NEWSLETTER

DRUG MAH SYSTEM AND MEDICAL DEVICE PILOT REGISTRANT SYSTEM

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PRC's Drug MAH System and Medical Device Pilot Registrant System

– What Do They Bring to Foreign Pharmaceutical/Meditech Companies' Business in China

ABSTRACT

In order to encourage the research and development, as well as innovation in the field of medical drugs and devices in China, a new system has been introduced that now separates the medical drug and device's manufacturing process from the certificate of approval process on a trial basis respectively since 2015 and 2017. It is currently referred to as the Marketing Authorization Holder (MAH) system for medical drugs and the Registrant system for medical devices. The latest changes in these two systems, especially those contained in the newly amended Drug Administration Law (which will be in effect starting from 1 December 2019), and their impacts on foreign pharmaceutical and meditech companies conducting business in China are summarized below.

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THE LATEST CHANGES IN THE DRUG MAH SYSTEM AND THE MEDICAL DEVICE PILOT REGISTRANT SYSTEM AND THEIR IMPACTS ON FOREIGN PHARMACEUTICAL/MEDITECH COMPANIES' BUSINESS IN CHINA

I - Medical Drug MAH System

In the past, Chinese domestic medical drug manufacturing and approval were linked together, meaning that the entity applying for the approval must not only possess its own manufacturing facilities, but also manufacture the drug itself. Nonetheless, as of promulgation of the Decision of the Standing Committee of the National People's Congress on Authorizing the State Council to Conduct the Pilot Program of the Drug Marketing Authorization Holder System in Certain Areas and the Relevant Issues (全国人民代表大会常务委员会关于授权国务院在部分地方开展药品上市许可持有人制度试点和有关问题的决定) on 4 November 2015, the MAH pilot program ("Pilot Program") has been implemented in ten pilot areas in China for a period of four years, under which the drug approval title holder can be separate from the drug manufacturer. Thus, it means that it is no longer a requirement for the title holder of a drug registration certificate to manufacture its own drug(s). The amended Drug Administration Law ("Amended DAL") will come into effect on the 1 December 2019, and henceforth the MAH system will be implemented across the country.

The Amended DAL contains a specific chapter on the MAH system (Chapter III Drug Marketing Authorization Holder), which sets forth a concrete and consolidated list of MAH responsibilities and establishes a comprehensive pharmacovigilance and post-market surveillance system.

It is as outlined below:

1. Re-defined types of entities that can become a MAH

Accoding to Article 30 of the Amended DAL, the MAH refers to the **enterprise or drug research institution or other entities** that obtain a **drug registration certificate**. In contrast to the practices set up by the Pilot Program, the MAH under the Amended DAL cannot be an individual natural person, such as an individual scientific researcher.

2. Foreign pharmaceutical companies allowed to become a MAH

The Amended DAL further specifies that a foreign pharmaceutical company may become a MAH (Article 38), provided that a Chinese enterprise shall be designated by the foreign MAH and perform all the obligations imposed on the MAH ("Designated Chinese Enterprise"). In the meantime, it is explicitly stipulated that the foreign MAH and the Designated Chinese Enterprise shall bear joint and several liabilities. This implies that foreign enterprises will have the opportunity to become deeply involved in this MAH system and carry out business in the field of mandated manufacture and transfer of the marketing authorization to a qualified Chinese enterprise (to be discussed below) etc.

3. Re-structured allocation of responsibilities

The Amended DAL makes it clear that MAHs are responsible for all pre and post-approval activities during the entire product's life cycle. This includes the pre-clinical research, clinical trials, drug manufacturing, marketing and sales, post-marketing studies, adverse reaction monitoring, and risk management (Articles 6, 30). Meanwhile, the entities and individuals engaged in the research, manufacture, sale, storage, transportation, use and other activities of the drug shall bear corresponding responsibilities. MAHs are, therefore, accountable for the entire life span of the drug's management cycle, which diverges from the past where multiple parties were respectively liable for different phases of the drug.

4. Broad duties and obligations of a MAH under the Amended DAL

i. Quality management obligations in the event of mandated service providers

A MAH may entrust qualified entities to conduct drug manufacturing, sales, transportation and storage (Articles 32, 34, 35). In the event of a manufacturing mandate, the MAH and the mandated manufacturer shall execute a **mandate agreement** and a **quality agreement**, and strictly fulfil the obligations stipulated therein. The State Council will develop guidelines about the quality agreement for the delegated production of drugs to guide and supervise MAHs and entrusted manufacturers in performing their drug quality assurance obligations. A **mandate agreement** shall be concluded in cases of mandated sales, storage and transportation of drugs. Moreover, the quality assurance and risk management capabilities of the mandated party shall be assessed before the storage and transportation of drugs are mandated.

ii. Setting up release procedures for the marketing of drugs

It is further provided that a MAH shall set up release procedures for the marketing of drugs. Drugs cannot be launched in the marketplace unless examined and approved by the relevant qualified person (Article 33). Specific requirements on the release procedures are expected to be detailed in the implementation rules of the Amended DAL.

iii. Building a drug traceability system

As required by the Amended DAL, a drug traceability system shall be established and implemented by the MAH, as well as drug manufacturers, drug distributors and medical institutions. This is aimed to ensure the traceability of a drug's entire life-cycle - from research through to production and usage (Articles 7, 36). The goal is to prevent counterfeit or substandard drugs, and to conduct recalls accurately.

Over the last few years, the National Medical Products Administration ("NMPA") has been working on a traceability system under which MAHs, drug manufacturers, drug distributors, and relevant medical institutions are required to keep records of their activities and provide traceability data to NMPA. This information will be made publicly available through an online platform. MAHs and drug manufacturers are required to assign a unique traceability mark on each product's packaging unit, which will be generated in accordance with the uniform coding rules. It is likely that NMPA will release more rules to clarify each party's responsibilities and the timing for implementation.

iv. Obligations during the drug's post-marketing management stage

A MAH shall form a risk management plan and conduct post-marketing research (Article 77) that regularly assess the safety, efficacy and quality of listed drugs (Article 83). The Amended DAL also requires a MAH to monitor and **report adverse drug reactions** (Articles 80, 81), recall drugs with quality defect(s) or other safety risks (Article 82), and **report annually** to the provincial drug administration authorities regarding their drug's production and sale, post-marketing research and risk management measures (Article 37). The precise details of the reporting obligations may be addressed in the implementing rules.

v. Overall liabilities of relevant individuals

It is explicitly stipulated in the Amended DAL that the **legal representative and principal persons** of a MAH shall take full responsibilities for the drug's quality (Article 30).

5. Permitted transfer of a drug's marketing authorization

Under the current legal framework, a transfer of rights relating to a drug is usually recognized through the transfer of a drug's production technology to a transferee, which the transferee then applies or re-applies for a drug registration certificate. In contrast, the Amended DAL allows the transfer of a drug marketing authorization (i.e. drug registration certificate) upon the approval of the NMPA. However, this approval is based on the transferee being able to demonstrate that it possesses the capacities for quality control, risk management, and compensation for claims to ensure the safety, efficacy, and quality of drugs (Article 40). However, details on how a transferee can demonstrate sufficient capacities in this regard have not yet been made clear, but it is expected to be the regulator's focus in the future.

II. Pilot Registrant System of Medical Devices

Under the current *Regulations on the Supervision and Administration of Medical Devices* (2017 Revision), a manufacturer licence will only be granted to an applicant that has already obtained the medical device registration certificate. This means that the registration and production of medical devices are linked together and must be completed by one market player. In October 2017, the State Council issued the *Opinions on Deepening the Reform of Review and Approval System to Encourage the Innovation of Drugs and Medical Devices* (Guo Fa [2017] No.23) (中共中央办公厅、国务院办公厅印发《关于深化审评审批制度改革鼓励药品医疗器械创新的意见》), which established a pilot registrant system ("Pilot Registrant System") for medical devices. The Pilot Registration System is similar to the MAH system for drugs, in that eligible medical device registration applicants are entitled to apply for a medical device approval independently, while outsourcing the production to qualified enterprises.

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In December 2017, the Pilot Registrant System was launched in Shanghai's Pilot Free Trade Zone. In August 2018, it was extended to Tianjin and Guangdong, and then Beijing in February 2019. On 1 August 2019, the NMPA issued the *Circular of the National Medical Products Administration on Expanding the Pilot Medical Device Registrant System* (Guo Yao Jian Xie Zhu [2019] No. 33) ("No.33 Circular") (国家药监局关于扩大医疗器械注册人制度试点工作的通知) and announced the expansion of the current Pilot Registrant System from Shanghai, Guangdong, Tianjin and Beijing **to twenty-one provinces or provincial cities**. This covers most of the medical device industry's footprint in China. The scale and speed of this expansion exceeded the industry's previous expectations.

The Pilot Registrant System provides key conditions and obligations for the Registrant and delegated manufacturers involved in the Pilot Registrant System. These conditions include (i) the Registrant shall be staffed with full-time technical and management personnel for quality management and regulatory compliance; (ii) the Registrant is held responsible for the entire life cycle of a medical device, including research and development, clinical trial, production, sale, after-sale service, product recall, adverse reaction report, etc., and shall sign a mandate agreement and quality agreement with the mandated manufacturer, specifying the technical requirements, quality assurance, division of responsibilities and product release requirements; (iii) the Registrant shall also supervise and regularly assess the mandated manufacturer for their quality management abilities and strengthen the monitor of adverse events, etc. Generally speaking, there are many similarities between the Pilot Registrant System for medical devices and the Pilot Program for drugs.

Notwithstanding the expansion of the Pilot Registrant System, the system is not yet open to foreign meditech enterprises. This is because, in accordance with the No.33 Circular, the domicile or production site of the Registrant shall be located in a pilot province, autonomous region or municipality directly under the Central Government. Nevertheless, considering the Pilot Registrant System will be implemented thoroughly across China in the future, it would be essential to keep updated on any forthcoming developments made in the Pilot Registrant System.

III. Impacts on Foreign Pharmaceutical/Meditech Companies' Business in China

The Chinese government has been continuously reshaping the competitive landscape in the pharmaceutical and meditech industry for several years now. The drug MAH system will be implemented nationwide from 1 December 2019, while the Pilot Registrant System for medical devices has expanded to more regions. These reform initiatives may affect business models and commercialization strategies for specific foreign companies in China.

1. Impacts of the drug MAH system

i. Potential changes in business flow for imported drugs

Up until now, drug importation and localization in China is usually handled through two steps, i.e. license-in model: (1) First, based on an agreement, a Chinese pharmaceutical company will assist its foreign partner in applying for and obtaining the imported drug certificate. Upon receiving the certificate under the name of the foreign pharmaceutical company, the domestic pharmaceutical company will import and distribute the drugs into the Chinese market; and (2) Separately, the Chinese pharmaceutical company would set up the manufacturing capacity in order to get the technology licensed-in, so as to localize the drug.

This two-step model allows for quick occupation of the market, especially when the technology contains patents that will expire after a fixed period of time. However, this model poses aspects of uncertainty and potential problems if the Chinese pharmaceutical company is not able to immediately get a hold of a registration certificate.

Under the MAH system, thanks to the separation of the registration certificate title holder from the manufacturer, the Chinese pharmaceutical company might be able to directly apply for and act as a MAH at the beginning of the cooperation deal. It can thus continue to entrusted a foreign manufacturer to produce the drug(s) until production in China becomes feasible.

This new business model is yet to be confirmed by the ancillary regulations of the DAL that are to be updated in accordance with the Amended DAL.

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ii. A foreigner's MAH liabilities

The foreign MAH will be held liable for all aspects of the product life cycle, and must designate a Chinese enterprise to fulfil the obligations of the MAH. The foreign MAH will undertake joint and several liabilities with the Designated Chinese Enterprise and the outsourcing service provider(s). For instance, in cases of a drug quality defect, the customer has the right to claim compensation from any of the MAH, the Designated Chinese Enterprise, the mandated production enterprise or mandated distributor. If the customer demands compensation directly from the MAH, the MAH is obligated to compensate the customer first, even if the mandated production enterprise is at fault. Afterwards, the MAH is entitled to pursue recovery costs from the entrusted manufacturer to the extent of the manufacturer's corresponding liabilities. Therefore, in order to guarantee the quality and security of drugs in the research and development, manufacture, sale, storage and transportation of drugs, it is vital for a foreign MAH to conduct a thorough investigation, keep constant supervision over the manufacturing process and uphold a certain degree of control on the Designated Chinese Enterprise and outsourcing service providers before and throughout the cooperation process.

iii. Properly Organising Intellectual Property protection

The protection of the patent(s), trademark(s) and other intellectual property ("IP") is at the heart of a mandated production (to be specific, the mandate agreement) and transfer of a marketing authorization (such as in a merger & acquisition transaction). The IP protection should be made clear in writing, in particular (i) whether to transfer or license the IP; (ii) restrictions on use of the licensed IP; (iii) confidentiality obligations relating to protection of IP; (iv) attribution and protection of the newly developed IP in the course of cooperation; (v) whether to license the newly developed IP for the other party's use; (vi) dispose of IP infringement by a third party, etc. A foreign pharmaceutical enterprise should reach a proper agreement in terms of IP protection with its partners before entering into a partnership. Otherwise, a foreign enterprise may experience economic losses, and even potential market blockage.

2. Impacts of medical device Pilot Registrant System

As mentioned previously, while the Pilot Registrant System has expanded rapidly, foreign meditech enterprises are yet to have access to the Pilot Registrant System. Currently, in order to sell imported medical devices in China, a foreign meditech enterprise needs to have its medical devices registered in China through its own representative office or a Chinese enterprise acting on its behalf. Only after registration should the medical device then be imported from abroad into China.

It is important to note that if spare parts of the foreign meditech enterprise's medical device are exported to and assembled by a Chinese partner in China, it would then be deemed that the Chinese partner is the manufacturer of the medical device. From the regulator's perspective, the Chinese partner would then be the eligible applicant for the medical device's registration certificate.

In this situation, if the foreign meditech enterprise decides to stop cooperating with the Chinese partner, it is still possible for the foreign enterprise to register the imported medical device in China under its own name, even if the Chinese partner has been granted the registration certificate for the same medical device (which is processed with the spare parts supplied previously by the the foreign meditech enterprise). This is because innovativeness is not a mandatory factor for a medical device's registration approval.

Nevertheless, the key factor in securing a place in the Chinese market is for IP issues to be arranged appropriately. Otherwise, problems may occur if the Chinese partner obtains any patent rights or trademark rights over the medical device. In extreme circumstances, the foreign enterprise may lose the Chinese market in that the Chinese partner may no longer need the supply of spare parts, and the foreign enterprise may not be able to have the imported medical device registered in China if the Chinese partner raises objections to regulatory authority by claiming IP infringement .

Hence, it is advised that foreign meditech enterprises have their own IP, especially patent, registered in China when entering the Chinese market and be well-arranged where licensing is concerned. It is more secure to have medical devices registered only in the foreign meditech enterprise's own name to tackle the risks of losing the Chinese market. However, it will be a different scenario if the Registrant system is applicable to foreign enterprises, under which the foreign enterprise will be able to obtain the medical device registrastion - even if its Chinese partner is entrusted to carry out the production. However, the issues surrounding IP protection still need to be negotiated and included in the mandate agreement.

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