Baker McKenzie.

IPTech
China

Client Alert
October 2019

China: Drug administrative law amended to encourage innovation and deter safety violations

For further information, please contact:

Isabella Liu
Partner
+852 2846 1689
isabella.liu@bakermckenzie.com

Yilan Yang
Associate
+86 10 6535 3906
yilan.yang@bakermckenzie.com

The second amendment to the Drug Administrative Law (the "**Amended Law**") was approved by the Standing Committee of the National People's Congress on 26 August 2019 and will take effect from 1 December 2019. This is the first set of major changes to the law since its last amendment in 2001.

The Amended Law consolidates trial measures and orders issued by the State Council and the National Medical Products Administration of China ("NMPA", formerly known as the China Food and Drug Administration "CFDA") in the past four years, including in particular, the introduction of a system of drug lifecycle management centered around market authorization holders, and expedited drug review process. The Amended Law also provides harsher penalties for drug safety violations.

Market authorization holders and their responsibilities

While drug approval has always been a requirement, it is the first time that the term "market authorization holder" ("**MAH**") is explicitly used under the Drug Administrative Law in China. Article 30 provides that MAH refers to enterprises or drug R&D institutions that have obtained drug registration certificates. Core to the Amended Law, a MAH is required to manage the full lifecycle of drugs, including R&D (non-clinical and clinical processes), manufacturing and supply, post-marketing study, adverse effect monitoring and annual reporting, etc. For a foreign MAH, the relevant responsibilities should be carried out by its designated onshore entity in China.

In the past, there was a strong connection between drug manufacturing and drug approval (now market authorization): in order to obtain drug approval, one needs to have its own drug manufacturing facility. In addition, the previous regulatory regime did not provide a mechanism for the transfer of market authorization.[1] Under the Amended Law, the holding of market authorization can be separated from actual manufacturing activities. A MAH can engage third parties for drug manufacturing and sale, though it is obligated to conduct periodical audit of the third parties' quality management system in order to ensure drug safety. In addition, Article 40 of the Amended Law explicitly allows the transfer of market authorization.

The Amended Law also extends the scope of MAH to all enterprises, as opposed to drug R&D institutions only. Individuals cannot be a MAH, likely out of concern that they may lack the necessary resources to bear the

[1] In November 2015, the State Council approved a pilot trial of the MAH mechanism in ten selected cities, allowing drug R&D institutions and researchers to obtain and hold market authorization. Under the pilot, a MAH was allowed to engage qualified third parties for drug manufacturing and/or sale. Although the pilot allows for amendment of the MAH and/or the contracted manufacturer, it was unclear whether transfer of MAH can be regarded as a mere "amendment". The pilot was also limited to companies/individuals in the selected cities and did not involve imported drugs.

responsibilities for drug safety. If a researcher desires to be a MAH, he or she would need to invest in or establish a company.

Expedited drug review process

Previously, the review and approval of clinical trial applications were lengthy, taking six to eighteen months in practice. The negative notification system has been in place since July 2018 pursuant to the NMPA's Order No. 50 [2018] (*Notice on Adjustment of Drug Clinical Trial Review and Approval Procedures*), significantly expediting the review process. Under Order No. 50 [2018], a clinical trial applicant should discuss with the Center for Drug Evaluation ("**CDE**") before filing the clinical trial application and the sixty-day period starts counting from the CDE's formal acceptance of the application.

Article 19 of the Amended Law confirms the negative notification system for clinical trial approvals. Consistent with Order No. 50 [2018], after the CDE accepts an application for clinical trial, the application is deemed to have been approved if no negative comments are received within sixty days. After completing the required trials, the applicant can apply for marketing authorization and become a MAH.

In line with the CFDA's Order No. 126 [2017] (*Opinion on Encouraging Drug Innovation and Implementing Priority Review and Approval*), the Amended Law also confirms the policy of encouraging the development of drugs for treating orphan diseases and pediatric drugs. For drugs urgently needed for public health and drugs treating a life-threatening disease for which there is no other effective treatment, conditional approval can be granted based on existing clinical trial data suggesting effectiveness.

Online sale of prescription drugs

Article 61 of the Amended Law provides that MAH and drug suppliers can sell drugs through online channels, provided that they satisfy other requirements generally applicable to drug suppliers. This provision does not distinguish between prescription and over-the-counter drugs.

According to members of the legislative committee, the initial proposal was to prohibit the online sale of prescription drugs. Having balanced the interests of various parties, the committee finally decided to leave open the possibility of online sale of prescription drugs for further regulations by the NMPA.

Revised definition of "fake drug"

A "fake drug" as defined in the Amended Law refers to (i) a drug whose ingredients are inconsistent with the designated ingredients in China's national standards; (ii) a non-medicinal substance pretended to be a drug or a drug pretended to be a different type of drug; (iii) a drug of deteriorated quality; and (iv) a drug whose claimed indications or functions exceed those as approved. Although Article 98 of the Amended Law continues to prohibit the manufacturing and import of unapproved drugs, unapproved drugs have been removed from the definition of fake drugs.

The manufacturing and/or sale of fake drugs are subject to forfeiture of illegal turnover, suspension of manufacturing and sales activities, revocation of drug approvals, and a fine of fifteen to thirty times the illegal turnover. In serious cases, the drug manufacturing and/or sales permit can be revoked with a

black-list period of ten years, i.e., the same manufacturer/seller cannot re-apply for permits in the next ten years. Individuals responsible for the manufacturing and/or sale of fake drugs can also be subject to additional fine up to three times the individuals' incomes received from the manufacturer/seller during the period of violation, and be barred from participating in drug related activities for life.

Compared to the previous law, the Amended Law has imposed much harsher penalties. The fine is significantly increased at up to thirty times versus five times the illegal turnover. The Amended Law also assumes a minimum turnover of CNY100,000 if the amount is in fact lower, meaning that if one is found liable for the manufacturing or sale of fake drugs, the minimum amount of fine issued would be CNY1.5 million (being fifteen times of CNY100,000). Further, the Amended Law introduces a black-list period for serious violations, prohibiting the relevant manufacturer/seller from re-entering / importing into the market for the next ten years and responsible individuals can be permanently barred from the pharmaceutical industry.

Similar penalties are provided for the manufacturing and import of unapproved drugs. That said, Article 124 of the Amended Law provides a potential exemption of liabilities for small-scale parallel import of drugs. Under this provision, the penalties can be reduced or even exempted if a small amount of drugs that have been legally marketed overseas are imported into China without authorization and the circumstances are relatively minor. While it remains unclear at this time how the exemption may be carried out in practice (e.g., the permitted amount of drugs, etc.), this revision appears to respond to recent social debates over liabilities for selling "fake drugs"[2] of individuals who purchased and resold small amount of drugs from overseas markets. According to members of the legislative committee, the general principle remains unchanged that the importation of drugs requires approval, including drugs that have received market authorization in foreign markets. The Amended Law, however, seeks to clarify that such drugs do not fall within the definition of fake drugs, though unauthorized importation remains prohibited and is subject to a different penalty clause with potential exemption.

Latest drafts on implementing measures

On implementing the Amended Law, the NMPA in late September 2019 published three draft measures for public consultation on (1) drug registration, (2) drug manufacturing and (3) drug supply, respectively. Drug GMP (Good Manufacturing Practice) certification and the drug GSP (Good Supply Practice) certification are no longer required. The regulatory authorities will instead conduct the necessary review when examining applications for drug manufacturing permits and drug supply permits.

For a MAH who does not have manufacturing capacity, the NMPA proposes that the MAH still needs to obtain a drug manufacturing permit, but the application should be based on the MAH's agreement with the contracted manufacturer and the permit granted would be restricted accordingly.

[2] Under the previous *Drug Administrative Law* (2015), "fake drugs" include drugs that are unapproved in China but have received market authorization in foreign markets. This definition has been changed in the Amended Law.

Despite anticipation by the industry, issues such as updated mechanisms for patent linkage and data exclusivity[3] are not addressed in the draft implementing measures. The NMPA noted that these require further consideration and will be subject to further enactments.

Overall observations

The nationwide implementation of the MAH mechanism and the allowed transfer of market authorization present key improvements over the previous regulatory regime. The MAH mechanism separates market authorization holding from actual manufacturing and supply activities, allowing companies and R&D institutions to more flexibly engage in suitable business models for drug development and commercialization in China.

The various measures adopted under the Amended Law to speed up drug approval are welcome changes to the current framework. However, harsher penalties are imposed for drug safety violation in post-marketing activities. Overall and in line with the Chinese government's shift from extensive pre-market regulatory security to post-market vigilance by enterprises, the Amended Law seeks to expedite market entry while tightening post-marketing scrutiny for drug safety.

[3] In its *Opinion on Deepening Reformation of Review and Assessment in Encouraging Innovation in Drugs and Medical Devices* issued in October 2017, the State Council stated that China will explore to establish a patent linkage system, and to provide data exclusivity for innovative pharmaceuticals and therapeutic biologics, orphan drugs, paediatric drugs, and the first generic that successfully challenge the innovator's patent. Detailed measures remain to be enacted.

www.bakermckenzie.com

Suite 3401, China World Tower 2
1 Jianguomenwai Dajie
Beijing 100004, China
Tel: +86 10 6535 3800
Fax: +86 10 6505 2309

14th Floor, One Taikoo Place
979 King's Road, Quarry Bay
Hong Kong SAR, China
Tel: +852 2846 1888
Fax: +852 2845 0476

Unit 1601, Jin Mao Tower
88 Century Avenue, Pudong
Shanghai 200121, China
Tel: +86 21 6105 8558
Fax: +86 21 5047 0020