Further Strengthening the Supervision of Entrusted Manufacturing of Medical Devices: Key Takeaways from NMPA's New Notice

On 3 April 2024, the National Medical Products Administration ("NMPA") released the *Notice on Further Strengthening the Supervision and Management of Entrusted Manufacturing by Registrants of Medical Devices* (the "**Notice**"), taking effect from 1 June 2024. For information, the People's Republic of China ("**PRC**") introduced the regime of entrusted manufacturing of medical device in 2021, with the amendment of the *Regulation on Supervision and Administration of Medical Devices* under which Market Authorization Holders ("**MAHs**") can entrust qualified manufacturers for manufacturing without having production facilities in China by themselves.

The Notice is a part of NMPA's recent efforts on a well-regulated entrusted manufacturing system, covering three topics, including strict implementation of principal responsibilities of medical device registrants, enhanced management of registration of entrusted manufacturing and continued and strengthened entrusted manufacturing supervision. Below is a brief introduction of the main content of the Notice:

1. Principal Responsibility of Medical Device Registrants

   a) **Whole lifecycle QMS.** A quality management system ("**QMS**") covering the whole lifecycle of medical devices is a key responsibility of medical device registrants. The Notice specifies that even for MAHs who solely rely on entrusted manufacturing, they shall keep QMS complete and effective, by equipping standalone quality management organs and sufficient management and technical personnel. MAHs need also to equip themselves with the ability to pay compensation in proportion to product risks, market share and personal injury compensation standards, for instance by way of purchasing commercial insurances. Before carrying out entrusted manufacturing, MAHs shall ask the entrusted parties to submit credit information statement, and have a full knowledge of the credit status of the entrusted entities.

   b) **Implantable Medical Device**. All implantable medical devices on the *List of Medical Devices Prohibited from Entrusted Manufacturing* shall be only manufactured by the MAHs themselves. For other implantable medical devices, in principle the registrants shall designate personnel with relevant experience and knowledge to remain on-site at the entrusted manufacturer to carry out on-site guidance and supervision. The duties of such designated personnel should be specified in the quality agreement.

c) **Quality Agreement**. The quality agreement must be developed in accordance with *Guidelines for the Preparation of Quality Agreements for Entrusted Manufacturing of Medical Devices.* In principle, the term of a quality agreement shall not be longer than that of registration certification or production license, whichever is earlier. MAHs and the entrusted manufacturers may have their discretion in deciding on implementation details related to the control of documents, purchase, production process, testing, release and change control, while the communication and coordination requirements must be specified. Moreover, both parties shall formulate and execute management policies to carry out the quality agreement. They should also conduct an annual assessment of the suitability, adequacy and efficacy of the quality agreement to help verify relevant management policies and to ensure that actual production do not depart from the quality agreement.

d) **Purchase**. MAHs shall, together with their entrusted manufacturers, decide on the management of purchased goods and suppliers based on the importance of purchased goods. For critical goods or raw materials (such as those of animal origin, outsourced sterilization process, key components of active products and antigens and antibodies for in vitro diagnostic reagents), if the purchase thereof is carried out by entrusted manufacturers, MAHs shall determine by themselves, or together with their entrusted manufacturers, the inspection and acceptance criteria for purchasing and carry out examination on relevant suppliers.

e) **Market Release**. MAHs shall carry out the product market release by themselves and they cannot entrust product market release to any other entity. Entrusted products can only be released to the market upon signature of the designated personnel of MAHs.

f) **Prevention and Correction of Quality Issues**. The quality agreement shall include prevention and correction measures. Where the quality is significantly deteriorating, substandard intermediate or finished products are found in multiple batches or the risk incident after market release is beyond acceptable guidelines, both parties are obligated to investigate into and analyze the issue and take the measures and assess its efficacy.

g) **Change Control**. MAHs shall work with their entrusted manufacturers to develop change control procedures. For any introduction or changes of entrusted research, entrusted service and entrusted manufacturing, risk assessment shall be conducted to determine whether such change will have an impact on QMS.

h) **Adverse Events Monitoring**. MAHs shall take measures to perform their obligations under the *Administrative Measures for Monitoring and Re-evaluation of Adverse Events of Medical Devices*. Duties of both parties related to adverse events shall be included in the quality agreement and MAHs shall not shift their statutory obligations of adverse events monitoring to their entrusted manufacturers.

2. Enhanced Management of Registration

The Notice also clarifies some concerns in the registration process. For example, it requires that the entrusted manufacturing process shall be included in the QMS documents of MAHs. When inspecting the QMS, local NMPA will focus on the internal quality management organs, key management personnel, quality agreement and entrusted manufacturing management, etc.

Furthermore, the Notice specifies some record-filing requirements. Name change of the entrusted manufacturers is exempted from record-filing. In the case of changing production address, if a change of production license is not involved and the production scope can still cover the contracted products, a statement from local NMPA will be needed in record-filing. If an MAH terminates entrusted manufacturing, it shall apply to competent local NMPA to examine and delete the relevant entrusted manufacturing address and former entrusted manufacturers shall report such change to provincial NMPA.

3. Strengthened Administrative Supervision Measures

Provincial NMPAs shall continuously supervise the quality management of MAHs and the production compliance of the entrusted manufacturers throughout the whole lifecycle of medical devices. If MAHs intend to opt for entrusted manufacturing, or to change the entrusted manufacturers, MAHs shall notify provincial NMPA, who will subsequently undertake a QMS inspection on both the MAHs and their entrusted manufacturers.

Penalties for non-compliance are also stipulated in the Notice. If an MAH or its entrusted manufacturer's QMS fails to function properly, they will be subject to a rectification order. Provincial NMPAs will take measures, such as warnings or interrogation, if an MAH or its entrusted manufacturer fails to eliminate quality risks. For serious violation of quality management rules that jeopardize human health, provincial NMPAs can suspend the production and operation and punish responsible parties according to *Regulation on Supervision and Administration of Medical Devices*. Relevant penalties may include confiscation of relevant medical devices, fines of up to 20 times the value of medical devices, and suspension of medical device registration, production license and trading license. The responsible managers of the parties involved will be forfeited of income earned through illegal conduct, along with a fine ranging from 30% to 300% of such income and a 10-years ban from entering the medical devices industry.

4. Takeaways

Since the regime of entrusted manufacturing is relatively new in the PRC, the MAHs and entrusted manufacturers need to grow in awareness of the specific requirements issued by the NMPA and ensure their implementation in operation and production. We noticed that in practice non-compliance can happen quite often. The NMPA's annual statistics of 2023 shows that 25 MAHs out of 1,556 inspected were ordered to cease production and rectify the conditions, while 13 entrusted manufacturers of 1,180 inspected were imposed the same penalty.[1]

We advise the MAHs who adopt entrusted manufacturing mode should review their QMS on a regular basis to ensure full and continuous compliance. The MAHs should regularly coordinate with their entrusted manufacturers and carry out examination, guidance and supervision on their entrusted manufacturers in strict compliance with the statutory requirements.

In case you have questions or for further information, please contact the authors of this newsletter:

Nicolas Zhu
Partner
Head of Lifesciences Sector Group
CMS, China

T +86 21 6289 6363
E Nicolas.Zhu@cmslegal.cn

Laila Lu
Associate

CMS, China

T + 86 21 6289 6363
E Laila.Lu@cmslegal.cn

[1] https://www.nmpa.gov.cn/directory/web/nmpa/images/1716192390012090771.pdf

CMS Hasche Sigle Shanghai
Representative Office (Germany)
3108 Plaza 66, Tower 2
1266 Nanjing Road West
Shanghai 200040, China

CMS Cameron McKenna LLP Beijing
Representative Office (UK)
Room 1909, China Youth Plaza,
No. 19 Dongsanhuan North Road,
Chaoyang District
Beijing 100026, China