China’s Medical Device Market: New Policies, Higher Stakes

Presentation for MassMEDIC webinar

Katherine Wang & Florian Then

October 20, 2015
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- Update on recent regulatory changes
- Implications for the industry
Order 650 Set the Stage for Considerable Regulatory Changes

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<th>Distribution and Post-market</th>
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<td>▪ More clinical trial waivers available</td>
<td>▪ Fast track approvals available for innovative devices</td>
<td>▪ Replacing QMS with the new device GMP, with new annexes for IVDs, implantable and sterile devices</td>
<td>▪ New device GSP tightening control over device distribution</td>
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<td>▪ CTAs for Class III devices with higher risk profiles and mandatory record filing for all clinical trials</td>
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<td>▪ Increasing post-approval enforcement activities</td>
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In principle, clinical trials on certain Class II and III devices can be waived if:

- The operating mechanism and design of a device is definite, the manufacturing processes are mature, products of the same type have been in clinical applications for multiple years without severe adverse events, and there is no change to the regular intended use; or

- The safety and efficacy of a device can be demonstrated through non-clinical performance evaluation, or through analysis of data derived from clinical studies or clinical uses of products of the same type.
  - China’s Food and Drug Administration (“CFDA”) released two “Clinical Trial Waiver Catalogues” listing 79 Class III devices and 488 Class II devices.
  - Also possible to waive clinical trials through comparison to a predicate device (the “Equivalence Route”)

- Clinical trials can be waived on a case-by-case basis, if the applicant can establish equivalence to a predicate device already approved in China, and can use the clinical data of the predicate device to establish safety and effectiveness of the device under review.
In May 2015, the CFDA released the *Technical Guideline Governing Medical Device Clinical Evaluation*, further elaborating the conditions for clinical trial waivers:

- If the device under review is deemed “basically equivalent” to the same type of devices previously approved by the CFDA, the applicant can waive the clinical trials of the device under review by using the clinical study and empirical data derived from the previously approved equivalent devices.

- Two devices are deemed “basically equivalent” if differences in their operating principles, structures, materials, production processes, safety evaluation, applicable national /industry standards, and intended use do not cause a negative impact on product safety and effectiveness.

With respect to the clinical study requirement for imported devices, the applicant may reference foreign study data, provided that:

- The study design meets the CFDA’s requirements for in-country registration studies, e.g., minimum sample size, selection of the control group, study end point, and outcome of therapeutic effects.

- The applicants can present data showing no ethnicity differences.
CFDA released a Catalogue of Class III Medical Devices subject to CTAs:

- Implantable pacemakers, implantable defibrillators, implantable cardiac resynchronization defibrillator (with new design or new indication)
- Implantable blood pumps (with new design or new indication)
- Implantable drug infusion pumps (with new design or new indication)
- Intravascular stents not yet marketed in China
- Implantable artificial organs, touch-type artificial organs, orthopedic internal fixation products and orthopedic filler materials not yet marketed in China
- Absorbable internal fixation products used within long bones in limbs
- Nano orthopedic implants
- Customized additive manufacturing (3D-printed) orthopedic implants
  - All clinical trials are required to be filed for record with local health authorities as well as local FDAs, upon an internal approval by the hospital undertaking the study:
    - Filings with the local counterpart of NHFPC which has granted the hospital’s medical practice license; and in parallel
    - Filings with the provincial FDA where the sponsor is located, or where the legal agent of a foreign sponsor is located (concerning an imported device)
CFDA’s *Fast Track Approval Process for Innovative Medical Devices*  

- The applicant must own or be licensed to use a granted or published *Chinese invention patent on the core technology*. That technology must stem from R&D activities under the applicant’s leadership;  
- The product’s working mechanism was *first seen in China*, its performance or safety *improved significantly* compared to similar products, and its technology is the state of the art worldwide and has apparent value in clinical applications; and  
- The manufacturer has completed early stage R&D and the product’s basic design, the R&D activities are authentic and performed with control, and the R&D data is complete and traceable.

**Major benefits of the fast track approval process**

- **Priority in the waiting list for technical review, reduced approval timeline**  
  (reportedly a domestic corneal implant was approved within 80 working days after the submission), and abundant opportunities to communicate with examiners.

- Both domestic and foreign medical device manufacturers are eligible (40 products admitted to date and 4 being imported device), but the foreign device makers may be concerned with the in-country patent requirement.
The CFDA recently replaced the 2011 Device GMP with an updated new Device GMP, effective as of March 1, 2015.

- End-to-end control
- Traceability
- Detailed Requirements for workshops and equipment

**Newly opened device manufacturers** must immediately conform to the Device GMP. For **existing device manufacturers**:

- All Class III manufacturers must conform to the Device GMP as of Jan 1, 2016.
- All device manufacturers must conform to the Device GMP as of Jan 1, 2018.

Annexes to the new GMP have been finalized on July 10, 2015, including the annexes for IVDs, sterile devices, and implanted devices.

Device manufacturers must establish and operate GMP-compliant facilities and periodically report self-evaluation results to the relevant provincial FDAs.
New Device GSP Tightening Control over Device Distribution

- The CFDA issued its first ever Device GSP in December 12, 2014 to tighten control over device distribution.
  - Higher requirements for devices with high-risk profiles
  - Independence and veto power of quality management personnel
  - High requirements for the IT systems of Class III device distributors
  - Traceability of products from delivery, acceptance, to sale; wholesalers of Class II and III devices, as well as retailers of Class III devices, must maintain complete sales records.

- Distribution of Class II devices no longer requires a distribution permit.
  - A prior filing with the municipal FDA where the distributor is located is sufficient.

- All device distributors must establish a GSP-compliant system; Class III device distributors must obtain GSP certification before it can be issued the Medical Device Distribution Permit, and must periodically report the self-evaluation results to the relevant local FDAs.
“Rectifications of Five Common Types of Noncompliance Concerning Medical Devices”, a 5-month enforcement campaign launched by the CFDA in March 2014. Several hundreds of device companies were subject to business suspension and license revocation during the campaign.

- Fraud and misrepresentation relating to product registrations
- Non-compliance relating to product manufacturing, especially manufacture of sterile devices
- Non-compliance relating to product distribution, e.g., illegal sale in user experience programs
- Non-compliance relating to product promotions and advertisements
- Use of unregistered products, especially the clinical use of unregistered IVD products at hospitals

The CFDA newly published the draft *Administrative Measures of Medical Device Supervisory Inspectors* and plans to bring in external technical experts to join the official device inspections led by the CFDA and local FDAs.

Most recent campaign focusing on the supervision of IVD products.
Contents

- Update on recent regulatory changes
- Implications for the industry
Regulatory changes have become the top concern of medical device leaders in China

<table>
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<tr>
<th>What are your key worries about the China market?</th>
<th>Critical issue</th>
<th>Important but not top of mind</th>
<th>Less important</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regulatory changes (pricing, access etc.)</td>
<td>81%</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>Talent sourcing and retention</td>
<td>69%</td>
<td>31%</td>
<td>6%</td>
</tr>
<tr>
<td>Increasing local competition</td>
<td>63%</td>
<td>31%</td>
<td>6%</td>
</tr>
<tr>
<td>Compliance risks</td>
<td>50%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Rising cost of doing business</td>
<td>44%</td>
<td>44%</td>
<td>13%</td>
</tr>
<tr>
<td>Sustainability of commercial/channel model</td>
<td>25%</td>
<td>63%</td>
<td>13%</td>
</tr>
<tr>
<td>Overall slow-down of China’s economy</td>
<td>13%</td>
<td>38%</td>
<td>50%</td>
</tr>
<tr>
<td>Increasing MNC competition</td>
<td>6%</td>
<td>31%</td>
<td>63%</td>
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SOURCE: McKinsey Medical Device China CEO Survey 2014
From industry perspective, several challenges

<table>
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<tr>
<th>Cost</th>
<th>Time</th>
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<tbody>
<tr>
<td>• Increasing regulatory fees</td>
<td>• Long administrative processes (e.g. turnaround times for approvals, inquiries)</td>
</tr>
<tr>
<td>• Need for more costly trials</td>
<td>• Concerns about “clogging” of the process</td>
</tr>
<tr>
<td>• Upgrades in facilities, processes</td>
<td>• Clinical trial requirements potentially adding years to approval time lines</td>
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<td>• Need for more, and more qualified, RA talent driving cost of the function</td>
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<table>
<thead>
<tr>
<th>Competitive impact</th>
<th>Variable implementation</th>
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<tr>
<td>• Government support for local medical device industry</td>
<td>• Implementation of regulatory guidance overall work in progress</td>
</tr>
<tr>
<td>• Divergent regulation (e.g. for market access) regarding locally produced vs. imported products</td>
<td>• Different interpretations of national policy at province- and city level</td>
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<tr>
<td></td>
<td>• External events influencing trajectory of policy implementation</td>
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<tr>
<td></td>
<td>• Difficulty to obtain definitive answers</td>
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Approval time lines are expanding

**Average process time (including queuing time) for CFDA approval**

- Minimum: 11 months
- Medium: 21 months
- Maximum: 24 months

**“Is it becoming longer than before?”**

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<tbody>
<tr>
<td>Yes</td>
<td>71%</td>
</tr>
<tr>
<td>No</td>
<td>29%</td>
</tr>
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</table>

If no product changes are introduced, license renewal is faster (used to take 1.5 to 2 years, now takes 9 months). However, substantive changes take a very long time to be approved now.

*SOURCE: Regulatory Competitiveness Questionnaire 2015 by McKinsey & Company, Ropes & Gray*
# Stretched regulatory resources contribute to process bottlenecks

<table>
<thead>
<tr>
<th># of medical device regulatory reviewers</th>
<th>Total # of registration submission, 2014</th>
<th>Workload (Average submission per staff), 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>~100</td>
<td>~10,000(^1)</td>
<td>~100</td>
</tr>
<tr>
<td>~100</td>
<td>~1,200</td>
<td>~12</td>
</tr>
<tr>
<td>600~800</td>
<td>~3200(^2)</td>
<td>4~6</td>
</tr>
</tbody>
</table>

1 Not including Class II products which are reviewed by provincial level regulatory body
2 Includes 501K and PMA originals

SOURCE: Expert interview, Press search, PMDA, SFDA, FDA
At the same time, “green channel” process provides some promise to speed up approvals for innovative products.

- In total **196 applications**, of which
  - 40 approved
  - 40 in progress
  - 116 rejected
- All approved products are **class III**, mainly CVS implants, gene sequencing related, or artificial tissue type products
- 4 successful applications from **MNC**
  - Fully bio-absorbable stent from **Abbott**
  - Endovascular aneurysm sealing system from **Endologix**
  - Mitral clip and catheter delivery system from **Abbott**
  - Transcatheter wireless pace maker from **Medtronic**

SOURCE: Government announcement, team analysis
China's government intends to support the local medical device industry

April 2014
“We plan to include percentage of domestic devices procured as one of the metrics for public hospital performance evaluation.”

– Shen Ji, Chief of Sichuan HFPC

May 2014
“We need to accelerate the domestication progress of high-end medical equipment, reduce the cost, and promote the continuous development of national brands.”

- President Xi Jinping, visit to United Imaging

August 2014
“Class III hospitals should give more consideration to local products in purchases of large medical equipment.”

– Li Bin, NHFPC Commissioner

May 2015
Public hospitals should procure domestic medical equipment in preference...
We encourage procurement of domestic high-value consumables on the premise of quality assurance...

– State Council “2015 Guideline for Municipal Public Hospital Trial Reform”

1 Health and Family Planning Commission

SOURCE: McKinsey analysis; Literature search; Xinhua.net; People Daily
### Different flavors of local implementation of government guidance

<table>
<thead>
<tr>
<th>Description</th>
<th>Examples</th>
</tr>
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<tbody>
<tr>
<td>▪ Imported products are given <strong>higher scores in technical review</strong> of tender process if manufacturers have local factory in China</td>
<td>▪ Shandong</td>
</tr>
<tr>
<td>▪ Local <strong>products that are exported</strong> to certain countries (e.g. USA, Japan, Europe, Australia etc.) are categorized in the <strong>same quality group</strong> with imported products</td>
<td>▪ Guangdong</td>
</tr>
<tr>
<td>▪ <strong>Imported products can only be used in</strong> provincial- and city-level hospitals ▪ <strong>Percentage of volume</strong> cannot be higher than 30% and 20% respectively</td>
<td>▪ Ningxia</td>
</tr>
<tr>
<td>▪ <strong>License restrictions</strong> for large equipment (PET-CT, CyberKnife, CT, MRI, LA etc.) were removed selectively for local products</td>
<td>▪ Shanghai</td>
</tr>
<tr>
<td></td>
<td>▪ Jiangsu</td>
</tr>
<tr>
<td></td>
<td>▪ Zhejiang</td>
</tr>
</tbody>
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**SOURCE:** McKinsey analysis
“After the latest round of regulatory changes in China, I expect no or little changes in the next 3-5 years.”

- Completely agree: 17%
- Somewhat agree: 50%
- Somewhat disagree: 25%
- Completely disagree: 8%

“I expect that the new device regulations will be very differently implemented by individual provinces/cities in China.”

- Completely agree: 42%
- Somewhat agree: 33%
- Somewhat disagree: 17%
- Completely disagree: 8%

SOURCE: Regulatory Competitiveness Questionnaire 2015 by McKinsey & Company, Ropes & Gray, n=14 RA leaders from leading MNCs
Confidence regarding readiness to cope with regulatory challenges is relatively low

McKinsey / Ropes & Gray annual Medical Device Round Table (participants from ~20 MNC Medical Device companies)

<table>
<thead>
<tr>
<th>Question</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) One of our strengths – we have achieved excellence in these areas</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>2) We are doing OK right now, but need an upgrade of numbers and/or to cope with future challenges</td>
<td>64</td>
<td>53</td>
</tr>
<tr>
<td>3) These are currently areas of concern where we urgently need to build more expertise and a stronger team</td>
<td>32</td>
<td>40</td>
</tr>
<tr>
<td>4) These functions are not that important for the success of our organization and hence not a focus</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
Implications for MNCs: How to succeed in China’s regulatory environment

1. Develop a seamless way of working between local regulatory affairs function and the global team – continuous involvement in product planning cycle and business plans from the get-go

2. Become a valuable partner to regulatory bodies – bringing cutting edge knowledge and best practices to regulatory stakeholders in China, while being sensitive to unique local needs

3. Build best in class capabilities within the regulatory team – content expertise (regulation, quality, compliance) as well as mindsets, leadership and strategic thinking
Questions?
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