China Medical Device Regulatory Update

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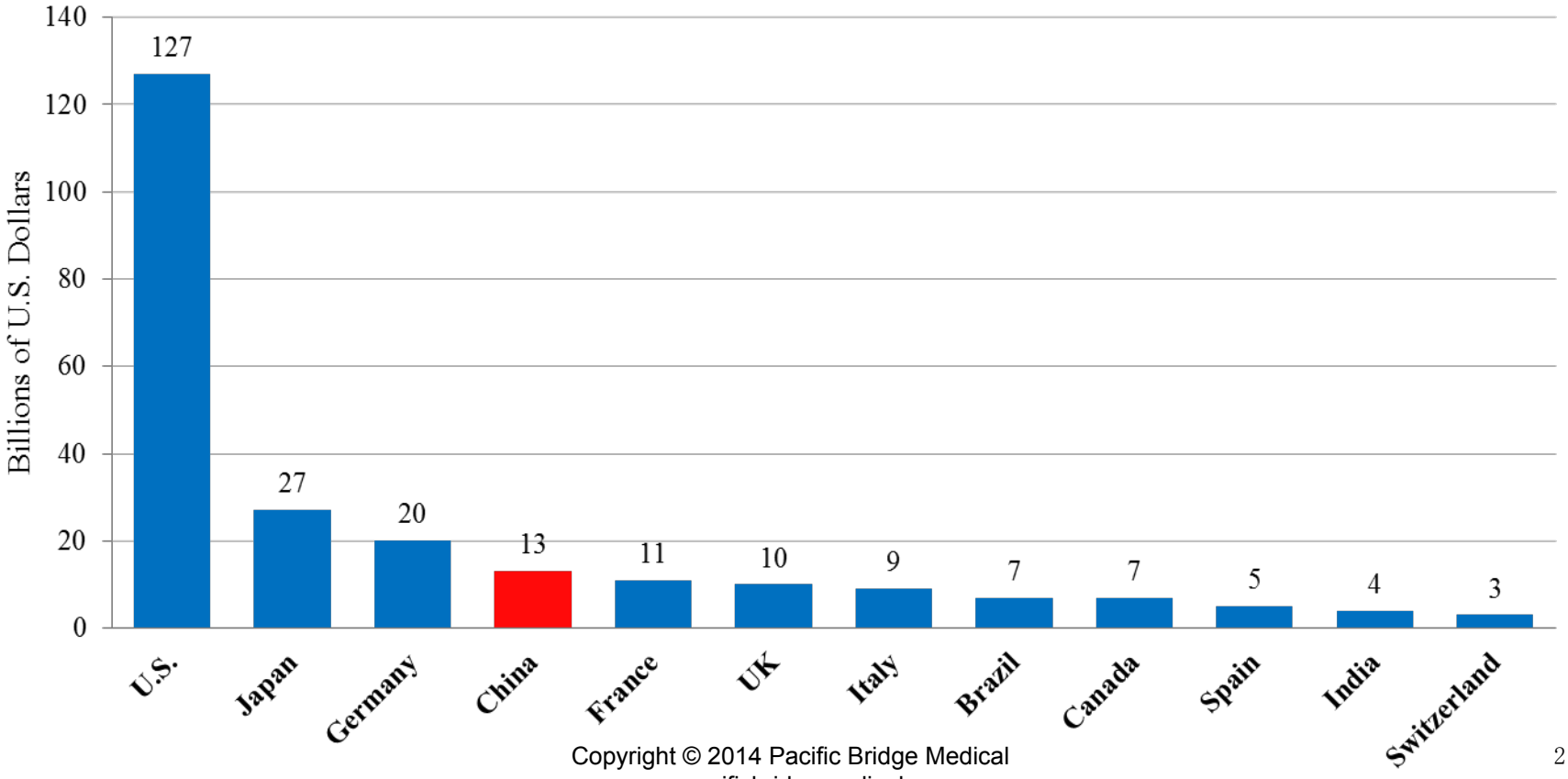
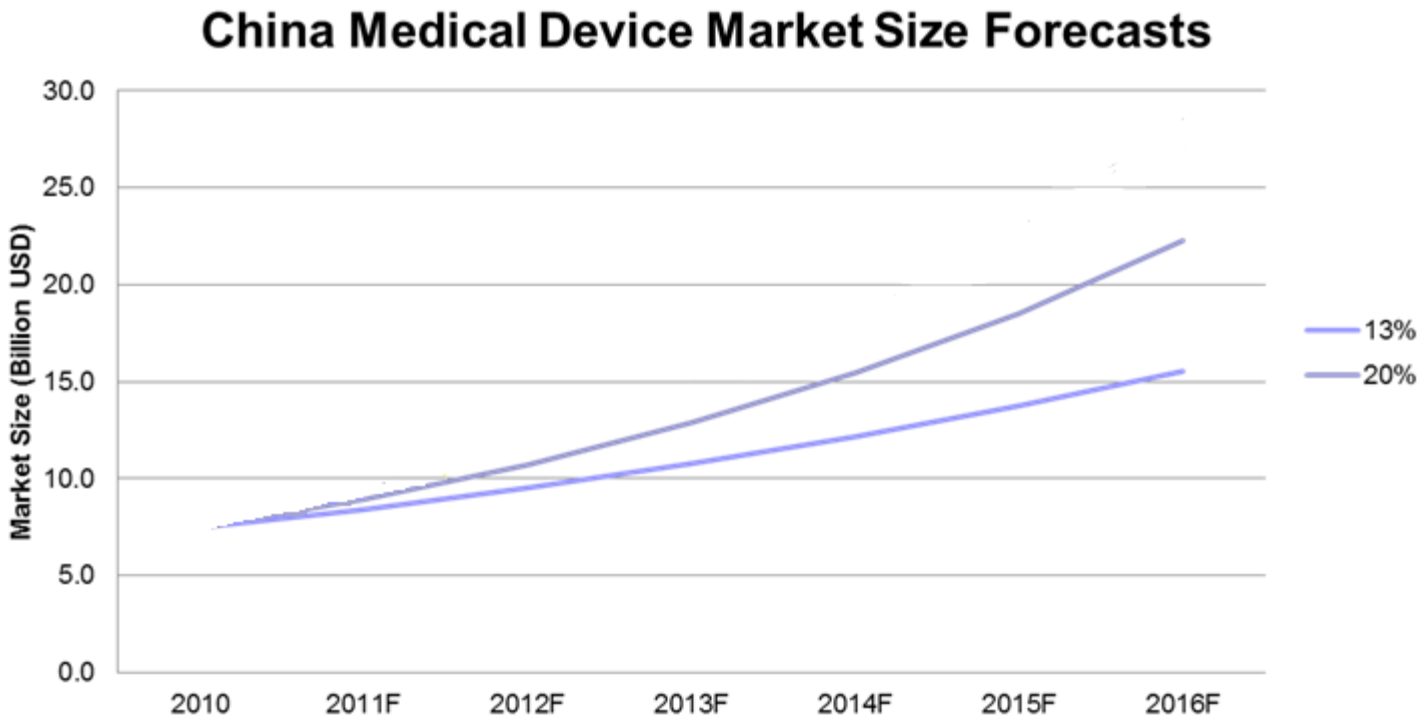
China's Medical Device Market (2013)

Medical device markets, by country



Chinese Medical Device Market Growth



Chinese Agents

- Legal Agent
  - Must be a registered entity in China
- After Sales Agent
  - Must be a registered entity in China
- Registration Agent
  - Must be a registered entity in China

China: Medical Device Regulatory Authorities

China Food & Drug Administration (CFDA)

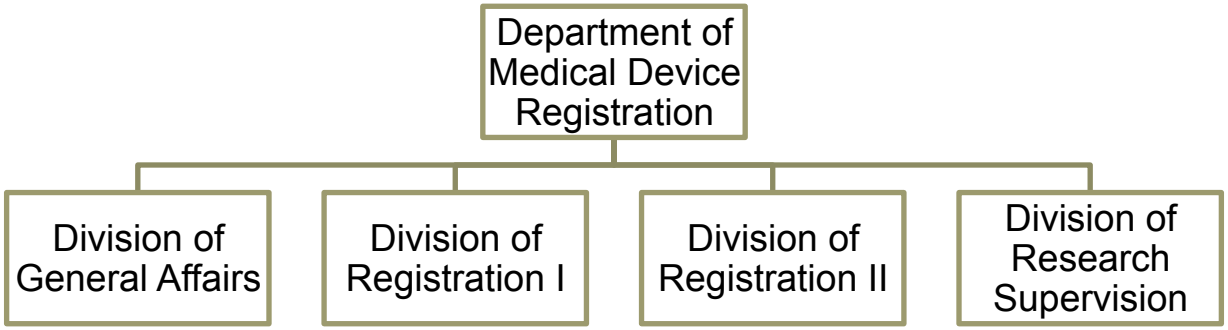
- Founded in 1998
- Equivalent to the U.S. FDA
- Responsible for medical devices, drugs, healthcare services, cosmetics, food
- Headquarters is located in Beijing, with offices in each province

General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ)

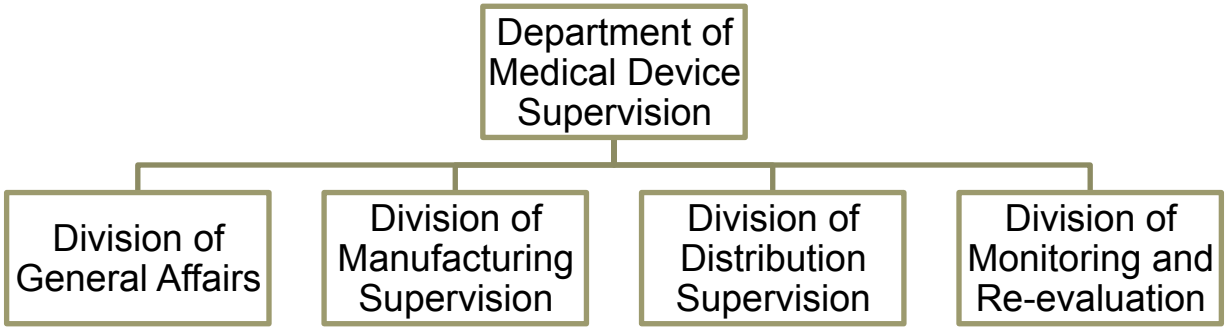
- Conducts mandatory safety registration, certification, and inspection for certain devices

CFDA Organization for Medical Devices

- **Pre-market approval: Department of Medical Device Registration**



- **Post-market supervision: Department of Medical Device Supervision**



Medical Device Regulation and Classification

- Regulation on Supervision and Administration of Medical Devices (Order 276, 2002)
- Device Classification is the basis for determining regulatory requirements:
  - **Class I** – Those which safety and effectiveness can be ensured through routine administration
  - **Class II** – Those which further control is required to ensure their safety and effectiveness
  - **Class III**– Those which are implanted into the human body, or used for life support or sustenance, or pose potential risk to the human body and thus must be strictly controlled in respect to safety and effectiveness

Medical Device Regulation and Classification

- For innovative products and combination products, getting an official CFDA classification can be very helpful
  - The classification process can take from 3 to 12 months
- On December 24, 2013, the CFDA released a *draft* revision of the Classification Rules of Medical Devices
  - Draft amendment adds a new category for IVD reagents

Example from the CFDA Medical Device Classification Catalogue

CFDA Classification Code 6825 for High Frequency Medical Devices (English translation)

编码代号 Classification Category Code	序 Subcategory	名称 Product Type	品名举例 Examples	管理类别 Class
6825医用高频仪器设备 6825 high frequency medical devices	1	高频手术和电凝设备 high frequency devices for surgery and electric coagulation	高频电刀(high frequency electric knife)、高频扁桃体手术器(high frequency surgical equipments for tonsillectomy)、内窥镜高频手术器(endoscopic high frequency electro surgical unit)、后尿道电切开刀(posterior urethra electric resecter)、高频眼科电凝器(high frequency ophthalmological electric coagulation apparatus)、高频息肉手术器(HF polypus surgical unit)、高频鼻甲电凝器(HF nosepiece electric coagulation unit)、射频控温热凝器(radio frequency temperature-controlled electric coagulation apparatus)	III
			高频腋臭治疗仪(HF treatment apparatus for underarm odour)、高频痔疮治疗仪(HF treatment apparatus for hemorrhoids)、高频电灼器(HF electric cautery)	II
	2	高频电熨设备 high frequency electric ironing devices	高频妇科电熨器(high frequency electric ironing for Gynaecology)、高频五官科电熨器(high frequency electric ironing for Ophthalmology and Otorhinolaryngology)	II
	3	微波治疗设备 microwave therapeutical devices	微波手术刀(microwave surgery scalpel)、微波肿瘤热疗仪(microwave tumor thermotherapy apparatus)、微波前列腺治疗仪(microwave prostate therapeutic equipment)、微波治疗机(microwave therapeutic equipment)	III
	4	射频治疗设备 radio frequency therapeutical equipments	射频前列腺治疗仪(radio frequency prostate therapeutic equipment)、射频消融心脏治疗仪(heart radiofrequency ablation treatment equipment)、射频消融前列腺治疗仪(prostate radiofrequency ablation treatment equipment)、内生物/场?肿瘤热疗系统(Endogenetic field tumor hyperthermia system)、肿瘤射频热疗机(radio-frequency tumor hyperthermia treatment equipment)	III
			短波治疗机(short wave treatment apparatus)、超短波治疗机(ultrashort wave treatment apparatus)	II
	5	高频电极 high frequency electrodes	电凝钳(electric coagulation pincers)、电凝镊(electric coagulation forceps)、阴极板(negative plate)、手术电极(surgery electrode)	II

Product Standard

- The Product Standard is the **most important** part of the registration:
  - Because the product standard is not reviewed by the CMDE before testing, sample testing is done on the company's product standard.
  - If the testing result is deemed unsatisfactory, the CMDE/CFDA may request the company to revise the product standard and re-test.
- Make sure to provide sufficient information to support the drafting of Chinese product standard by the registration agent
- The product standard should describe the product and include the appropriate Chinese standards it complies with
- Many of the Chinese standards correspond to international standards
- Any product information (like product numbers, dimensions, etc.) noted in the product standard should exactly match other legal documents
- Once the Type Testing is complete, the Product Standard CANNOT be revised. So make sure to have all the information correct and supported by legal documents.

Updates – New Standards Released

- The CFDA released 107 new medical device industry standards in November 2013
  - 31 mandatory
  - 73 recommended
- At the same time, the CFDA revised 2 medical device standards
- Both of the above will come into effect on October 1, 2014

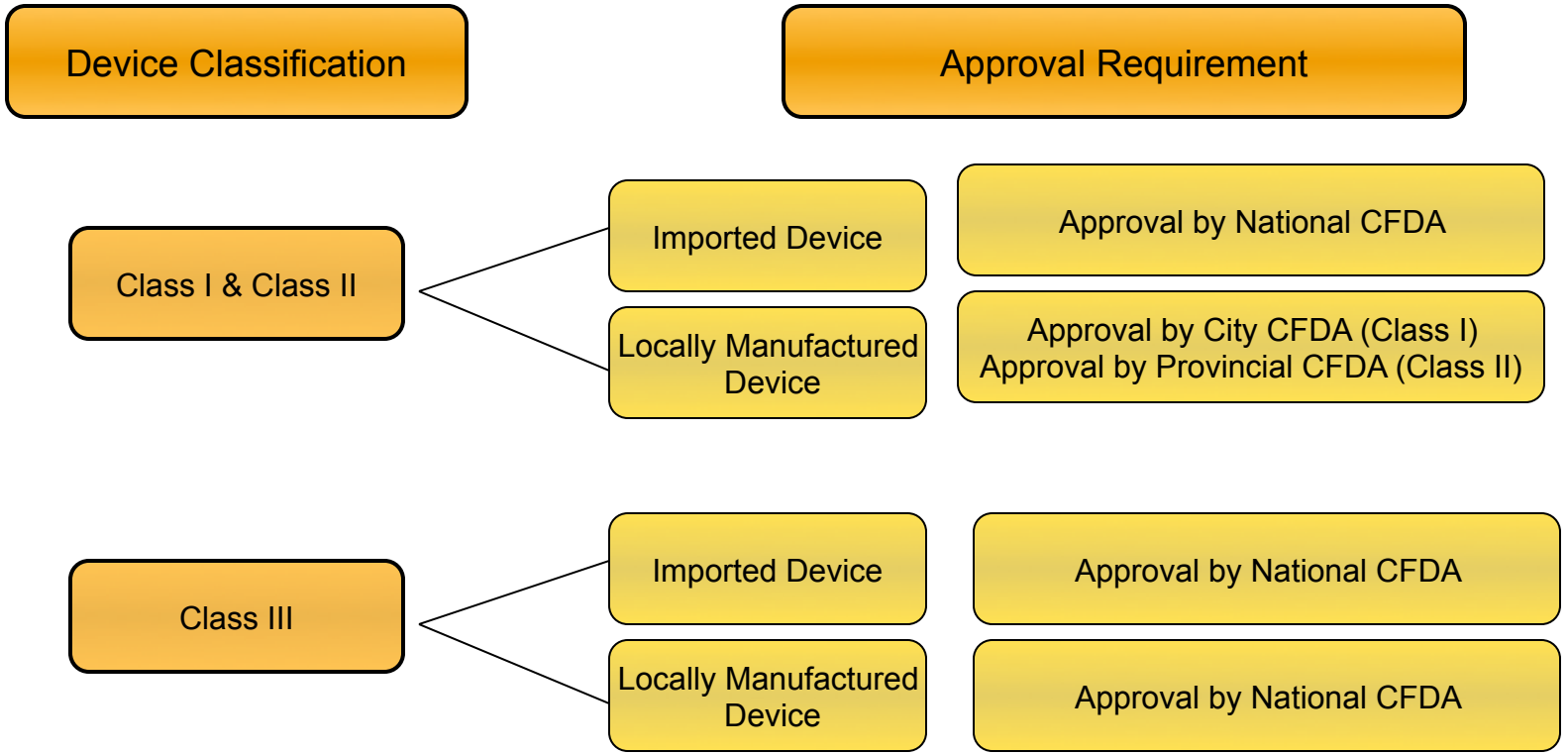
Type Testing

- In almost all situations, the CFDA will request samples for type testing
  - Often the CFDA might request too many samples or ask for propriety information
- The testing centers will use the Product Standard to determine what tests to conduct
- Once the final testing report has been issued, no changes can be made on the Product Standard
- If testing is currently in progress, it is possible to try and update the Product Standard
- Testing certificate only valid for one year
- Can have problems with initial registration if the product standard is too vague or if the international standard is different than the Chinese standard
- The CFDA has not accredited any foreign lab for ISO 10993 – only CFDA approved labs can be used for type testing
  - A third party lab testing market could open soon

Testing Centers

- There are 10 national testing labs around the country that are CFDA certified:
  - National Testing Institute (Beijing)
  - Beijing Testing Institute
  - School of Dentistry, Beijing University (“Beida”)
  - Shanghai Testing Institute
  - Jinan Testing Institute
  - Shenyang Testing Institute
  - Tianjin Testing Institute
  - Wuhan Testing Institute
  - Hangzhou Testing Institute
  - Guangzhou Testing Institute
- There are also over 40 affiliated testing institutes
- Increasing acceptance of foreign test reports
  - ISO 10993 is equivalent to GB/T 16886

Product Approval by Classification

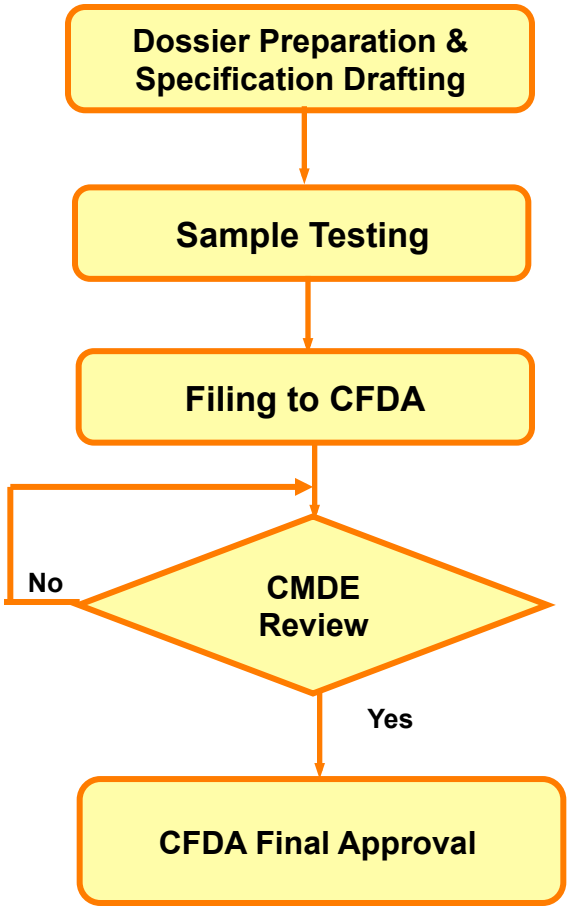


China Product Registration: Key Points

- Third Party Review ***not*** allowed; need approval from the CFDA
- Some classifications are different from the U.S.
- Class I medical devices also need CFDA approval
- Need to submit Chinese Specification for CFDA review and approval

Product Registration Process for Classes II & III

NORMAL TIMELINE	
1) Chinese specification drafting	Depends on the company and product
2) Sample testing	6 months
3) CFDA preliminary review & issues acceptance notice	5 working days
4) CMDE review	6 months
5) CFDA final approval	10 working days
APPROXIMATE TOTAL	**12-18 months**



Registration Requirements for Dossier

- A total 13 items of documents must be collected and submitted to the CFDA
- Three parts of these 13 items:
  - Legal Documents (9)
  - Technical Documents (3)
  - Testing report issued by CFDA certified testing center (if applicable)

Supplementary Review Process

- After technical review by the CFDA, they will likely request further information
- Additional testing might also be required, based on the supplementary document reviews
- As of June 1, 2013, a new rule requires a more stringent timeline for the supplementary review process
  - Supplementary documents must be submitted to the CFDA in 60 days
  - Applicants may request an extension of an extra 60 working days.
  - If the supplementary information is still not sufficient, the applicant has 15 days to submit further materials.
  - Now, there is a maximum of two rounds of supplementary review – if the issues are still not resolved, the application will be rejected

China Compulsory Certification (CCC) – Update

- In May 2013, the CFDA announced that the China Compulsory Certification (CCC) was no long necessary for eight products
- Instead, these devices only need to have a medical device registration certificate from the CFDA (Class III and imported devices) or local FDA (domestic Class I and II)

Device Re-Registration Requirements

- Product registration is valid for 4 years
- Renewal application must be submitted 6 months before import license expires. Start process 1 year in advance.

Update – Device Re-Registration Requirements

- In December 2013 the CFDA announced simplified renewal process; took effect January 1, 2014
  - If the product's manuals or basic standards have not been changed
  - *Not* need to re-submit manuals, inspection reports, product standard
  - *Do* need to submit a declaration that the products comply with current CFDA standards and that no changes have been made to the products
- If the product's manufacturing location changes:
  - *Not* need to re-submit user manuals, inspection reports, product standards
  - *Do* need to submit a declaration of the change, self-test reports on devices made at the new site(s), inspection reports of quality system compliance
- If the product's changes involve the components, standard, intended use, model or components:
  - *Not* need a new application that includes user manuals, inspection reports, product standards
  - *Do* need to submit a declaration of the change, relevant technical information
- *These changes do not apply to IVD reagents*

Country of Origin

- If product made in U.S. but no FDA approval, cannot register in China
- Many U.S. companies get CE Mark and do some manufacturing in Europe; product approved in country of origin

Updates – Issues with Raw Materials

- Over the past year, the CFDA has been asking for increased information about the raw materials used in medical devices
- Working with your supplier is crucial for registering your product in China successfully

Labeling Requirements for Medical Devices

- CFDA Notice 280 on labeling for medical devices entering China became effective April 1, 2013
- Chinese *must* be used as part of the outside packaging and for the text of labels
- Below are some examples of information required by CFDA on a label. Other Chinese government agencies may require additional information
  - Product Name, model ID or number
  - Manufacturer's name and contact information
  - Product Registration Serial No.
  - Product Standard Serial No.
  - Intended Use
  - Contraindication, precaution and warnings
  - Required marks, symbols
  - Installation and user instruction
  - Maintenance, cleaning and storage conditions
  - Shelf life (if applicable)

Clinical Trials

- Clinical trial is required for medical devices when:
  - New Class II & III medical device, which has not been approved anywhere in the world
  - Some Class III implant products. It is the first medical device product of the foreign company applying for registration in China, and this product has already been approved in the foreign country

Clinical Trials in China

- All clinical trials (if necessary) for medical devices must follow China's Good Clinical Practices (GCP)
- *Regulation on Medical Device Clinical Trial Requirements* became effective April 2004
  - Can only draw on previous clinical trial experiences of similar products

GCP (Good Clinical Practice)

- The CFDA published a *draft* revised *Regulation on Medical Device Clinical Trial Requirements*
- The revised Chinese GCP will be in accordance with international GCP standards
  - Strengthening management of technical aspects of clinical trials
  - Establishing quick and effective mechanism to coordinate trials with medical device registration

Clinical Trials for Products Not Yet Registered in China

- The CFDA has been organizing expert review meetings with top doctors to determine if clinical trials are required for product registration
- More and more, the CFDA has been getting stricter in requiring local clinical trials, even for some Class II products

Clinical Trials Going Forward

- More local Chinese clinical trials required to supplement overseas trials
- September 30, 2013 – CFDA announced a *draft* guidance that requires local clinical trials for 15 types of high risk medical devices
  - Manufacturers will need to submit a clinical trial application to the CFDA
  - A supplementary application is necessary if there are significant changes to the study

Clinical Trials – Update

- In October 2013, the CFDA published a second set of Class II medical devices that will be exempt from doing clinical trials in China
  - This announcement covers 142 products from 25 categories of Class II devices
  - Manufacturers that are applying for registration of one of these now-exempted medical devices would be able to submit a written application to the CFDA to receive an exemption from undertaking clinical trials in China

Contract Manufacturing

- A foreign device company contracts with a Chinese medical device manufacturer and your own company sells their products in China.

Key information under this option:

- The legal manufacturer will be the Chinese manufacturer
  - Your company's China office then acts as the distributor to sell the product in China

Contract Manufacturer as Supplier

- The foreign device company has its own factory in China and would like to contract another Chinese manufacturer, too
- Foreign company can have registration in their name:
  - The foreign device company's facility in China must be China GMP

Transfer Manufacturing Site from One Location to Another in China (Capacity Issues)

- Class III device
- Initial registration 18 months plus 12 months = 30 months
- Set up exact same factory at different site (must re-reregister) -- another 18 months, total now 48 months
- Best to set up new site with capacity originally only 30 months
- Site can be idle waiting for product registration

GMP in China

- SFDA released GMP regulations for medical devices in December 2009:
  - Good Manufacturing Practice (GMP) for Medical Devices (Interim)
  - Regulations on Inspection of Good Manufacturing Practice (GMP) for Medical Devices (Interim)
  - Implementation Guidelines and Inspection Criteria of Good Manufacturing Practice (GMP) for Implantable Medical Devices (Interim)
  - Implementation Guidelines and Inspection Criteria of Good Manufacturing Practice (GMP) for Sterile Medical Devices (Interim)
- All came into effect January 1, 2011

GMP in China

- For **domestic** manufacturers, the CFDA issues GMP qualification certificates
- There are differences between international (U.S. FDA and ISO) and CFDA GMP, QC and QA standards
- The CFDA requires **foreign** manufacturers who export medical devices to China to conform to quality system standards
  - The CFDA accepts conformance to either ISO13485 or the U.S. FDA's 21 CFR Part 820 quality system standards

GMP in China - Updates

- On December 11, 2013, the CFDA released the *draft* "Medical Device GMP Inspection Assessment Standards"
  - This draft includes 179 items that local FDAs would need to assess to approve manufacturing certificates

Adverse Event Reporting for Medical Devices

- The medical device AE monitoring network and reporting system began in 2010, but it is often ignored
- SFDA Decree 425, issued in 2011, is the current medical device AE guidance
- All manufacturers, distributors, and medical institutions must establish internal supervision systems for medical device adverse event monitoring
- The following parties are responsible for filing a "Report on Suspicious Medical Device Adverse Event" for any adverse event, no matter its seriousness, with their local medical device monitoring institution and legal agent
  - Medical device manufacturer
  - Distributor
  - Medical institution (i.e., hospital)
  - CFDA offices

Adverse Event Reporting for Medical Devices

- Serious AEs *outside* of China must be reported to the CFDA within 15 working days
  - Within 20 working days of the initial report, the medical device manufacturer must also file a "Supplementary Report on Medical Device Adverse Event," providing more details about the adverse event
- Additionally, manufacturers of Class II and III medical devices must file an "Annual Report on Medical Device Adverse Events" with their local monitoring institution each year by the end of January, summarizing and analyzing the AEs over the past year

Adverse Event Reporting for Devices - Update

- In July 2013, the CFDA released a guidance update entitled "Further improvement on construction of a medical device adverse event monitoring system (draft)"
- In October 2013, the CFDA released a guidance document that sets out a 2 year plan to increase local government capacity to report, evaluate, inform, and control adverse events
- The CFDA aims to have a functioning system in place by the end of 2014 followed by a 1-year trial period before the system's official start in 2015
- The final system will include
  - Comprehensive coverage of county-level administrative regions, including requirements for hospitals and distributors
  - Daily monitoring of medical device AEs
  - Required submission of annual reports and assessments, even if there have *not* been any AEs

Recalls of Medical Devices

- CFDA Decree 82, effective from July 1, 2011, has 38 articles regarding the Medical Device Recall Management Guidelines
- Liability and responsibility is shared by everyone, extending from the distributor to the manufacturer
- Three levels of recalls:
  - Class I: If the device has caused or could cause serious and permanent hazards to health
  - Class II: If the device could cause a temporary health issue
  - Class III: If the device is defective but is not likely to cause any harm
- How do you know if a recall is required?
  - The foreign manufacturer and the distributor much research and report to the CFDA before a potential recall

Device Reimbursement in China

- Medical devices can be reimbursed
  - They are commonly reimbursed as a part of a medical procedure
- Certain medical devices (such as stents, bone plates) are reimbursed separately on their own

Device Reimbursement in China

- Local hospital submits coding and pricing at the provincial level
- Can include procedure fees
- High prices where hospital can make some profit is best
- Imported medical devices have very limited reimbursement via medical procedures and almost always require some self-pay
- Reimbursable devices are enumerated on a medical device insurance list that is released by the provincial social security bureau

Updates – Unannounced CFDA Inspections

- The CFDA announced in June 2012 that all medical device manufacturing facilities are now subject to unannounced inspections
- Inspection teams will consist of at least two officers of either the CFDA or local provincial FDA
- The CFDA team must prepare documents telling the manufacturer the reason behind the inspection and the results of the inspection

Updates – High Value Device Purchasing

China's Ministry of Health (MOH) announced that centralized purchasing would take place for specific high value medical devices. Furthermore:

- The purchasing process will be organized and monitored by centralized purchasing agencies established by local governments
- All public hospitals are to follow the new procedure, submitting in advance their purchasing plan for high value medical devices

Updates – Advertisement Monitoring

The CFDA launched a national database in January 2013 for monitoring the *illegal advertising* of drugs, medical devices and health food products. Furthermore:

- Local CFDA offices must use the database to file quarterly reports
- Local CFDA offices are encouraged to *strictly* interpret the law if they encounter false advertising in the following categories: exaggerated product indications, fake seals of approval or misleading testimony from patients, doctors, medical professionals, officials or academics

Updates – Fast Track Approval

- On February 7, 2014, the CFDA released the "Procedure for Examination and Approval of Innovative Medical Devices (Trial)," which will go into effect starting March 1, 2014
- To qualify:
  - The company applying needs to be a legal entity in China
  - The device must be manufactured in China
  - The device must be the first of its kind functionally in China
  - The device must provide significant improvement in safety or efficacy
  - The device must have significant clinical application value
  - The intellectual property must be *owned in China* by the applicant
  - The device must have gone through the initial R&D stages and a prototype must already be developed

Updates – Fast Track Approval Application Process

- Domestic applicants submit the special application form and accompanying data to the Provincial FDA
- If the application has passed the preliminary examination, the Provincial FDA submits the application to the CFDA
- Overseas applicants should submit their application and data directly to the CFDA
- The CFDA's new Examination Office for Innovative Medical Devices will review the application and provide a review comment within 40 working days
- The testing lab will pre-asses the product standards and suggest modifications, followed by testing of the device
- Clinical trials will be the same
- A special form for communicating with the CMDE can be used
- CMDE will examine the registration and provide administrative approval

Updates – Increased penalties for violations

- The National Health and Family Planning Commission announced in December 2013 that a national bribery blacklist will be published online starting in March 2014
- Healthcare institutes that accept public financial subsidies would be prohibited from buying medical devices, consumables or drugs for 2 years from blacklisted companies in the region(s) in which the companies were implicated
- If these companies make bids on public tenders, public healthcare institutes must assign a lower grade to the bid
- If a firm is blacklisted twice, it will not be allowed to sell its products for 2+ years
- Punishment will also be given to medical practitioners who accept bribes

Update – Good Supply Practice (GSP)

- On December 26, 2013, the CFDA released a *draft* Good Supply Practice (GSP) for medical devices, "Medical Device Quality Management Standards (draft)," seeking local FDA opinions
  - Gives specific regulations on:
    - Medical device company responsibilities
    - Equipment and facilities standards
    - Training and qualification of personnel
  - Follows updated international standards – like ISO9001 and ISO13485:2003
  - Uses a risk-based classification system
  - Applies to the whole distribution chain
  - 3rd party logistics companies will need to provide technology and conditions to make sure products can be traced
  - Class III device companies are required to set up an IT management system

Updates – Expected CFDA Regulation Changes

- The CFDA announced on December 11, 2013 that a new Regulation on Supervision and Administration of Medical Devices (regulation 276) will soon be released
  - Key *expected* changes:
    - Chinese clinical trials will be mandatory for imported Class II and III medical devices
    - Clinical trial exemptions will also be included
    - If the product does not change prior to re-registration, the product approval certificate number will stay the same
    - Some medical devices will be upgraded to Class II

Updates – Expected CFDA Regulation Changes

- At the same time, approximately 15 sub-regulations will also change after the revision of CFDA regulation 276 is announced, including:
  - Administration of medical device trials
  - Medical device testing
  - Medical device standards
  - Medical device registrations
  - Instructions for labels, packaging, use of medical devices
  - Licensing of medical device companies
  - Clinical trial organization certification
  - IVD reagent registrations
- And, 19 new guidelines will be released around the same time, including:
  - Unique device ID system
  - Medical device naming rules
  - Brochure labeling, labeling and packaging of medical devices
  - Administration of importing and customs of medical devices
  - Provisions for clinical trial approval of medical devices
  - GCP
  - Medical device quality arbitration and appeal
- Finally, 600 industry and national standards will also be revised

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China Medical Device Regulatory

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