Successful approval of medical devices in China – a road with many obstacles

China represents a promising market for medical devices from the United Kingdom. However, the road to approval is long and requires an appropriate budget. In the following, the regulatory consultant Anna King from Cisema explains in great detail the approval of medical devices in China including instructions for registration, certification issues and process control.

Risk classification - determination of product category or classification request

The approval of medical devices in China starts with their classification following the Medical Device Classification Catalogue, the current version of which was published on 01 August 2018 by the National Medical Products Administration (NMPA, formerly CFDA). China uses the three risk classes I, II, and III for medical devices and in-vitro diagnostics (IVD). European classifications merely serve as an indication for the class as products are frequently assigned one risk class higher in China. The classification catalogue is clearly illustrated with a large number of examples. In-vitro diagnostics reagents still utilize the classification guidelines from 2013 (CFDA Notice No. 2013-242). If a medical device cannot be unequivocally classified into one of the 22 specified product categories, the Rules for Medical Device Classification are to be used.

Classification application

In borderline cases, there exists the option of applying for official classification with the NMPA. However, it can take the NMPA months to process such applications. Potential risks, specific characteristics, and the use of the device must be described in the application. The manufacturer must submit a detailed functional description and proof of classification of the device in the manufacturer's country of origin together with the application.

If the device is assigned risk class II or III, the next step of the registration process comprises the creation of the Product Technical Requirements (PTR, formerly Registration Standard), which map out the requirements for type tests for the particular device. Active medical devices are subject to performance, electrical safety, and electromagnetic compatibility (EMC) tests in China. China has its own system of standardisation, which is based on European standardization, but which always lags behind by a few years. Obligatory Chinese standards are called GuoBiao (GB), which is literally translated as "national standard". Chinese industry standards for medical devices are called YY standards. The test standard for electrical safety is called GB 9706.1-2007. It is based on IEC 60601-1: 1988, 2005, 2012. The standards are equivalent but not completely equal. The test standard for EMC in China is YY 0505-2012 and is identical to IEC 60601-1-2: 2004. Nevertheless, tests must be carried out at a test laboratory accredited by the NMPA in China. In China, biocompatibility tests for devices which come into contact with the patient's body are carried out in accordance with GB/T 16886.

1-201 1, which is in turn identical to ISO 1 0993- 1:2009. Here, the opportunity exists that the test, which was carried out abroad, is recognised in China. The prerequisites are that the test was performed in accordance with ISO 10993-1 :2009 and the test report was issued by a test laboratory following Good Laboratory Practices (GLP).

Importance of test reports and clinical trial in China

Preparation of the application dossier can begin in parallel to the type tests. The type test reports and the Clinical Evaluation Report (CER) are the cornerstones of the application. Whether a clinical trial in China is required for the CER can be determined using various exclusion criteria. The NMPA has published multiple batches of clinical trial exemption lists, detailing which Class II and III medical devices and IVDs do not require clinical trials in China for registration; instead, a highly simplified CER suffices. On 20.12.2019, the China NMPA (National Medical Products Administration) announced (No.91-2019) that it would add 148 medical devices and 23 in-vitro diagnostic reagents to the clinical trial exemption list, as well as to revise the names and descriptions of 48 medical devices and 4 in-vitro diagnostic reagents already on the list.

Class I medical devices do not need to undergo a type test or clinical trial in China; for these, a simple clinical evaluation suffices.

In instances where a product does not appear on the clinical trial exemption list, clinical data which were collected in a clinical trial performed outside of China can be used to create the CER if these meet Chinese requirements. This was introduced in 2018. If such data are not available, there is the option of finding a predicate device approved in China and use its clinical data. However, obtaining the clinical data in a legal manner can pose a challenge. A clinical trial for the product is only unavoidable if these three approaches are fruitless. Currently, another alternative to the clinical trial in China is emerging, because on December 13, 2019 the NMPA released a draft for the use of real-world data for the creation of a CER, “The Technical Guidelines for the Application of Real-World Data in Clinical Evaluation of Medical Devices”. Real-world data refers to observational data as opposed to data gathered in an experimental setting such as a randomized controlled trial (RCT). Possible sources can include patient-generated data or data derived from electronic health records. Certain guidelines have yet to be released before real-world data will be accepted as another clinical pathway for device approval in China.

Challenge through technical inspection of the product lifetime

The guidelines on the technical review of product lifetime, updated on 14 May 2019, form a new challenge in the registration of active medical devices (no. 23-2019). As part of the registration process, applicants must prove the lifetime of their products. Here, the lifetime is the period during which safe operation of the product is guaranteed.

Product registration by foreign manufacturers with a legal representative

Under the NMPA provisions, only a legal entity with residency in China can apply for the registration of medical devices. For the registration of their products, foreign producers thus require a legal representative, the NMPA Legal Agent. The manufacturer must issue a written power of attorney for representation at the NMPA. The NMPA Legal Agent plays a significant role in applying for, changing, and extending certificates as well as importing devices to China. Therefore, this position should be selected carefully, with the most important selection criteria being experience in dealing with regulatory matters, the relevant product standards, the competent authorities, as well as his/her loyalty and integrity.

Three options for choosing the NMPA Legal Agent in China

There are generally three options available:

» 1. A Chinese subsidiary of the producer assumes the function of legal agent.

» 2. The distributor is appointed as the legal agent; in this case, however, a company is to a large extent dependent on the distributor, who is virtually given exclusivity. With this option, you have to be aware that the distributor receives insight into very sensitive information including the product and the manufacturing process. In addition, the NMPA hands over the original certificates with appendices - the Product Technical Requirements - to the NMPA Legal Agent. Should the NMPA Legal Agent decide not to pass these originals on to the manufacturer or not to cooperate anymore, renewal applications are impossible.

» 3. A consultancy company responsible for the NMPA registration is appointed as the NMPA Legal Agent. This has the advantage of the foreign manufacturer remaining independent and being able to use as many Chinese distributors as required, as well as the flexibility to change them.

Technical requirements for submitting the application dossier

On 7 May 2019, the Center for Medical Device Evaluation (CMDE), a department of the NMPA, announced the introduction of an electronic platform to submit the application dossier (http://erps.cmde.org.cn). The system electronically manages medical device registrations. In future, all documents for the NMPA registration are to be submitted through this eRPS system (electronic Regulated Product Submission), with the paper form no longer being necessary.

Since 10 May 2019, it is thus possible to apply for a Certificate Authority (CA). The CA certificate is required to log into the eRPS system. With imported medical devices, the NMPA Legal Agent must apply for a CA certificate on behalf of the foreign manufacturer. The application dossier is to be submitted in Chinese and in complete form, together with all accompanying documents such as test reports, certificates, evidence, etc.

Review of documents and expiry date of certificates

The NMPA checks the submitted documents for compliance with the formal requirements within a week. For Class II medical devices, the CMDE requires approximately 60 working days for the technical evaluation of the documents, and 90 working days for Class III medical devices. After this initial technical evaluation, the CMDE expert issues a Supplementary Notice. Within one year of this notice, the manufacturer has a single chance to submit all supplementary documents to the NMPA. Applicants can request up to three face-to-face meetings with NMPA. Then follows the final technical evaluation, which will again take around 60 working days. The NMPA requires another 30 working days for administrative approval of the registration and to issue the certificate.

Certificates for Class II and III medical devices are valid for five years. Certificate renewals must be applied for at least six months before the expiration date at the latest. However, we advise manufacturers to start the procedure much earlier by checking whether relevant standards have changed. In some cases, changed regulatory requirements necessitate additional type tests before the renewal. If the deadline for renewal is missed, medical devices have to undergo a completely new NMPA registration. There is no expiration date for certificates for Class I medical devices.

Requirements for the local legal representatives of foreign companies

To safeguard product quality in the life sciences sector, the NMPA expects proactive cooperation of the NMPA Legal Agent and the foreign manufacturers. The NMPA published a guideline on responsibilities – the Guideline for Imported Medical Device Legal Agent. This includes supporting the manufacturer in the approval of its products and regulation compliant Chinese IFUs (instructions for use). From 1 January 2019, the Chinese company name of all imported Class II and III medical devices must be included in the Chinese IFU and on the Chinese label, and the name must match the name on the NMPA certificate. This request is illustrative of the importance of a well-informed, proactive, and cooperative NMPA Legal Agent for the timely implementation of current regulations in China.

Monitoring and reporting of adverse events

Further responsibilities of the NMPA Legal Agent comprise monitoring and reporting adverse events in China as well as notifying and supporting the supervisory authorities in quality control. To this end, the NMPA has released Decree No. 1 on the reporting of adverse events for medical devices on 31 August 2018. The Decree states that adverse events that occur overseas must be reported to the NMPA and a report must be created by the NMPA Legal Agent in China. This regulation assigns the responsibility for controlling, proactive monitoring, and providing information on quality problems to the manufacturer and the NMPA Legal Agent in equal parts. A minor adverse event does not require immediate reporting, while a suspected serious adverse event – involving serious injury of death – requires a report to be sent to the provincial counterparts of the NMPA.

The official timeline varies between 12 hours and 45 days depending on the severity and also if it is an individual or group adverse event. The system serves to improve risk management of medical devices by targeting the monitoring, evaluation, and remedying of adverse events for medical devices. The NMPA Legal Agent plays a much more important role than before, which aligns with the new regulatory emphasis on post-approval supervision. As the local legal representatives, they are responsible for meeting requirements after the product is brought to market, without the producer having to establish its own Chinese office.

Regulations for the recall of defective imported goods

With regards to the issue of adverse events, the State Administration of Market Regulation (SAMR) published a joint declaration together with the General Administration of Customs of China (GACC) on 30 October 2018, announcing closer cooperation in the recall of defective imported goods. With this reform, the SAMR was given the main responsibility for product recalls in China, with greater focus placed on life sciences products and foods, such as medical devices, pharmaceuticals, and cosmetics, in addition to health food and infant milk. The GACC reports to the SAMR on products identified as defective during customs inspections. The SAMR in turn informs the GACC on infringements in the event of recalls, to allow the GACC to initiate measures against the involved companies. Moreover, producers and consumers can find information about recalls on the website of SAMR. The WeChat Messenger services of the SAMR and GACC also regularly publish information on recalls.

Product safety control through factory inspections of overseas manufacturers

Further reinforcement of product safety controls was enacted in the "Directive on the Administration of Medical Devices and Medicine Overseas", passed on 28 December 2018. This regulation specifies that the NMPA will also carry out factory inspections for overseas manufacturers, to guarantee the safety and effectiveness of imported medical devices and pharmaceuticals.

The goal is not to inspect every single foreign manufacturer; sampling will take place on the basis of risk assessments. To date, primarily Chinese producers were regularly inspected. It is to be expected that about 30 foreign companies are subjected to an inspection each year. Deficiencies were identified in all instances. The respective problems can be looked up online on the NMPA website. Producers then have 50 working days to take corrective measures.

Introduction of the UDI system for medical devices in China

On 23 August 2020, the NMPA announced the introduction of the UDI system (Unique Device Identification) for medical devices in China. The implementation is going to take place step by step for certain product batches. The first product batch contains high-risk products such as catheters and pacemakers. For these products, the new UDI rule comes into force on October 1st, 2020.To date, four important documents have been published on the UDI ("NMPA Announcement on Issuing the Rule of UDI System for Medical Devices", "Rule for UDI System of Medical Devices in China", "YY/T 1630-2018 Fundamental Requirements for the UDI", and the "NMPA UDI Interpretation Rule"). Foreign producers of medical devices as announced in the batches must carry out the following steps:

» 1. Creation of a DI code (Device Identification) in line with the UDI code standard of the Chinese approval authority ANCC (Article Numbering Center of China) and determining the PI code structure (Production Identification)

» 2. From 1 October 2020, the applicant must submit the relevant DI code to the NMPA for applications for approval of medical devices — such as new approvals, renewed approvals, and changes to the approval of medical devices.

» 3. Selection of a suitable data carrier — such as a barcode, QR code, or RFID code — in accordance with the ANCC Standard and applying it to the product or packaging.

» 4. Uploading the DI code and the associated information to the UDI database for medical devices before it is imported to China. Important — this UDI database has not yet been made available by the NMPA.

» 5. If there are changes to the DI code and the associated information, the applicant must update the information in the UDI database.

Implementation of Hong Kong-registered medical devices in China's Greater Bay Area

On 06.11.2019, the Central Government of PRC has accepted the HKSAR government's proposal for the use of Hong Kong registered pharmaceutical products and common medical devices in designated Hong Kong-owned medical institutions in the Greater Bay Area.

This measure will help attract local and multinational companies to introduce medical devices to Hong Kong with a view to expanding their businesses in Hong Kong and Mainland cities in the Greater Bay Area, benefiting patients in both places.

The Food and Health Bureau will be in discussion with relevant Mainland authorities on the implementation details, including the measure at the University of Hong Kong-Shenzhen Hospital on a pilot basis. Once implemented, this may enable an additional regulatory pathway to China by first registering in Hong Kong.

Conclusion - a long but worthwhile way to China

Major regulatory challenges must be overcome to enter the Chinese market. Therefore, companies should schedule plenty of time and arrange for an appropriate budget. The door to this promising market opens when successfully completing the required tests and creating a solid application dossier.

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