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Research on the Problems and Countermeasures of Mah in China's Drug Marketing Authorization Holder System

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Abstract: To study the strategies for better implementation of China's drug listing holder system. Method: By comparing the implementation of the MAH system for drug marketing license holders at home and abroad, analyze the problems existing in each link of the system in the pilot implementation of the system in China and propose targeted improvement measures. Conclusion: It is recommended to learn from developed countries' mature experience to make the drug marketing authorization holder system a policy dividend for promoting the scientific and technological progress and long-term development of the pharmaceutical industry.

1. Introduction

1.1 Background of the Implementation of the Mah System

China's previous drug registration system was a system that tied the drug production licenses to the marketing license. The low-level repeated construction under this system resulted in many “salted fish licenses,” “selling young crops,” and “multiple marriages for one girl,” which are serious. It affects the development and innovation of China's pharmaceutical industry. At the same time, due to the lack of a body responsible for the full life cycle of drugs, the quality of drugs cannot be effectively guaranteed. At the same time, the entire production cycle of drugs requires the participation of multiple parties, and the legal relationship between R&D personnel, manufacturers and other participants also needs to be clarified and supervised. Therefore, the MAH system was put on the agenda [1].

1.2 The Main Content of the Mah System

After implementing the drug marketing authorization holder system, the holder will conduct unified management and assume responsibility for all the drug's full life cycle links. In contrast, the subjects of other links shall bear corresponding responsibilities in accordance with the law.

The pilot program started in 2016. After nearly four years of pilot practice, it has proved feasible. In the newly revised Drug Administration Law, a drug marketing authorization holder system has

been established. The drug marketing authorization holder system requires that drug marketing authorization holders should be equipped with specialized personnel independently responsible for drug quality management, and establish a complete quality management system to comprehensively manage the quality of drug research, production, operation and use, and clarify the drug marketing authorization The holder is responsible for the safety, effectiveness and quality controllability of the drug throughout its life cycle in accordance with the law. [3]

2. Comparison of the Implementation of the Mah System At Home and Abroad

The MAH system originated in European and American countries. As a policy dividend, it has alleviated the problems under China's previous so-called "bundling" management model. It has also effectively suppressed the low-level, repetitive construction of pharmaceutical companies, and the enthusiasm for new drug research and development has been dramatically improved indirectly. Promote the prosperity of commissioned production and promote the rapid development of the international pharmaceutical industry. The specific implementation status is shown in Table 2.1 (Comparison of the MAH system's implementation status in the EU, Japan and China).

Table 2.1 Comparison of the Implementation of the Mah System in the Eu, Japan and China

Country	EU	Japan	China
Time	1965	2005	2016
Law	65/65/EEC Directive	"Pharmaceutical Affairs Law"	"Pilot Plan for Drug Marketing Authorization Holder System"
Type	Separation of drug marketing authorizer and drug production authorizer	Qualification access type MAH system	Combination of drug marketing authorization and production authorization
Content	MAA (marketing authorization applicant) can be a drug research and development institution, a manufacturing company, business enterprise or individual. After approval, MAA becomes MAH. If MAH meets the production conditions, it can be entrusted to a drug production license that has obtained a GMP certificate. Human production or self-production. MAH is responsible for drug safety. [4].	A "MAH license" was proposed. T Only after obtaining a particular type of MAH license can the listing application of a specific product be submitted. [5] Japan's MAH system requires the establishment of three qualified full-time managers.The core "is the production/sales three-person management[7].	The drug marketing authorization holder can directly transfer the drug marketing authorization to a qualified enterprise or drug development institution, The holder of the drug marketing license will conduct unified management and assume responsibility for all links of the drug's lifecycle, while the subjects of other links shall bear corresponding responsibilities in accordance with the law.[6].

3. Risk Analysis and Countermeasure Discussion of Mah System Implementation

3.1 Drug Quality Risks and Improvement Measures in Drug r&d and Commissioned Production

Risk:①The holder may not have established a quality management system suitable for its products, and the "Quality Agreement" signed with the entrusted company may not be correctly implemented in accordance with the agreement. ②he entrusted company may not have the qualifications to produce drugs, and the holder cannot guarantee the evaluation support of the GMP standard when auditing the entrusted manufacturer [8]. ③the laws and regulations for entrusted

production are not yet complete.

Improvements:①Strengthen the awareness of MAH drug risk management and GMP standard audit to ensure continuous compliance throughout the development process. ②Holders must improve their awareness of risk prevention and form a sound risk prevention mechanism. ③The drug regulatory authority in the place where the manufacturer belongs shall bear the responsibility of review and supervision to ensure that the manufacturer has qualified production qualifications. ④Further improve the quality management system and constantly formulate the legal provisions on commissioned production[9].

3.2 Safety Risks and Improvement Measures That Exist after the Drug is Marketed

Risks:①The supervision model needs to be optimized. The current model belongs to localized supervision, and the MAH system is difficult to be compatible with the current system [10]. ②The drug regulatory information system cannot keep up with the implementation needs of the MAH system, and the situation of comprehensively grasping the basic information of the holder, the registration verification of the product variety and GMP inspection and other regulatory information is out of reach.

Improvements:①Explore a localized supervision model, further strengthen the responsibility supervision of both the holder and the entrusted party, ②Improve relevant laws and regulations, establish a sound national-level drug regulatory information system, and ensure the traceability of drugs.

3.3 There Are Risks and Improvement Measures in the Protection of Consumer Rights

Risks:①R&D institutions and scientific researchers lack financial and human support.② It is difficult for drug R&D institutions and scientific researchers to ensure that the risk of drug sales and circulation is controllable [11]. ③The ADR burden of the proof distribution system and the ADR damage identification system need to be improved, and relevant laws and regulations need to be improved urgently. ④ The protection of rights and interests is lacking. Once a drug accident occurs, the huge amount of compensation responsibility will have to be borne by the research and development personnel, and the rights and interests of consumers are not guaranteed.

Improvements:① We can learn from the Japanese management model of “three-person management of production/sales”, so that the power and responsibility of drugs can be clearly defined in the small-scale research and development process. ②Improve the assessment standards to ensure that the holder has the relevant training on certain basic sales knowledge. ③ Speeding up the ADR relief legislation reasonably allocates the burden of proof for ADR damage, formulate ADR damage technical appraisal procedures, and protect the rights and interests of consumers.

4. Conclusion

The implementation of the MAH system has effectively stimulated the vitality of innovation in pharmaceutical companies and Strengthen lifecycle management. However, due to China's large, small, scattered and chaotic phenomenon will still exist, the industry regulatory system needs to be improved. Therefore, China should fully learn from the development and regulatory experience of the pharmaceutical industry in the European Union, the United States, Japan and other developed countries and regions, makes the drug marketing license holder system a policy dividend that

promotes the scientific and technological progress and long-term development of the pharmaceutical industry. It is also necessary for pharmaceutical companies implement safety management throughout the lifecycle of drugs to ensure the quality of drug production.

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