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COLUMNS

China market access for MedTech via Hong Kong and the Greater Bay Area Initiative

The stringent regulatory requirements in Mainland China can be overly onerous for many MedTech manufacturers looking to sell into one of the world's largest and fastest growing healthcare markets. By contrast, Hong Kong's certification requirements for imported MedTech devices are voluntary and, in any case, less burdensome provided the manufacturer has already obtained certification in their home country.

Recent policy changes could enable MedTech companies to register their products in Hong Kong and then sell into Hong Kong-owned healthcare institutions in the Greater Bay Area, effectively allowing some Mainland China sales. With real-world data from Greater Bay Area sales, a MedTech manufacturer can thereafter make a simplified registration application to sell throughout the rest of Mainland China.

The Chinese registration requirements

MedTech manufacturers looking to sell their devices into China must first register them with the National Medical Products Administration (NMPA, formerly CFDA).[1] Similar to other global registration frameworks, the NMPA uses three risk classes – I, II and III – for medical devices and in-vitro diagnostics (IVD), with Class III having the most potential risk for users. Classification is made pursuant to a classification catalogue which has a large number of examples.

If a MedTech device is determined to fall into Class I, then filing with the NMPA will be sufficient prior to China sales. There is no need to undergo a type test or clinical trial for Class I devices. Timing from start to finish can be as quick as seven weeks, depending on the documentation available and other practical considerations (e.g. translation and notarization timing because filings need to be submitted to the NMPA in Chinese).

For all three risk classes, the Product Technical Requirements (PTR, formerly Registration Standards) will need to be compiled. The PTR maps out the requirements for type tests for the particular device. Tests must be carried out at a test laboratory accredited by the NMPA in China.

In addition, a Class II or Class III device might require a clinical trial in China to complete the Clinical Evaluation Report (CER) and the application dossier, unless the device can be categorized under one of the exemptions. The NMPA has published multiple batches of clinical trial exemption lists, the most recently in December 2019 when 148 medical devices and 23 IVD reagents were added to the exemption list.

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SPOTLIGHT

Clinical trials can add one to two years or more to a registration application and cost upwards of US$200,000. On top of a registration timeline of around 18 months for Class II and 21 months for Class III devices, this adds significantly to cost and time to market. Therefore, MedTech companies looking to sell into the huge Chinese healthcare market will benefit from avoiding conducting a clinical trial in China unless absolutely necessary.

MedTech manufacturers now have a number of other options in the last few years even if their devices do not fall within one of the exemption lists:

1. using clinical data collected in clinical trials meeting the Chinese requirements gathered outside of China to create the CER: this has been available since 2018 but there are significant subtleties to its application because of the Chinese requirements, which are not always intuitive or consistent with other regulatory frameworks. Therefore, the original clinical trial in the home country will need to be conducted with prior advice and an eventual China NMPA application in mind;

2. using clinical data from a predicate device: however, predicate devices are usually owned by direct competitors who will generally be unwilling to share the detailed clinical data required;

3. using "real-world data" to prepare the CER: recently in December 2019, the NMPA released a draft for the use of real-world data for creation of a CER.[2] Real-world data refers to observational data as opposed to data gathered in an experimental setting as randomised controlled trials. The NMPA is still to publish additional guidelines and so this promising pathway is in its testing stages but there has been momentum for this pathway and developments in the Hainan Pilot Zone, where in March 2020 the first device was approved by the NMPA according to the real-world data requirements. The device approved was US firm Allergan's glaucoma drainage tube.

Only a legal entity with residency in China can apply for registration with the NMPA. But this does not mean a non-Chinese MedTech company needs to establish a Chinese subsidiary, although this is one option.

Local distributors can act as NMPA Legal Agent, but this brings its own risks:

1. practical exclusivity is effectively granted because the distributor will generally retain the original certificates with appendices, making renewal or amendment applications without their cooperation extremely difficult, if not impossible;

2. the distributor receives detailed technical and sensitive information including product and manufacturing processes.

Alternatively, an independent third-party service provider can act as NMPA Legal Agent which has the advantage of the foreign manufacturer retaining its independence and flexibility with respect to its local Chinese distributors and more stringent information controls.

Hong Kong registration

Hong Kong has a unique regulatory system, with the Medical Device Division ("MDD", formerly the Medical Device Control Office) of the Department of Health overseeing the Medical Device Administrative Control System ("MDACS").[3] Unlike NMPA registration in China, MDACS listing for medical devices in Hong Kong is currently voluntary. The practical effect is that few will list their devices under MDACS.

Hong Kong has four risk levels for medical devices and four for IVDs, which are summarised in the accompanying tables:

Medical Devices

Class	Risk Level	Examples for reference
I	Low	Stethoscope, Bandages, Wheelchairs, Walking aid, Compression hosiery
II	Low-moderate	Electrocardiograph (ECG), Transcutaneous electrical neuromuscular stimulator (TENS), Hearing aids, Electronic blood pressure monitor, Urinary catheter
III	Moderate-high	Contact lens care solutions, Diagnostic X-ray machines, Automated external defibrillator, Insulin pen, Prosthetic joint
IV	High	Artificial heart valves, Implantable cardiac pacemakers, Neuro-endoscopes, Breast implant

In Vitro Diagnostic (IVD)

Class	Risk Level	Examples for reference
A	Low	Plain urine cup, Identification kits for cultured microorganism
B	Low-moderate	Urine test strips, Pregnancy test kits
C	Moderate-high	Home use blood glucose meters and their test strips, Screening test for Spina Bifida in foetus, Diagnostic assay for Chlamydia pneumonia
D	High	Tests to detect Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV), Hepatitis B Virus (HBV)

The key documents required to apply for registration under the voluntary system are:

- MDACS Form;
- Instructions for Use (IFU);
- ISO 12485;
- Summaries of available clinical data; and
- Home jurisdiction test reports (as required).

The application can be done in English. Neither local testing nor clinical trials are required, which significantly reduces approval times although approval will still generally take 9 to 12 months. A non-Hong Kong company will need to designate a local responsible person, or LRP, for the application.

One reason for registration is Hong Kong's procurement system is highly influenced by the Hospital Authority, which gives precedence to products registered with MDACS. Therefore, there is increased likelihood of public (and private) purchases if the product is MDACS listed.

Greater Bay Area initiative as new potential regulatory pathway

Listing in Hong Kong has recently become more attractive. As part of the Chinese Government's push to develop the Greater Bay Area (also known as the Pearl River Delta),[5] a new policy initiative is to allow Hong Kong-registered MedTech to be sold into Hong Kong-owned medical institutions in the Greater Bay Area.

The Greater Bay Area includes the mega cities of Guangdong, Hong Kong, Shenzhen and Macau and has a total population exceeding 72 million.[6] This is larger than the population of the UK and nearly as big as Germany's. The area's GDP was approximately US$1.5 trillion in 2018, the last years for which numbers are available, making it larger than half the size of France's economy, or greater than the Austrian and Swiss economies combined.[7]

China aims to build the Greater Bay Area into a hub of global technological innovation and an important source of emerging industries. For the past years, more medical institutions owned or managed by Hong Kong enterprises have been providing healthcare services in the Greater Bay Area.

The new policy regarding sale of Hong Kong-registered medical devices into Hong Kong-owned medical institutions in the Greater Bay Area was announced by the People's Republic of China (PRC) Central Government on 6 November 2019 as part of a broader list of 16 policy measures.[8] The measure is intended to attract local and multinational pharma, biotech and HealthTech companies to introduce products 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".[9]

Implementation of the policy measure is still to be determined by Hong Kong and Mainland authorities,[10] but the potential new regulatory pathway into Mainland China is exciting for MedTech manufacturers.

We suggest in broad outline that the pathway could look as follows. A MedTech company begins immediately selling their product into Hong Kong while simultaneously applying for listing under MDACS. Following MDACS approval, distribution of the device can be widened to the Greater Bay Area. There is no specific list yet of institutions into which such products can be sold, however the University of Hong Kong-Shenzhen Hospital is specifically named on the government website[11] and a non-official list of other institutions is provided on an HKSAR Government website.[12]

With sales into the Greater Bay Area, a MedTech company can receive income and gather real-world data in China itself. This will likely look similar to the existing Hainan health Pilot Zone. Demonstrated usage in China itself is important because data can be gathered on Chinese patients, which is often a specific requirement for NMPA approval of higher risk class devices. From a practical perspective, it is also clearly positive because revenues can be earned and the market tested for the particular product, rather than the typical dead zone of zero revenues while waiting for approvals in-country.

Assuming the real-world data regulatory pathway in China is finalised without significant changes, then the Greater Bay Area sales will provide persuasive real-world data. With such data, a simplified application made to the China NMPA without the need for an expensive and time-consuming clinical trial. The ultimate approval timeline will be shorter than or at least similar to existing timelines for NMPA Class II or III applications, but with the considerable benefits of incoming revenues and sales records throughout the pathway timeline, as well as reduced cost and the introduction of optionality given that a company has multiple milestones at which to determine whether to proceed or not.

Whilst the details of the programme are still to be finalised, there is considerable interest and optimism about this potential new regulatory pathway. Once the final details are implemented, we expect Hong Kong's voluntary registration regime will be significantly busier, and patients will benefit as they can obtain leading treatment and devices, wherever developed, sooner.

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