inspection organized by PRC drug administrative departments.

According to the Opinions on Deepening the Reform on Examination and Approval System and Encouraging the Innovation of 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 clinical trial data obtained from overseas multi-centers may be used to apply for drug registration in China if they meet the relevant requirements for the drug registration in China. For drugs that apply for a New Drug Application (NDA) for the first time in China, the applicant for registration shall provide clinical trial data on whether there are ethnic differences (if any).

According to the Announcement on Promulgation of the Guiding Technical Principles for the Acceptance of Overseas Clinical Trial Data of Drugs (《關於發佈<接受藥品境外臨床試驗數據的技術指導原則>的通告》), if drug registration applicants use overseas clinical trials for drug registration applications in China, all overseas clinical trial data shall be provided, rather than selectively. If drug registration applicants plan to carry out follow-up clinical research and development following the early overseas clinical trials, they shall evaluate the early clinical trial data and only after having obtained complete clinical trial data and communicated with the CDE, these data could be used to support the follow-up clinical trials.

Gathering, Collection and Filing of Human Genetic Resources

Pursuant to the Service Guide for Administrative Licensing of Gathering, Collection, Deal, Export and Exit Approval of Human Genetic Resources (《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》), the gathering and collection of human genetic resources through clinical trials by a foreign-invested sponsor shall file for the record with the China Human Genetic Resources Management Office through an online system. The Regulations on the Management of Human Genetic Resources of the PRC (《中華人民共和國人類遺傳資源管理條例》) regulates the collection, preservation, utilization and external provision of human genetic resources in China. Foreign organizations, individuals and institutions established or actually controlled by them shall not gather or preserve Chinese human genetic resources in China, or provide Chinese human genetic resources to foreign countries. Where a foreign entity needs to use Chinese human genetic resources to conduct scientific research activities or clinical trials, it shall cooperate with Chinese scientific research institutions, institutions of higher education, medical institutions or enterprises.

The Administrative Regulation on Human Genetic Resources (《人類遺傳資源管理條例實施細則》) further provided specific provisions on the collection, preservation, utilization and external provision of human genetic resources of the PRC.

According to the Bio-security Law of the PRC (《中華人民共和國生物安全法》), the competent health department under the State Council shall be the competent authority for the approval or filing of using China's human genetic resources.

New Drug Application, Approval and Renewal

According to the Administrative Measures for Drug Registration (《藥品註冊管理辦法》), an applicant shall, upon completion of studies including pharmacy, pharmacology and toxicology and clinical trial of drugs which support the registration of drug marketing, determination of quality standards, and verification of commercial scale manufacturing processes, and preparation to undergo examination and inspection for drug registration, submit an application for drug marketing authorization, and submit the relevant research materials in accordance with the submission requirements. The CDE shall organize pharmacist, medical and other technical personnel to comprehensively review the application regarding the safety, effectiveness and quality control of the drug. Where the application is approved by the comprehensive review, the drug shall be approved for marketing and a drug registration certificate shall be issued.

According to the Special Approval Procedures for Drugs of the China Food and Drug Administration (《國家食品藥品監督管理局藥品特別審批程序》), the NMPA may initiate special approval procedures for certain drugs needed in response to public health emergencies.

According to the Working Procedures for the Evaluation of Breakthrough Therapy Designation Drugs (for Trial Implementation) (《突破性治療藥物審評工作程序(試行)》), during the clinical trials of a drug, for innovative drugs or improved new drugs for the prevention and treatment of diseases that are life-threatening or severely affect the quality of life, and there is no effective prevention and treatment method or sufficient evidence demonstrating significant clinical advantages over current therapies, the applicant may apply for the breakthrough therapy designation process during the Phase I or Phase II clinical trial (generally no later than Phase III clinical trial).

Meanwhile, according to the Working Procedures for the Prioritized Review and Approval of Drug Marketing Authorization (for Trial Implementation) (《藥品上市許可優先審評審批工作程序(試行)》) and he Announcement on Matters concerning the Optimization of Drug Registration Review and Approval (《關於優化藥品註冊審評審批有關事宜的公告》), a drug marketing authorization holder may apply for prioritized review and approval for drugs included in the breakthrough therapy designation process.

The CDE will prioritize the allocation of resources for review, inspection, examination and approval of registration applications that have been included in the scope of priority evaluation and approval to speed up the review and approval progress.

The Administrative Measures for Drug Registration provides more detailed standards, procedures and policy support for different expedited drug marketing authorization pathways, including breakthrough therapy designation, conditional approval, prioritized review and approval and special approval procedures.

Pursuant to the Drug Administration Law, an applicant who has obtained a drug registration certificate shall be recognized as a drug marketing authorization holder, responsible for non-clinical laboratory studies, clinical trials, production and distribution, post-market studies, and the monitoring, reporting and handling of adverse reactions in connection with pharmaceuticals in accordance with the provisions of the Drug Administration Law. The drug marketing authorization holder may engage in manufacturing or sales on their own or to entrust a licensed third party. According to the Administrative Measures for Drug Registration, at the time of application for drug marketing authorization, the applicant and the manufacturing enterprise shall have held the corresponding pharmaceutical manufacturing permit.

Pursuant to the Administrative Measures for Drug Registration, the validity period of a drug registration certificate shall be five years. The drug marketing authorization holder of the drug registration certificate shall ensure the safety, effectiveness and quality control of the marketed drug at all times during the validity period of the certificate and apply for re-registration of the drug six months before the expiry of such validity period. After the drug re-registration application is accepted, the local provincial-level drug regulatory authorities or the CDE shall conduct post-marketing reevaluation and adverse reaction monitoring on the drug marketing authorization holder, carry out relevant work in accordance with the drug approval documents and the requirements of the drug regulatory authorities, and review all material changes based on the information stated in the drug approval documents.

Drug Manufacturing

According to the Administrative Measures on Supervision of Pharmaceutical Manufacturing (《藥品生產監督管理辦法》), all facilities that manufacture drugs in China must apply for a pharmaceutical manufacturing permit which is issued by the provincial drug supervision and administration department, autonomous region or municipality directly under the central government where it is domiciled. The drug marketing authorization holder who entrusts another party to produce preparations shall meet the requirements as specified in Administrative Measures on Supervision of Pharmaceutical Manufacturing, sign an entrustment agreement and a quality agreement with a qualified drug producer, and submit the relevant agreements and the application materials of the actual production site to the provincial drug supervision and administration department where the drug marketing authorization holder is located to apply for the pharmaceutical manufacturing permit. According to the Administrative Measures for Drug Registration, when an application for marketing authorization is submitted, the applicant and the drug manufacturer shall have obtained the corresponding pharmaceutical manufacturing permit.

These drug manufacturing facilities shall comply with drug manufacturing quality management norms, establish a sound drug manufacturing quality management system and ensure the whole drug manufacturing process continuously comply with statutory requirements. The drug marketing authorization holder shall establish a quality assurance system for pharmaceuticals, and employ designated personnel to be independently in charge of quality control for pharmaceuticals.

Drug Operation

According to the Measures for the Supervision and Administration of the Quality of Drug Operation and Use (《藥品經營和使用質量監督管理辦法》), operation of drug business, including drug wholesale and drug retail, is prohibited without a drug business permit.

According to the Good Manufacturing Practice for Pharmaceutical Products (2010 Revision) (《藥品生產質量管理規範(2010年版)》), drug business operators shall comply with the drug operation quality management norms, establish and improve their drug operation quality management system, and ensure that the whole drug business process continuously comply with statutory requirements.

In China, governmental pricing controls on drugs (other than narcotic and certain psychiatric drugs) have been lifted since June 2015 when the Opinions on Advancing Drug Price Reform (《推進藥品價格改革意見》) came into effect. Instead of direct governmental controls, the government exercises control over the drugs through establishing a centralized tender process or centralized procurement mechanism, revising the National Medical Insurance Drug Catalogue or provincial medical insurance drug catalogue and strengthening regulation of medical and pricing practices. Also, according to the Opinions of the State Council on the Reform of Review and Approval System for Drugs and Medical Devices (《國務院關於改革藥品醫療器械審評審批制度的意見》), enterprises which apply for the registration of new drugs shall promise that the prices of their products on the PRC market shall not be higher than the comparable market prices in original countries or the surrounding area of the PRC.

Regulations on Dual Invoicing System

According to the Implementing Opinions on Promoting the "Dual Invoicing System" for Drug Procurement by Public Medical Institutions (for Trial Implementation) (《關於在公立醫療機構藥品採購中推行"兩票制"的實施意見(試行)》) (the "**Dual Invoicing System Notice**"), the dual invoicing system refers to a system that requires one invoice to be issued from pharmaceutical manufacturers to pharmaceutical distributors and the other invoice to be issued by pharmaceutical distributors to medical institutions.

Monitoring Period of New Drugs

According to the Implementation Regulations for the Drug Administration Law of the PRC, the NMPA may impose an administrative monitoring period of up to five years on newly approved drugs to safeguard public health, during which the safety of such new drugs shall undergo continuous monitoring. No other manufacturer may produce or import such new drugs during the monitoring period.

Drug Advertisements

The Advertising Law of the PRC (《中華人民共和國廣告法》) outlines the regulatory framework for the advertising industry. Advertisers, advertising service providers and advertising publishers are required to ensure that the contents of the advertisements they prepare or distribute are true and in full compliance with applicable laws and regulations. For advertisement of drugs, the advertisement contents shall be examined by the relevant authorities prior to the publication. Pursuant to the Interim Administrative Measures for the Review of Advertisements for Drugs, Medical Devices, Health Food and Formula Food for Special Medical Purposes (《藥品、醫療器械、保健食品、特殊醫學用途配方食品廣告審查管理暫行辦法》), advertisements for drugs shall not contain any false or misleading contents. Advertisers shall be responsible for the veracity and legitimacy of the contents of advertisements for drugs, medical devices, health food and formula food for special medical purposes.

Drug Recalls

According to the Measures for Administration of Drug Recall (《藥品召回管理辦法》), a marketing authorization holder shall establish and improve its drug recall system by collecting relevant information about drug safety and conducting investigation and evaluation with respect to the drugs with potential safety hazards. If there are any potential safety hazards that endanger human health and life in respect of any drugs sold in the PRC, such manufacturer must start the drug recall procedures.

Regulations on Medical Insurance Systems

The General Office of the State Council further released the Guidance of the General Office of the State Council on Further Deepening the Reform of the Payment Method of Basic Medical Insurance (《國務院辦公廳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. 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.

Regulations on Product Liability

According to the Product Quality Law of the PRC (《中華人民共和國產品質量法》), a manufacturer shall be liable for compensating for any personal injury or property damage.

Pursuant to the Civil Code or the PRC (《中華人民共和國民法典》), where a patient suffers damage due to defects in drugs, the patient may seek compensation from the drug marketing authorization holder or the medical institution. Where the patient seeks compensation from the medical institution, the medical institution, after it has made the compensation, shall have the right to recover the compensation from the liable drug marketing authorization holder.

Laws and Regulations on Anti-Unfair Competition

According to the Anti-Unfair Competition Law of the PRC (《中華人民共和國反不正當競爭法》) (the "**Anti-Unfair Competition Law**"), operators shall abide by the principle of voluntariness, equality, impartiality, integrity and adhere to laws and business ethics during market transactions. Operators in violation of the Anti-Unfair Competition Law shall bear corresponding civil, administrative or criminal liabilities depending on the specific circumstances.

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》), where the production and operation enterprises of drugs, medical devices and medical disposables, as well as their agencies and individuals bribe the staff of medical institutions responsible for the procurement and use of their drugs, medical devices and medical disposables with property or other benefits, they shall be listed in the adverse records of commercial bribery provided such conduct falls within the circumstances specified in the aforementioned regulations. If medical production and operation enterprises are listed into the adverse records of commercial bribery for more than once in five years, their products shall not be purchased by public medical institutions, and shall not be purchased by medical and health institutions receiving financial subsidies nationwide for two years from the date of the record's publication.

Regulations on Company Establishment and Foreign Investment

Company Law

The establishment, operation and management of corporate entities in the PRC is governed by the Company Law of the PRC (《中華人民共和國公司法》) (the "**PRC Company Law**").

The shareholders' meeting is the authority of the company, which exercises its powers in accordance with the PRC Company Law.

Foreign Investment Law and Relevant Catalogue of Industries

According to the Foreign Investment Law of the PRC (《中華人民共和國外商投資法》), the organizational form, structure, and operations of foreign-invested enterprises are subject to the Company Law and other applicable laws and regulations. Foreign investors or foreign-funded enterprises shall report investment information to the commerce departments through the enterprise registration system and the enterprise credit information publicity system.

According to the Regulation for Implementing the Foreign Investment Law of the PRC (《中華人民共和國外商投資法實施條例》) and the MOFCOM and the Foreign Investment Access Special Management Measures (Negative List) (2024 Version) (《外商投資准入特別管理措施(負面清單)(2024年版)》), China adopts the management system of pre-establishment national treatment and negative list for foreign investment. Foreign investors shall not invest in any field prohibited by the negative list for foreign investment access. Foreign investors shall meet the investment conditions stipulated under the negative list for any field with investment restricted by the negative list for foreign investment access. For the fields not included in the negative list for foreign investment access, management shall be conducted under the principle of consistency for domestic and foreign investment.

Regulations on Intellectual Property Rights

Trademark Law

According to the Trademark Law of the PRC (《中華人民共和國商標法》) and the Implementation Regulations for the PRC Trademark Law (《中華人民共和國商標法實施條例》), the trademark registrants shall enjoy the exclusive right to use the marks, which shall be protected by law. The Trademark Law of the PRC has adopted the "first-to-file" principle with respect to trademark registration.

Patent Law

According to the Patent Law of the PRC (《中華人民共和國專利法》) and the Implementation Regulations for the Patent Law of the PRC (《中華人民共和國專利法實施細則》), the patent right entitled to its owner shall be protected by the laws. Unauthorized exploitation of a patent may constitute infringement, subject to applicable exceptions under the law, such as experimental use, Bolar exception, prior use rights, or compulsory licensing.

Trade Secret

According to the Anti-Unfair Competition Law, 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 Anti-Unfair Competition Law, business operators are prohibited from infringing 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 impose fines on the infringing parties.

Domain Names

According to the Administrative Measure for Internet Domain Names (《互聯網域名管理辦法》), the domain name services follow a "first come, first file" principle. Use of domain names by providers of internet information services shall comply with laws and regulations and the relevant provisions of the telecommunication administrative authorities and shall not use a domain name to carry out illegal acts.

Regulations on Tax

Enterprise Income Tax

Pursuant to the Enterprise Income Tax Law of the PRC (《中華人民共和國企業所得稅法》) and the Implementation Regulations for 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》), the Enterprise Income Tax Law applies a uniform 25% enterprise income tax rate to both foreign-invested enterprises and domestic enterprises, except where tax incentives are granted to special industries and projects. However, if non-resident enterprises have not established institutions or premises in the PRC, or have established institutions or premises in the PRC but the income derived has no actual connection with such established institutions or premises, the enterprise income tax is, in that case, set at the rate of 10% for their income sourced from inside the PRC.

In February 2015, the State Administration of Taxation (the "**SAT**") issued the Announcement of the SAT on Several Issues Concerning the Enterprise Income Tax on Indirect Property Transfer by Non-Resident Enterprises (《國家稅務總局關於非居民企業間接轉讓財產企業所得稅若干問題的公告》) (the "**SAT Circular 7**"). According to the SAT Circular 7, an "indirect transfer" of assets, including equity interests in a PRC resident enterprise, by non-PRC resident enterprises may be re-characterized and treated as a direct transfer of PRC taxable assets, if such arrangement does not have a reasonable commercial purpose and was established for the purpose of avoiding payment of PRC enterprise income tax. As a result, gains derived from such indirect transfer may be subject to PRC enterprise income tax.

The Announcement of the SAT on Issues Relating to Withholding at Source of Income Tax of Non-resident Enterprises (《國家税務總局關於非居民企業所得税源泉扣繳有關問題的公告》) (the "**SAT Circular 37**"), replaced or supplemented certain previous provisions in the Circular 7. The SAT Circular 37 purports to clarify certain issues in the implementation of the SAT Circular 7 and other regulations, by providing, among others, the definition of equity transfer income and tax basis, the foreign exchange rate to be used in the calculation of withholding amount, and the date of occurrence of the withholding obligation.

Withholding Tax

Pursuant to the Enterprise Income Tax Law and the Implementation Regulations for the Enterprise Income Tax Law, if non-resident enterprises have not established institutions or premises in the PRC, or have established institutions or premises in the PRC but the income derived has no actual connection with such established institutions or premises, they shall be subject to withholding tax on their PRC-sourced income at a rate of 10%. According to the Arrangement between Chinese Mainland and the Hong Kong Special Administrative Region for the Avoidance of Double Taxation and Tax Evasion on Income (《內地和香港特別行政區關於對所得避免雙重徵税和防止偷漏税的安排》), dividends repatriated from a PRC entity to its Hong Kong shareholder owning more than 25% of its capital would be entitled to a reduced withholding tax rate of 5% subject to certain conditions.

Value-added Tax

According to the Interim Regulations of the PRC on Value-added Tax (《中華人民共和國增值税暫行條例》) and the Detailed Rules for the Implementation of the Interim Regulations of the PRC on Value-Added Tax (《中華人民共和國增值税暫行條例實施細則》), all entities and individuals in the PRC engaging in sale of goods or labor services of processing, repairing and replacement, sale of services, intangible assets, or immovables, or import of goods are required to pay value-added tax for the added value derived from the process of manufacture, sale or services.

According to the Circular of the MOF and the SAT on Adjusting Value-added Tax Rates (《財政部、國家税務總局關於調整增值税税率的通知》), where a taxpayer engages in value-added tax taxable sales activities or import of goods, the previous applicable value-added tax rates of 17% and 11% are adjusted to be 16% and 10% respectively.

According to the Circular on Policies to Deepen Value-added Tax Reform (《關於深化增值税改革有關政策的公告》), where a general VAT taxpayer engages in VAT-taxable sales activities or import of goods, the previous applicable VAT rates of 16% and 10% have been adjusted to be 13% and 9% respectively.

Regulations on Labor Protection

Labor Law and Labor Contract Law

The Labor Law of the PRC (《中華人民共和國勞動法》) and the Labor Contract Law of the PRC (《中華人民共和國勞動合同法》) together stipulate the labor contracts, settlement of labor disputes, labor remuneration, protection of occupational safety and healthcare, social insurance and welfare, etc. Written labor contracts must be entered into for the establishment of an employment relationship between employers and employees. Employers are also required to pay wages no lower than the local minimum wage standards to their employees.

Social Insurance and Housing Provident Funds

The Social Insurance Law of the PRC (《中華人民共和國社會保險法》), governs the PRC social insurance system. It requires employers and/or employees (as the case may be) to register social insurance with competent authorities and contribute the required amount of social insurance funds, including funds for basic pension insurance, unemployment insurance, basic medical insurance, occupational injury insurance and maternity insurance. Employers who fail to complete

social security registration shall be ordered by the social security administrative authorities to make correction within a stipulated period; where correction is not made within the stipulated period, the employer shall be subject to a fine ranging from one to three times the amount of the social security premiums payable, and the directly accountable person (s)-in-charge and other relevant responsible personnel shall be subject to a fine ranging from RMB500 to RMB3,000. Employers who failed to promptly contribute social security premiums in full amount shall be ordered by the social security premium collection agency to make or supplement contributions within a stipulated period, and shall be subject to a late payment fine computed from the due date at the rate of 0.05% per day; where payment is not made within the stipulated period, the relevant administrative authorities shall impose a fine of one to three times the amount in arrears.

According to the Interim Measures for the Participation in Social Insurance of Foreigners Employed in China (《在中國境內就業的外國人參加社會保險暫行辦法》), employers who hire foreigners shall register them for social insurance within 30 days of obtaining employment certificates. Foreigners who participate in social insurance and meet the requirements shall enjoy social insurance benefits in accordance with the law.

Under the Regulations on the Administration of Housing Provident Fund (《住房公積金管理條例》), an employer shall complete contribution registration with the housing provident fund management center and complete the formalities of opening housing provident fund accounts for its employees. Where an employer fails to complete payment and deposit registration of housing provident fund or fails to go through the formalities of opening housing provident fund accounts for its employees, the housing provident fund management center shall order it to go through the formalities within a prescribed time limit; where failing to do so at the expiration of the time limit, a fine of not less than RMB10,000 nor more than RMB50,000 shall be imposed. Where an employer is overdue in the payment of, or underpays, the housing provident fund, the housing provident fund management center shall order it to make the payment within a prescribed time limit; where the payment has not been made after the expiration of the time limit, an application may be made to a people's court for compulsory enforcement.

According to Interpretation (II) of the Supreme People's Court on Issues Concerning the Application of Law in the Trial of Labor Dispute Cases (《最高人民法院關於審理勞動爭議案件適用法律問題的解釋(二)》) ("**Interpretation (II) for Trial of Labor Dispute Cases**"), which became effective on September 1, 2025, if the employer and laborer agree or the laborer promises that social insurance premiums need not be paid, the people's court shall deem such agreement or promise invalid. If the employer fails to pay social insurance premiums as required by law, and the laborer requests termination of the labor contract and economic compensation under Article 38(3) of the Labor Contract Law, the court shall support the claim. If the above conditions are met and the employer, after legally making up the premiums, requests the laborer to return the social insurance compensation already paid, the court shall support the claim.

Regulations on Environmental Protection

According to the Environmental Protection Law of the PRC (《中華人民共和國環境保護法》) (the "**Environmental Protection Law**"), the Environmental Impact Assessment Law of the PRC (《中華人民共和國環境影響評價法》) and the Administrative Regulations on the Environmental Protection of Construction Project (《建設項目環境保護管理條例》), enterprises which plan to construct projects shall engage qualified professionals to provide the assessment reports, assessment form, or registration form on the environmental impact of such projects. The assessment reports, assessment form, or registration form shall be filed with or approved by the relevant environmental protection bureau prior to the commencement of any construction work.

According to the Environmental Protection Law and the Regulation on Administration of Discharge Permit (《排污許可管理條例》), public institutions and other producers and operators that are subject to the administration of discharge permit shall discharge pollutants in accordance with the requirements of the discharge permit; and those who have not obtained the discharge permit shall not discharge pollutants.

According to the Classification Management List for Fixed Source Pollution Permits (2019 Edition) (《固定污染源排污許可分類管理名錄(2019年版)》), the manufacturing of biological drugs and products falls into the classification management scope for fixed source pollution permits.

Regulations on Foreign Exchange and Overseas Investment and Dividend Distribution

Foreign Exchange and Overseas Investment

Foreign exchange in the PRC is mainly regulated by the Foreign Exchange Administration Regulations of the PRC (《中華人民共和國外匯管理條例》). Renminbi is freely convertible for current account items, including the distribution of dividends, interest payments, trade and service-related foreign exchange transactions, but is not freely convertible for capital account items, such as direct investments, loans, repatriation of investments and investments in securities outside of the PRC, unless prior approval is obtained from the SAFE and/or prior registration with the SAFE is made.

According to the Notice of SAFE on Issues Concerning the Foreign Exchange Administration of Overseas Listing (《國家外匯管理局關於境外上市外匯管理有關問題的通知》), the SAFE and its branch offices and administrative offices shall oversee, regulate and inspect domestic companies regarding their business registration, opening and use of accounts, trans-border payments and receipts, exchange of funds and other conduct involved in overseas listing. Domestic companies shall, within 15 working days upon the end of their public offering overseas, complete overseas listing registration formalities with the foreign exchange authority at their place of registration with the required materials.

According to the Notice on Further Simplifying and Improving Foreign Exchange Administration Policy on 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》), the banks shall review and carry out foreign exchange registration under domestic direct investment as well as foreign exchange registration under overseas direct investment directly, and the SAFE and its branches shall implement indirect supervision over foreign exchange registration of direct investment via the banks.

According to the Circular on Reforming the Management Approach regarding the Settlement of Foreign Exchange Capital of Foreign-invested Enterprises (《關於改革外商投資企業外匯資本金結匯管理方式的通知》), the foreign exchange capital of foreign-invested enterprises shall be subject to the Discretional Foreign Exchange Settlement. The proportion of Discretional Foreign Exchange Settlement of the foreign exchange capital of a foreign-invested enterprise is temporarily determined as 100%. The Renminbi converted from the foreign exchange capital will be kept in a designated account. If a foreign-invested enterprise needs to make a further payment from such designated accounts, it still needs to provide supporting documents and go through the banks' review process.

Dividend Distribution

The SAFE promulgated the Notice of the SAFE on Further Promoting the Reform of Foreign Exchange Administration and Improving the Examination of Authenticity and Compliance (《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》), which stipulates several capital control measures with respect to the outbound remittance of profits of a domestic entity equivalent to more than USD50,000 (exclusive) including the following: (1) under the principle of genuine transaction, banks shall check board resolutions regarding profit distribution (or the partners' 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 provide detailed explanations of the sources of capital and the intended use of funds, and provide board resolutions (or the partners' resolutions), contracts and other proof when completing the registration procedures in connection with an outbound investment.

Regulations on Information Security and Data Privacy

Pursuant to the Civil Code of the PRC, the personal information of a natural person shall be protected by the law. Any organization or individual that needs to obtain personal information of others shall obtain such information legally and ensure the safety of such information, and shall not illegally collect, use, process or transmit personal information of others, or illegally purchase or sell, provide or make public personal information of others.

The Personal Information Protection Law of the PRC (《中華人民共和國個人信息保護法》) stipulates the scope of personal information and establishes rules for processing personal information of natural persons within the territory of the PRC, including but not limited to more specific informed consent requirements in various contexts, strengthened and classified obligations of personal information processors, and more limitations and rules on processing of personal information.

The Data Security Law of the PRC (《中華人民共和國數據安全法》) stipulates that each organization or individual collecting data shall adopt legal and proper methods, and shall not steal or obtain data by other illegal methods, and the data processing activities shall comply with laws and regulations, respect social mores and ethics, comply with commercial ethics and professional ethics, be honest and trustworthy, perform obligations to protect data security, and undertake social responsibility; it shall not harm national security, the public interest, or the legitimate rights and interests of citizens or organizations. Pursuant to the Cybersecurity Review (《網絡安全審查辦法》), (i) the purchase of network products and services of a critical information infrastructure operator and data processing activities of an online platform operator that affect or may affect national security shall be subject to the cybersecurity review, (ii) particularly, if a critical information infrastructure operator purchase network products and services that affect or may affect national security, or an online platform operator possessing personal information of over one million users and pursues a listing abroad, such operator must apply for cybersecurity review, and (iii) relevant governmental authorities in the PRC may initiate cybersecurity review if such governmental authorities determine any network products and services, and data processing activities affect or may affect national security. In addition, the Cyber Data Security (《網絡數據安全管理條例》), provides clear stipulation on carrying out cyber data processing activities and the security supervision and management thereof.

The Measures for the Security Assessment of Outbound Data Transfers (《數據出境安全評估辦法》) outlines the possible security assessment process for outbound data transfers. In addition, the Measures for the Administration of Standard Contractual Clauses for the Cross-Border Transfer of Personal Information (《個人信息出境標準合同辦法》), attach the prescribed template for the standard contract on the outbound transfer of personal information that could be used as an available option to satisfy the condition for cross-border transfer of personal information under Article 38 of the Personal Information Protection Law.

On March 22, 2024, the CAC issued Provisions on Facilitating and Regulating Cross-border Data Flows (《促進和規範數據跨境流動規定》), which provide provisions for the implementation of outbound data transfer systems including security assessment for outbound data transfers, standard contracts for outbound transfer of personal information, and personal information protection certification. In accordance with these provisions, unless otherwise stipulated, (I) data processors who provide data abroad, and meet any of the following conditions, are required to declare the security assessment of outbound data transfer to the national cyberspace administration authority through the provincial-level cyberspace administration authority where they are located: (A) critical information infrastructure operators providing personal information or important data abroad; (B) data processors other than critical information infrastructure operators providing important data abroad or cumulatively providing abroad personal information (excluding sensitive personal information) of more than one million individuals, or sensitive personal information of more than 10,000 individuals since January 1 of the current year; and (C) data processors other than critical information infrastructure operators have cumulatively provided abroad personal information (excluding sensitive personal information) of more than 100,000 and less than

1,000,000 individuals, or sensitive personal information of less than 10,000 individuals as of January 1 of the current year, shall enter into a standard contract for outbound transfer of personal information with the overseas recipient or obtain personal information protection certification in accordance with the law.

Regulations on Overseas Securities [REDACTED] and [REDACTED] by Domestic Enterprises

According to the Trial Administrative Measures of Overseas Securities Offering and Listing by Domestic Enterprises (《境內企業境外發行證券和上市管理試行辦法》), the Overseas Listing Trial Measures comprehensively reformed the regulatory regime for overseas offering and listing of securities by the PRC domestic enterprises, either directly or indirectly, into a filing-based system. The PRC domestic enterprises that seek to offer and list securities in overseas markets, either directly or indirectly, are required to fulfill the filing procedure with the CSRC and report relevant information. The Overseas Listing Trial Measures provides that an overseas listing or offering is explicitly prohibited, if any of the following applies: (i) such securities offering or listing is explicitly prohibited by provisions in PRC laws, administrative regulations or relevant state rules; (ii) the securities offering or listing may endanger national security as reviewed and determined by competent authorities under the State Council in accordance with laws; (iii) the domestic enterprise or its controlling shareholder(s) and the actual controller, have committed crimes such as corruption, bribery, embezzlement, misappropriation of property or undermining the order of the socialist market economy during the latest three years; (iv) the domestic enterprise is currently under investigations for suspicion of criminal offenses or major violations of laws and regulations, and no conclusion has yet been made thereof; or (v) there are material ownership disputes over equity held by the controlling shareholder(s) or by other shareholder(s) that are controlled by the controlling shareholder(s) or actual controller.

According to the Provisions on Strengthening the Confidentiality and Archives Administration of Overseas Securities Issuance and Listing by Domestic Enterprises (《關於加強境內企業境外發行證券和上市相關保密和檔案管理工作的規定》), where a domestic enterprise provides or publicly discloses to the relevant securities companies, securities service institutions, overseas regulatory authorities and other entities and individuals, or provides or publicly discloses through its overseas listing subjects, documents and materials involving state secrets and working secrets of state organs, it shall report the same to the competent department with the examination and approval authority for approval in accordance with the law, and submit the same to the secrecy administration department of the same level for filing. Domestic enterprises providing accounting archives or copies thereof to the relevant securities companies, securities service institutions, overseas regulatory authorities and other entities and individuals shall perform the corresponding procedures pursuant to the relevant provisions of the State. The working papers formed within the territory of the PRC by the securities companies and securities service institutions that provide corresponding services for the overseas issuance and listing of domestic enterprises shall be kept within the territory of the PRC, and cross-border transfer shall go through the examination and approval formalities in accordance with the relevant provisions of the State.

Regulations on "Full Circulation" of H Shares

According to the Guidelines on Application for "Full Circulation" of Domestic Unlisted Shares of H Share Companies (《H股公司境內未上市股份申請"全流通"業務指引》), "Full Circulation" refers to the listing and circulation of the domestic unlisted shares of an H-share company (including unlisted domestic shares held by domestic shareholders prior to overseas listing, unlisted domestic shares that are further issued in the PRC after overseas listing and unlisted shares held by foreign shareholders) on the Hong Kong Stock Exchange. Holders of unlisted domestic shares may, at their own discretion, negotiate and determine the number and proportion of shares to be applied for circulation, and entrust H-share companies to apply for "full circulation", as well as entrust H-share companies to submit the "full circulation" filing documents to the CSRC, subject to compliance with relevant laws and regulations as well as policy requirements in respect

of state-owned assets management, foreign investment and industry regulation. According to the Guidelines, shareholders of domestic unlisted shares should handle the transfer of shares in accordance with the relevant business rules of CSDC, and H-share companies should submit a report on the relevant situation to the CSRC within 15 days after the completion of the transfer of the shares involved in the application to CSDC.

The Measures for Implementation of H-share Full Circulation Business (《H股"全流通"業務實施細則》) is in relation to the H-share full circulation business, such as cross-border transfer registration, maintenance of deposit and holding details, transaction entrustment and instruction transmission, settlement, management of settlement participants, services of nominal holders, etc. are subject to the Measures for Implementation.

According to the Guide to the Program for Full Circulation of H-shares of China Securities Depository and Clearing Corporation Limited Shenzhen Branch (《中國證券登記結算有限責任公司深圳分公司H股"全流通"業務指南》), the business preparation, cross-border share transfer registration, arrangement for settlement and delivery, risk management measures and other relevant matters are specified.

OVERVIEW OF U.S. LAWS, REGULATIONS AND REGULATORY DEPARTMENTS

U.S. Government Regulation of Drug and Biological Products

In the U.S., the FDA regulates drugs under the FDCA, its implementing regulations and biologics under the FDCA and the Public Health Service Act (the "PHSA") and their implementing regulations. Both drugs and biologics are also subject to other federal, state and local statutes and regulations, such as those related to competition. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or following approval may subject an applicant to administrative actions or judicial sanctions. These actions and sanctions could include, among other actions, the FDA's refusal to approve pending applications, withdrawal of an approval, license revocation, a clinical hold, untitled or warning letters, voluntary or mandatory product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal fines or penalties.

Pre-clinical testing of a product candidate is conducted in accordance with FDA's Good Laboratory Practice regulations. A sponsor of IND must submit the results of the pre-clinical testing, manufacturing information, analytical data, the clinical trial protocol, and any available clinical data or literature to the FDA. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions and places the trial on a clinical hold within that 30-day period. FDA may also impose clinical holds or partial clinical holds at any time during clinical trials due to safety concerns or non-compliance.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with Good Clinical Practice regulations, including the requirement that all research subjects provide informed consent in writing before their participation in any clinical trial. Further, an Institutional Review Board ("IRB"), must review and approve the plan for any clinical trial before it commences at any institution, and the IRB must conduct continuing review and reapprove the study at least annually. Each new clinical protocol and any amendments to the protocol must be submitted for FDA review, and to the IRBs for approval. An IRB can suspend or terminate approval of a clinical trial at its institution if the trial is not being conducted in accordance with the IRB's requirements or if the product has been associated with unexpected serious harm to subjects.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA. Safety reports must be submitted to the FDA and the investigators' 15 calendar days after the trial sponsor determines that the information qualifies for reporting. The sponsor also must notify FDA of any unexpected fatal or life-threatening suspected adverse reaction as soon as

possible but in no case later than 7 calendar days after the sponsor's initial receipt of the information. Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information, which is publicly available at www.clinicaltrials.gov.

Concurrent with clinical trials, companies usually complete additional animal studies and must also finalize a process for manufacturing the product in commercial quantities in accordance with GMP requirements. Failure to comply with the applicable U.S. requirements may subject an applicant to administrative or judicial sanctions.

U.S. Review and Approval Processes

The results of product development, pre-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the product, proposed labeling and other relevant information, are submitted to the FDA as part of an NDA or BLA. Unless deferred or waived, NDAs or BLAs, or supplements must contain data adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The submission of an NDA or a BLA is subject to the payment of a substantial user fee and an annual prescription drug product program fee.

Within 60 days of its receipt, the FDA reviews the NDA/BLA to ensure that it is sufficiently complete for substantive review before it accepts the NDA/BLA for filing. After accepting the NDA/BLA filing, the FDA begins an in-depth substantive review to determine, among other things, whether a product is safe and effective for its intended use. The FDA also evaluates whether the product's manufacturing is GMP-compliant to assure the product's identity, strength, quality and purity. Before approving the NDA/BLA, the FDA typically will inspect whether the manufacturing processes and facilities are in compliance with GMP requirements and adequate to assure consistent production of the product within required specifications. The FDA may refer the NDA/BLA to an advisory committee, a panel of experts, for review whether the application should be approved and under what conditions and considers such recommendations when making decisions.

The FDA may refuse to approve the NDA/BLA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. The FDA will issue a complete response letter describing all of the specific deficiencies that the FDA identified in the NDA/BLA that must be satisfactorily addressed before it can be approved. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. The applicant may either resubmit the NDA/BLA, addressing all of the deficiencies identified in the letter, or withdraw the application or request an opportunity for a hearing.

The regulatory approval may be limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post-approval studies, including Phase IV clinical trials, to further assess a product's safety and effectiveness after NDA/BLA approval and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

In the U.S., products composed of components that would normally be regulated by different centers at the FDA are known as combination products. Typically, the FDA's Office of Combination Products assigns a combination product to a specific Agency Center as the lead reviewer. The FDA determines which Center will lead a product's review based upon the product's primary mode of action. Depending on the type of combination product, its approval, clearance or licensure may usually be obtained through the submission of a single marketing application. However, the FDA sometimes will require separate marketing applications for individual constituent parts of the

combination product, which may require additional time, effort, and information. Even when a single marketing application is required for a combination product, the relevant Centers may participate in the review. An applicant will also need to discuss with the Agency how to apply certain premarket requirements and post-marketing regulatory requirements, including conduct of clinical trials, adverse event reporting and good manufacturing practices, to their combination product.

FDA Acceptance of Foreign Clinical Data in NDA

An application based solely on foreign clinical data meeting U.S. criteria for marketing approval may be approved if: (1) the foreign data are applicable to the U.S. population and U.S. medical practice; (2) the studies have been performed by clinical investigators of recognized competence; and (3) the data may be considered valid without the need for an on-site inspection by FDA or, if FDA considers such an inspection to be necessary, FDA is able to validate the data through an on-site inspection or other appropriate means. Failure of an application to meet any of these criteria will result in the application not being approvable based on the foreign data alone. FDA will apply this policy in a flexible manner according to the nature of the drug and the data being considered.

Expedited Development and Review Programs

The FDA has various programs that are intended to expedite or streamline the process for the development and FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

Fast Track Designation

To be eligible for a fast-track designation, the FDA must determine, based on the request of a sponsor, that a drug is intended to treat a serious or life-threatening disease or condition for which there is no effective treatment and demonstrates the potential to address an unmet medical need for the disease or condition. Under the fast-track program, the sponsor of a drug candidate may request FDA to designate the product for a specific indication as a fast-track product concurrent with or after the filing of the IND for the drug candidate. The FDA must make a fast-track designation determination within 60 days after receipt of the sponsor's request.

In addition to other benefits, such as the ability to use surrogate endpoints and have more interactions with FDA, FDA may initiate review of sections of a fast-track product's NDA before the application is complete. This rolling review is available if the applicant provides, and FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, FDA's time period goal for reviewing a fast-track application does not begin until the last section of the NDA is submitted. In addition, the fast-track designation may be withdrawn by FDA if FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Orphan Drug Designation

Under The Orphan Drug Act of 1983, the FDA may grant orphan drug designation to drugs or biologic candidates intended to treat a rare disease or condition generally affecting fewer than 200,000 individuals in the U.S. or for which a manufacturer has no reasonable expectation of recovering drug treatment research and development costs. The first applicant to receive FDA approval for the disease or indication for which it has orphan drug designation is entitled to a seven-year exclusive marketing period. During the exclusivity period, the FDA may not approve any other applications to market the same product for the same disease or condition except in limited circumstances.

Accelerated Approval

Under FDA's accelerated approval regulations, the FDA may approve a drug or biologic candidate for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments and demonstrates an effect on either a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality ("IMM"), that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the disease or condition and the availability or lack of alternative treatments. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of post-approval clinical trial to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Breakthrough Therapy Designation

A drug or biologic may be eligible for designation as a breakthrough therapy if the product is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A sponsor may request that a product be designated as a breakthrough therapy concurrently with, or at any time after, the submission of IND, and the FDA must determine if the candidate qualifies for such designation within 60 days of receipt of the request. If so designated, the FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather pre-clinical and clinical data is as efficient as practicable.

Priority Review

The FDA may give a priority review designation to drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under the Prescription Drug User Fee Act guidelines. These six- and ten-month review periods are measured from the "filing" date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast-track designation are also likely to be considered appropriate to receive a priority review.

Post-Marketing Requirements

Following the approval of a new product, the manufacturer and the approved product are subject to continuing regulation by the FDA, including, among other things, monitoring and record-keeping activities, reporting of adverse experiences, complying with promotion and advertising requirements, which include restrictions on promoting products for unapproved uses or patient populations (known as "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability, including investigation by federal and state authorities. Prescription drug promotional materials must be submitted to the FDA in conjunction with their first use or first publication. Further, if there are any modifications to the drug or biologic, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA/BLA or NDA/BLA supplement, which may require the development of additional data or preclinical studies and clinical trials. The FDA may also place other conditions on approvals including the requirement for a risk evaluation and mitigation strategy ("REMS"), to assure the safe use of the product.

If the FDA concludes a REMS is needed, the sponsor of the NDA/BLA must submit a proposed REMS. The FDA will not approve the NDA/BLA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations that require, among other things, quality control and quality assurance, the maintenance of records and documentation, and the obligation to investigate and correct any deviations from cGMP.

Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP requirements and other laws. The discovery of violative conditions, including failure to conform to cGMP regulations, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA/BLA, including recall.

Once an approval is granted, the FDA may issue enforcement letters or withdraw the approval of the product if compliance with regulatory requirements and standards is not maintained or if problems occur after the drug or biologic reaches the market. Corrective action could delay drug or biologic distribution and require significant time and financial expenditures. Later discovery of previously unknown problems with a drug or biologic, including AEs of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things: restrictions on the marketing or manufacturing of the drug or biologic, suspension of the approval, complete withdrawal of the drug from the market or product recalls; fines, warning letters or holds on post-approval clinical trials; refusal of the FDA to approve applications or supplements to approved applications, or suspension or revocation of drug or biologic approvals; drug or biologic seizure or detention, or refusal to permit the import or export of drugs; or injunctions or the imposition of civil or criminal penalties.

OVERVIEW OF AUSTRALIAN LAWS, REGULATIONS AND REGULATORY DEPARTMENTS

Regulations on Clinical Development

Clinical trials conducted in Australia are regulated by the Therapeutic Goods Administration ("TGA"). Clinical trials must comply with a number of laws and regulations in Australia at the Commonwealth and State/Territory levels, including the Therapeutic Goods Act 1989 (Cth) and the Therapeutic Goods Regulations 1990 (Cth). Clinical trials must also comply with: the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guidelines for Good Clinical Practice, as adopted and annotated by the TGA (the "ICH GCP Guidelines"); the National Statement on Ethical Conduct in Human Research (the "National Statement") and the protocol approved by the Human Research Ethics Committee ("HREC") responsible for monitoring the conduct of the trial.

There are two schemes for the approval of clinical trials involving 'unapproved' therapeutic goods in Australia: the Clinical Trial Notification ("CTN") scheme; and the Clinical Trial Approval ("CTA") scheme. The CTN scheme involves the TGA being notified of the clinical trial, but not undertaking any evaluation of the clinical trial. The CTA scheme involves the TGA not only being notified of the clinical trial, but also conducting an evaluation and assessment of the clinical trial prior to its commencement with a primary focus on reviewing the safety of the therapeutic goods.

The CTN scheme is generally used for earlier phase studies when there is adequate preclinical information about the product, particularly in relation to safety. The CTA scheme is generally used for high-risk or novel treatments, where there is little known or no knowledge about the safety of the goods. The decision regarding which scheme to follow is generally up to the sponsor of the trial and the applicable HREC, although the CTA scheme is mandatory for certain types of biological medicines.

Clinical trials in Australia require the approval of the research institute that is conducting the trial, following a review by its HREC before the trial commences. HRECs are responsible for assessing the scientific validity of the trial design, the balance of risk versus harm of the therapeutic goods and the overall ethical acceptability of the trial. HRECs are also responsible for overseeing clinical trials. Clinical trials conducted in Australia must have a trial sponsor that is an Australian company. It is permissible for a foreign corporation to engage an Australian company to act as the sponsor of a clinical trial in Australia, often referred to as the Local Sponsor. In this situation, the foreign corporation does not, itself, need to obtain any licenses or authorizations in respect of the clinical trial. The Australian trial sponsor is responsible for the initiation, management and financing (or arranging the financing) for the clinical trial and is legally responsible for the conduct of the clinical trial, including obtaining the requisite licenses or authorizations. The trial sponsor does not need to be the manufacturer of the product being trialed. The product manufacturer may rely on the results of the trial when seeking to have the product registered on the Australian Register of Therapeutic Goods.

Clinical trials in Australia must follow the ICH GCP Guidelines as annotated by the TGA. The TGA's annotations provide additional guidance regarding compliance with the National Statement, obtaining informed consent in special cases, responsibility for the conduct of the trial (including management, data handling and record keeping), the manufacturing, packaging, labelling and coding of investigational products, and reporting for adverse drug reactions. The approval of a clinical trial in Australia is conditional upon compliance with the ICH GCP Guidelines as annotated by the TGA.

Clinical trials in Australia must also comply with the National Statement. The National Statement sets out the Australian ethical standards against which all research involving humans, including clinical trials, are reviewed. The approval of a clinical trial in Australia is conditional upon compliance with the National Statement.

In relation to safety reporting requirements, clinical trials conducted in Australia must follow: the Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (CPMP/ICH/377/95), as annotated by the TGA; and the National Health and Medical Research Council ("NHMRC") Guidance: Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods.

Additionally, per the ICH GCP Guidelines as annotated by the TGA, products used in clinical trial must comply with the applicable good manufacturing practices ("GMP"). For investigational products manufactured in Australia, the relevant manufacturing standards are set out in the Therapeutic Goods (Manufacturing Principles) Determination 2020 (Cth). Generally, therapeutic goods (other than blood, blood components, haematopoietic progenitor cells and biologicals that do not comprise or contain live animal cells, tissues or organs) must be manufactured in accordance with the Guide to Good Manufacturing Practice of Medicinal Products (PE 009-15, 1 May 2021) published by PIC/S.

Under both the CTN and CTA schemes, the clinical trial sponsor for a trial involving medicines or biological products must provide to the TGA information about the proposed dosage form, route of administration, formulation, dosage, and frequency of administration of the product (amongst other information), prior to the commencement of the clinical trial. If a change to the dosage is proposed to be made following the completion of a phase I clinical trial, then that change must be either notified to the TGA (if the clinical trial falls under the CTN scheme), or approved by the TGA (if the clinical trial falls under the CTA scheme). The change would also require review and approval by the HREC overseeing the trial.