LAWS AND REGULATIONS RELATED TO OUR BUSINESS IN THE PRC

Regulations on 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 adopted by the Standing Committee of the National People's Congress ("**SCNPC**") on December 29, 1993, implemented on July 1, 1994, and subsequently amended on December 25, 1999, August 28, 2004, October 27, 2005, December 28, 2013 and October 26, 2018. Under 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. Pursuant 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 on February 11, 2002 and came into effect on April 1, 2002, and the Special Administrative Measures (Negative List) for Foreign Investment Access (《外商投資准入特別管理措施(負面清單)(2019年版)》, the "**Negative List (2019 Edition)**"), which was amended and promulgated by the MOFCOM and NDRC on June 30, 2019 and took effect on July 30, 2019. The Negative List set out in a unified manner the restrictive measures, 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 People's Republic of China (《中華人民共和國外商投資法》) ("**Foreign Investment Law**") was promulgated by SCNPC on March 15, 2019 and become effective on January 1, 2020. After the Foreign Investment Law came into force, the law on wholly foreign-owned enterprises (《中華人民共和國外資企業法》), the law on Sino-foreign equity joint ventures (《中華人民共和國中外合資經營企業法》) and the law on Sino-foreign contractual joint ventures (《中華人民共和國中外合作經營企業法》) have been repealed simultaneously.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: 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; 4) other forms of investment prescribed by laws, administrative regulations or the State Council.

On December 26, 2019, the State Council issued 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 on January 1, 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 (《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 Law (《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 (《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 (《中華人民共和國外資企業法實施細則》) have been repealed simultaneously.

On December 30, 2019, the MOFCOM issued the Measures for the Reporting of Foreign Investment Information (《外商投資信息報告辦法》), which came into effect on January 1, 2020. After the Measures for the Reporting of Foreign Investment Information came into effect, the Interim Measures on the Administration of Filing for Establishment and Change of Foreign Investment Enterprises (《外商投資企業設立及變更備案管理暫行辦法》) has 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 commerce authorities pursuant to these measures.

Regulations on Overseas Investment

Pursuant to the Administrative Measures for Outbound Investment (《境外投資管理辦法》) (Order No. 3 [2014] of the MOFCOM, effective on October 6, 2014) promulgated by the MOFCOM, the MOFCOM and Provincial Competent Commerce Departments shall carry out administration either by record-filing or approval, depending on different circumstances of outbound investment by enterprises. Outbound investment by enterprises that involves sensitive countries and regions or sensitive industries shall be subject to administration by approval. Outbound investment by enterprises that falls under any other circumstances shall be subject to administration by record-filing.

Pursuant to the Administrative Measures for Outbound Investment by Enterprises (《企業境外投資管理辦法》) (Order No. 11 of the NDRC, effective on March 1, 2018), a domestic enterprise (the "**Investor**") making an outbound investment shall obtain approval, conduct record-filing or other procedures applicable to outbound investment projects (the "**Projects**"), reporting relevant information, and cooperating with the supervision and inspection. Sensitive Projects carried out by Investors directly or through overseas enterprises controlled by them shall be subject to approval; non-sensitive Projects directly carried out by Investors, namely, non-sensitive projects involving investors' direct contribution of assets or rights and interests or provision of financing or guarantee shall be subject to record-filing. The aforementioned "sensitive project" means a project involving a sensitive country or region or a sensitive industry. The NDRC promulgated the Catalog of Sensitive Sectors for Outbound Investment (2018 Edition) (《境外投資敏感行業目錄(2018年版)》), effective on March 1, 2018 to list the current sensitive industries in detail.

Regulations on Drug Research and Development & Registration Services

Research and Development of New Drugs

Pursuant to the Drug Administration Law of the PRC (《中華人民共和國藥品管理法》, last amended on August 26, 2019 and effective on December 1, 2019), the dossier on a new drug research and development, including the manufacturing method, quality specifications, results of pharmacological and toxicological tests and the related data, documents and the samples, shall, in accordance with the regulations of NMPA be truthfully submitted to the said department for approval before clinical trial is conducted. The medical products administration under the State Council shall, within 60 working days from the date on which the application for such clinical trial is accepted, decide on whether to approve it and then notify the clinical trial applicant. In the case of failure to notify the applicant within the prescribed time limit, it shall be deemed as approved. When a new drug has gone through the clinical trial and passed the evaluation, a drug registration certificate shall be issued upon approval by NMPA. The institutions for non-clinical safety evaluation and study and clinical trial organizations shall respectively implement the Good Laboratory Practice for Non-Clinical Laboratory Studies (the "**GLP**") (《藥物非臨床研究質量管理規範》, Order No. 34 of the State Food

and Drug Administration, effective on September 1, 2017) and Good Clinical Practice (the "**GCP**") (《藥物臨床試驗質量管理規範》, Order No. 3 of the State Food and Drug Administration (the "**SFDA**"), effective on September 1, 2003). If certain actions in the preclinical trial research and clinical research conducted for a clinical application trial, and/or in the application procedures for registration of medicines, are in violation of the relevant rules and regulations, the CFDA is authorized to handle such cases pursuant to the Measures regarding Noncompliance with Relevant Rules of Research and Application for Registration of Medicines (《藥品研究和申報註冊違規處理辦法(試行)》) promulgated on and effective from September 1, 1999. On July 22, 2015, the CFDA issued Notice No. 117 (CFDA notice in relation to self-review of clinical trials data) (《國家食品藥品監督管理總局關于開展藥物臨床試驗數據自查核查工作的公告》), which required the current applicants in respect of the existing 1,622 drug manufacturing or drug import applications to the CFDA to reassess the clinical trials data in respect of each application. On April 23, 2020, the NMPA and NHC further revised the Good Clinical Practice of Pharmaceutical Products (《藥物臨床試驗質量管理規範》) which will become effective on July 1, 2020, in order to further improve the quality of clinical trials and encourage innovation.

Drug Registration

Examination and Approval of New Drug Application

On July 10, 2007, the NMPA promulgated the Amended version of the Administrative Measures for Drug Registration（《藥品注冊管理辦法》）, or the Registration Measures, which became effective on October 1, 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. Under the Registration Measures, new drugs generally refer to those drugs that have not been previously marketed in China. In addition, certain marketed drugs may also be treated as new drugs if the type or application method of these drugs has been changed or new therapeutic functions have been added to these drugs. If all the regulatory requirements are satisfied, the NMPA will grant a new drug certificate and a drug registration number (assuming the applicant has a valid Pharmaceutical Manufacturing Permit and the requisite production conditions for the new medicine have been met). All pharmaceutical products that are produced in China must bear drug registration numbers issued by the NMPA, with the exception of certain Chinese herbs and Chinese herbal medicines in soluble form. Drug manufacturing enterprises must obtain the drug registration numbers before manufacturing any drug. A drug registration number issued by the NMPA is valid for five years and the applicant shall apply for renewal six months prior to its expiration date.

On January 22, 2020, the State Administration for Market Regulation promulgated the Revised Administrative Measures for Drug Registration which will become effective on July 1, 2020 (the "**Drug Registration Measures (2020)**") (《藥品註冊管理辦法 (2020) 》). According to the Drug Registration Measures (2020), drug registration is regulated according to the classification into Chinese medicine, chemical medicine and biological products. Where overseas research materials and data are used in an application to support drug registration, its source, research institutes or laboratory criteria, quality system requirements and other management criteria shall comply with the general principles of the ICH, and comply with the relevant requirements with regard to the drug registration. The NMPA

shall establish a system to expedite drug registration, and support drug innovation guided by clinical value. Where an application for drug registration satisfies the criteria, the applicant may apply for breakthrough therapy drug, conditional approval, prioritized/special review and approval. Drug registration inspection for overseas-manufactured drug shall be implemented by port pharmaceutical inspection agencies organized by the National Institutes for Food and Drug Control (中國食品藥品檢定研究院, the "NIFDC"), and for application for registration of overseas-manufactured drug, where an applicant applies for drug registration inspection prior to acceptance of the application for drug registration, it shall request for random sampling pursuant to the provisions, and deliver the samples, materials required for inspection and standard substances to the NIFDC.

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》) (the ''**Reform Plan**''), which outlined the reclassifications of drug applications under the Registration Measures. Under the Reform Plan, Category 1 drugs refer to 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. Generic drugs, that have equivalent quality and efficacy to the originator's drugs have been marketed abroad but not yet in China, fall into Category 3. Generic drugs, that have equivalent quality and efficacy to the originator's drugs and have been marketed in China, fall into Category 4. 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 NDA and the Imported Drug Application procedures under the Registration Measures, respectively.

According to the Special Examination and Approval of Registration of New Drugs (《新藥注冊特殊審批管理規定》), or the Special Examination and Approval Provisions, which was promulgated and implemented since January 7, 2009 by the SFDA, the NMPA 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 and abroad; (3) the new drugs are for treating AIDS, malignant tumors and orphan diseases, etc., and have obvious advantages in clinic treatment; or (4) the new drugs are for treating diseases with no effective methods of treatment.

The Special Examination and Approval Provisions provide 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.

Fast Track Approval for Clinical Trial and Registration

In November 2015, the CFDA released the Circular Concerning Several Policies on Drug Registration Review and Approval (《關于藥品注冊審評審批若干政策的公告》), which further clarified the following policies, potentially 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; (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 innovative 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 European Union 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 European Union 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.

On December 21, 2017, the NMPA promulgated the Opinions on Implementing Priority Review and Approval to Encourage Drug Innovation (《關於鼓勵藥品創新實行優先審評審批的意見》), which further clarified that a fast track clinical trial approval or drug registration pathway will be available to innovative drugs.

On May 17, 2018, the NMPA and NHC jointly promulgated the Circular on Issues Concerning Optimizing Drug Registration Review and Approval (《關於優化藥品註冊審評審批有關事宜的公告》), which further simplified and accelerated the clinical trial approval process.

Sampling and Collecting Human Genetic Resources Filing

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 on June 10, 1998, aimed at protecting and fair utilizing human genetic resources in the PRC. On July 2, 2015, the Ministry of Science and Technology issued 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》) ("**Service Guide**"), which became effective on October 1, 2015. According to the Service Guide, the sampling and collection of human genetic resources though clinical trials shall be required to be filed with the China Human Genetic Resources Management Office through the online system. On October 26, 2017, the Ministry of Science and Technology 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》), simplifying the approval of sampling and collecting human genetic resources for the purpose of listing a drug in the PRC.

According to the Regulations of 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 on May 28, 2019 and implemented on July 1, 2019, collecting human genetic resources of China's important genetic families and specific regions, or collection of those human genetic resources in such categories and quantities as prescribed by the administrative department for science and technology under the State Council, as well as preserving China's human genetic resources and providing the basic platform for scientific research shall be subject to the approval of the administrative department for science and technology under the State Council.

As for utilisation of China's human genetic resources for international cooperation in scientific research shall submit an application to the administrative department for science and technology under the State Council for approval. No approval is required in international clinical trial cooperation using China's human genetic resources at clinical institutions in order to obtain marketing authorization for relevant drugs and medical devices in China, which will not involve exit of materials of human genetic resources. However, the two parties shall file the type, quantity and usage of the human genetic resource to be used with the administrative department of science and technology under the State Council before clinical trials. If it is necessary to transport, deliver by post or carry China's materials of human genetic resources abroad for the purpose of international cooperation in scientific research on the basis of China's human genetic resources or due to other special circumstances, the exit certification of materials of human genetic resources issued by the administrative department for science and technology under the State Council shall be secured.

Administrative Protection and Monitoring Periods for New Drugs

According to the Registration Measures, the Implementing Regulations of the Drug Administration Law (《藥品管理法實施條例》) and the Reform Plan, the NMPA may, for the purpose of protecting public health, provide for an administrative monitoring period of 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.

Registration of Generic Drugs

According to the Registration Measures, the applicants which apply for registration of generic drugs shall be manufacturer of the same drugs. The applicant's drugs shall also be within the manufacturing scope specified in the Pharmaceutical Manufacturing Permit. Furthermore, clinical trials are required to be conducted in accordance with the Registration Measures. According to the Circular on Implementation of Record-filing Management of Bioequivalence Trials of Chemical Drug (《關于化學藥生物等效性試驗實行備案管理的公告》), the management of bioequivalence trials of chemical drug has been changed from examination and approval to record-filing. After completion of clinical trials, applicants for registration of generic drugs should submit materials of the respective clinical trials to the CDE. With reference to the technical review opinions, the NMPA will either grant a drug registration number or issue a disapproval notice.

Pursuant to the Opinions on Conducting the Consistency Evaluation for the Quality and Efficacy of Generic Drugs issued by the General Office of the State Council (《國務院辦公廳關于開展仿製藥質量和療效一致性評價的意見》) promulgated on February 6, 2016 and the Opinions of Relevant Matters Concerning Implementing the Opinions on Conducting the Consistency Evaluation for the Quality and Efficacy of Generic Drugs issued by the NMPA (《關于落實〈國務院辦公廳關于開展仿製藥質量和療效一致性評價的意見〉的有關事項的意見》) promulgated on March 31, 2016, generic drugs approved for marketing before the implementation of the new registration classification of chemical drugs, including domestic generic drugs, imported generic drugs and the indigenous varieties of the

original developed drugs, shall carry out consistency evaluation. In principle, the consistency evaluation should be completed before the end of 2018 for the oral solid preparations of generic chemicals approved for sale before October 1, 2007 listed in the National Essential Drug List (2012 version) (《國家基本藥物目錄(2012年版)》). For any other generic drugs approved for marketing before the implementation of the new classification of registration of chemical drugs, after a drug produced by a pharmaceutical enterprise passes the consistency evaluation, other pharmaceutical enterprises shall complete the consistency evaluation for their identical drugs within three years in principle; no registration will be granted in case of failure to do so as required within the prescribed time limit.

Pursuant to the Circular on Relevant Matters Concerning Consistency Evaluation for Quality and Curative Effect of Generic Drugs (《關于仿製藥質量和療效一致性評價有關事項的公告》) further promulgated by NMPA on December 28, 2018, the time limit for evaluation of the varieties included in the National Essential Drug List (2018 version) will no longer be set uniformly. For generic drugs, including essential drug varieties, approved for listing before the implementation of new registration and classification of chemical drugs, after the first variety has passed the consistency evaluation, the same variety of other drug manufacturers should complete the consistency evaluation within 3 years in principle. If it is not completed within the time limit, the enterprise may apply to the local provincial drug regulatory authority for an extension of the evaluation if it is deemed to be clinically necessary and in short supply in the market. If the registration is not completed within the prescribed time limit, it shall not be re-registered.

Regulations on Drug Manufacturing

Pursuant to the Drug Administration Law of the PRC and the Implementing Regulations of the Drug Administration Law, a drug manufacturing enterprise is required to obtain a drug manufacturing license (藥品生產許可證) 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. Pursuant to the Regulations of Implementation of the Drug Administration Law of the PRC and the Measures on the Supervision and Administration of the Manufacture of Drugs (《藥品生產監督管理辦法》, effective on August 5, 2004 and amended on November 17, 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.

The Good Manufacturing Practice for Drugs (2010 revised edition) (《藥品生產質量管理規範》, effective on March 1, 2011), 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 manner of handling customer complaints.

Pursuant to the Drug Administration Law of the PRC, the Measures on the Supervision and Administration of the Manufacture of Drugs (《藥品生產監督管理辦法》) and the Administrative Measures for Certification of the Good Manufacturing Practice for Drugs (《藥品生產質量管理規範認證管理辦法》, effective on August 2, 2011), the application for Good Manufacturing Practice (the

"**GMP**") certificate shall be made to the relevant drug supervision and administration department by the new drug manufacturer or existing drug manufacturer which builds a new drug production workshop or adds new production forms in 30 days after obtaining the drug manufacturing license or production approval, in order to obtain the relevant certificate. A GMP certificate shall be renewed at least six months prior to its expiration date upon re-examination by the relevant authority.

On 22 January 2020, the State Administration for Market Regulation promulgated the newly revised Administrative Measures on Supervision of Drug Manufacturing (the "**Revised Administrative Measures of Drug Manufacturing**") (《藥品生產監督管理辦法 (2020)》), which will take effect on 1 July 2020. The Revised Administrative Measures of Drug Manufacturing further implement the dug marketing authorisation holder system as stipulated in the Drug Administration Law of the PRC (《中華人民共和國藥品管理法》). Drug marketing authorisation holder entrusting others to manufacture preparations shall enter into an outsourcing agreement and a quality agreement with a qualified drug manufacturing enterprise and submit the relevant agreements together with the actual manufacturing site application materials to the competent drug administrative authority to apply for a drug manufacturing license. The Revised Administrative Measures of Drug Manufacturing no longer require GMP certificate for drug manufacturing enterprises, but the competent drug administrative authorities shall, based on regulatory needs, conduct compliance inspection of drug manufacturing quality control examination before drug marketing procedure.

Regulations on Drug Distribution

Medicine operation certificate

According to the PRC 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 issued by the SFDA on January 31, 2007 and came into effect on May 1, 2007, detailed provisions are imposed on aspects such as the purchase, sale, transportation and storage of medicines.

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 an Operation Certificate in respect of the retail pharmacy store. Once these permits are received, the wholesale or retail pharmaceutical company (as the case may be) shall be registered with the relevant local branch of the SAIC.

Under the Measures for the Administration of Pharmaceutical Operation Certificate (《藥品經營許可證管理辦法》) promulgated on February 4, 2004 and became effective from April 1, 2004 and amended on November 17, 2017 by the NMPA, 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.

Good supply practices

Each retail or wholesale operator of pharmaceutical products is required to obtain a GSP certificate from the relevant medicine administrative authorities prior to commencing its business. GSP

constitutes the basic standards in management of operation quality of medicines and shall apply to enterprises exclusively or concurrently engaged in medicine operation within China. The current applicable GSP standards require pharmaceutical operators to implement strict controls on its operation of pharmaceutical products, including standards regarding staff qualifications, premises, warehouses, inspection equipment and facilities, management and quality control. Under the Administrative Measures for Certification of Good Supply Practices (《藥品經營質量管理規範認證管理辦法》) promulgated on and became effective from April 24, 2003 by the NMPA, the GSP certificate is generally valid for five years and may be extended three months prior to the expiry of its valid term.

Regulations on Import and Export of Goods

Import and Export of Goods

Pursuant to the Administrative Provisions on the Registration of Customs Declaration Entities of the PRC (《中華人民共和國海關報關單位註冊登記管理規定》) (Order No. 221 of the General Administration of Customs, effective on March 13, 2014, amended on December 20, 2017 and May 29, 2018 respectively), the import and export of goods shall be declared by the consignor or consignee itself, or by a customs declaration enterprise entrusted by the consignor or consignee and duly registered with the customs authority. Consignors and consignees of imported and exported goods shall go through customs declaration entity registration formalities with the competent customs departments in accordance with the applicable provisions. After completing the registration formalities with the customs, consignors and consignees of the imported and exported goods may handle their own customs declarations at customs ports or localities where customs supervisory affairs are concentrated within the customs territory of the PRC.

Import and Export of Special Articles

Pursuant to the Administrative Provisions on the Sanitation and Quarantine of Entry/Exit Special Articles (《出入境特殊物品衛生檢疫管理規定》) (Order No. 160 of the General Administration of Quality Supervision, Inspection and Quarantine, effective on March 1, 2015 and amended on October 18, 2016, April 28, 2018, May 29, 2018 and November 23, 2018 respectively), the import or export of special articles, including micro-organisms, human tissues, biological products, blood and blood products shall be subject to the supervision and administration over health quarantine. The customs office is responsible for the health quarantine and approval of import and export of special articles in its relevant jurisdictions. The enterprise conducting import or export of special articles shall establish safety management system for special articles, and shall produce, use or sell the special articles in strict accordance with the purposes for the approval of such special articles.

Export of Drugs

According to the Approval by NMPA on Certain Issues of Pharmaceutical Products Export (《國家藥品監督管理局關于藥品出口有關問題的批覆》), promulgated and effective on September 20, 1999, whether the enterprise can obtain the right to operate import and export business and the qualification shall be approved by relevant foreign trade authority. The pharmaceutical products export shall mainly comply with the requirements of the importing country, so long as there is no special requirement by the importation country, the NMPA support the export in principal based on the national policy of encouraging exports. However, under the Pharmaceutical Administration Law, the export licenses issued by the relevant NMPA are required for the export of narcotics and psychotropic substances falling within the restricted scope prescribed by the State.

Other Related Regulations in the PRC Pharmaceutical Industry

Reimbursement under the National Medical Insurance Program

Pursuant to the Decision of the State Council on the Establishment of the Urban Employee Basic Medical Insurance Program (《國務院關于建立城鎮職工基本醫療保險制度的决定》) issued by the State Council on December 14, 1998 which took effect on the same day, 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 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》) on July 10, 2007 which took effect on the same day, under which urban residents of the pilot district, rather than urban employees, may voluntarily join Urban Resident Basic Medical Insurance. Pursuant 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 SCNPC on October 28, 2010, became effective on July 1, 2011, and amended on December 29, 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.

The Notice Regarding the Tentative Measures for the Administration of the Scope of Medical Insurance Coverage for Pharmaceutical Products for Urban Employee (《關于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》) ("**Measures for the Administration of the Scope of Medical Insurance Coverage for Pharmaceutical Products**"), jointly issued by several authorities including the Ministry of Labor and Social Security and the Ministry of Finance of the PRC ("**MOF**"), among others, on May 12, 1999, 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.

According to Measures for the Administration of the Scope of Medical Insurance Coverage for Pharmaceutical Products, the PRC Ministry of Labor and Social Security, together with other government authorities, has the power to determine the medicines included in the National Medical Insurance Catalog, which is divided into two parts, Part A and Part B. Provincial governments are required to include all Part A medicines listed on the National Medical Insurance Catalog in their provincial Medical Insurance Catalog, but have the discretion to adjust upwards or downwards by no more than 15% from the number of Part B medicines listed in the National Medical Insurance Catalog. As a result, the contents of Part B of the provincial Medical Insurance Catalogs may differ from region to region in the PRC.

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. The percentage of reimbursement for Part B medicines is stipulated by local authorities and in result may differs from region to region in the PRC.

National Essential Drug List

On August 18, 2009, MOH and eight other ministries and commissions in the PRC issued the Measures on the Administration of the National Essential Drug (Trial) and the Guidelines on the Implementation of the National List of Essential Drugs System (《關于建立國家基本藥物制度的實施意見》) which became effective on the same day, and the Provisional Measures on the Administration of the National Essential Drug List (《國家基本藥物目錄管理辦法》) (the "**Measures on Essential Drugs**") amended on February 13, 2015, which aim to promote essential medicines sold to consumers at fair prices in the PRC and ensure that the general public in the PRC has equal access to the drugs contained in the National Essential Drug List. NHC and NATCM ("**National Administration of Traditional Chinese Medicine**"(國家中醫藥管理局)) promulgated the National Essential Drug List (《國家基本藥物目錄(2018年版)》) on September 30, 2018 which became effective on November 1, 2018.

According to these regulations, basic healthcare institutions funded by government, which primarily include county-level hospitals, county-level Chinese medicine hospitals, rural clinics and community clinics, shall store up and use drugs listed in National Essential Drug List. The drugs listed in National Essential Drug List shall be purchased by centralized tender process and shall be subject to the price control by NDRC. Remedial drugs in the National Essential Drug List are all listed in the Medical Insurance Catalog and the entire amount of the purchase price of such drugs is entitled to reimbursement.

Price Controls

According to the Pharmaceutical Administration Law, the Regulations of Implementation of the Law of the People's Republic of China on the Administration of Pharmaceuticals, the pharmaceutical products are subject to fixed or directive pricing system or to be adjusted by the market. Those pharmaceutical products included in the Medical Insurance Catalogs and the National Essential Drug List and those drugs the production or trading of which are deemed to constitute monopolies, are subject to price controls by the PRC government in the form of fixed retail prices or maximum retail prices. Manufacturers and distributors cannot set the actual retail price for any given price-controlled product above the maximum retail price or deviate from the fixed retail price set by the government. The retail prices of pharmaceutical products that are subject to price controls are administered by the NDRC and provincial and regional price control authorities. From time to time, the NDRC publishes and updates a list of pharmaceutical products that are subject to price controls. According to the Notice Regarding Measures on Government Pricing of Pharmaceutical Products Issued by NDRC (《國家計委關于印發藥品政府定價辦法的通知》) effective on December 25, 2000, Maximum retail prices for pharmaceutical products shall be determined based on a variety of factors, including production costs, the profit margins that the relevant government authorities deem reasonable, the product's type, and quality, as well as the prices of substitute pharmaceutical products.

Further, pursuant to the Notice Regarding Further Improvement of the Order of Market Price of Pharmaceutical Products and Medical Services (《關於進一步整頓藥品和醫療服務市場價格秩序的意見》) jointly promulgated by the NDRC, the State Council Legislative Affairs Office and the State Council Office for Rectifying, the MOH, the NMPA, the MOFCOM, the MOF and Ministry of Labor and Social Security on May 19, 2006 and effective on the same day, the PRC government exercises price control over pharmaceutical products included in the Medical Insurance Catalogs and made an overall adjustment of their prices by reducing the retail price of certain overpriced pharmaceutical products and increasing the retail price of certain underpriced pharmaceutical products in demand for clinical use but that have not been produced in large quantities by manufacturers due to their low retail

price level. In particular, the retail price charged by hospitals at the county level or above may not exceed 115% of the procurement cost of the relevant pharmaceutical products or 125% for Chinese herbal pieces.

On May 4, 2015, the NDRC, the NHFPC, the MOHRSS, the Ministry of Industry and Information Technology of the PRC, the MOF, the MOFCOM and the NMPA issued the Opinion on Furthering Pharmaceutical Price Reform (《推進藥品價格改革的意見》) (the "**Price Reform Opinion**") and the Notice on Issuing the Opinion on Furthering Pharmaceutical Price Reform (《關於印發推進藥品價格改革意見的通知》) (the "**Price Reform Notice**"). Pursuant to the Price Reform Notice, government price controls on pharmaceutical products (other than narcotic drugs and psychiatric drugs of category I) will be lifted on June 1, 2015. According to the Price Reform Opinion, after price controls are lifted, prices of pharmaceutical products will be mainly determined by market competition. Instead of direct price controls, the government will regulate prices mainly by establishing a consolidated procurement mechanism, revising medical insurance reimbursement standards and strengthening regulation of medical and pricing practices.

Drug Purchases by Hospitals

According to the Opinion on the Guidance of the Reform of Urban Medical and Health Care System (《關于城鎮醫藥衛生體制改革的指導意見》) promulgated and took into effect on February 16, 2000 and the Opinion on the Implementation of Classification Management of Urban Medical Institutions (《關于城鎮醫療機構分類管理的實施意見》) promulgated on July 18, 2000 and became effective from September 1, 2000, a medical institution must be defined as a profit-making or non-profit-making institution at the time when it is established. A non-profit-making medical institution is established to provide services to the general public, with its revenue used for maintaining and developing such institution, while a profit-making medical institution is established by investors for the purpose of investment return. The PRC government does not establish any profit-making medical institutions, while non-government entities may establish profit-making medical institutions. Any non-profit-making medical institutions must implement a collective tender system in respect of any drug purchases and any profit-making medical institutions need not to implement such a system according to PRC law.

According to the Notice on the Trial Implementation of the Centralized Tender with Respect to Drug Purchases by Medical Institutions (《關于印發醫療機構藥品集中招標采購試點工作若干規定的通知》) promulgated and was effective on July 7, 2000, the Notice on the Further Standardizing of the Centralized Tender with respect to Drug Purchases By Medical Institutions (《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 and became effective on August 8, 2001 and the Opinions concerning Further Regulating Purchase of Medicines by Medical Institutions through Centralized Tendering (《關於進一步規範醫療機構藥品集中採購工作的意見》) promulgated and took into effect on January 17, 2009, any non-profit- making medical institutions established and/or controlled by any government at a county level or above must implement the centralized tender system in respect of purchase of any drugs which are contained in the Medicines List for National Basic Medical Insurance and are generally used for clinical purposes and purchased in relatively large amount.

The Circular on the Good Practice of Medical Institutions with respect to Centralized Procurement of Drugs (《醫療機構藥品集中採購工作規範》) promulgated and was effective on July 7, 2010, provides stipulations in detail in respect of the catalog for centralized procurement and methods,

procedures, evaluators, expert database construction and management of drugs, further regulating the centralized drug procurement and clarifying the code of conduct on the part of purchasing parties. According to the Good Practice of Medical Institutions with respect to Centralized Procurement of Drugs, any non-profit-making medical institutions established by the government at the county level or above or state-owned enterprises (including stock-holding enterprises) must participate in the centralized procurement of medical institutions. The centralized procurement management authority at provincial (municipal or district) level is responsible for compiling the catalog of drugs for centralized procurement by medical institutions within its own administrative region, and narcotic drugs and first class psychoactive drugs with respect to which the special administration is carried out by the state are not included in such catalog for centralized procurement; second class psychoactive drugs, radioactive pharmaceuticals, toxic drugs for medical use, crude drugs, traditional Chinese medicinal materials and traditional Chinese medicine decoction pieces may be excluded from such catalog for centralized procurement.

According to the Guidance Opinion of the General Office of the State Council on the Improvement of the Drug Centralized Procurement Work 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 and came into effect on February 9, 2015, the centralized procurement work of public hospitals will be improved through the classification purchase of drugs. All drugs used by public hospitals (with the exception of traditional Chinese medicine decoction pieces) should be procured through a provincial centralized pharmaceutical procurement platform. The provincial procurement agency should work out a summary of the procurement plans and budget submitted by hospitals and compile reasonably a drug procurement catalog of the hospitals with its own administration region, listing by classification the drugs to be procured through bids, negotiations, direct purchases by hospitals or to be manufactured by appointed manufacturers.

The Drug Centralized Procurement in "4+7 Cities" and Wider Areas

On November 15, 2018, the Joint Procurement Office published the Papers on Drug Centralized Procurement in "4+7 Cities" (《4+7藥品集中採購文件》, the "**Paper**"), which launched the national pilot scheme for drugs centralized tendering with minimum procurement quantities. The pilot scheme will be carried out in 11 cities, including Beijing, Tianjin, Shanghai, Chongqing, Shenyang, Dalian, Xiamen, Guangzhou, Shenzhen, Chengdu and Xian (the "**4+7 cities**").

On January 1, 2019, the General Office of the State Council also published the Notice of Issuing Pilot Program of the Centralized Procurement and Use of Drugs Organized 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》), which provides the detailed measures in the implementation of the national pilot scheme for drugs centralized tendering with minimum procurement quantities in the 4+7 cities.

According to the Implementing Opinions on Expanding the Pilot Program for Conducting Centralized Procurement and Use of Drugs by the State to Wider Areas (《關於國家組織藥品集中採購和使用試點擴大區域範圍的實施意見》) promulgated and came into effect September 25, 2019, together with the Documents on National Centralized Drug Procurement (GY-YD2019-2) (《全國藥品集中採購文件》) issued by the Joint Procurement Office on December 29, 2019, the model of centralized procurement with target quantity in the pilot program for conducting centralized procurement and use of drugs by the State will be promoted nationwide and all manufacturers of drugs within the scope of centralized procurement marketed in Mainland China, with the approval of the medical products administration, may participate in the pilot program.

The drug being offered for tender must belong to one of the following categories:

- an originator drug or reference preparations used for consistency evaluation designated by NMPA;
- a generic drug that has passed the consistency evaluation;
- a generic drug approved for registration according to the NMPA Notice No. 51(2016); or
- a drug included in the Catalogue of the Drugs Marketed in China.

The tenderer must also ensure that its annual production and sales capacity can satisfy the intended minimum quantity requirement.

Public hospitals must prioritize their drug purchasing from the successful bidder during the procurement cycle, calculated from the execution date of the successful bid result, until the quantity commitment has been satisfied. If the quantity commitment is satisfied, the excess is still procured at the selected price until the expiration of the procurement cycle.

Two-invoice System

In order to further optimize the order of purchasing and selling pharmaceutical products and reduce circulation steps, as required at the executive meeting of the State Council dated April 6, 2016 and under the 2016 List of Major Tasks in Furtherance of the Healthcare and Pharmaceutical Reforms (《深化醫藥衛生體制改革2016年重點工作任務》) issued by the General Office of the State Council on April 21, 2016, the ''two-invoice System'' (兩票制) will be fully implemented in the PRC. According to the Circular on Issuing the Implementing Opinions on Carrying out the Two-invoice System for Drug Procurement among Public Medical Institutions (for Trial Implementation) 《印發〈關於在公立醫療機(構藥品采購中推行「兩票制」的實施意見(試行)〉的通知》) (the ''**Circular**''), which was effective from December 26, 2016, the two-invoice system means one invoice between the pharmaceutical manufacturer and the pharmaceutical distributor, and one invoice between the pharmaceutical distributor and the hospital, and thereby only allows a single level of distributor for the sale of pharmaceutical products from the pharmaceutical manufacturer to the hospital. According to the Circular, two-invoice system will be promoted in pilot provinces (autonomous regions and municipalities directly under the Central Government) involved in the comprehensive medical reform program and pilot cities for public hospital reform on a priority basis, while other regions are encouraged to implement such system, so that such system can be promoted in full swing nationwide in 2018.

Drug recall

According to the Measures on Drug Recall (《藥品召回管理辦法》) effective from December 10, 2007, a drug manufacturer should establish and improve its recall system by collecting relevant information about drug safety and making an investigation and evaluation with respect to any drugs with potential safety hazards. If there are any potential safety hazards that endanger human health and life safety in respect of any drugs sold in PRC, such manufacturer must start the drug recall procedures. Where a drug is recalled, the drug operating units and users should assist such manufacturer to satisfy its recall obligations by communicating the drug recall information and any feedback, controlling and recovering such drugs according to the recall plan.

Advertising Restriction

Pursuant to the Drug Administration Law of the PRC and the Measures on the Examination of Pharmaceuticals Products Advertisement (《藥品廣告審查辦法》) promulgated on March 13, 2007 and amended on December 21, 2018, an enterprise seeking to advertise its pharmaceutical products must apply for an advertising approval code number. The code number is issued by the relevant local administrative authority. The validity term of an advertisement approval number for pharmaceutical drugs is one year. The content of an approved advertisement may not be altered without prior approval. Where any alteration to the content of the advertisement is needed, a new advertisement approval number shall be obtained by submitting a reapplication. On October 26, 2018, the SCNPC promulgated the PRC Advertising Law (《中華人民共和國廣告法》) (as amended in 2018), according to which certain contents shall not be included in advertisement of drugs, such as an assertion or guarantee on the efficacy or the safety, stating a cure rate or effective rate.

Pharmaceutical Directions and Labels of Pharmaceutical Products

According to the Measures for the Administration of the Pharmaceutical Directions and Labels of Drugs (《藥品説明書和標籤管理規定》) effective on June 1, 2006, the Pharmaceutical Directions and labels of drugs should be reviewed and approved by the NMPA. A Pharmaceutical Directions should include the scientific data, conclusions and information concerning drug safety and efficacy in order to direct the safe and rational use of drugs. The inner label of a drug should bear such information as the drug's name, indication or function, strength, dose and usage, production date, batch number, expiry date and drug manufacturer, and the outer label of a drug should indicate such information as the drug's name, ingredients, character, specifications, description of the drug's indications and contraindications, precautions, dosage, date of production, product batch number, valid term, approval number, manufacturing enterprise and any adverse reactions.

Commercial Briberies in Pharmaceutical Industry

Pursuant to the Regulations on the Establishment of Adverse Records with Respect to Commercial Briberies in the Medicine Purchase and Sales Industry (2013 revision) (《關於建立醫藥購銷領域商業賄賂不良記錄的規定(2013年修訂)》) enforced by the NHFPC and effective on March 1, 2014, 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 industrial and commercial administration, 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 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.

Environmental Regulations

Environmental Assessment and Acceptance of Environmental Protection Facilities

Pursuant to the Law of Environmental Impact Assessment of the PRC (《中華人民共和國環境影響評價法》) (Order No. 77 of the PRC President, effective on September 1, 2003 and amended on July 2, 2016, and December 29, 2018 respectively), Regulations on Environmental Protection Management for Construction Projects (《建設項目環境保護管理條例》) (Order No. 253 of the State Council, effective on November 29, 1998 and amended on July 16, 2017), Measures for the Administration of Environmental Protection Acceptance of Completed Construction Projects (《建設項目竣工環境保護驗收管理辦法》) (Order No. 13 of the State Environmental Protection Administration, effective on February 1, 2002 and amended on December 22, 2010), where effects may be exerted on the environment after the completion of construction projects, the construction enterprise shall submit an environmental impact report (form) or environmental impact registration form to the relevant environmental protection department. The project that is required to prepare the environmental impact report (form) in accordance with the law shall obtain the approval from the relevant environmental protection department for its environmental impact assessment documents; otherwise it shall not start the construction. After the construction project is completed, the construction enterprise shall apply for environmental protection acceptance of the construction project and make acceptance report pursuant to the standard and formality set by the environmental protection authority.

Regulations on Pollution Permit

Pursuant to the Administrative Measures on Pollutant Emission Permits (Trial) (《排污許可管理辦法(試行)》) (Order No. 48 of the Ministry of Environmental Protection, effective on January 10, 2018), enterprises, institutions and other producers and operators (the "pollutant discharge enterprises") that have been included in the Classification Management List for Fixed Source Pollution Permits shall apply for and obtain a discharge permit in accordance with the prescribed time limit. The pollutant discharge enterprises that are not included in the Classification Management List do not need to apply for a pollutant discharge permit. The pollutant discharge enterprise shall hold a pollutant discharge permit in accordance with the law and discharge pollutants in accordance with the discharge permit.

Pursuant to the Notice of the General Office of the State Council on Issuing the Implementation Plan for the Control of Pollutant Release Permit System (《國務院辦公廳關于印發控制污染物排放許可制實施方案的通知》) (No. 81 [2016] of the State Council's Office, effective on November 10, 2016) and 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)》) (Order No. 11 of the Ministry of Ecology and Environment, effective on December 20, 2019), the state implements a focused management, a simplification management and a registration management of emission permits based on the pollutant-discharging enterprises and other manufacturing businesses' amount of pollutants, emissions and the extent of environmental damage. The manufacturing of drug substance and manufacturing dose for chemical drugs (except for manufacturing of manufacturing dose for chemical drugs that are simply mixed or

repackaged) fall within the industries that are strictly regulated, shall obtain the discharge permit in accordance with the prescribed time limit.

Safety Management Supervision

Pursuant to the Law on Work Safety of the PRC (《中華人民共和國安全生產法》) (Order No. 70 of the PRC President, effective on November 1, 2002 and amended on August 27, 2009 and August 31, 2014 respectively), enterprises engaged in production activities must strengthen safety production management, establish and improve the responsibility system for safe production and ensure a safe production environment. The state establishes and implements a system for the accountability of production safety accidents. If the company fails to comply with the provisions of the Law on Work Safety, the supervisory authority on production safety may issue a rectification order, impose a fine, order the company to cease production and operation, or revoke the relevant permit.

Some chemical materials needed for new drug research and development, such as toluene and hydrochloric acid, are hazardous chemicals. Pursuant to the Regulations on Safety Management of Hazardous Chemicals (《危險化學品安全管理條例》) (Order No. 344 of the State Council, effective on March 15, 2002 and amended on March 2, 2011 and December 7, 2013, respectively), the production, storage, use, operation, and transportation of hazardous chemicals must be in accordance with the safety management regulations. The hazardous chemical units shall oblige to the safety conditions required by laws and administrative regulations and state and industry standards, establish and improve safety management rules and post safety responsibility systems, and provide safety education and legal education and occupation technical training for employees. Employees should accept such education and training, and may begin working only after qualifying the relevant assessment. Where it requires employees to have certain qualification to assume a post, an enterprise shall only designated employees having such qualification to assume the post.

Regulations on Employment

The Labor Contract Law of the PRC (《中華人民共和國勞動合同法》) (Order No. 65 of the PRC President, effective on January 1, 2008 and amended on December 28, 2012) and the Regulations on Implementation of the Labor Contract Law of the PRC (《中華人民共和國勞動合同法實施條例》) (Order No. 535 of the State Council, effective on September 18, 2008) provide for the establishment of labor relationship between employing entities and workers, as well as the concluding, performance, dissolution and revision of the labor contracts. To establish a labor relationship, a written labor contract shall be signed. In the event that no written labor contract is signed at the time when a labor relationship is established, such contract shall be signed within one month as of the date when the employing enterprise employs the employee.

Pursuant to Social Insurance Law of the PRC (《中華人民共和國社會保險法》), (Order No. 35 of the PRC President, effective on July 1, 2011, and amended on December 29, 2018), Interim Regulations on Collection and Payment of Social Insurance Premiums (《社會保險費徵繳暫行條例》) (Order No. 259 of the State Council, effective on January 22, 1999 and amended on March 24, 2019), Trial Measures for Enterprise Staff Maternity Insurance (《企業職工生育保險試行辦法》) (No. 504 [1994] the Ministry of Labor, effective on January 1, 1995), Regulations on Work-Related Injury Insurance (《工傷保險條例》) (Order No. 375 of the State Council, effective on January 1, 2004 and amended on December 20, 2010), and Regulations on Management of Housing Provident Fund (《住房公積金管理條例》) (Order No. 262 of the State Council, effective on April 3, 1999 and amended on

March 24, 2002, March 24, 2019, respectively), employing entity must pay basic pension insurance, unemployment insurance, basic medical insurance, work-related injury insurance, maternity insurance and housing provident fund for its employees. If an employing entity fails to go through the formalities or does not pay the full amount as scheduled, the relevant administration department shall order it to make rectification or make up the payment within the prescribed time limit. If the rectification for social insurance registration is not made within the stipulated period, the employing entity shall be imposed a fine. If the payment for social insurance premiums is not made within the stipulated period, the relevant administration department shall impose a fine. If an employing entity fails to undertake payment and deposit registration of housing provident fund or fails to go through the formalities of opening housing provident fund account for its employees by the expiration of the time limit, a fine shall be imposed. If an employing entity fails to make the payment and deposit of the housing provident fund within a prescribed time limit, an application may be made to the people's court for compulsory enforcement.

Product Liability

Under current PRC law, manufacturers and vendors of defective products in the PRC may incur liability for loss and injury caused by such products. Pursuant to the General Principles of the Civil Law of the PRC (《中華人民共和國民法通則》), or the PRC Civil Law, promulgated on April 12, 1986 and amended on August 27, 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.

On February 22, 1993, the Product Quality Law of the PRC (《中華人民共和國產品質量法》) was promulgated to supplement the PRC Civil Law aiming to define responsibilities for product quality 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 amended by the Ninth National People's Congress on July 8, 2000 and was later amended by the Eleventh National People's Congress on August 27, 2009 and the Thirteenth National People's Congress on December 29, 2018. Pursuant to the amended Product Quality Law, manufacturers who produce defective products may be subject to civil or criminal liability and have their business licenses revoked.

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 on October 31, 1993 and was amended on October 25, 2013 to protect consumers' rights when they purchase or use goods and accept services. All business operators must comply with this law when they manufacture or sell goods and/or provide services to customers. Under the amendment on October 25, 2013, all business operators shall pay high attention to protect the customers' privacy which they obtain during the business operation. In addition, in extreme situations, pharmaceutical product manufacturers and operators may be subject to criminal liabilities under applicable laws of the PRC if their goods or services lead to the death or injuries of customers or other third parties.

On May 28, 2020, the Civil Code of the PRC (《中華人民共和國民法典》) was adopted by the third session of the 13th NPC, which will become effective on January 1, 2021 and simultaneously replace the current effective General Principles of the Civil Law of the PRC, according to which, a patient may make a claim against the drug marketing authorization holder, a medical institution or producer for any damage arising from defects of drugs.

Regulations on Intellectual Property

Patent

Pursuant to the Patent Law of the PRC (《中華人民共和國專利法》) which was promulgated by the SCNPC on March 12, 1984 which became effective on April 1, 1985 and amended on September 4, 1992, August 25, 2000 and December 27, 2008, there are three types of patents in the PRC, namely invention patents, utility model patents and design patents and a patentable invention or utility model must meet three conditions: novelty, inventiveness and practical applicability. The State Intellectual CNIPA Property Office is responsible for receiving, examining and approving patent applications. A patent is valid for a term of 20 years in the case of an invention and a term of 10 years in the case of a utility model and design, starting from the application date. A third-party user must obtain consent or a proper license from the patent owner to use the patent except for certain specific circumstances provided by law. Otherwise, the use will constitute an infringement of the patent rights.

Trademark

Pursuant to the Trademark Law of the PRC (the "**Trademark Law**," 《中華人民共和國商標法》) which was promulgated by the SCNPC on August 23, 1982 and revised on February 22, 1993, October 27, 2001, August 30, 2013 and April 23, 2019, the revised provisions became effective on November 1, 2019 and the Regulation on the Implementation of Trademark Law of the PRC (《中華人民共和國商標法實施條例》), which was promulgated on August 3, 2002 and last amended on April 29, 2014 and became effective on May 1, 2014, trademarks are registered with the Trademark Office of the State Administration of Industry and Commerce. The Trademark Law adopts the principle of "first-to-file" while handling trademark registration. Where registration is sought for a trademark that is identical or similar to another trademark which has already been registered or pending in application for use in the same or similar category of commodities or services, the application for registration of such trademark may be rejected. Trademark registrations are effective for a renewable ten-year period, unless otherwise revoked. Trademark license agreements must be filed with the Trademark Office. The licensor shall supervise the quality of the commodities on which the trademark is used, and the licensee shall guarantee the quality of such commodities.

Trade Secrets

Pursuant to the PRC Anti-Unfair Competition Law (《中華人民共和國反不正當競爭法》) promulgated by the SCNPC on September 2, 1993 and as amended on November 4, 2017, 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, solicitation or coercion; (2) disclosing, using or permitting others to use the trade secrets obtained illegally under item (1) above; or (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. 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 on Taxation

Enterprise Income Tax

According to the Enterprise Income Tax Law of PRC (《中華人民共和國企業所得税法》), which was promulgated by the NPC on March 16, 2007, implemented on January 1, 2008, and subsequently revised on February 24, 2017 and December 29, 2018 respectively, and the Implementation Rules for the Enterprise Income Tax Law of the PRC (《中華人民共和國企業所得税法實施條例》) enacted on December 6, 2007 by the State Council and became effective on January 1, 2008, and amended on April 23, 2019 (collectively, the "**EIT Law**"), a resident enterprise shall pay EIT on its income originating from both inside and outside PRC at an EIT rate of 25%. Foreign invested enterprises in the PRC falls into the category of resident enterprises, which shall pay EIT for the income originated from domestic and overseas sources at an EIT rate of 25%. A non-resident enterprise having no office or establishment inside China, or for a non-resident enterprise whose incomes has no actual connection to its office or establishment inside China must pay enterprise income tax on the incomes derived from China at a rate of 10%.

Pursuant to the Administrative Measures on Accreditation of High-tech Enterprises (《高新技術企業認定管理辦法》), which was adopted by the Ministry of Science and Technology, the MOF and SAT on January 29, 2016, and took effect from January 1, 2016, qualifications of an accredited high-tech enterprise shall be valid for three years from the date of issuance of the certificate Upon obtaining the qualification as a high-tech enterprise, the enterprise shall complete tax reduction and exemption formalities with the tax authorities in charge pursuant to the provisions of Article 4 of these Measures.

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》) which was promulgated by the State Council on December 13, 1993, and amended on November 10, 2008, February 6, 2016 and November 19, 2017, and the Detailed Rules for the Implementation of the Provisional 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》) which was promulgated by the Ministry of Finance on December 25, 1993 and subsequently amended on December 15, 2008 and October 28, 2011 (collectively, the "**VAT Law**"), all enterprises and individuals that engage in the sale of goods, the provision of processing, repair and replacement services, sales of service, intangible assets and real estate and the importation of goods within the territory of the PRC shall pay value-added tax at the rate of 17%, except when specified otherwise.

In accordance with Circular on Comprehensively Promoting the Pilot Program of the Collection of Value-added Tax in Lieu of Business Tax (《關于全面推開營業税改徵增值税試點的通知》(財税[2016]36號)), which was promulgated on March 23, 2016 and came into effect on May 1, 2016, upon approval of the State Council, the pilot program of the collection of VAT in lieu of business tax shall be promoted nationwide in a comprehensive manner starting from May 1, 2016.

The Notice on the Adjustment to VAT Rates (《關於調整增值税税率的通知》), promulgated by the MOF and the SAT on April 4, 2018 and became effective as of May 1, 2018 adjusted the applicative rate of VAT, and the deduction rates of 17% and 11% applicable to the taxpayers who have VAT taxable sales activities or imported goods are adjusted to 16% and 10%, respectively.

According to the Announcement on Relevant Policies for Deepening Value-Added Tax Reform (《關於深化增值税改革有關政策的公告》(財政部、税務總局、海關總署公告2019年第39號)) promulgated by

MOF, SAT and General Administration of Customs on March 21, 2019 and became effective on April 1, 2019, with respect to VAT taxable sales or imported goods of a VAT general taxpayer, where the VAT rate of 16% applies currently, it shall be adjusted to 13%.

LAWS AND REGULATIONS RELATED TO OUR BUSINESS IN THE U.S.

Regulation of Drugs and Biologics

In the U.S., the FDA regulates drugs and biologics under the Federal Food, Drug, and Cosmetic Act, the Public Health Services Act, and their implementing regulations. Before a new drug or biologic may be approved and marketed, it must undergo extensive testing, development and regulatory review to determine that it is safe and effective and that its manufacturing processes are capable of ensuring the product candidate's identity, strength, quality, purity and potency. It is not possible to estimate the duration of this testing and development with respect to a given product candidate, although it often lasts many years and requires the expenditure of significant financial resources. The stages of this development process in the U.S. are generally as follows:

NDA, ANDA or BLA Preparation and Submission

Upon completion of product and manufacturing development, and preclinical and clinical trials, the sponsor assembles the statistically analyzed data from all phases of development, along with the chemistry and manufacturing and preclinical data and the proposed labelling, among other things, into a single marketing application, which, depending on the product candidate, may be a new drug application ("**NDA**"), a full biologic license application ("**BLA**"), an ANDA, or a BLA for a biosimilar product. The FDA carefully scrutinizes the submitted information and data to determine whether the sponsors and any other companies, such as CROs and laboratories working on the sponsor's behalf, have complied with the applicable regulations, and whether the drug or biologic is safe and effective for the specific use. Additionally, the FDA typically will inspect the facility or facilities where the product is manufactured, and will not approve an application unless it determines that the manufacturing processes and facilities, including contract manufacturers and subcontractors, are in compliance with GMP requirements and are capable of assuring consistent production of the product within required specifications. Additionally, before approving a marketing application, the FDA may inspect one or more clinical trial sites to assure compliance with GCPs. The FDA may also inspect others involved in the product candidate development process, such as preclinical trial sites and laboratories. Even after accepting the submission for review, the FDA may require additional testing or information before approval of the application. The FDA must deny approval of an application if applicable regulatory requirements are not satisfied. Moreover, after approval, some types of changes to the approved product, such as adding new indications, manufacturing and testing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval. Following product approval, drug and biologic products must continue to be manufactured and tested in accordance with the FDA's regulatory requirements, including GMPs.

FDA Enforcement

In the U.S., the FDA has authority to inspect facilities that conduct research on product candidates which are ultimately intended for marketing in the U.S., as well as facilities that manufacture and test products and product candidates intended for use in clinical trials or for marketing in the U.S. following FDA approval. The FDA may inspect such facilities, regardless of whether such facilities are located in the U.S. or overseas, including facilities belonging to entities

other than the product or product candidate sponsor. Inspections by the FDA have the objective of confirming compliance with FDA regulatory requirements, including GLPs, GCPs and GMPs, and identifying and requiring correction of noncompliant conditions.

Inspections undertaken by the FDA, in which the inspector observes conditions that do not comply with the applicable regulatory requirements, may result in the FDA issuing a Form 483. A Form 483 contains observations which, in the inspector's judgement, may constitute potential violations ranging from relatively minor to critical issues. The Form 483 does not constitute a final FDA determination of whether any condition constitutes a violation. Rather, the Form 483 is considered by the FDA, along with a full written report, evidence or documentation collected during the inspection, and any company responses. Based upon this information, the FDA determines what further action, if any, is appropriate. The inspected company is responsible for responding directly to the FDA with a corrective action plan addressing any cited objectionable conditions in the Form 483 and implementing that plan expeditiously.

The production of a Form 483 with significant or critical observations, or other determinations by the FDA of regulatory noncompliance can precipitate immediate and severe action by the FDA on the facility's operations and business, and may cause serious and sometimes irreparable damage to a company's reputation. Such actions may include, without limitation, costly corrective actions, rejection of study results as a basis for approval of marketing applications or supplements, restrictions on operations, including the discontinuation of services or closing of facilities, clinical holds, discontinuations or suspension of studies, warning letters, untitled letters, cyber letters, regulatory authority issuance of adverse public statements or alerts, product recalls, fines, restitution, disgorgement of profits or revenue, product seizure or detention, FDA debarment or suspension, FDA disqualification of testing facilities and investigators, consent decrees or other settlement agreements, injunctions, and civil and criminal penalties.

Good Laboratory Practice ("GLP"), Good Clinical Practice ("GCP") and Good Manufacturing Practice ("GMP")

Certain regulatory authorities, including the FDA, require that submissions made to them are based on research, analysis or development studies conducted in accordance with GLP and GCP provisions and guidelines.

GLPs set forth the minimum basic requirements for the conduct of *in vivo* or *in vitro* experiments in which a test article is studied prospectively in a test system under laboratory conditions to determine its safety. In the U.S., GLPs include a number of requirements relating to the conduct of preclinical studies, internal company organization and personnel, facilities, equipment, operations, test and control articles, study protocols, operating procedures, records and reporting, quality assurance, and the care and use of animals in testing. Other agencies, such as the U.S. Department of Agriculture, also have requirements concerning the conduct of certain animal research and may have requirements for registrations, licenses, approvals, assurances, permits, certificates and similar authorizations. Moreover, Institutional Animal Care and Use Committees review animal research protocols before animal research may commence.

GCPs set forth standards for the conduct of clinical trials in order to ensure that data and reported results are credible and accurate, and that the rights, safety, well-being, integrity and confidentiality of trial participants are protected. GCPs include requirements concerning clinical study

design, conduct, monitoring, auditing, analysis, recording and reporting, among other requirements. GCPs also require that all research subjects provide their informed consent in writing for their participation in any clinical trial and that all studies be reviewed and approved by an IRB.

Regulatory authorities also require that drugs and biologics, and their active pharmaceutical ingredients ("**API**"), intended for use in clinical trials or for the commercial market be manufactured and tested in accordance with GMP provisions and guidelines. The FDA requires that drug and biologic products used in clinical trials, approved products, and their API, be manufactured under GMPs. GMPs require that manufacturers and entities conducting certain laboratory testing adequately control manufacturing operations, which includes establishing quality management systems, quality control and assurance, obtaining raw materials that meet quality requirements, establishing operating procedures, detecting and investigating deviations, maintaining laboratory quality, maintaining records, samples and documentation, and ensuring the integrity of manufacturing and testing data. Poor control of production and testing processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of products or product candidates. Manufacturers and other entities involved in the manufacture of drugs and biologics, including control and contract laboratories, are required to annually register their establishments with the FDA. Certain facilities identified in regulatory applications and submissions, including facilities approved to produce finished dosage forms or API, biolanalytical study sites, CROs, and contract analytical testing sites must also annually provide identification information to the FDA. Additional state licenses, permits, and registrations may also be required.

Records for laboratory research, clinical studies, and manufacturing and testing must be maintained for specified periods for inspection by the FDA and other regulators. The FDA requires that electronic records and electronic signatures meet additional requirements to be considered trustworthy, reliable and generally equivalent to paper records and handwritten signatures. Noncompliance with GLP, GCP or GMP requirements can result in the disqualification of data collected during the clinical trial, as well as other enforcement actions.

Regulation of Controlled Substances

The use, research, testing, import and export, and manufacture of controlled substances and listed chemicals is regulated in the U.S. by the DEA through the Controlled Substances Act and the DEA's implementing regulations. The DEA regulations cover registration, security, recordkeeping, reporting, storage, shipping, distribution, acquisition, inventory and other requirements relating to controlled substances. The DEA regulates controlled substances as Schedule I, II, III, IV or V substances. The DEA also regulates chemicals that, in addition to legitimate uses, are used in the manufacture of controlled substances, and designates such chemicals as List I or List II chemicals. The DEA imposes additional requirements for Scheduled Listed Chemicals and requires registration for entities that manufacture, import, distribute, sell or export List I and Scheduled Listed Chemicals and also imposes record-keeping, security and reporting requirements. The DEA also establishes quotas for the manufacture, importation, and procurement of Scheduled Listed Chemicals. In addition, the DEA imposes specific requirements and restrictions for the retail sale of drug products containing a Scheduled Listed Chemical. Entities that handle only List II chemicals are not required to register with DEA but are subject to certain record-keeping and reporting requirements.

Fraud and Abuse and Anti-Corruption Laws and Regulations

Existing U.S. laws governing federal healthcare programs, including Medicare and Medicaid, as well as similar state laws, impose a variety of broadly described fraud and abuse prohibitions on healthcare providers, including clinical laboratories. These laws are interpreted liberally and enforced aggressively by multiple government agencies, including the U.S. Department of Justice, the U.S. Department of Health and Human Services' Office of Inspector General, and various state agencies.

In the event we collaborate with or invest in CROs, we may be subject to many federal and state healthcare laws, such as the federal Anti-Kickback Statute, the federal civil and criminal False Claims Acts, the civil monetary penalties statute and other laws relating to patient inducements, the Medicaid Drug Rebate statute and other price reporting requirements, the Veterans Health Care Act of 1992, the Patient Protection and Affordable Care Act of 2010, and similar state laws. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse, reimbursement programs, government procurement, and patients' rights may be applicable to our business. We would be subject to healthcare fraud and abuse regulation by both the federal government and the states in which we conduct our business.

We seek to conduct our business in compliance with all U.S. and state fraud and abuse laws. Sanctions for violations of these laws may include penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, suspension and debarment from government contracts, and refusal of orders under existing government contracts exclusion from participation in U.S. federal or state healthcare programs, corporate integrity agreements, and the curtailment or restructuring of our operations, any of which could materially adversely affect our ability to operate our business and our financial results.

Achieving and sustaining compliance with applicable federal and state reimbursement and fraud laws can prove costly. Any action against us for violation of these laws, even if we successfully defend against it could cause us to incur significant legal expenses and divert our management's attention from the operation of our business.

We are required to comply with the U.S. Foreign Corrupt Practices Act ("**FCPA**") and other U.S. and non-U.S. anti-corruption laws, which prohibit companies from engaging in bribery, including improperly offering, promising or providing money or anything else of value to non-U.S. officials and certain other recipients. It is our policy to implement safeguards to prohibit these practices by our employees and business partners with respect to our operations. In some cases, companies that violate the FCPA may be debarred by the U.S. government and/or lose their U.S. export privileges.

The Defense Production Act of 1950

Under the Defense Production Act of 1950, as amended by several later pieces of legislation, including most recently the Foreign Investment Risk Review Modernization Act of 2018 ("**DPA**"), the president of the U.S. is authorized to prohibit or suspend acquisitions, mergers or takeovers by foreign persons engaged in interstate commerce in the U.S. if the president determines that there is credible evidence that such foreign persons in exercising control of such acquired persons might take action that threatens to impair the national security of the U.S. and that other provisions of existing law do not provide adequate authority to protect national security. On October 10, 2018, the U.S. Department of Treasury (as the chair of CFIUS) issued interim regulations implementing certain provisions of the

Foreign Investment Risk Review Modernization Act of 2018 (the "**FIRRMA interim regulations**"). The FIRRMA interim regulations initiate a pilot program which, among other changes, expands CFIUS jurisdiction to cover not only controlling investments, but also certain non-controlling investments involving foreign persons in U.S. businesses that utilize "critical technologies" in activity within or aimed at one of twenty-seven (27) designated industry sectors ("**Pilot Program Industries**"), and requires mandatory declarations advising CFIUS of foreign investments in such businesses (the "**CFIUS Pilot Program**"). The DPA and the FIRRMA interim regulations define "critical technologies" broadly, in a manner which includes certain biotechnology-related products, services or materials, and the definition may expand over time, as the U.S. government has the authority to further develop the set of technologies of interest through rulemaking. The FIRRMA interim regulations formally took effect on November 10, 2018 and are expected to remain in effect until such time as they are replaced by final regulations implementing the DPA.

Under the CFIUS Pilot Program, a party or parties to certain transactions that (i) close after November 10, 2018; (ii) involve certain types of investments by foreign persons in U.S. businesses; (iii) involve a U.S. business that produces, designs, tests, manufactures, fabricates or develops one or more critical technologies; and (iv) involves a U.S. Business that utilizes those critical technologies in activity within or aimed at one or more Pilot Program Industries, must submit a declaration with basic information regarding such transaction with CFIUS (unless the parties elect to file a notice instead) prior to the closing of the investment. Filing a declaration with CFIUS will be mandatory in such cases when the foreign party in the transaction will gain control of the U.S. target business as a result of such transaction or when the transaction grants the foreign party (i) a board seat, observer or nomination right, (ii) access to non-public information about the target's technologies, or (iii) any other form of involvement in the use, development, acquisition or release of the target's critical technologies. Declarations must be filed no later than forty-five (45) days before the closing of the transaction. Once a declaration has been accepted by CFIUS, CFIUS has thirty (30) calendar days to determine its subsequent action, including approving the transaction, requesting that the parties file a notice or initiating a unilateral review, among others.

As we may be deemed a "foreign person" under the DPA, some biotechnology products and their applications may fall under the scope of critical technologies and may involve Pilot Program Industries. As a result, our future investments in or acquisitions of U.S. biotechnology businesses may be subject to the mandatory CFIUS filing and review process if and to the extent the U.S. target business produces, designs, tests, manufactures, fabricates or develops critical technology.

The FIRRMA interim regulations generally do not limit the scope and sustainability of ongoing research and development activities or revenue-generating services provided by us to our customers. Nor do the FIRRMA interim regulations generally limit arm's-length research collaborations and business partnerships between us and academic/industrial institutions, except to the extent that such relationships involve us taking an equity stake in a U.S. business or joint venture involving a U.S. business, in which case the FIRRMA interim regulations may be implicated.

The breach of the above prohibition may lead to personal civil liability of its author. In addition, the French judge may take temporary measures in order to stop such breach, such as the prohibition of any action whereby the protected trade secret would be used or disclosed, the destruction of any support on which the trade secret has been reproduced illegally etc.

Notwithstanding the above, trade secrets cannot trump freedom of speech, including freedom of the press as proclaimed in the Charter of Fundamental Rights of the European Union. Neither can trade

secrets be invoked against the exercise of the right of alert, nor against the right of information and consultation of employee representatives.

LAWS AND REGULATIONS RELATED TO OUR BUSINESS IN THE EU

Drug Authorisation

Drugs may only be marketed within the EU/EEA, if the competent authority has granted a valid Marketing Authorisation ("MA") for the respective product. Before a MA is issued, the competent authority will assess the quality, efficacy and safety of a product. The national regulations on the authorisation of drugs for human use have been harmonized in the European Union ("EU")/European Economic Area ("EEA") by the Directive 2001/83/EC. It covers regulations for drugs on their (a) placing on the market, (b) manufacture and importation, (c) labelling a packaging, (d) wholesale distribution, (e) advertising, (f) pharmacovigilance and (g) supervision. Marketing Authorisations on basis of this Directive may only be granted to an applicant established in the European Community. Marketing Authorisations on basis of this Directive may only be granted to an applicant established in the European Community.

General Procedures of Marketing Authorisation

A marketing authorisation is either granted by the national regulatory authorities of the member states, or by the European Commission (with such process handled by the European Medicines Agency ("EMA"), depending on the procedure that is used to obtain the marketing authorisation. There are four different types of procedures: (1) the national procedure, (2) the mutual recognition procedure, (3) the decentralized procedure and (4) the centralized procedure.

The national procedure should be used by an applicant that is seeking a MA in only one member state and which is not compelled to use the centralized procedure due to the nature of the product (for example biosimilars). The national procedure is not permitted where a MA is already held in any member state of the EU.

The mutual recognition procedure ("MRP") is used to facilitate the grant of a MA where the pharmaceutical product already holds a national MA in a member state at the time of application. One member state known as the Reference Member State ("RMS") assesses the product first and further MAs can be sought from other member states, known as concerned member states ("CMS").

The decentralized procedure ("DCP") is used to simultaneously apply for MAs in more than one member state if the pharmaceutical product has not yet been authorized in any member state. If a MA has already been granted or applied for in another member state, the MRP should be used.

In the centralized procedure the EMA is responsible for the scientific evaluation of centralized marketing authorisation applications (MAA). Once granted by the European Commission, the centralized MA is valid in all EU member states, Iceland, Norway and Liechtenstein. The legal framework of this procedure is governed in Regulation 726/2004/EC, which requires or declares eligible certain drugs (such as biological drugs, orphan drugs and advanced therapy drugs) to use the centralized procedure.

This authorisation procedure allows pharmaceutical companies to submit a single marketing authorisation application to the EMA and to market the drug and make it available to patients and healthcare professionals throughout the European Economic Area on the basis of a single marketing authorisation.

Mandatory Centralized Procedure for Biosimilars

For some kind of drugs, applicants are compelled to use the centralized procedure. This is the case with biosimilars. A biosimilar is a biological drug highly similar to another already approved biological drug in the EU, for which marketing exclusivity rights have expired. The EMA is responsible for evaluating the majority of applications to market biosimilars before they can be approved and marketed in the EU. In this regard developers of biosimilars are required to demonstrate through comprehensive comparability studies with the 'reference' biological drug that (1) their biological drug is highly similar to the reference drug, notwithstanding natural variability inherent to all biological drugs and (2) there are no clinically meaningful differences between the biosimilar and the reference drug in terms of safety, quality and efficacy.

In contrast to generics, biosimilars must undergo phase III clinical trials in a particularly sensitive patient population to demonstrate similarity to the reference product. The clinical studies are designed to show that differences between the reference product and the biosimilar are not clinically significant.

The clinical development of a biosimilar starts with investigations to prove pharmacodynamics and pharmacokinetics comparable to the reference product. Studies to prove tolerability (including immunogenicity studies) are a part of these analyses. These data are then supplemented by a Phase III study to establish clinical comparability and confirm the biosimilar's tolerability and efficacy in a sensitive patient population.

Based on those requirements, Techdow had to prove the similarity of its Enoxaparin-Biosimilar (Inhixa®) to its reference product (Clexane®) by providing results of appropriate preclinical tests or clinical trials as part of the centralized marketing authorization procedure.

Legal effect of a Marketing Authorisation issued within the centralized procedure

A granted MA allows the Marketing Authorisation Holder ("MAH") as well as a local representative of the MAH to place the drug on the market of all EU member states, Iceland, Norway and Liechtenstein.

The marketing authorisation is granted exclusively to the applicant for the authorisation of the specific drug in Europe. The drugs have the same packaging sizes all over Europe and are listed under the same name.

Authorised drugs are registered in the Union Register of medicinal products. It lists all medicinal products for human and veterinary use as well as orphan medicinal products that have received a marketing authorisation by the Commission through the centralised procedure.

A marketing authorisation is generally issued for a term of five years and can be renewed upon application. Thereafter, the marketing authorisation should normally be of unlimited validity unless otherwise determined by the competent regulatory authority. However, there are some circumstances that lead to the expiry of a marketing authorisation. For example a marketing authorisation shall expire, if the authorised drug is not placed on the market within three years of the granting of the marketing authorisation, or if the authorised drug, that was placed on the market in accordance with the marketing authorisation, is not placed on the market for three successive years (sunset clause).

Requirements for the MAH after obtaining a MA

Pharmacovigilance

Due to the fact, that the knowledge of the safety of drugs is not complete at the time of their first market authorisation, experiences gained from the use of a pharmaceutical product have to be systematically collected and evaluated after the approval. Therefore, the MAH must operate a pharmacovigilance system. The overall EU pharmacovigilance system operates through cooperation between the EU Member States, EMA and the European Commission. In some Member States, regional centres are in place under the coordination of the national competent authority.

Legal requirements related to the European Medicines Agency (EMA or the Agency) pharmacovigilance system for human medicines are laid down in Regulation (EC) No 726/2004, Directive 2001/83/EC and Commission Implementing Regulation (EU) No 520/2012.

The safety of biosimilars is monitored through pharmacovigilance activities in the same way as for other medicines.

To monitor the pharmacovigilance requirements pharmaceutical entrepreneurs are obliged to engage a Qualified Person for Pharmacovigilance (QPPV). This person is an individual residing within the European Economic Area (EEA) and is personally responsible for the safety of a human pharmaceutical product within the EEA. His/her key roles are to establish and maintain pharmacovigilance system, to act as the contact person for competent authorities and to oversee the safety profiles of marketed products and any emerging safety concerns.

Compliance with Directive on falsified medicines for human use

In July 2011, the EU strengthened the protection of patients and consumers by adopting a new Directive on falsified medicines for human use. The Directive came into force on 21 July 2011 and aims to prevent falsified medicines entering the legal supply chain and reaching patients.

As one introduced safety control measure, MAHs are – as of 9 February 2019 – obliged to place two safety features on the packaging of most prescription-only medicines and some over-the-counter medicines. These are a unique identifier (a 2-dimension barcode) and an anti-tampering device placed on the packaging of their products.

Additionally, pharmaceutical entrepreneurs must fulfil a number of obligations, that require the connection to the European Medicines Verification System ("EMVS").

Drug Manufacturing and Import in the EU

The manufacture and import of drugs in the EU are subject to a manufacturing and import authorisation. In order to obtain a manufacturing authorisation the applicant shall have at his disposal, suitable and sufficient premises, technical equipment and control facilities complying with the requirements for manufacture, control and storage of drugs. Furthermore, it is compulsory to have at least one qualified person that is responsible to guarantee compliance with manufacturing requirements. To ensure this obligation, a manufacturer can relate to the principles and guidelines of the good manufacturing practice (GMP), he also has to act compliant with.

According to the Directive 2003/94/EG for compliance with GMP, all manufacturers should operate an effective quality management system of their manufacturing operations, which requires the

implementation of a pharmaceutical quality assurance system. The principles and guidelines of GMP should be set out in relation to quality management, personnel, premises and equipment, documentation, production, quality control, contracting out, complaints and product recall, and self-inspection.

To ensure that a drug manufacturer complies with GMP, the competent authorities of the Member States conduct repeated inspections according to Article 111 of the Directive 2001/83/EG. If the competent authority determines the compliance of the activities of the manufacturer with GMP it grants a GMP-certificate, that confirms the status of the permanent establishment at the time of the inspection.

In the EU, international GMP certificates by foreign public authorities may be recognized by the competent authority. The EU member states generally accept GMP audits/inspections and approvals of the competent national authorities of other EU member states because of the harmonization of the quality and pharmacovigilance regulations on the EU level. However, the sale and import of pharmaceuticals in other countries outside of the EU often requires an additional inspection and approval of the concrete manufacturing site by the foreign national public authority responsible for the supervision of manufacturing activities in the targeted country/market (e.g. the FDA concerning imports to the US). This concept applies for most Western countries.

Furthermore, for drugs imported from third countries, the importer shall ensure that they have been manufactured in accordance with standards which are at least equivalent to the GMP standards laid down by the EU.

From a regulation standpoint, the manufacturing of biosimilars follows in principe the same rules as the manufacturing of other drugs. However, due to its complex and sensitive product characteristics, the manufacturing of biosimilars requires particular care, as even the smallest changes in the manufacturing process may pose safety risks on the product.

Drug Distribution in the EU

In countries of the EU, entities active in the distribution of pharmaceutical products require a wholesale authorisation to permissibly procure, store and/or distribute pharmaceutical products. The wholesale authorisation is issued by the national competent authority of the Member State where the entity carries out the distribution activities. The same national authority is also responsible for inspecting the wholesale distributor.

Wholesale distributors must comply with the EU Good Distribution Practice (GDP) to obtain a wholesale authorisation. They can ensure that they meet all their legal obligations, laid down in Article 84 of the Directive 2001/83/EC, by following the GDP guidelines.

The compliance with GDP is approved with the granting of a GDP-certificate by the competent authority. According to the process in regard to a GMP-certificate, the competent authority conducts an inspection of the site of the wholesale distributor and examines its activities in respect of GDP-compliance. The GDP-certificate reflects the status of the premises at the time of inspections and should be renewed latest five years after the inspection, unless otherwise determined by the competent regulatory authority.

Reimbursement in the EU

Reimbursement of prescription-only pharmaceutical products under the existing social security systems is key for successfully marketing such products in the EU and internationally. However, there

is no EU harmonization on the level of healthcare provided under national social security systems for the pricing and reimbursement for prescription-only pharmaceutical products. Rather, national legislators and the respective authorities in the EU (and elsewhere) are generally free to decide on the medicinal treatments they wish to reimburse and the prices they are willing to pay under their social security systems.

That being said, the pharmaceutical pricing and reimbursement systems established by EU countries differ significantly and are relatively complex. Each country uses different schemes and policies, adapted to its own economic and health needs. Also, these national systems are regularly reviewed or adapted in order to take account of political priorities, market developments, and patients' needs.

LAWS AND REGULATIONS RELATED TO OUR BUSINESS IN SELECTED EU COUNTRIES

Poland

General Regulatory Framework

Key legal acts concerning the medicinal products for human use:

(a) Polish act on Pharmaceutical law dated September 6, 2001 (Journal of laws 2019 item 499, as amended) ("**Pharmaceutical Law**");

(b) Directive 2001/83/EC of the European Parliament and of the Council of November 6, 2001 on the Community code relating to medicinal products for human use;

(c) Commission Directive 2003/94/EC of October 8, 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use;

(d) Regulation (EC) no 726/2004 of the European Parliament and of the Council of March 31, 2004 laying down Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency; and

(e) Numerous secondary legislation, in particular ordinances of the Polish Ministry of Health, such as the Ordinance of the Minister of Health on the Requirements of Good Manufacturing Practice dated November 9, 2015.

Marketing Authorization

No medicinal product may be placed on the market unless the relevant authorization has been issued by the competent authority. A marketing authorization is a decision issued by the competent authority confirming that a medicinal product may be marketed in a specific territory. The authorization is issued on the basis of the evaluation of the product's safety, therapeutic efficacy and quality.

The system for authorizing the marketing of a medicinal product within the broadly defined EU legal system involves the existence of separate national procedures in this respect, provided, however, that Member States' legal systems contain similar categories of procedures based on the same standards created by Directive 2001/83. This system also provides for the participation of the European

Commission and the EMA in the so-called centralized procedure, under which certain categories of medicinal products are authorized. Decisions made in the centralized procedure enable a medicinal product to be authorized throughout the EU. Other medicinal products (not being subject to the centralized procedure), to be placed on the market in EU countries are subject to national procedures. The President of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products (President of the URPL) is the authority authorizing medicinal products for marketing in the territory of the Republic of Poland. The President of the URPL has been granted the competence to issue marketing authorizations for medicinal products. The description of the procedures for authorizing medicinal products for marketing and all the related formal requirements, are contained in the Pharmaceutical Law.

Import Authorization

Importation is any activity consisting in importing finished medicinal products from outside the EU or the European Free Trade Association (EFTA) Member States—parties to the European Economic Area (EEA) Agreement, including in particular the storage, quality control at batch release and distribution of such products. Consequently, the sole transport of medicinal products between EU or EFTA Member States is not considered as importation of medicinal products, but rather as wholesale trade in medicinal products.

Pursuant to Article 38(1) of the Pharmaceutical Law, in order to commence business activity in the field of importing medicinal products, it is necessary to obtain an importation authorization. The Main Pharmaceutical Inspectorate (Główny Inspektor Farmaceutyczny, GIF) is the authority competent to issue, refuse to issue, withdraw, or change the authorisations. GIF is also obliged to send a copy of the decision to grant an authorization for the manufacturing and/or importation of medicinal products to the European Medicines Agency (EMA).

Pursuant to Article 39(1) of the Pharmaceutical Law, the applicant seeking an authorization to import a medicinal product must append the application for the authorization with the Place of Business Documentation prepared in accordance with the requirements of the Good Manufacturing Practice, and a list containing the names, doses and pharmaceutical forms of the medicinal products to be imported.

Applications for medicinal product importation authorisations are processed within 90 days of the date of their submission. The running of this period may be suspended if the application needs to be supplemented.

Importation authorisations for medicinal products are granted for an unlimited period of time. If the importer of a medicinal product no longer fulfills the obligations laid down in Article 43(1) of the Pharmaceutical Law or the requirements specified in the authorization, the GIF will revoke, by way of a decision, the authorization to import medicinal products.

Importers of medicinal products are obliged to, without limitation:

(a) import only those medicinal products which are covered by the authorization; (b) distribute the imported medicinal products;

(c) give written notice to the GIF at least 30 days in advance of any intended modification of the conditions of importation of the medicinal product, and in particular to notify the GIF without undue delay of the need to replace a qualified person;

(d) send the following to the GIF: an up-to-date place of business documentation, an up-to-date complete list of imported medicinal products;

(e) keep archive samples of products;

(f) make available to the GIF, for inspection, the premises where the medicine importation activity is carried out, the documentation and other data regarding the importation of the product, and enable the GIF to take samples;

(g) enable the qualified person to perform his or her duties;

(h) comply with the requirements of Good Manufacturing Practice;

(i) ensure, on the basis of a risk assessment, that excipients for the manufacture of medicinal products have been manufactured in accordance with the Good Manufacturing Practice for excipients;

(j) notify the GIF and the Marketing Authorization Holder of any suspected falsification of the product.

Reimbursement

In Poland, the main purpose of reimbursement is to ensure that the public payer (the National Health Fund) contributes to the purchase cost of a given product. However, this contribution should be understood more broadly as the fulfillment of the obligation to protect the health of citizens, which is regulated in Article 68(1) and (2) of the Constitution of the Republic of Poland. In fact, the protection of life and health is treated as a public subjective right realized through a system of guaranteed services financed from public funds, which also includes the reimbursement system. This care is to be based on equal access to health care services financed from state funds, independent of the income criterion. The rules for establishing the reimbursement budget, the manner of setting fixed prices and margins for pharmacy reimbursement and maximum prices and margins for the inpatient sector, the regulation of decision-making criteria concerning inclusion in the list of reimbursed products and setting of the official purchase price, and the maximum time limits for the completion of the reimbursement procedure, are set out in the act on reimbursement of medicines, foodstuffs for special nutritional uses and medical devices dated 12 May 2011 (Journal of laws 2019, item 784, as amended) ("**Reimbursement Act**").

Official prices and margins used in the trading of reimbursed products are one of the cornerstones of the current reimbursement system. This involves the obligation for the individual marketing participants to comply with the official prices calculated as the official purchase prices plus the margins due in accordance with the Reimbursement Act. In the case of reimbursed products these margins can be broken down into fixed prices and margins for prescription products available in pharmacies and maximum prices and margins for reimbursed products used in the inpatient system: included in the chemotherapy list and drug programs.

Based on the current regulations, the analyzed budget is established as a maximum amount—the amount of funds spent on reimbursement may not exceed 17% of the total amount of public funds allocated for financing guaranteed services from public funds in the National Health Fund's financial plan.

The Reimbursement Act provides for a statutory payback mechanism consisting in the obligation for the recipients of reimbursement decisions (businesses) to return a portion of the amounts obtained from reimbursement.

Applications for reimbursement can be submitted by marketing authorization holders, foodstuff business operators, manufacturers or distributors of medical devices, or their representatives (applicants).

The second stage of the reimbursement procedure, once the application has been submitted, consists of price negotiations with the Economic Committee, concluding with the Committee's presenting its position in a resolution. The negotiations are conducted by the Committee's negotiating team consisting of five members, who discuss the reimbursement terms proposed by the applicant. The maximum time limit for the completion of all reimbursement procedures is 180 days irrespective of whether or not the product applied for has reimbursed equivalents. However, in practice, decisions in procedures concerning reimbursed equivalents are issued within a shorter time, usually within 60 days from the date of submission of the reimbursement application. Such procedures do not involve the evaluation of pharmacoeconomic analyzes, which are therefore not attached to the reimbursement application.

If there is no reimbursed equivalent, the whole range of HTA analyzes must be submitted and then evaluated by expert bodies, along with an additional fee for the verification analysis. Reimbursement for a given product is granted by way of an administrative decision issued by the Minister of Health.

All reimbursement decisions—regardless of the availability category of the given product—include: the identity of the applicant, the identification details of the product to be refunded, the reimbursement availability category, the level of co-payment and definition of the limit group, and also the official purchase price, the date of the decision's becoming effective and the validity period of the decision.

Under the Reimbursement Act, the final reimbursement decision creates the basis for the inclusion of a given product in the list of reimbursed products as of the effective date indicated in the decision. Importantly, the reimbursement notice not only includes all the information contained in the reimbursement decision, but also new items calculated on the basis of statutory mechanisms. However, according to administrative courts, the notice remains informative only and it is rather the valid reimbursement decision that is the grounds for the reimbursement of a given product.

Brokers Arrangement

The Pharmaceutical Law provides also requirements for entities that intends only to act as an agent in trading medicinal products.

The major requirement from such entity is registration in the (Polish) National Register of Brokers of Medicinal Products runned by GIF.

The intermediation cannot cover wholesale trade in medicinal products and the supply of such products.

Intellectual Property

Legal Framework

Protection of industrial property in Poland includes inventions, industrial designs, trademarks, utility models, geographical indications and topographies of semiconductor products. The first three

categories of goods are most significant in business practice. Thus the following overview will provide more detail in this respect.

In order to obtain protection for an invention, utility design, trademark or industrial design, an application should be filed with the Polish Patent Office (PPO). Two main institutions responsible for industrial property protection in the EU are EUIPO (European Union Intellectual Property Office), which provides trademark and design protection, and the EPO (European Patent Office), which grants patent protection.

From the IP perspective the key Polish legal acts are the following:

(a) the Polish industrial protection law dated June 30, 2000 (Journal of laws 2017, item 776, as amended) ("**Industrial Property Act**");

(b) the Polish act on copyright and related rights dated February 4, 1994 (Journal of laws 2019, item 1231, as amended); and

(c) the Polish civil code dated April 23, 1964 (Journal of Laws 2019 number 1145, consolidated text dated June 19, 2019).

Types of IP rights

Trademarks

Trademarks may be any marking if it is capable of distinguishing the goods or services of one entrepreneur undertaking from those of another. A trademark may in particular be words, drawings, letters, numerals, colors, spatial forms, including the form of the goods or of their packaging, and sound.

If the goods and services are offered in different European countries, it is worth considering registering the European Union trademark. A single registration made in the European Union Intellectual Property Office (EUIPO) in Alicante gives protection of a trademark in all 28 member states. The period of protection for Polish and European trademarks lasts for 10 years from filing the application for registration, but this term may be extended for successive 10-year periods.

The trademark registered in Poland may become protectable on the international market, by extending the right to countries, which are parties to the Madrid Agreement concluded in 1891. The international registration of trademarks is governed by the World Intellectual Property Organization (WIPO) in Geneva.

Industrial design

The Industrial Property Act offers the following definition of the term industrial design: "An industrial design is a form of a product or of its part which is new and has an individual character given to it especially by the characteristics of lines, contours, shapes, colors, product structure or material, and by its ornamentation".

Registration of a new industrial design takes approx. 7 months in the PPO. The protection for Polish industrial design rights, is granted for a maximum period of 25 years, provided that every 5 years the right will be extended along with payment of fees.

Industrial design protection in Poland may also be obtained via registration of a Community Design. Registration of a Community Design is conducted by filing one application to EUIPO and is valid in all 28 European Union countries. Community Design application may include several design variants in one application. Applicants outside the EU must appoint an agent, or patent attorney is registered before any EU member state.

Patents

A patent is a right protecting an invention. Patents are granted for inventions which are new, involve an inventive step and which are susceptible to industrial application. The protection of an invention starts from the moment of filing the patent application. However, it is subject to the subsequent granting of the patent.

The filing procedure lasts approx. 4 to 6 years. The PPO is obligated to publish the patent application within 18 months from its submission date. Nevertheless, publication may be expedited upon the applicant's request.

The term of a patent is 20 years from the filing date, provided that the annuity payments are made regularly. The patent protection does not have to be limited to the territory of Poland, but may also be granted for the European and international market. Through application with the PPO, a European patent may be granted, providing protection for an invention in over 30 European countries. In comparison, an international patent covers 148 countries, under the Patent Cooperation Treaty (PCT).

Enforcement of IP rights

Infringing intellectual property rights entails liability of the infringing party on civil, as well as criminal grounds. Criminal liability includes penalties for an appropriation of authorship (plagiarism), unlawful distribution of protected work, imitation, and counterfeiting of protected marks, or removal of original designations from products.

Civil lawsuits

In the case of infringement, the rights holder may use a variety of civil claims against the infringer, including a demand to cease the infringing activity, to reinstate a status compliant with the law, or repay the wrongly received benefit.

It should be also noted, that there are a number of procedural legal measures, which facilitate protection of intellectual property such as preliminary injunction, securing of the evidence and disclosure of information.

Typical remedies granted by a court in infringement actions:

- Cessation of infringement;
- Disposal of unlawfully manufactured/marketed goods;
- Publication of the judgment;
- Surrender of unlawfully obtained profit; and
- Compensation for damages.

Oppositions

Trademarks

Since April 15, 2016 the trademark registration procedure in Poland has been changed into an opposition system. Up to that time, the PPO would have examined all prerequisites of trademark registration (both relative and absolute grounds for refusal of trademark registration). At present, the PPO examines only absolute grounds and owners of earlier rights will need to file opposition to prevent later identical or similar registrations. The objection must be submitted to the PPO in writing, within 3 months from the date of the publication of the application for the trademarked in the Patent Office Bulletin.

Patent/Industrial Designs

Anyone may submit a substantiated opposition to a final and non-revisable the PPO decision to grant a patent, protection for a utility model or a right in registration within 6 months of the day information on the granting of the right is published in the "Patent Office's Official Gazette". The grounds for opposition will be circumstances that justify the cancelation of the patent (lack of patentability or protection- as described in more detail below).

Invalidations/ Cancelations

Trademarks

The protection right is subject to invalidation if the statutory requirements for the granting of that right have not been fulfilled or due to the existence of an earlier right. Any person may file a request for invalidation. The procedure includes the examination of grounds, pleadings and evidence submitted by the parties, and hearing of the involved parties. The PPO will then issue a decision invalidating a trademark or dismissing the request. The decision is subject to a judicial review before the administrative court in respect of any errors in law.

Patent/Industrial Designs

A patent may be invalidated in whole or in part on the request of a person who has a legal interest therein if this person demonstrates that the conditions to obtain a patent are not met or the invention was not depicted sufficiently clearly and completely for it to be carried out by a person skilled in the art, or addition if the patent was granted for an invention not covered by the scope of the application or the original application. Grounds for invalidating a right in registration to industrial designs may also be evidence that using an industrial design infringes third party moral or economic rights.

There is no administrative recourse. The decision is subject to judicial review before the administrative courts in respect of an error in law. The judgment of the regional administrative court may be further appealed in cassation proceedings before the Supreme Administrative Court. Both courts may revoke the decision only if the error was made in law and this error had an impact on the PPO's decision.

Germany

Drug authorisation

In the event an applicant is seeking a MA only in Germany, the German Drug Law (*Arzneimittelgesetz, AMG*) regulates the relevant requirements. According to Section 21 AMG finished drugs in general may only be placed on the market, if they have been authorised by the competent authority (or in one of the other European procedures). Therefore, the German pharmaceutical entrepreneur may also rely on a MA granted in the centralized EMA procedure, e.g. as for a biosimilar. Finished drugs are drugs that are manufactured beforehand and placed on the market in packaging intended for distribution to the consumer, or other drugs intended for distribution to the consumer in the preparation of which any form of industrial process is used, or drugs that are produced commercially, except in pharmacies.

Exceptionally, for some drugs a marketing authorisation is not required (Section 21 Para 2, Section 36, Section 38 and 39a, Section 73 AMG), for example for drugs that are intended for use in clinical trials or homeopathic drugs, that only require a registration.

Formally a marketing authorisation requires an application of the pharmaceutical entrepreneur, i. e. the person who wishes to hold the marketing authorisation or any person who wishes to place the drug by parallel distribution or otherwise on the market under his/her own name.

The application must be addressed to the competent authority. According to Section 77 AMG the competent regulatory authority in Germany to grant a MA for human medicines is either the

Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM or the *Paul-Ehrlich-Institut, PEI* (inter alia for sera, vaccines, blood preparations). They examine whether a drug is effective and harmless and whether it has the required pharmaceutical quality.

The necessary approval documents are submitted by the pharmaceutical entrepreneur. They shall include analytical, pharmacological-toxicological and clinical tests as well as expert opinions. In addition, the pharmaceutical entrepreneur must submit instructions for use and technical information, labelling texts and information on package sizes. Additionally, the exact description of the intended pharmacovigilance or risk management system is part of the marketing authorisation documents.

According to Section 25 Para 2 AMG the competent authority may only refuse to grant the marketing authorisation if for example the submitted documents are incomplete, the drug has not been sufficiently tested in accordance with the confirmed state of scientific knowledge, the drug is not manufactured in accordance with recognised pharmaceutical rules or does not meet appropriate quality standards or any other reason stated in Section 25 Para 2 No. 1 to 7 AMG.

If there is no such reason, the competent authority issues the marketing authorisation, together with a marketing authorisation number.

Manufacturing Authorisation

For the manufacture of drugs at whatever stage in the manufacturing process a manufacturing authorisation is required in Germany according to Section 13 AMG Such manufacturing authorisation is connected to, and issued for, specific premises and covers specific manufacturing activities and product classes. In Germany, the public authority competent for granting such manufacturing authorisation is the regional authority competent for the supervision of pharmaceutical manufacturing. It is determined by the states and is usually the general regional government authority (*Regierungspräsidium*) or the local or regional public health authority (*Gesundheitsamt*).

The European Directive on GMP-requirements (Directive 2003/83/EG) has been implemented in Germany in particular by the Pharmaceuticals and Active Ingredient Manufacturing Regulation (*Arzneimittel- und Wirkstoffherstellungsverordnung, AMWHV*) and related guidelines. According to Section 3 AMWHV compliance with the GMP-guideline is required. Therefore, the issuance of a manufacturing authorisation requires the compliance of premises and processes with applicable GMP-requirements, inter alia, the engagement of a qualified person (*Sachkundige Person*) responsible for the manufacturing and quality control activities as well as premises appropriate for the manufacturing steps concerned.

The procedure of evaluating the compliance with GMP in Germany does not differ from the procedure at European level. Thus, the competent authority issues the manufacturing authorisation after an inspection of the applicants premise and activities and in combination with the issuance of a GMP-certificate.

In Germany, manufacturing authorisations are in principle issued for an indefinite period. However, the competent public authority audits the compliance with applicable GMP-requirements on a regular basis (usually every second year). The results of these audits/inspections provide the basis for the authority's decision to either maintain or potentially withdraw or suspend the manufacturing authorisation. Any deficiencies detected are classified according to the potential impact on the health of patients as critical deficiencies (potentially life-threatening or serious damage to patient health),

serious deficiencies (potential or concrete impact on pharmaceutical but not critical) and other deficiencies (no noticeable impact on pharmaceutical and no demonstrable significant risk).

According to Section 96 No. 4 AMG the manufacturing of pharmaceuticals without a manufacturing authorisation is prohibited and even constitutes a criminal offense.

Import Authorisation

According to Section 72 AMG the professional or commercial import of drugs from countries which are not Member States of the EU or EEA, requires an import authorisation. The requirements are predominantly based on the regulations on the manufacturing authorisation. In practice, manufacturing and import authorisations are often issued together, because mostly pharmaceutical entrepreneurs perform manufacturing activities as well as import activities in relation to one drug.

Nevertheless, the existence of an import authorisation alone does not permit the import of the products mentioned in the authorisation. Rather, according to Section 72a Para 1 AMG it is required, to prove by certificate or attest of the competent authority that (a) the manufacture was performed in compliance with all requirements in relation to the manufacturing of drugs or (b) import is in the interests of the general public. Furthermore, the import authorisation does not replace the marketing authorisation or registration. According to Section 73 Para 1 AMG the introduction, i.e. the transport of drugs into the scope of the AMG is in principle only permitted if a corresponding authorisation or registration has been obtained or the medicinal product is exempted from authorisation or registration and the importer holds an import authorisation.

Wholesale authorization

In Germany, such wholesale authorisation is again issued by the competent regional authority for specific premises only. According to Section 52a para. 6 AMG, a manufacturing authorisation and/or import authorisation includes the authorisation to engage in wholesale activities regarding all products covered by the scope of the respective manufacturing and/or import authorisation.

To obtain a wholesale authorisation, the applicant shall (1) name the specific sites, as well as the activities and drugs for which the authorisation is to be issued, (2) submit evidence that he/she is in possession of suitable and adequate premises, installations and facilities in order to ensure the proper storage and distribution and, where envisaged, proper decanting, packaging and labelling of drugs, (3) appoint a responsible person who possesses the required expert knowledge to perform the activity ("*Großhandelsbeauftragter*") and (4) enclose a statement in which he/she commits himself in writing to observe the regulations governing the proper operation of a wholesale enterprise.

The regulations the applicant shall observe are, in addition to the provisions of the AMG, the guidelines on good distribution practice (GDP) and the German Regulation on Wholesale Trade and Mediation of Drugs (AM-HandelsV).

Reimbursement and pricing in Germany

For the vast majority of the German population, healthcare is provided by the statutory health insurance ("GKV").

Under the present GKV-system, all prescription-only drugs with MA are generally eligible for reimbursement unless the product and/or indication has been excluded by statute or directive issued by

the Joint Federal Committee (*Gemeinsamer Bundesausschuss—GBA*). An example for such statutory exclusion are drugs for so-called 'life style' indications (obesity, erectile dysfunction, etc.).

Special rules may apply for drugs directly applied on patients by doctors in their practice or in a hospital. Such products are typically reimbursed as part of the lump-sum reimbursement for a certain type of treatment ("DRG-System").

In relation to the pricing of drugs pharmaceutical entrepreneurs are initially free to determine the price for their drugs. However, to keep health insurance contributions affordable, the German legislator has introduced various pricing regulations for prescription-only drugs.

Pharmacies and wholesalers impose surcharges on their purchase prices to cover their own costs and fees. The amount of these surcharges is limited by the German Drug Price Regulation (*Arzneimittelpreisverordnung, AMPreisV*).

Furthermore, there are fixed prices for groups of similar drugs in Germany. Although those fixed prices are not prices for drugs set by law, they form the maximum amounts for the reimbursement of drugs by the statutory health insurance funds. This means, that the GKV will only pay the costs for a drug up to the fixed amount.

Fixed amounts are determined in a two-stage procedure: First, the GBA determines for which groups of drugs reference prices can be set. In these groups, drugs with the same or pharmacologically and therapeutically comparable active substances as well as with therapeutically comparable effects are grouped together. Secondly, the Federal Association of Health Insurance Funds (*GKV-Spitzenverband*) sets a fixed price for each fixed group formed by the GBA (based on Section 35 German Social Code V (SGB V).

According to the database of the German Institute for Medical Documentation and Information (*DIMDI*) Inhixa® is part of a reference price group. Despite this resulting fixed price, health insurance funds can negotiate further discounts or price reductions with pharmaceutical entrepreneurs in rebate agreements (typically through tender procedures). This is relevant as the pharmacies are obliged to dispense the cheapest of substitutable drugs, unless otherwise prescribed by the doctor (Section 129 SGB V).

In general, the above rules apply to all drugs including biosimilars and in particular for generic drugs. However, in relation to the substitutability of drugs, Section 129 SGB V does not yet provide for an automatic substitution of biosimilars with its reference drugs. However, the new "Law for more security in the supply of medicines" (*Gesetzes für mehr Sicherheit in der Arzneimittelversorgung—GSAV)* entered into force in August 2019 will establish rules that shall increase the substitution rate of biological reference drugs with biosimilars as of 2022 by pharmacists.There are concerns that the new law may lead to a similar developments that have been observed with regard to generic drugs in Germany. Drug experts argue that through rebate agreements and the associated substitution obligation for pharmacists it would in future be the GKV (i. e. the lowest agreed price) and no longer the physicians who would decide which biosimilar the patients received.

For manufacturers and / or distributors of biosimilars in Germany, there is a risk that the new regulations in Germany provided by the GSAV may lead to price reductions in the market for biosimilars (comparable to the generic drugs market).

Intellectual Property

German National IP Rights

German law recognizes various forms of intellectual property rights ("**IP**"), most importantly patents, utility models, trademarks, design rights and copyrights.

Patents are in general granted for technical inventions which are new and involve an inventive step. They have a maximum protection period of 20 years. By way of so-called supplemental protection certificates, this can be prolonged by 5 years for medical products and plant protection products. Patents must be registered with the German Patent and Trademark Office, and are examined for formal and material requirements.

Trademarks grant protection for signs that give an indication of origin (including words, devices, colors, shapes, sounds, and other forms.) and which are neither descriptive nor generic. Trademarks can be registered with the German Patent and Trademark Office, and are examined for formal and material requirements. Older third party rights are however not considered during registration examination, but must be raised by their respective owners (e.g. by way of opposition). Trademarks can be renewed every 10 years, no maximum protection period exists. Beside registered trademarks, German law recognizes trademarks by use (also called common-law trademarks) as well as certain protection for (company) names and titles.

Design rights grant protection for the form of a product if the design is new, has individual character, and where the design is not due to technically requirements. Design rights need to be registered with the German Patent and Trademark Office, but are only examined for formal requirements. The maximum protection period is 25 years.

Copyrights grant protection for individual works of art, including software. Comparable rights exist for e.g. photographs, or databases. They do not need to be (and cannot be) registered but come into existence with creation. The maximum protection period is 70 years after the death of the author. Other than all other IP rights listed above, copyrights cannot be transferred under German law, but only usage and exploitation rights can be granted by way of license agreement.

European Union IP Rights

Beside the German national IP rights, the European Union IP rights apply to Germany as part of the EU. These are the European Union Trade Mark ("**EUTM**") and the European Union Design Right (*Community Design Right*, ("**CDR**")), which grant a uniform protection for all then-current EU Member States. A pan-European patent right does not exist at the moment.

EUTMs need to be applied for with the EU Intellectual Property Office ("**EUIPO**"), and can be registered after a formal and material examination. Third party rights are not considered ex officio but need to be raised by their respective owners (e.g. by way of opposition). EUTMs can be renewed every 10 years, no maximum protection period exists.

Registered CDRs also need to be applied for and registered with the EUIPO, but are only checked for formal requirements. They have a maximum protection period of 25 years. Also unregistered CDRs are recognized; these have a maximum protection period of 3 years and come into existence with the first public disclosure of the object that shall be protected.

Similar protection rights

German law further provides for protection of trade secrets. Under the Trade Secret Protection Act, which was enacted in April 2019, any kind of information that (i) is not generally known amongst the relevant circles of trade, (ii) is of commercial value, and (iii) is subject to reasonable protection measures enjoys protection against unlawful acquisition, use and disclosure. Especially the requirements to implement reasonable protection measures is new for Germany, requiring companies to review their conduct. If a company uses trade secrets of others and was (or should have been aware) that the trade secret was acquired unlawfully, this may also constitute unlawful conduct.

In addition, German law provides for specific rules against unfair competition. These primarily prohibit aggressive or misleading advertising, and to some degree also grant protection against imitation of goods. For medicinal products, specific rules exist that further specify and narrow the scope of allowed advertising.

Claims and enforcement

All of the above IP rights, trade secrets and unfair competition law grant claims for, amongst other, cease-and-desist, damages, and (mostly) recall or destruction of infringing goods. These claims are often enforced by way of interim injunction proceedings.

Spain

Marketing authorization

In the event an applicant is seeking a marketing authorization only in Spain, the Spanish Royal Legislative Decree 1/2015 of 24 July, approving the revised text of the Law on Guarantees and the Rational Use of Medicines and Medical Devices ("**RLD 1/2015**"), regulates the relevant requirements.

According to article 9 of RLD 1/2015, industrially manufactured medicines may only be placed on the market if they have been previously authorised by the competent authority—the Spanish Agency of Medicines and Medical Devices (the **"AEMPS"**)- or in one of the other European procedures. Therefore, the Spanish pharmaceutical entrepreneur may also rely on a marketing authorization granted in the centralized EMA procedure, e.g. as for a biosimilar. Additionally, the aforementioned products shall be registered with the Spanish Registry of Medicines. In this regard, the AEMPS shall proceed *ex officio* to incorporate a marketing authorization granted in the EMA procedure to the mentioned registry.

Moreover, pursuant to article 9.2 of RLD 1/2015, when a medicine has obtained a marketing authorization, all additional doses, pharmaceutical forms, routes of administration and additional presentations, as well as any other changes and additions to the authorization dossier, must be authorised or notified, as the case may be. Such variations shall be considered as belonging to the same global marketing authorization, in particular for the purposes of applying the period of data exclusivity (i.e. period in which another company cannot use the originator's data in support of another marketing authorization application). Furthermore, any amendment, transfer or termination of the marketing authorization shall be registered in the Spanish Registry of Medicines.

Marketing authorization applications must be addressed to the AEMPS, which will examine whether the relevant medicine is effective and harmless and whether it has the required pharmaceutical quality. Applications shall also contain details of any precautionary and safety measures to be taken for

the storage of the medicines, its administration to patients and for the disposal of waste products, together with an indication of any potential risks which the medicinal product might pose to the environment. In addition, a qualified person responsible for pharmacovigilance is required. Finally, the administrative file for a marketing authorization shall include expert reports, chemical, pharmaceutical and biological information for medicines containing chemical and/or biological active ingredients, and the results of pharmaceutical, preclinical and clinical tests, among others.

According to article 20 of RLD 1/2015, the AEMPS may only refuse to grant the marketing authorization in the following scenarios: (i) when the risk-benefit balance is not favourable; (ii) when the therapeutic effectiveness is not sufficiently justified; (iii) when the qualitative and quantitative composition of the medicine is not as declared or is not of appropriate quality; and (iv) when the data and information contained in documents provided with the application are incorrect or do not comply with the relevant implementing regulations.

The marketing authorization shall be valid for five years and it can be renewed subject to a reassessment of the risk/benefit balance. Renewal of the marketing authorization shall be for an unlimited period, unless pharmacovigilance reasons justify a new procedure for renewal.

In addition to the above, the applicant shall take into consideration the provisions of Royal Decree 1345/2007, of 11 of October, regulating the authorization procedure, registration and conditions of dispensing of industrially manufactured medicines, in regards to the specific procedures depending on the type of medicine.

Manufacturing authorization

Medicine manufacturing at whatever stage in the manufacturing process, including the fractioning, packaging and presentation for sale, even if the medicine is manufactured exclusively with the purpose of exporting, requires the prior authorization of the AEMPS according to article 63 of RLD 1/2015. Such Manufacturing authorization shall be made public by the AEMPS, as well as any amendment thereof, or its termination.

Royal Decree 824/2010, of 25 of June, regulating pharmaceutical laboratories, manufacturers of active pharmaceutical ingredients and foreign trade in medicines and investigational medicines (**"RD 824/2010"**) implements RLD 1/2015 in this regard.

In order to obtain a manufacturing authorization, the applicant shall: (i) detail the medicines and pharmaceutical forms which it intends to manufacture, as well as the place, establishment or laboratory of manufacture and control; (ii) hold the possession of premises, adequate and sufficient technical and control equipment for proper manufacture, control and preservation in accordance with legal requirements; and (iii) appoint a person responsible for the manufacture, a person responsible for quality control and a responsible person who possesses the required expert knowledge to perform the activity ("*Director Técnico*").

Additionally, the manufacturing authorization must be registered with the Spanish Registry of Pharmaceutical Laboratories and the Spanish Registry of Manufacturers, Importers or Distributors of Active Ingredients, as appropriate.

The European Directive on GMP requirements (Directive 2001/83/EC) has been implemented in Spain by RD 824/2010, which requires GMP-guideline compliance.

The procedure of evaluating the compliance with GMP in Spain does not differ from the procedure at European level. When an inspection visit has been carried out and conformity with the rules of correct manufacture has been verified, the relevant authorities will issue a certificate of compliance with said rules (GMP-certificate) (in accordance with article 43 and 45 of RD 824/2010).

In Spain, manufacturing authorizations are generally issued for an indefinite period. However, the competent public authority audits the compliance with the general and GMP requirements on a regular basis (usually every three years). The results of these audits/inspections provide the basis for the authority's decision to either maintain or potentially withdraw or suspend the manufacturing authorization.

Import authorization

According to article 63 of RLD 1/2015, the professional or commercial import of medicines from countries which are not Member States of the EU or EEA, requires an import authorization. The requirements are predominantly similar to those required for the manufacturing authorization.

In practice, manufacturing and import authorizations are often issued together, because mostly pharmaceutical entrepreneurs perform manufacturing activities as well as import activities in relation to one medicine.

Together with the import authorization, the following requirements shall be complied with when importing active ingredients: (i) they shall be manufactured in accordance with the provisions in force in the exporting country regarding standards of good manufacturing practice at least equivalent to those laid down in the legal framework for the European Union; and (ii) they have to be accompanied of a certificate or attest of the competent authority of the export country stating: (a) that the provisions in force, in the exporting country, regarding standards of good manufacturing practice applicable to the premises in which the exported active ingredients are manufactured, are at least equivalent to those established in the legal framework of the European Union; (b) that the manufacturing premises concerned is subject to regular, strict and transparent controls and effective enforcement of good manufacturing practice, including repeated and unannounced inspections, so as to ensure protection of public health at least equivalent to that established in the European Union; and (c) that in cases of non-compliance, the exporting third country shall report to the European Union without delay (according to article 57 of RD 824/2010).

Wholesale authorization

According to article 68 of RLD 1/2015, the wholesale authorization is granted by the competent regional authority in which the applicant's storehouse has its domicile, notwithstanding the obligation of reporting its activities to the health authorities of the Autonomous Communities ("*Comunidades Autónomas"*) in which it carries out a wholesale activity. Moreover, the initiation of the wholesale activity must be reported to the AEMPS.

Notwithstanding the above, the AEMPS is the competent authority to grant authorizations regarding the wholesale of medicines under customs control or supervision, in accordance with article 16 of Royal Decree 782/2013, of 11 of October, regulating the distribution of medicines for human use (**"RD 782/2013"**).

Pursuant to article 14 of RD 782/2013 the competent authority issues the wholesale authorization after an inspection of the applicants premises and activities, with the purpose of verifying

the existence of appropriate personnel, material and operational resources to guarantee the correct development of their activity.

To obtain a wholesale authorization, the applicant shall comply with the requirements provided for in article 69 of RLD 1/2015 and article 8 of RD 782/2013, including the appointment of a responsible person with the expert knowledge to perform the activity ("*Director Técnico*").

The wholesale authorization shall be granted notwithstanding the obligation to obtain a good distribution practice certificate (GDP).

Finally, according to article 110 *et seq.* of RLD 1/2015, the marketing, manufacturing or distribution of pharmaceuticals without the corresponding authorization constitutes a very serious infringement and may even be considered a criminal offense.

Reimbursement and pricing in Spain

For the vast majority of the Spanish population, healthcare is provided by the National Health System ("*Sistema Nacional de Salud")*.

On the one hand, articles 92 and 93 of RLD 1/2015 regulate the inclusion of medicines within the financing of the National Health System through a "selective" and "non-indiscriminate" financing, taking into account general, objective and published criteria, including, amongst others, the severity, duration and sequels of the different pathologies for which they are indicated, and the specific needs of certain groups.

The Ministry of Health, Social Services and Equality (**"Ministry of Health"**) will review the groups, subgroups, categories and/or classes of medicines whose financing is not deemed necessary to cover the basic health needs of the Spanish population. In any case, medicines not subject to medical prescription, medicines not used for the treatment of a clearly determined pathology and products for cosmetic, dietetic and other similar products will not be included in the pharmaceutical provision. Neither will the National Health System finance medicines indicated for the treatment of syndromes and/or symptoms of less severity, nor those which, although authorised in accordance with the regulations in force at the time, do not meet current therapeutic needs, understanding as such an unfavourable benefit/risk balance in the diseases for which they are indicated.

The relevant body within the Ministry of Health will update, by means of a reasoned decision, the list of medicines excluded from pharmaceutical provision in the National Health System.

Furthermore, pursuant to article 102 of RLD 1/2015, medicines shall be dispensed to the patient by means of a medical prescription or hospital dispensing order, through pharmacy offices or services. The patient shall pay a contribution at the time the medicine is dispensed, which shall be proportional to his or her level of income.

On the other hand, article 94 of RLD 1/2015 regulates the pricing of medicines. In general, the scope of the administrative intervention on industrial medicine prices in Spain is currently limited to medicines financed by the National Health System, hence, excluding (i) medicines excluded from public financing, and (ii) medicines not subject to medical prescription. However, when there is an exceptional health situation, in order to protect public health, the Interministerial Committee on the Price of Medicines ("*Comisión Interministerial de Precios de los Medicamentos*") may set the maximum sales price of these medicines for the duration of said exceptional situation.

In any case, marketing authorization holders may commercialise medicines not subject to medical prescription in the Spanish territory at "notified prices", meaning that the price is communicated to the Ministry of Health, so that the latter may object to it on grounds of public interest.

Regarding medicines financed by the National Health System and those medicines which require a medical prescription, the Interministerial Committee on the Price of Medicines, subject to the Ministry of Health, shall set, on a reasoned basis and in accordance with objective criteria, the prices of said medicines.

Finally, in 2019, the Ministry of Health published an action plan to promote the use of "market regulating medicines" in the National Health System in reference to biosimilar medicines and generic medicines ("*Plan de Acción para fomentar la utilización de los medicamentos reguladores del mercado en el Sistema Nacional de Salud: medicamentos biosimilares y medicamentos genéricos"*).

Intellectual Property

Spanish national IP rights

Spanish law recognizes various forms of intellectual property rights (IP), most importantly patents, utility models, trademarks, design rights and copyrights.

Patents are in general granted for technical inventions which are new and provide for an invention. They have a maximum protection period of 20 years. By way of so-called supplemental protection certificates (*Certificado Complementario de Protección*), this can be prolonged by 5 years for medical products and plant protection products. Patents must be registered with the Spanish Patent and Trademark Office (*Oficina Española de Patentes y Marcas*), and are examined for formal and material requirements.

Trademarks grant protection for signs that give an indication of origin (including words, devices, colors, shapes, sounds, and other forms) and which are neither descriptive nor generic. Trademarks must be registered with the Spanish Patent and Trademark Office, and are examined for formal and material requirements. Older third party rights are however not considered during registration examination, but must be raised by their respective owners (e.g. by way of opposition). Trademarks can be renewed every 10 years, no maximum protection period exists. Beside registered trademarks, German law recognizes trademarks by use (also called common-law trademarks) as well as certain protection for (company) names and titles.

Design rights grant protection for the form of a product if the design is new, has individual character, and where the design is not due to technically requirements. Design rights need to be registered with the Spanish Patent and Trademark Office, but are only examined for formal requirements. The maximum protection period is 25 years.

Copyrights grant protection for individual works of art; also e.g. photographs, software, or databases can qualify as such. They do not need to be (and cannot be) registered but come into existence with creation. The maximum protection period is 70 years after the death of the author. Other than all other IP rights listed above, copyrights cannot be transferred under Spanish law, but only usage and exploitation rights can be granted by way of license agreement.

Similar protection rights

Spanish law further provides for protection of trade secrets. Under the Trade Secret Protection Act (*Ley de Secretos Empresariales*), which was enacted in February 2019, any kind of information that (i) is not generally known amongst the relevant circles of trade, (ii) is of commercial value, and (iii) is subject to reasonable protection measures enjoys protection against unlawful acquisition, use and disclosure. If a company uses trade secrets of others and was (or should have been aware) that the trade secret was acquired unlawfully, this may also constitute unlawful conduct.

In addition, Spanish law provides for specific rules against unfair competition (*Ley de Competencia Desleal*). These primarily prohibit aggressive or misleading advertising, and to some degree also grant protection against imitation of goods.

Claims and enforcement

All of the above IP rights, trade secrets protection and unfair competition law grant claims for, amongst other, cease-and-desist, damages, and (mostly) recall or destruction of infringing goods. These claims are often enforced by way of interim injunction proceedings.

UK

General Regulatory Framework

Currently, the regulatory regime for medicines in the UK is similar to that in other EU Member States, as medicines regulation is significantly harmonised under EU law. Directive 2001/83/EC is transposed into English law primarily through the Human Medicines Regulations 2012 (SI 2012/1916) (the **"UK Regulations"**).

Regulatory oversight of medicines in the UK is principally carried out by the Medicines and Healthcare Products Regulatory Agency (**"MHRA"**), which is the national competent authority. Alongside the MHRA, there are a number of other government bodies involved in the wider regulatory framework, including the EMA at the supra-national level.

However, this position and the overview set out below only apply at present in the UK. The decision of the UK to leave the European Union in 2016, known as 'Brexit', has raised uncertainties as to the UK's future approach to medicines regulation. The impact of Brexit vis-à-vis medicines regulation is addressed further at the section headed "Brexit" below.

Drug authorization

As mentioned in the section headed "General Procedures of Marketing Authorization" above, there are four routes that can be taken across the EU to obtain drug authorizations in Member States (such as the UK), including the national procedure which can be used by applicants to market drugs solely in the UK. According to Regulation 46 of the UK Regulations, medicinal products must not be sold, supplied or offered for sale or supply in the UK without a marketing authorization obtained via one of these four procedures.

In certain circumstances the national procedure is not available to market drugs in the UK and instead the centralized EU procedure must be used (for instance, for biosimilars). Although the Inhixa product, as a biosimilar, was authorised via the centralized procedure, it is likely that the rules relating to UK national marketing authorizations will become relevant after Brexit, for the reasons set out in the section headed "Brexit" below.

Applications for a UK marketing authorization are made directly to the MHRA in accordance with Regulation 49 of the UK Regulations, which sets out a number of key requirements for the application. Once granted, a UK marketing authorization is valid for an initial term of five years (Regulation 65(1)(a)). Thereafter, once it has been successfully renewed the marketing authorization is typically valid indefinitely unless a safety concern subsequently arises (Regulation 65(1)(b)).

However, if the medicine is not placed on the UK market within three years of the marketing authorization being granted, or if taken off the market for a period of three consecutive years, the authorization will no longer be valid under Regulation 67. Further, the MHRA may revoke a UK marketing authorization at any time if any of the conditions under Regulation 68 are met, such as the MHRA determining that the product to which the authorization relates is harmful and/or that its positive therapeutic effects do not outweigh the risks to public health.

Holders of UK marketing authorizations must comply with a number of obligations prescribed by Regulations 73-78 of the UK Regulations.

Finally, there are a number of exceptions to the general requirement for a marketing authorization pursuant to Regulation 46. These exceptions are specified in Part 10 of the UK Regulations.

Manufacturing/Importations authorizations

Regulation 17 of the UK Regulations requires an entity to have a manufacturer's licence in the UK in order to manufacture, assemble or import from a non-EEA state any medicinal product, or possess a medicinal product for the purposes of any of these activities.[1]

There are various types of manufacturer's licence available in the UK, the most common of which is a manufacturer/importer licence. Applications for a manufacturer's licence in the UK are made to the MHRA and must indicate the descriptions of the medicinal products for which the licence is required (Regulation 21). The MHRA must then decide to grant or refuse the application within a period of 90 days beginning immediately the day on which the application was received (Regulation 23).

The relevant factors that the MHRA takes into account in its determination whether or not to grant a manufacturer's licence are listed at Regulation 22(1), and the statutory conditions for a manufacturer's licence are set out at Regulations 37-41 of the UK Regulations, and have effect as if they were provisions of the licence. In particular, Regulation 37(2) specifies that the holder of a manufacturer's licence must comply with the principles and guidelines of GMP as set out in the Good Manufacturing Practice Directive (defined in the UK Regulations as Directive 2003/94/EC). This obligation applies to both (i) the manufacture/assembly of products and (ii) the importation of products from outside the EEA.

Compliance with GMP in the UK is overseen by the MHRA, which also issues its own guidance to UK-based holders of manufacturer's licences. As is the case in other EU Member States, a 'qualified person' must be named on the licence to ensure that the legal requirements of GMP are met in accordance with Regulation 41 of the UK Regulations. Regular inspections are carried out by the

[1] There is an exception to the need for this licence for entities which solely provide facilities for transporting the product, or act as an 'import agent' by importing the medicinal product solely to the order of another entity which itself possesses a manufacturer's licence authorising such importation.

MHRA every 2-3 years on these sites to ensure ongoing compliance with GMP, and licence holders are also issued with a corresponding certificate of GMP compliance to demonstrate this.

Manufacturer licences granted by the MHRA remain in force until the licence is revoked by the MHRA, or the licence is surrendered by the holder (Regulation 25). Once granted, any changes to the information shown on the manufacturer's licence must be notified and approved by the MHRA through the submission of a variation application.

Wholesale authorization

According to Regulation 18 of the UK Regulations, an entity in the UK cannot distribute a medicinal product by way of wholesale dealing or possess a medicinal product for the purpose of such distribution without having first obtained a wholesale dealer's licence. Broadly, a wholesale dealer's licence is required in the three following circumstances:

(a) procuring, holding, supplying or selling medicinal products for human use sourced in the UK or another EEA Member State, to anyone other than members of the public;

(b) importing medicinal products from a non-EEA Member State for export to a non-EEA Member State; and/or

(c) exporting medicinal products to a non-EEA Member State.

The above includes virtual operations where no physical handling of the products takes place.

Applications for a wholesale dealer's licence are made to the MHRA, and as with manufacturer's licences in the UK, will not be granted unless and until the MHRA is satisfied that the information in the application is accurate and legally compliant following an initial site inspection.

The holder of a wholesale dealer's licence must comply with the obligations set out under Regulations 43-45 of the UK Regulations These include an obligation to comply with principles of GDP published by the European Commission in accordance with Article 84 of Directive 2001/83/EC (Regulation 43(1)), and to appoint a "responsible person" who is sufficiently qualified and trained in GDP to have ultimate responsibility for ensuring that the conditions under which the licence was granted are complied with (Regulation 45). Routine site inspections are also carried out on the sites named on wholesale dealer's licences to ensure continued compliance with the principles of GDP.

Reimbursement

The UK medicines market is highly complex, and it differs from most other European markets due to the existence of the National Health Service ("NHS"), where patients are not required to have either statutory or private health insurance.

The manner in which the NHS procures medicines differs between England, Scotland, Wales and Northern Ireland, and within England there are ten regional pharmacy purchasing groups.

Separate from centralized NHS procurement, there is also a system of reimbursing private pharmacies for the dispensing of prescriptions to out-patients, which is intended to incentivise the use of generic rather than branded medicines where possible. The systems of payment for prescriptions also differ between the constituent countries of the UK.

The full details of the reimbursement system in the UK are beyond the scope of this document.

Brexit

The UK formally left the EU on January 31, 2020 ("**Exit Day**"). Prior to Exit Day, the UK and the EU ratified a withdrawal agreement which was agreed in October 2019 (the "**Withdrawal Agreement**") and which set out the terms of the UK's departure in accordance with Article 50 of the Treaty on the Functioning of the European Union ("**TFEU**"). The UK is now in a so-called "**Transition Period**" until 31 December 2020, during which all EU laws continue to apply in the UK in the same way they applied before Exit Day. The UK's full departure from the EU has now been deferred until 31 December 2020.

In the case of medicines regulation in the UK which is currently subject to directly applicable EU law, the status of such regulation after 31 December 2020 will depend on whether: 1.) the Transition Period is extended (the UK Government's position at the time of writing is that the Transition Period will not be extended); and 2.) whether a trade agreement is concluded between the UK and the EU before the end of the Transition Period.

If a trade deal is concluded between the UK and the EU, it is highly likely that medicines regulation will be covered by such trade deal. At the time of writing, the UK government has published a draft proposal for the text of a trade deal, which does address medicines regulation. However, the draft proposal has yet to be negotiated with the EU, and it is currently too early to predict with any degree of certainty what the final text of any final trade deal will say.

If no trade deal is concluded between the UK and the EU by the end of the Transition Period, the U would be in a so-called 'no deal' scenario.

No deal Brexit scenario

Before the Withdrawal Agreement was ratified, there had been a risk that the UK would leave the EU on 31 January 2020 without any transitional agreement in place, which was known as a 'no deal' scenario. To prepare for a potential no deal scenario, the UK Parliament had enacted the European Union (Withdrawal) Act 2018 ("**EUWA**"). This had provided for the repeal of the European Communities Act 1972 on Exit Day, effectively rendering EU law no longer applicable in the UK, and for the incorporation of all EU law that had effect in the UK immediately prior to Exit Day directly into UK law. The EUWA also gave UK ministers powers to pass secondary legislation to amend UK law, so that any necessary changes can be quickly made to reflect the UK's departure from the EU.

The UK government has exercised these powers in respect of medicines regulation primarily through the Human Medicines (Amendment etc.) (EU Exit) Regulations 2019 (SI 2019/775) (the "Brexit SI"), in order to ensure that UK law in this area is fit for purpose in a no deal scenario.

The Brexit SI would have amended the UK Regulations in the event of no deal with immediate effect following Exit Day to enable the MHRA to act as a standalone regulator outside of the EU framework on the basis of UK law.

However, the EUWA (and secondary legislation enacted pursuant to the EUWA, such as the Brexit SI) has since been amended to ensure that EU law continues to apply in the UK for the duration of the Transition Period. Certain provisions of the EUWA (and related secondary legislation) could now potentially take effect at the end of the Transition Period in the event of a no deal scenario, rather than on Exit Day.

Subject to any further variations that the UK government may make between the time of writing and the end of the Transition Period, the key changes to UK law that would apply in a no deal scenario pursuant to the Brexit SI and the EUWA are set out below:

(a) All EU centrally authorised marketing authorizations in place immediately prior to exit day will be converted into UK marketing authorizations;

(b) To sell medicines in the UK after exit day which do not have a prior marketing authorization in place, a UK marketing authorization will need to be obtained via one of the three new national routes (targeted assessment, accelerated assessment, and rolling review);

(c) wholesale dealer licences will initially remain in force, but may need to be reviewed and various new requirements will apply, including the appointment of a Responsible Person for imports; and

(d) in relation to pharmacovigilance, after a 21 month grace period the QPPV will need to be based in the UK, as opposed to within the EEA as prescribed under the current rules.

Other functions currently exercised by the EMA with respect to UK medicines regulation would also be transferred to the MHRA under the Brexit SI.

Finally, the Withdrawal Agreement contains a Protocol on Ireland and Northern Ireland, pursuant to which Northern Ireland will be treated differently from the rest of the UK and would have to align with specific EU rules, including rules on the authorization and supervision of medicines. In practice, this would result in the MHRA having to apply a different set of rules and standards in Northern Ireland from the rest of the UK. This could potentially raise a number of issues from a legal and regulatory standpoint.

Intellectual Property

The Intellectual Property Act 2014 protects businesses' IP rights in the UK and abroad as it synchronizes UK law with that of EU intellectual property law. There are several different forms of intellectual property rights available in the UK, each with its own formality, level of protection, and duration period.

In the UK, patents are subject to the Patents Act 1977. To obtain patent rights an application can be filed either directly with the UK patent office, the European Patent Office, or under the Patent Cooperation Treaty, of which the UK is a member. A patent will exist for 20 years from the original application date.

The Registered Designs Act 1949 is the governing piece of legislation regarding design rights and it defines a 'registered design' under s1(2) as: "…the appearance of the whole or part of a product resulting from the features of, in particular the lines, contours, shape, texture and/or materials of the product itself and/ or its ornamentation". A registered design right lasts for 25 years from the registration date.

In terms of copyright, no formality is required to register this right in the UK. Copyright will subsist in the artistic work for 70 years from the death of the creator.

A trademark is obtained through registration and shall be protected for 10 years, however, you can choose to renew this to offer a further 10 years' protection upon the first 10 years expiry.

European Union IP Rights

As noted above, the UK left the EU on 31 January 2020. During the Transition Period between Exit Day and 31 December 2020, EU laws continue to apply. The EU IP rights already described above in respect of Germany are also available in the UK, and will continue to be available until 31 December 2020. The position after 31 December 2020 will depend on the terms of any trade agreement between the UK and the EU.

If a trade agreement is agreed prior to 31 December 2020, such deal will almost certainly address the position of EU trade mark and design rights in the UK. However, at the time of writing it is too early to sate with certainty what the position under any agreed deal would be.

If there is no trade agreement by 31 December 2020, and if no extension to the Transition Period is agreed, existing EU trade marks and design rights will automatically be 'cloned' to create equivalent UK rights at the end of the Transition Period. Such rights will then need to be renewed at the UK Intellectual Property Office rather than at the EU Intellectual Property Office, if the owner of the applicable trade mark or registered design right wishes to maintain protection in the UK.

National IP Rights

The UK is a member of the World Trade Organisation ("**WTO**"), and it is a signatory to the Agreement on Trade-Related Aspects of Intellectual Property Rights (the "**TRIPS Agreement**"). UK IP law is therefore harmonized with other WTO member states to the extent required under the TRIPS Agreement.

UK patent law is governed by the terms of the Patents Act 1977, as amended by various subsequent pieces of secondary legislation. The UK is a signatory to the European Patent Convention ("EPC"), and the Patents Act 1977 therefore reflects the provisions of the EPC. The Patents Act 1977 also reflects the terms of the Community Patent Convention (76/76/EEC). UK patent law is therefore similar to that in other EU member states. However, as EU law has a very limited role in patent law, Brexit will have only a limited impact on patent law, at least in the short term. The UK is also a signatory to the Patent Cooperation Treaty and the Paris Convention for the Protection of Industrial Property.

UK copyright law is governed by the terms of the Copyright, Designs and Patents Act 1988. UK copyright law has been harmonized with the law in other EU members states to a limited extent pursuant to several EU directives. The UK is a signatory to the Berne Convention for the Protection of Literary and Artistic Works, and recognizes copyright in literary, dramatic, musical and artistic works, and computer software code is protected as a literary work. The term of copyright protection is 70 years from the death of the author of the applicable copyright work. The UK also recognizes copyright in films, sound recordings, databases and typographical arrangements.

UK trade mark law has been substantially harmonized with that of other EU member states pursuant to the EU trade marks directives. UK trade mark law is therefore very similar to the law of the other EU member states described above. The UK is also a signatory to the Madrid Agreement and Protocol for the Concerning the International registration of Marks. The common law in each jurisdiction within the UK also recognizes rights equivalent to unregistered trade marks through bringing an action for passing off, which permits the owner of goodwill in a trading name or trade 'get up' to bring a claim against persons making misrepresentations 40 as to the origin or (in some cases) qualities of their goods or services.

UK registered design law has been substantially harmonized with that of other EU members states pursuant to the EU designs directive. UK registered design law is therefore very similar to the law of the other EU member states described above. UK unregistered design law differs from the law in other EU member states. A specific UK unregistered design right was created under the Copyright, Designs and Patents Act 1988. The UK unregistered design right only applies in the UK, and is conceptually similar to copyright, as protection arises automatically and copying is a prerequisite for infringement; unlike trade marks, patents and registered design rights, UK unregistered design rights are not monopoly rights. The UK unregistered design right protects 'articles' made to a design, and protection lasts for up to 15 years from the year in which the design was first recorded in a design document or an article was first made to the design. If articles made to the design are first put on sale within the first 5 years of that term, protection lasts only for 10 years from the date of first sale.

Italy

Drug authorization

Medicinal products may only be placed on the market in Italy on the basis of an Autorizzazione all'Immissione in Commercio (AIC), i.e. a marketing licence (marketing authorization (MA)) (Article 6 Legislative Decree no. 219/2006 (implementing Directives 2001/83/EC and 2003/94/EC). The Ministry of Health issues the MA by a Ministerial Decree.

In order to obtain the MA the applicant has to file an application in the form of a dossier including information concerning chemical-pharmaceutical, preclinical and clinical studies, having a standard format structure (CTD—Common Technical Document). The data and the studies submitted in support of the MA application have to comply with the guidelines established at European level.

AIFA (Agenzia Italiana del Farmaco—the Italian Medicines Agency) is the body responsible for both granting MAs and negotiating reimbursement prices for medicinal products.

AIFA verifies the conformity of the documentation submitted by the applicant and verifies that the medicinal product is manufactured according to good manufacturing practices (GMP), that its components (active substance and other components) are suitable and that the control methods used by the manufacturer are satisfactory.

With the support of the Technical Scientific Commission (CTS) and the Istituto Superiore di Sanità (ISS), AIFA carries out the evaluation of the data submitted by pharmaceutical companies concerning the chemical-pharmaceutical, biological, pharmaco-toxicological and clinical characteristics of each medicinal product intended to be placed on the Italian market, in order to ensure its safety and efficacy requirements.

A CTS sub-commission checks the documentation and issues an opinion on the possibility of granting an MA for the medicinal product. The CTS plenary session then ratifies the opinion expressed by the sub-commission and designates the class for price reimbursement. Price negotiations are managed by AIFA's Price & Reimbursement Committee.

Historically in Italy a medicinal product could only be sold once the MA had been published in the Official Journal of the Italian Republic (OJIR), which was not before the reimbursement price had also been determined. The publication in the OJIR would then include not only the MA but also the relevant reimbursement price and category. Therefore, the grant of an MA in Italy often lagged

significantly behind those of linked MAs in other EU countries. However, Law Decree 158/2012 converted into Law no. 189/2012 (the "Balduzzi Decree"), which came into force on 14 September 2012, allowed for demerger of grant of MAs and reimbursement prices. In May 2013, AIFA issued a communication to all pharmaceutical companies confirming that it would apply the Decree's provisions.

The overall timing from application to grant for national MAs is extremely difficult to estimate, albeit it is set by the law in 210 days.

In exceptional cases, in Italy, free access to a pharmacological therapy is allowed before AIFA authorizes its marketing or, for already authorised medicinal product, for indications other than those for which the latter has been authorised in Italy (off-label use).

The pathways for early access to a medicinal product are:

Law no. 648/1996

Compassionate use

AIFA National Fund (Law no. 326/2003—so-called "5% Fund")

Non-repetitive use of advanced therapies

Law no. 648/1996 and AIFA Fund provide for the reimbursement of the medicinal product, by the National Health Service and by AIFA, respectively.

The compassionate use provides for the direct and free supply by the manufacturer of the medicinal product.

The non-repetitive use of advanced therapies involves the preparation of the medicinal product directly from a cell factory and the requesting clinical centre takes charge of the related expenses.

Finally, it is possible to access treatment with a medicinal product on the market but for an indication other than that for which it has been authorised (Law no. 94/98 art.3, paragraph 2—former Di Bella Law), even in the presence of regularly authorised therapeutic alternatives. In this case, however, the therapy is at the patient's expense or at the expense of the hospital in case of hospitalization.

Manufacturing authorization

For the manufacture of medicinal product at whatever stage in the manufacturing process a manufacturing authorization is required in Italy according to Article 50 and ff. of Legislative Decree no. 219/2006. Such manufacturing authorization is connected to, and issued for, specific premises and covers specific manufacturing activities and product classes. In Italy, the public authority competent for granting such manufacturing authorization is AIFA—Office for GMP Inspections and authorizations.

Recently, Law no. 37/2019 introduced additional amendments to Article 50 and ff. of Legislative Decree no. 219/2006 by implementation of the Commission Directive (EU) 2017/1572 supplementing Directive 2001/83/EC of the European Parliament and of the Council as regards the principles and guidelines of good manufacturing practice (GMP) for medicinal products for human use. These amendments establishes a strengthening of the obligations of the manufacturer (and importer—see below) to ensure quality and safety of the medicinal products.

Article 50 establishes inter alia that in order to obtain the manufacturing authorization, the applicant shall: a) specify the medicinal products and pharmaceutical forms that it intends to manufacture or import, as well as the place of manufacturing and controls; b) have at its disposal, for the manufacturing or import of the same medicinal products, adequate and sufficient premises, technical equipment and facilities and control possibilities, both for the manufacturing and control and for the storage of the medicinal products; c) have at least one qualified person (QP).

The procedure of evaluating the compliance with GMP in Italy is aligned to that at European level. Thus, AIFA issues the manufacturing authorization after an inspection of the applicant's premises and activities.

AIFA enters the information relating to the authorizations granted in the European Union database and publishes on its institutional website the list of premises authorised to manufacture and control medicinal products on 30 June each year.

AIFA controls the compliance with applicable GMP-requirements through audits/inspections. The results of these audits/inspections provide the basis for AIFA's decision to issue, maintain or potentially withdraw or suspend the manufacturing authorization. Any deficiency detected with respect to the GMP is classified according to the potential impact on the health of patients. They include: critical deficiencies (potentially life-threatening or serious damage to patient health), serious deficiencies (potential or concrete impact on pharmaceutical but not critical) and other deficiencies (no noticeable impact on pharmaceutical and no demonstrable significant risk but incorrect application of GMP).

Import authorization

Article 55 of Legislative Decree 219/2006 provides that the rules set forth in Articles 50-53 of the same Legislative Decree apply to the import of medicinal products from countries which are not Member States of the EU or EEA. This means that the importer requires an import authorization issued by AIFA and the regulations on the manufacturing authorization also apply to import of medicinal products. In practice, manufacturing and import authorizations are often issued together, because mostly pharmaceutical entrepreneurs perform manufacturing activities as well as import activities in relation to one drug.

When the drugs come from countries which are not Member States of the EU or EEA, in addition to the import authorization it is needed that their manufacture was performed in compliance with rules on manufacturing at least equivalent to those in force in the EU and by a duly authorised manufacturer (Article 61 of Legislative Decree 219/2006).

Wholesale authorization

In Italy, wholesale distribution of medicinal products is subject to the possession of an authorization issued by the autonomous region or province or other competent authorities, as identified by the legislation of the regions or autonomous provinces themselves. This authorization specifies for which premises, established on their territory, it is valid (Article 100, paragraph 1, of Legislative Decree 219/2006).

Wholesale distribution of pharmaceutical products is allowed only for authorised products.

According to Article 100, paragraph 3, a manufacturing authorization includes the authorization to engage in wholesale activities regarding the products covered by the scope of the respective manufacturing authorization.

To obtain a wholesale authorization, the applicant shall (1) have suitable premises, installations and equipment sufficient to ensure the proper storage and distribution of medicinal products; (2) have adequate personnel and appoint a responsible person having certain requirements, including inter alia a degree in pharmacy or chemistry or pharmaceutical chemistry and technology or industrial chemistry (3) undertake to comply with the applicable obligations. The specific premises and medicinal products for which the wholesale distribution is performed shall be indicated in the authorization. In order to carry out wholesale distribution through several warehouses located in different regions, the applicant must obtain separate authorizations, applying to each competent authority. Prior to the issue of the wholesale authorization an inspection of the premises is carried out.

The holder of the wholesale authorization for distribution must purchase medicines only from authorised entities and it is authorised to sell them only to persons/companies/entities authorised to distribute/purchase drugs.

The wholesaler is obliged to comply with defined delivery times and an assortment obligation (Article 105 of Legislative Decree 219/2006).

With exception for the obligations set forth in Article 105, paragraphs 1 and 3, the rules on the wholesale authorization also apply to the activities of those holding, for subsequent distribution, medicinal products for human use on the basis of storage contracts concluded with the MA holders of medicinal products or their representatives (so-called "custodians" or first-line distribution opposed to the so-called second-line distribution by the wholesalers properly called).

Currently, in Italy the European GDP of 1994 have been implemented by the Ministerial Decree of July 6, 1999—Approval of the guidelines on Good Practice in the Distribution of Medicines for Human Use.

Although Article 110 of Legislative Decree 219/2006 requires timely implementation of the guidelines, the 2013 European GDP have not yet been formally implemented in Italy.

Reimbursement in Italy

In Italy a medicinal product may be given one of the following price classifications: "A" (reimbursed), "H" (hospital only reimbursed), "C" (not reimbursed), and "C-nn" (i.e. "C-non-negotiated"). "C-nn" was introduced under the Balduzzi Decree, to allow for the possibility of splitting the grants of the MA and reimbursement price. A medicinal product will have the C-nn price classification if the MA has been published in the OJIR before the determination of the price—which can occur if: (i) no request for price negotiation has yet been filed by the applicant; or (ii) if the price negotiation procedure has not been completed when the time limit for publication of the MA has been reached (AIFA now has much shorter time limits for MA publication). The C-nn classification will then be changed once the reimbursement price negotiation procedure is concluded.

Article 11(1bis) of the Balduzzi Decree provides for a pricing linkage system. The Balduzzi Decree directed AIFA to refrain from granting a reimbursement price to an approved generic product when the reference product is still protected by a patent or SPC. Where the price negotiation is

completed before the expiry of patent /SPC rights, the order publishing the reimbursement price for the product will indicate that the product has been included in class C-nn until the expiry of the patent/SPC rights. It will also indicate the prospective classification of the product as a reimbursed product along with the relevant price, such classification to enter into force as of the date of expiry of the patent/SPC rights identified by the Ministry of Economic Development (which is in charge of the Italian Patent Office). Lists of relevant patents (not covered by SPCs) and SPCs were published.

The Balduzzi Decree also introduced a shortcut to the process of agreeing a generic or biosimilar product a price by negotiation between the generic company and AIFA, that process typically requiring several sessions of AIFA's price committee and taking a period of months. The shortcut allows the automatic grant of a reimbursement price of a generic or biosimilar product, and this process was clarified by a further Decree of April 4, 2013 which came into force on July 1, 2013. The Balduzzi Decree stated that generic or biosimilar products would be automatically granted a reimbursement price provided that the generic company proposed a price of clear convenience to the National Health Service. However, the Balduzzi Decree left open the question of what "clear convenience" meant. Under the Decree, a table was published on 6 June 2013 setting out a series of percentage discounts over the originator's price, depending on the value of annual sales of the originator's product. A reimbursement price will be granted automatically if the generic or biosimilar proposes a price with a percentage reduction at least as great as the relevant percentage set out in the Decree. The percentage thresholds range between 45% to 75% off the public price of the originator's product for category A products (reimbursed products) and between 30% and 50% off the ex-factory price for category H products (hospital only reimbursed).

Pricing of the drugs applicable to Inhixa, specifically pricing of biosimilars

The procedure for the determination of the reimbursable price of medicinal products is regulated by Articles 11 and 12 of the "Balduzzi Decree".

For biosimilars the above provisions foresee that within 60 days from the publication of the MA grant in the EU Official Gazette, AIFA will publish on the Italian Official Gazette an official "decree of acknowledgement" (DA) of the centralized MA. The actual timing of the procedure is heavily impacted by the duration of price negotiation with Italian health authority AIFA. There are two different scenarios here. The first is fast, the second may be a lot slower.

The first scenario is that the biosimilar will complete price negotiations with AIFA before the publication of the DA. The DA will automatically classify the biosimilar as reimbursable either in "Class A" or "Class H" (Class H is specifically for hospital only products, whilst Class A is for all other reimbursable products). The DA will include the relevant price. In this scenario the biosimilar will have finalize the Italian part of regulatory procedure within the official deadline of 60 days from publication of MA grant in the EU Official Gazette.

In the second slower scenario, the biosimilar will not be able to complete price negotiations with AIFA before publication of the DA the Italian Official Gazette. In this case the DA will merely report a so-called "Cnn" price classification ("C" stands for "Class C" (i.e. NOT-reimbursable product and "nn" stands for "Not Negotiated"). At this point the biosimilar will have to complete price negotiation and only after a price has been determined AIFA will issue a formal notice (called "determina") which will contain both indication of the class (either H or A) and the price.

Based on Art. 12 of Law Decree no. 158/2012 (so called "Balduzzi Decree") in this second scenario the timing for price classification and negotiation should not exceed 180 days from the submission of the price proposal.

It is evident that the length of price negotiations will depend on the biosimilar's attitude in proposing their price. According to AIFA's "Second Position Paper on Biosimilars" dated 27 March 2018 the price of the latter must be at least 20% lower than the reference product. However, we know that AIFA is increasingly aggressive in requesting much more substantial price cuts.

A possibly highly relevant point concerns the application to biosimilars of Article 11 of the Balduzzi Decree—providing that medicinal products that are "equivalent" to products which are still protected by a patent or SPC cannot be included in "Class A" or "Class H", until after the expiry of the relevant rights which expressly mentions equivalent products ("normal" generic) but remains silent on biosimilars.

Specific regulations for biosimilar drug, if any, relating to the marketing/import of such drugs

We are not aware of specific regulations for biosimilar drug in Italy relating to the marketing/import of such drugs. The main issues concerning biosimilars in Italy as identified by AIFA's "Second Position Paper on Biosimilars" relate—in addition to the applicability of the pricing rules illustrated in answer F—to the possible application of Law no. 648/1996 (re: off-label use—see answer A) to biosimilar products and the automatic "substitutability" issue (Ref. EMEA/74562/2006 Rev. 1; EMA/837805/2011). Please let us know if you want us to further elaborate on this.

Intellectual Property

Industrial and intellectual property rights ("**IPRs**") are regulated in Italy by the general principles laid down in the Italian Civil Code and in the Italian Legislative Decree No. 30 of February 10, 2005, as further amended (the Intellectual Property Code, "**IPC**"), and, in relation to copyright, by Italian Law No. 633 of April 22, 1941 (the Italian Copyright Law, "**ICL**"), as further amended. Italy is also a party to several international treaties and conventions related to IPRs, including the European Patent Convention.

In general, IPRs, except for trademarks, are granted in Italy for a limited period and there is a right to obtain a declaration of voidness if the IPRs do not meet legal requirements for their protection.

All applications and requests, with the exception of what is provided for by international conventions and agreements, are to be filed with the Italian Patent and Trademark Office ("**IPTO**"). Once filed, depending on the type of IPRs, the IPTO carries out its examination and checks the occurrence of the formal and, to a certain extent, substantial requirements of the application.

IPRs are litigated in Italy before the specialized divisions established within Italian courts (i.e. *Sezioni Specializzate delle Imprese*).

The owner of IPRs has several options to react against infringement in Italy depending on the scale and type of infringement. The owner might commence civil and/or criminal proceedings and can alert the customs authorities in case of counterfeiting. A range of interim measures, including seizure, search order and preliminary injunction, is available in civil proceedings.

Patents for invention

Under Italian Law, the claimed invention must consist of patentable subject-matter; *inter alia*, discovery, scientific theories and mathematical methods are not *per se* patentable. In addition, the invention must: (i) be new; (ii) involve an inventive step; (iii) be capable of industrial application; and (iv) be disclosed in a clear and complete manner in the patent application.

Patent applications made on or after 1st July 2008 have been able to include a novelty search conducted by the European Patent Office on behalf of the IPTO, with the search results provided to the applicant.

Patents have a maximum duration of 20 years starting from the date on which the application is filed, and may not be renewed, nor may their duration be extended.

Patents may expire in case of failure to pay the relevant annual fees. By way of so-called supplemental protection certificates ("**SPC**"), the duration can be extended of further 5 years for medical products.

Utility models

They consists in a shape of a product capable to confer effectiveness to, or ease the application of, machines or parts of them, instruments, tools or objects of general use.

They last for 10 years from the date on which the application is filed.

Trade secrets

The IPC sets forth protection of trade secrets as IPR, even if not on the basis on a registration title.

Article 98 of the IPC requires that a trade secret must meet the following three requirements: (i) confidentiality, i.e. the information protected cannot be well-known or readily accessible to experts and operators in the field; (ii) commercial value, which must derive from the fact that the information is a trade secret; (iii) reasonable efforts must be made by the holder of the information to keep it confidential.

Trademarks and other distinctive signs

Marks, business names and trade names are the typical forms of distinctive sign in the Italian legal system. With specific respect to trade marks, there are various categories, which differ based on the nature of the sign. In principle, a trade mark is capable of registration where it has the essential purpose of identifying a specific product or business, and it has distinctiveness (consequently, descriptive or generic words cannot be registered as trademarks). Italian Legislative Decree No. 15 of February 20, 2019 no longer requires the graphic representation of the sign in order to register it as trademark. This amendment broadens the scope of protection of the trademark, considering that also new types of signs (such as smells or sounds) may be protected as a trademark.

Registered trademarks are protected for 10 years starting from the application date and can be renewed with respect to the same signs and the same products and services for further 10-year periods, for an indefinite number of times.

The last law amendments, enacted in 2019, sets forth the new category of "historical marks" (*marchi storici*).

The owners or exclusive licensees of trademarks registered since more than 50 years or the continued use of which for more than 50 years can be proved, may obtain registration of the mark in the newly established register of historical marks of national interest, where the mark is used in relation to goods or services produced or offered by a national manufacturing company of excellence, historically "connected" to the Italian territory.

In Italy, collective trade marks have instead the function of guaranteeing the origin, nature or quality of certain goods or services.

With the implementation of Directive no 2015/2436, the ownership of collective trademarks has been reserved to "associations of manufacturers, producers, service providers or traders". According to the last law amendments, persons constituted in non-associative form (and also those associations that do not respect the "open door" principle) may become owners of certification marks, but no longer collective marks. The main function of the certification mark is to certify the conformity of the certified goods and services with certain standards set by the owner of the mark itself (eg, in relation to the material, the manufacturing process of the goods or the provision of the service, quality, precision or other characteristics of the goods).

The Italian system also recognizes unregistered trademarks (or *de facto* trademarks).

The essential condition to be met to obtain trademark protection for unregistered trademarks is to demonstrate that the unregistered mark is perceived by the general public as an indication of the origin of the product or has become well known/notorious in the relevant market.

If the unregistered trademark is known only at a local level, the owner of the previous unregistered trademark is always allowed to continue the use of the sign within the limits of such use (so-called "*diritto di preuso*").

Copyright and software

Copyright protects works of the mind having a creative character and belonging to literature, music, figurative arts, architecture, theater or cinematography, whatever their mode or form of expression. The ICL indicates no specific level of creativity required to qualify for protection; in practice, a minimum of creativity is generally regarded as sufficient. Copyrights come into existence as a result of the creation itself. This means that registration is not compulsory. However, works can be registered with the Italian Society of Authors and Publishers (SIAE) and the Italian Ministry of Cultural Heritage and Activities (Mibact).

The ICL expressly lists software among copyrightable subject-matters and allows copyright protection on condition that the software is original and the result of the author's intellectual creation. In accordance with the European Patent Convention, software cannot be protected by patent law as such, but only if has a technical effect that is new and non-obvious.

Economic rights in copyright generally are protected for 70 years after the death of the author. The moral rights are instead perpetual.

Industrial Design

The registration as a design is subject pursuant to the IPC to the requirement of (i) novelty; (ii) individual character (i.e. the general impression of the appearance of the design); and (iii) lawfulness. The duration of the protection is 5 years, renewable for up to a maximum of 25 years.

Pursuant to the Italian legal framework, industrial design is also granted copyright protection provided that it displays not only creative features, but also 'artistic value' (*valore aristico*).

The 'artistic value' requires, as interpreted by the Italian courts, evidence of public rewards or acknowledgments by art critics, museums or exhibits. With "Cofemel decision" issued in September 2019 (decision no. 683/17), the Court of European Justice ruled that, as far as designs are concerned, no other requirement is mandated for copyright protection to arise under the so called "InfoSoc Directive" no 29/2001, but the sufficient originality of the design at issue. After that, in 2020 a fervid debate has been opened amongst Italian Scholars to establish as to whether the requirement of the "artistic value" is still compliant with the European Union principles.

Unfair competition

Italian law sets forth rules to prohibit unfair competition (see Article 2598 et seq. of the Italian Civil Code).

1. In particular acts of unfair competition are performed by anyone that: uses names or distinctive signs which are capable to trigger likelihood of confusion in the relevant market with the names or any distinctive signs legitimately used by any competitors or slavishly copies competitors' products;
2. spreads information and opinions, regarding products and activities of a competitor, which are capable to discredit the competitors, or treats as his/her own good qualities of a competitor;
3. use directly or indirectly any mean which does not comply with the principles of fair professional conduct and which is capable of harming other business

France

Medicinal product marketing authorization

In the event an applicant is seeking a MA (*autorisation de mise sur le marché*) only in France, the French Public Health Code (*Code de la santé publique* or "**CSP**") sets out the relevant requirements. According to Article L. 5121-8 of the CSP, proprietary medicinal products (*spécialités pharmaceutiques*) or any other industrially medicinal product for human use may only be placed on the market if they have been authorised by the competent authority (at French or EU level). Therefore, the French pharmaceutical entrepreneur may also rely on a MA granted through the centralized EMA procedure (e.g., biosimilars). Proprietary medicinal products are ready-prepared medicinal products that are placed on the market under a special trademark and in a special packaging.

As an exception, for some medicinal products a MA is not required (Articles L. 5121-12, L. 5121-13, L. 5121-14-1 and L. 5124-8 of the CSP). This is the case for example as regards certain homeopathic products or traditional herbal medicinal products that only require a registration.

Formally a MA requires an application of the French pharmaceutical entrepreneur, i.e. the person who wishes to be granted the MA.

For a French MA, the application must be addressed to the competent authority. According to Article L. 5121-8 of the CSP, the competent regulatory authority in France to grant a MA for human use medicinal products is the *Agence nationale de sécurité du médicament et des produits de santé* ("**ANSM**"). The ANSM examines whether a medicinal product is effective and harmless and whether it has the required pharmaceutical quality.

The required application documents submitted by the pharmaceutical entrepreneur shall include (among others) the full composition of the medicinal product, preclinical and clinical tests as well as experts opinions. In addition, the pharmaceutical entrepreneur must submit instructions for use and technical information. Additionally, the exact description of the intended pharmacovigilance or risk management system is part of the MA application documents.

According to Article L. 5121-9 of the CSP, the competent authority must deny the MA if the submitted documents and information do not comply with the required application file, if the assessment of the positive therapeutic effects of the medicinal product in relation to the risks for the patient's health or public health associated with its quality, safety or efficiency is not deemed favorable, if the medicinal product does not correspond to the declared qualitative and quantitative composition or if the claimed therapeutic effect is lacking or insufficiently evidenced by the applicant.

Otherwise, the competent authority shall issue the MA, as the case may be with requirements. The MA is issued for a five-year period and may be renewed without time limitation. It can be suspended, withdrawn or modified for specific reasons set out the CSP.

Manufacturing authorization

Medicinal products can only be manufactured by authorised pharmaceutical establishments (*établissements pharmaceutiques*) (Articles L. 5124-1 and R. 5124-2.1° of the CSP), it being understood that any entity (*entreprise*) having at least one pharmaceutical establishment must be owned by a pharmacist (*pharmacien*) or by a company having a pharmacist involved in its management or general management. This pharmacist is the "qualified person" within the meaning of EU regulations.

Any French pharmaceutical entrepreneur shall thus request the authorization to open a pharmaceutical establishment for medicinal products manufacturing purposes.

The authorization is issued for specific premises and covers specific medicinal products. Such authorization is granted by the ANSM.

The European Directive on GMP-requirements (Directive 2003/94/EG) has been implemented in France in particular by the Ministerial Decision of May 26, 2006 modifying the Ministerial Order of May 10, 1995 on the manufacturing guidelines (*Décision du 26 mai 2006 modifiant l'arrêté du mai 10 1995 modifié relatif aux bonnes pratiques de fabrication*) which has been repealed and ultimately replaced by the decision of May 6, 2019 on the manufacturing guidelines (*Décision du 06 mai modifiant la décision du 29/12/2015 modifiée relative aux bonnes pratiques de fabrication des médicaments*). According to articles R. 5124-3 and R. 5124-46 of the CSP, the authorised pharmaceutical establishments shall comply with the manufacturing guidelines and be granted with a GMP compliance certificate issued by the ANSM.

In France, manufacturing authorizations are in principle issued for an indefinite time period. However, the competent public authority may control the compliance with applicable GMP-

requirements (Article L. 5313-1 of the CSP). The results of these audits/inspections provide the basis for the authority's decision to either maintain or potentially withdraw or suspend the manufacturing authorization (Articles L. 5124-3 and R. 5124-15 of the CSP). Non-compliance with the GMP-requirements constitutes a criminal offence (Article L. 5421-1 of the CSP).

In addition, according to Article L. 5423-3 of the CSP, the manufacturing of medicinal products without a manufacturing authorization is prohibited and even constitutes a criminal offence.

Import authorization

Medicinal products can be imported by authorised pharmaceutical establishments (Articles L. 5124-1 and R. 5124-2.2° of the CSP). Any French pharmaceutical entrepreneur shall thus request the authorization to open a pharmaceutical establishment for medicinal products import purposes. Such authorization is granted by the ANSM. The requirements are predominantly based on those applicable to the manufacturing authorization. In practice, manufacturing and import authorizations are often both applied for, as most pharmaceutical entrepreneurs perform both medicinal products manufacturing and import activities. As a result, one unique authorization for the opening of a pharmaceutical establishment may be granted by the ANSM to a pharmaceutical establishment for the performance of several activities including medicinal products manufacturing and import.

Even if the pharmaceutical establishment has been granted a general import authorization, according to Article L. 5124-13 of the CSP, the import of medicinal products requires an import authorization for each product, even in the case where the medicinal products are imported from EU or EEA Member States.

However, such import authorization is not required when the medicinal product already benefits from a MA in France (see above).

There are two categories of import authorization:

- the general import authorization;
- the parallel import authorization.

General import authorization

For a finished product in its commercial packaging, an import authorization is required for each importation. For a product other than a finished product in its commercial packaging, the import authorization covers a set of import transactions over the course of a maximum one-year period and for a fixed aggregate quantity.

Such authorization is not required in the case where the medicinal product having been granted a MA in a EU Member State is imported from this EU Member State, provided that it is (i) stored in a pharmaceutical facility and (ii) intended exclusively for export to EU third-countries.

The general import authorization is issued by the ANSM and can be suspended or removed by the latter.

An import authorization differs from a MA authorization and does not replace it.

As already said, a medicinal product having been granted a MA in France does not require such an import authorization if the imported product complies with the French MA.

Parallel import authorization

A parallel import authorization refers to a medicinal product that is imported from a EU or EEA Member State in which a MA has been issued, and where (i) the quantitative and qualitative composition in terms of active substances and excipients, (ii) the pharmaceutical form and (iii) the therapeutic effects are identical to those of a proprietary medicinal product that has been granted a MA by the ANSM (Article R. 5121-115 of the CSP).

The parallel import authorization is issued by the ANSM for a five-year period and may be renewed (Articles R. 5121-123 and R. 5121-125 of the CSP). It can be suspended or removed in the case where the proprietary medicinal product does no longer comply with the conditions prescribed in the authorization (Article R. 5121-126 of the CSP).

A parallel import authorization does not replace a MA or a registration.

An advice to applicants of parallel importation of medicinal products (*avis aux demandeurs d'autorisations d'importation parallèle en France de spécialités pharmaceutiques à usage humain*) dated 5 March 2020 and issued by the ANSM provides more details on the parallel import authorization.

Wholesale authorization

The wholesale of medicinal products in France can only be performed by authorised pharmaceutical establishments (Articles L. 5124-1 and R. 5124-2.4° of the CSP for depositories which only stock medicinal products and Article R. 5124-2.5° of the CSP for wholesalers which buy and stock medicinal products). Any French pharmaceutical entrepreneur shall thus request the authorization to open a pharmaceutical establishment for medicinal products wholesale purposes. Such authorization is granted by the ANSM.

The granting of the wholesale authorization is subject to the filing of an application containing (among others) (1) the identification of the specific sites, as well as the activities and medicinal products for which the authorization is requested and (2) a technical note describing the installations and facilities in order to ensure the proper storage and distribution of the medicinal products.

In addition to the provisions of the CSP, the applicant shall comply with the guidelines on good distribution practice (GDP) of the ANSM published in May 2014, Official Gazette 2014/9 *bis* (*Décision du 20 février 2014 relative aux bonnes pratiques de distribution en gros de médicaments à usage humain et modifiant l'arrêté du 30 juin 2000*).

The social security financing law for 2020 ("**LFSS 2020**") No. 2019-1446 of 24 December 2019 provides a new legal regime for certain wholesale activities known as the parallel distribution.

A parallel distribution is related to a medicinal product having been granted an EU MA.

As a biosimilar must have been granted an EU MA, it can be subject to parallel distribution.

According to new Article L. 5124-13-2 of the CSP arising from the LFSS 2020, a new decree will determine (i) the obligations of the companies performing the parallel wholesale of medicinal products and (ii) the conditions under which the medicinal products that are subject to parallel wholesale are marketed in France.

Reimbursement and pricing

For the French population, healthcare is provided by the statutory health insurance (*sécurité sociale*).

Under the current social security-system, all prescription-only medicinal products with MA may be eligible for reimbursement. The prescription shall be issued by an health professional (*professionnel de santé*). In addition, such medicinal products shall be on one or two of the two following lists: the "list of reimbursed medicinal products" (*liste des médicaments remboursables*) and the "list of medicinal products approved by communities" (*liste des médicaments agréés à l'usage des collectivités et divers services publics*).

The medicinal products bought in a pharmacy may be fully or partially reimbursed, depending on the category of medicinal products, the prescription conditions and the issuance conditions.

As regards the pricing, a framework agreement between the Economic Committee of Health Products (*comité économique des produits de santé* or "**CEPS**") and the French syndicate of pharmaceutical industries (*les entreprises du médicament* or "**LEEM**") outlines the main priorities of the pricing policy of medicinal products.

In addition, for each medicinal product, based on the application filed by the pharmaceutical company (including the proposed price of the product), the CEPS will propose a price for the corresponding product based on the opinion of the Transparency Commission of the ASNM. Such opinion assesses the SMR (medical service rendered (*service médical rendu*) by the medicinal product) and the ASMR (improvement of the medical service rendered (*amélioration du service médical rendu*)). Generally, an agreement is signed between the CEPS and the pharmaceutical company regarding this medicinal product for a four-year period. This agreement may include obligations to comply with, including the carrying out of new clinical studies.

Specific regulations for biosimilars

A biosimilar is a medicinal product that is similar to a reference biological medicinal product which has been authorised in Europe for more than eight (8) years and whose patent has expired. Biosimilars are not generics. Those products differ from a pharmacologic point of view. As regards biosimilars, a similarity must exist with the reference biological medicinal product. Efficacy and side effects must be equivalent. In addition, the clinical development must demonstrate equivalent tolerance and efficacy.

The regulatory framework applicable to biosimilars is set out in Article L. 5121-1.15° and Articles R. 5121-9-1 to R. 5121-9-4 of the CSP.

A biosimilar is prescribed by a doctor under its International Nonproprietary Name (INN) and not its trademark.

On the website of the ANSM, there is a reference list of biosimilar biologic groups. The products with the same INN are in the same group.

Under EU regulations applicable to biosimilars, two notions plays a key role:

- interchangeability: which is a medical act, on initiative of the doctor, to replace a biological medicinal product by a biosimilar having the same clinical effect as the reference biological medicinal product or another biosimilar of this medicinal product. The initiative of the doctor may occur at any time during the treatment and has to be done in the interest of the patient under three conditions: inform the patient, obtain his agreement, ensure a proper clinical survey and traceability of the products.
- substitution: which means the delivery by a pharmacist of an equivalent medicinal product without referring to the doctor.

Under EU regulations applicable to biosimilars, the decision to authorise interchangeability and substitution is taken at Member State level.

Article 42 of the LFSS 2020 has removed from the CSP the provisions of Articles L. 5125-23-2 and L. 5125-23-3 which referred to a right of substitution of biosimilars by pharmacists. So, it is no longer applicable in France.

The LFSS 2020 has also (i) introduced the right for companies to file a MA application before the expiry of the patent of the reference biological medicinal product, and (ii) created a working group to determine the conditions of interchangeability of biosimilars. However, in any cases, the marketing remains only possible at the expiry of the reference biological medicinal product patent.

Pricing of biosimilars

There is no specific pricing procedure for biosimilars.

Contrary to the pricing of generics, a very strict scheme of rebate in comparison of the reference medicinal product price does not exist for biosimilars.

In the CEPS/LEEM framework agreement of December 31, 2015 (*Accord cadre du 31 décembre 2015 entre le Comité économique des produits de santé et les Entreprises du médicament*), which is in force until the July, 31 2020 (*Avenant à l'Accord cadre du 31/12/2015 entre le Comité économique des produits de santé et les Entreprises du médicament, conclu le 18 décembre 2019*), it is indicated that fixation and regulation of biosimilars prices and their reference biological medicinal products will be specified in an amendment to this framework agreement. This amendment has however not yet been concluded. It is also indicated that the procedure for admission of biosimilars to reimbursement will be accelerated (75 days after the Transparency Commission advice and if not, an explanation to justify it) (Article 22.b).

Intellectual Property

Under French law, intellectual property law is governed by the provisions of the French Intellectual Property Code (*Code de la propriété intellectuelle*) which is harmonized with the EU protection of intellectual work.

In France, the National Institute of Industrial Property (*Institut National de la Propriété Industrielle, or INPI*) is the main regulatory entity responsible for receiving, examining and deciding on the registry and protection of patents, trademarks and other intellectual property works such as creative rights and designs applications.

A third-party user must obtain consent or a proper license from the owners to use them except for certain specific circumstances provided by law. Otherwise, the use will constitute a counterfeit (i.e. an infringement of these exclusive rights).

Patent

The French Intellectual Property Code provides that an invention is patentable if it is new, inventive, susceptible of industrial application and is not excluded from patentable subject matter.

According to Article L 611-2 of the French Intellectual Property Code, a French patent is valid for a term of 20 years maximum, starting from the application date. Patents remain in force by the payment of annuities. They must be paid no later than the last day of the anniversary month of the application filing. After a maximum period of 20 years, the invention is in the public domain, i.e. it no longer enjoys protection and anyone can exploit it, however a supplementary protection certificate can be issued in very specific circumstances under the terms of Article L 611-3 of the French Intellectual Property Code.

A French patent is obtained through its registration before National Institute of Industrial Property (*Institut National de la Propriété Industrielle, or INPI*) and the application procedure is set out in Articles L 612-1 *et seq* and in Articles R 612-1 *et seq* of the French Intellectual Property Code.

Trademark

According to the French Intellectual Property Code, for a sign to be registered as a trademark, it has to meet the following conditions: it must be licit, distinctive, and available. French Government implemented the Directive (EU) 2015/2436 into the French Intellectual Property Code by the transposition Ordinance of November 13, 2019, published in the Official Journal on November 14, 2019. According to such Ordinance, a sign may be represented "in any appropriate form by means of commonly available technology, and therefore not necessarily by graphic means, provided that such representation offers satisfactory guarantees for this purpose", with the sole condition that the representation is "clear, precise, distinct, easily accessible, intelligible, durable and objective".

Therefore, a request for registration may be rejected if the sign is identical or similar to a trademark or a sign pending for registration in the same or similar category of commodities or services.

The ownership of a trademark is obtained through its registration before the French National Institute of Industrial Property and the application procedure is set out in Articles L 712-1 *et seq* of the French Intellectual Property Code.

French trademark registrations are effective for a 10 year period, indefinitely renewable.

Whenever a trademark is subject to transfer or license agreements, to a contribution to a company, or to pledges, these agreements must be published with the French National Institute of Industrial Property.

Industrial designs

Under the French Intellectual Property Code, industrial designs can be protected by an exclusive right if the two following conditions are met : to be new and to have a specific character. This protection grants to their creator a monopoly over the use of these designs. Indeed, French legislators believed that the appearance of products is of strategic importance for commercial and industrial companies at several levels : distinction from the competition, attraction of the consumers, result of financial and human investments, etc.

When eligible, protection is granted by the French National Institute of Industrial Property for a renewable five-year period starting from the application date, to a maximum of 25 years. However, it is possible to initially request a renewable ten-year period of protection upon filing (in exchange of payment of an additional fee), up to the same maximum period of 25 years.

Trade secrets

In 2018, French legislators implemented in the French Commercial Code (Article L.151-1&seq) a European Union Directive 2016/943 of the European Parliament and of the Council dated June 8, 2016 on the protection of undisclosed know-how and business information (trade secrets) against their unlawful acquisition, use and disclosure.

It provides for the protection of information which is not generally known or easily accessible for people in the concerned business or activity, and "*has an actual or potential commercial value because of its secret nature*" and "*is subject to reasonable protective measures by its legitimate holder, taking into account the circumstances, to maintain its secret nature*." This provision makes it illegal to obtain, use or disclose this information with no agreement of its legitimate holder.

SANCTIONS LAWS AND REGULATIONS

This section sets out a summary of the sanctions regimes imposed by the respective jurisdictions.

U.S.

Treasury regulations

OFAC is the primary agency responsible for administering U.S. sanctions programs against targeted countries, entities, and individuals. "Primary" U.S. sanctions apply to "U.S. persons" or activities involving a U.S. nexus (e.g., funds transfers in U.S. currency or activities involving U.S.-origin goods, software, technology or services even if performed by non-U.S. persons), and "secondary" U.S. sanctions apply extraterritorially to the activities of non-U.S. persons even when the transaction has no U.S. nexus. Generally, U.S. persons are defined as entities organized under U.S. law (such as companies and their U.S. subsidiaries); any U.S. entity's domestic and foreign branches (sanctions against Iran and Cuba also apply to U.S. companies' foreign subsidiaries or other non-U.S. entities owned or controlled by U.S. persons); U.S. citizens or permanent resident aliens ("green card" holders), regardless of their location in the world; individuals physically present in the United States; and U.S. branches or U.S. subsidiaries of non-U.S. companies.

Depending on the sanctions program and/or parties involved, U.S. law also may require a U.S. company or a U.S. person to "block" (freeze) any assets/property interests owned, controlled or

held for the benefit of a sanctioned country, entity, or individual when such assets/property interests are in the United States or within the possession or control of a U.S. person. Upon such blocking, no transaction may be undertaken or effected with respect to the asset/property interest—no payments, benefits, provision of services or other dealings or other type of performance (in case of contracts/ agreements)—except pursuant to an authorization or license from OFAC.

OFAC's comprehensive sanctions programs currently apply to Cuba, Iran, North Korea, Syria, and the Crimea region of Russia/Ukraine (the comprehensive OFAC sanctions program against Sudan was terminated on October 12, 2017). OFAC also prohibits virtually all business dealings with persons and entities identified in the SDN List. Entities that a party on the SDN List owns (defined as a direct or indirect ownership interest of 50% or more, individually or in the aggregate) are also blocked, regardless of whether that entity is expressly named on the SDN List. Additionally, U.S. persons, wherever located, are prohibited from approving, financing, facilitating, or guaranteeing any transaction by a non-U.S. person where the transaction by that non-U.S. person would be prohibited if performed by a U.S. person or within the United States.

United Nations

The United Nations Security Council (the "**UNSC**") can take action to maintain or restore international peace and security under Chapter VII of the United Nations Charter. Sanctions measures encompass a broad range of enforcement options that do not involve the use of armed force. Since 1966, the UNSC has established 30 sanctions regimes.

The UNSC sanctions have taken a number of different forms, in pursuit of a variety of goals. The measures have ranged from comprehensive economic and trade sanctions to more targeted measures such as arms embargoes, travel bans, and financial or commodity restrictions. The UNSC has applied sanctions to support peaceful transitions, deter non-constitutional changes, constrain terrorism, protect human rights and promote non-proliferation.

There are 14 ongoing sanctions regimes which focus on supporting political settlement of conflicts, nuclear non-proliferation, and counter-terrorism. Each regime is administered by a sanctions committee chaired by a non-permanent member of the UNSC. There are ten monitoring groups, teams and panels that support the work of the sanctions committees.

United Nations sanctions are imposed by the UNSC, usually acting under Chapter VII of the United Nations Charter. Decisions of the UNSC bind members of the United Nations and override other obligations of United Nations member states.

EU

Under EU sanction measures, there is no "blanket" ban on doing business in or with a jurisdiction targeted by sanctions measures. It is not generally prohibited or otherwise restricted for a person or entity to do business (involving non-controlled or unrestricted items) with a counterparty in a country subject to EU sanctions where that counterparty is not a Sanctioned Person or not engaged in prohibited activities, such as exporting, selling, transferring or making certain controlled or restricted products available (either directly or indirectly) to, or for use in a jurisdiction subject to sanctions measures.

Australia

The Australian restrictions and prohibitions arising from the sanctions laws apply broadly to any person in Australia, any Australian anywhere in the world, companies incorporated overseas that are owned or controlled by Australians or persons in Australia, and/or any person using an Australian flag vessel or aircraft to transport goods or transact services subject to United Nations sanctions.