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UPDATE

Food and Drug Law, Regulation and Education

FDLI
A PUBLICATION OF THE FOOD AND DRUG LAW INSTITUTE

China's New Regulations on Medical Devices

By Gordon Schatz and Michael Alper

Starting June 1, 2014, China's regulation of medical devices took a big step forward with the new Administrative Regulations on the Supervision and Administration of Medical Devices (State Council Order No. 650, released March 7, 2014).[1] For device companies already in China or considering how best to enter the China health care market, these regulations present important new regulatory dynamics.[2]

The new regulations carry particular authority because they were issued by China's State Council,[3] and will be implemented through the China Food and Drug Administration (CFDA), which has risen in the Chinese administrative government hierarchy compared to its predecessor – the State Food and Drug Administration. The new regulations significantly revise the prior regulations in place since 2000 and are intended to establish more efficient and scientific regulatory controls over

Gordon Schatz is Reed Smith's China Life Science Integration Partner and has worked from Reed Smith's offices in Washington, DC, Beijing and Shanghai, since 2009.

**Gordon represents medical device, diagnostic and drug companies on regulatory and reimbursement issues.*

Michael Alper is the managing director and CEO of NeuvoMedica, a Shanghai-based medical device distributor and consultancy. The NeuvoMedica team also includes native Chinese with experience in China's device regulations.

**Fluent in Mandarin Chinese, Michael has spent over eight years working in and representing in the medical device manufacturers including over six years in China.*

the safety and effectiveness of medical devices.[4] Major new provisions include:

- More streamlined filing process for Class I devices.
- Updates in clinical trial requirements with the possible future issuance of a catalogue identifying devices not subject to clinical trials.
- Potentially more expeditious sequence of getting a medical device registered first, then getting the manufacturing license.
- Compliance with good manufacturing practices (GMPs) and the implementation of quality control systems now include self-inspections and submission of a manufacturer's self-inspection report to CFDA's counterparts at the provincial level.
- Significantly higher penalties for violation of requirements.

Registration and Filing Requirements

The new regulations further align CFDA's regulatory controls with a device's level of risk to patients. For example, a more expedited filing procedure should be available to all Class I medical devices, including those manufactured in foreign countries. This filing procedure replaces the prior registration process for Class I devices. Higher risk devices in Class II and Class III still require registration, including a submission of more comprehensive data on the product.

Under the old regulations, a material change in a registered device required a new registration as a new device.[5] By comparison, under the new regulations, a material change only requires a change in registration. Generally, a material change in a registered medical device is when the device's safety and/or efficacy might be affected by any change in its design, raw material, manufacturing procedure, etc. In practice, CFDA's local counterparts have wide discretion in determining what changes constitute material changes.

An immaterial/minor change in a registered medical device is no longer subject to the approval by the original registration authority; filing such change with the authority is sufficient.

Consistent with prior regulations, classification of medical devices (I, II, or III) is based on the level of risk to the patient, considering intended uses, structural features, and method of usage. Following the issuance of the new regulations, updates to the classification catalog of medical device types are likely. This may re-position devices into lower-risk categories and less burdensome regulatory requirements, for example if the technology becomes more mature and there is evidence of a high safety profile.

Another significant change under the new regulations is that the term of a medical device registration is five years instead of four. Also, the registration can be extended through renewal, instead of re-registration. This should lower some of the regulatory burdens for manufacturers.

Clinical Trials

The very important issue of whether clinical trial data from outside China will satisfy CFDA data requirements is still under debate. The 2004 SFDA rule allowed clinical data from outside China for a number of devices.[6] A new "Measures for the Administration of Medical Device Registration" was released on August 1, 2014.

Under the new regulations, clinical trial reports shall be issued by qualified clinical trial institutions located in China. Further, a clinical trial of low-risk medical devices no longer requires the approval of CFDA or its counterparts, but a filing is required. Certain Category III medical devices that involve very high risks must still obtain the necessary approvals.

The new regulations continue the requirement for clinical trials for Class II and III devices. A clinical trial may not be necessary if similar devices have been on the market for a long time and there is a proven record of safety with no reports of serious adverse events. Additionally, clinical trials may not be needed if the safety and efficacy of the product can be proven without a clinical trial. The CFDA will develop a catalog listing devices that will not require a clinical trial and will be made public.

Manufacturers

The new regulations specifically stipulate that medical device enterprises shall comply that medical device enterprises shall comply with GMPs for manufacturing, operating conditions and quality control systems. Manufacturing enterprises must conduct self-inspections on a regular basis and submit self-inspection reports to CFDA's counterparts at the provincial level. CFDA and its counterparts can make regular and random inspections to check on compliance.

An enterprise that intends to manufacture Category II and/or Category III medical devices may apply for registration of its medical device first and then apply for its manufacturing license. Under the old regulations, it had to first obtain its manufacturing license. Also, before an enterprise was issued a medical device registration certificate, it had to establish qualified manufacturing facilities in order to be qualified for obtaining a manufacturing license. Under the new regulations, the enterprise can first get its medical device registered, and then

proceed to obtain the manufacturing license. This may provide for a speedier registration process, and possibly lower expenses for the manufacturer. CFDA officials have suggested that one reason for this change in regulation is due to the financial pressures on new manufacturers waiting to get their product approved. A new manufacturer had to continue paying for a manufacturing facility fee for several years without an approved product to sell. In general, this is part of a trend at CFDA in the government to increase the speed of approvals linked to other regulatory requirements, including early stage self-inspections, random inspections and heavier penalties.

The new regulations stipulate what information must be included in the instructions for use and labels of medical devices. Medical devices manufactured in foreign countries must have their Chinese labels attached before they are imported into China.

The new regulations contain a section on monitoring adverse incidents, reevaluating registered medical devices, and recalling defective medical devices. Every medical device enterprise must now establish an adverse incidents monitoring system to monitor and report adverse incidents. While some of these requirements are not new[7], they underscore the CFDA's commitment to a regulatory system designed to improve the safety and quality of medical devices and healthcare in China.

Changes for Distributors

Distributors of Category II medical devices may file with CFDA's counterparts at the municipal level instead of obtaining a permit as required by the old regulations. Distributors for Class III devices still need to obtain a permit, but from the municipal level CFDA agency, rather than from the provincial level. Implementing rules, here also, may make it clearer if filing will be easier.

Distributors and other sellers of medical devices are required to verify and inspect the qualifications of their manufacturers or providers, as well as the certificates of conformity of the devices they will purchase. Wholesalers of Category II medical devices and all Category III medical devices sellers (wholesalers and retailers) shall also establish a system to maintain their sales records.

Increased Legal Penalties and Liabilities

The new regulations increase liabilities and penalties for manufacturers and distributors. The old regulations imposed fines for certain serious violations based on two to five times of the illegal proceeds. Under the new regulations, however, it would be five to 10 times (or even 10 to 20 times) of the value of the involved medical devices.

Further, the new regulations clarify that the fine will be calculated based on the value of the medical devices concerned in its illegal activities, and manufacturing costs and other expenses incurred will not be deducted for the purpose of calculating the fine. Every failure to comply with the new requirements imposes significant new penalties. For instance, the new regulations present punishment for deceptive advertising on medical devices, and punishment for forgery, alteration, purchase, sale, and lease of any medical device certificates or permits.

Other changes include:

- The new regulations redefine the scope of "medical devices." It now includes vitro diagnostic reagents and calibrators. They also add the following to the description of the purpose of medical devices: (i) for life support or maintenance; and (ii) to provide information for medical treatment or diagnosis through human sample testing.
- The new regulations remove the requirement that Category III medical devices shall be subject to the China Compulsory Certification.
- The new regulations repeat and emphasize the major liabilities of manufacturing enterprises to recall defective medical devices that are stipulated in the Administrative Measures on Recall of Medical Devices (2011).

CFDA is developing a number of important rules, normative documents and guidelines that will implement many of these changes. These should clarify what manufacturers and distributors need to do to comply with the new regulations.

In addition to these new regulations, on May 15, CFDA released its *Measures on the Supervision and Administration of the Quality of Medical Devices in Use* for public comment.[8] Under the measures, medical device operators will be required to establish a quality management system especially for Class III devices. Features of this proposed system cover the purchase of medical devices, an incoming stock inspection and recording system, an inbound and outbound management system, a daily maintenance and recording system, a quality traceability recording system, a management system for disposable medical devices, and a management system for contracts and technical documents for products.

Conclusions

The new State Council device regulations set important new procedures for product registration, along with changing classification and clinical trial requirements. Penalties will be higher for violations of the regulations. Since

China is becoming such an important market for medical devices, companies seeking to introduce well known and innovative devices should plan carefully to follow these new regulations. The new procedures can play a significant role in the regulatory entry strategies for innovative devices. Furthermore, the US FDA has been building its presence in China, which is important for companies manufacturing in China and selling/exporting to the US. US manufacturers are no doubt familiar with "dual" regulatory systems, and a new dialogue on device regulations is developing between the US and China.

As a final note, some of the English translations of Chinese regulations may sound like US FDA regulations, companies should be alert that the authoritative Chinese language regulations and the Chinese FDA officials who administer the regulations control implementation of the regulations. These Chinese officials[9] bring the same commitment to protecting the public health and safety of the Chinese as US FDA officials bring to the safety of US citizens. Even with a trend in global regulatory harmonization around the world, China is both a brave new world and the wild, wild west when it comes to device regulation.

Device registrations, approvals and related regulatory requirements can be unpredictable and protracted. Understanding and complying with these new regulations can be crucial for the success of innovative medical devices.

1. On July 30, 2014, CFDA moved forward with implementing decrees: No. 4 for Medical Device registration, No. 5 for IVD Products Registration, No. 6 for Medical Device Labels and Instructions for Use, No. 7 for Medical Device Manufacturing, and No. 7 for Medical Device Distribution.
2. Note that CFDA has a Chinese language website and an English language website. The English language website can be accessed at: http://eng.sfda.gov.cn/WS03/CL0755/. No authorized English language translation is yet available for State Council Order No. 650. The Chinese language regulations are the authorized regulations. The CFDA references below are to the English translations of various CFDA regulations and notices. They are provided for convenience and accessibility by English readers, but Mr. Schatz and Mr. Alper strongly recommend review and reliance on the authoritative Chinese language regulations and policies.
3. China's State Council is the highest executive agency in China's federal government administration.
4. http://eng.sfda.gov.cn/WS03/CL0767/61641.html - Regulations for the Supervision and Administration of Medical Devices (State Council Order No. 276 - 2000) http://eng.sfda.gov.cn/WS03/CL0757/96865.html (State Council Passes Draft Amendments to Device Regulations (February 17, 2014).
5. http://eng.sfda.gov.cn/WS03/CL0770/98145.html
6. http://eng.sfda.gov.cn/WS03/CL0768/61644.html - Provisions for Clinical Trials for Medical Devices.

   SFDA Order # 5 (January 17, 2004)
7. http://eng.sfda.gov.cn/WS03/CL0757/99620.html. CFDA releases 2013 Annual Report for National Medical Device Adverse Event Monitoring (2014-05-12)
8. See English language notice at http://www.sfda.gov.cn/WS01/CL0779/99834.html. CFDA has also introduced 120 industry standards for medical devices. See notice http://eng.sfda.gov.cn/WS03/CL0757/102298.html (July 3, 2014)
9. The authors would like to thank Zhang Gaotong, Hubert Humphrey Fellow at Washington College of Law, American University, Washington DC, who has been on a fellowship during 2013-2014, and serves as Deputy Consultant to CFDA's Department of Legal Affairs, Division of Regulations II. The views expressed in this article are exclusively those of the authors and do not represent the positions of any government agency or offical; including any Chinese government agency.