TRADE AND REGULATORY COMPLIANCE FOR AGREEMENTS IN CHINA

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Contents

Introduction

Introduction

- P&L Scientific Inc.
  - Founded in Miami, USA in 2009
  - There are offices in Florida, New York and Beijing
  - To provide regulatory and market services for the medical equipment enterprises with development of international business.

Introduction

Our Services

- U.S. FDA regulatory services
- Brazil ANVISA regulatory services
- China CFDA regulatory services
- International Medical Exhibition

Introduction

About China

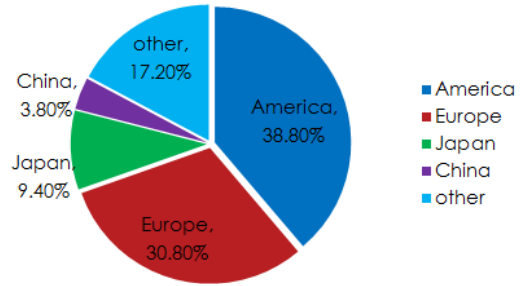
- Population: about 1.39 billion (2017);
- The third largest countries in the world;
- One of the TOP 10 largest economies in the world (2nd position);
- The total number of medical and health institutions in the country is 983394, about 29000 hospitals.

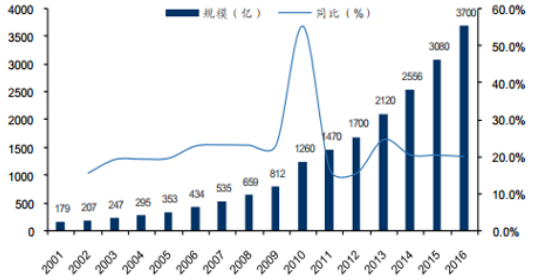
Introduction

About China-Trends

- The market share of medical devices in the world is increasing.
- Medical device market in China is in a stage of rapid expansion.
- Ageing of population.
- The support of the Chinese government.
- China is regarded as one of the most promising medical devices market in the world.

Global market share of medical devices(2015)





2001-2016 market scale of China's medical device (100 million yuan)

Introduction

	CHINA	Compare to U.S.
Population(2017)	1.39 billion	325 million
Total healthcare spending(2015)	$574 billion	$3 trillion
Healthcare expenditures total (% of GDP)	5.5% (2015)	17.1%(2015)
Healthcare expenditures per capita(2015)	$420 (USD)	$9403 (USD)
Expenditures on healthcare(2015)	Government: 56% Private: 44%	Government: 48% Private: 52%
Size of medical device market (USD) (2015)	$8.7 billion (USD)	$147.7 billion (USD)
Number of hospital beds(2015)	3.8 per 1000 people	2.9 per 1000 people
Age distribution (2015)	0-14 years: 17% 15-64 years: 73% 65 years and over: 10%	0-14 years: 19% 15-64 years: 66% 65 years and over: 15%
Life expectancy at birth (2015)	Male: 73 years Female: 78 years	Male: 77 years Female: 82 years
Currency	Renminbi yuan (¥)	US dollar ($)

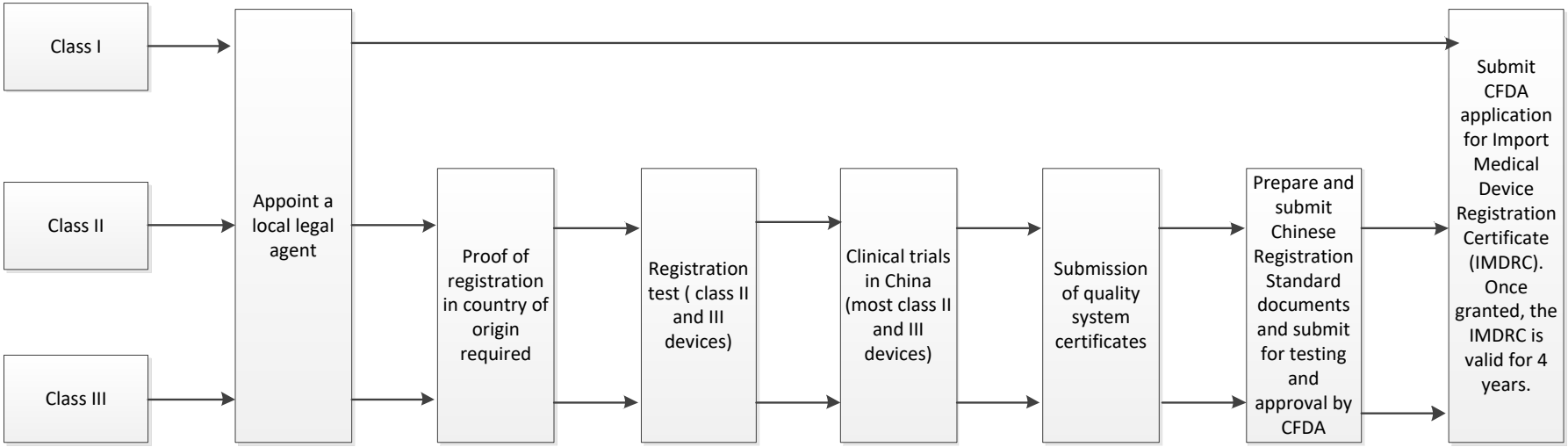
Introduction

About CFDA -China Food and Drug Administration

- The direct institution for the comprehensive supervision and administration of drugs, medical devices , cosmetics, health food , food and food safety by the State Council;
- Draft laws, regulations and rules and policy plans;
- Formulate the regulations on food administrative licensing and supervise their implementation;
- Organize and publish standards and classification system, and supervise their implementation;
- Establish recall and disposal system for defect products, and supervise the implementation;
- The CFDA reviews all device applications, and has strict requirements for submission documentation, testing, and clinical data.
- Manufacturers must register their devices with the CFDA before selling or distributing in China.

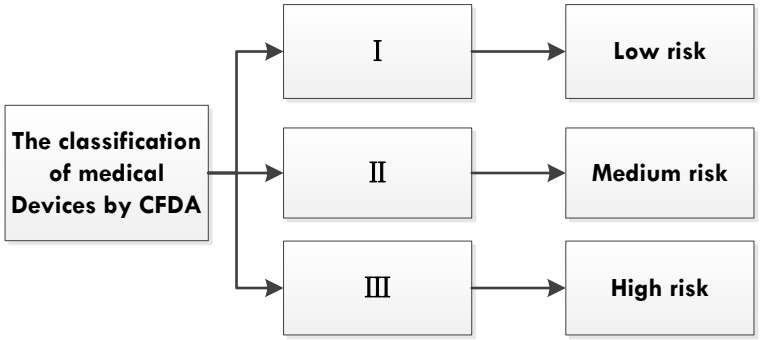
CFDA Regulations

- CFDA registration flow chart



CFDA Regulations

- CFDA Classification
- All classes require CFDA approval;
- Class I - Product Record ;
- Class II and Class III - Product Registration
- Comparison between the classification, in terms of risk, for Medical Devices (CFDA x FDA x CE Mark x ANVISA);



CFDA	FDA	CE Mark	ANVISA
Ⅰ	Ⅰ	Ⅰ	Ⅰ
Ⅱ	Ⅱ	Ⅱa	Ⅱ
Ⅲ	Ⅲ	Ⅱb	Ⅲ
		Ⅲ	Ⅳ

CFDA Regulations

- Appoint a local legal agent
  - The representative offices established in China or the enterprise legal persons designated in China
  - Liaison with CFDA and XXXXXX, collect information on medical device adverse events after the market and report to the corresponding registration management department, to recall the products that have problems after the medical device listed, and report to the corresponding food and drug supervision and management department. Truthfully and accurately convey relevant regulations and technical requirements to xxxxxx, and are jointly and severally liable for product quality and after sales service.

CFDA Regulations

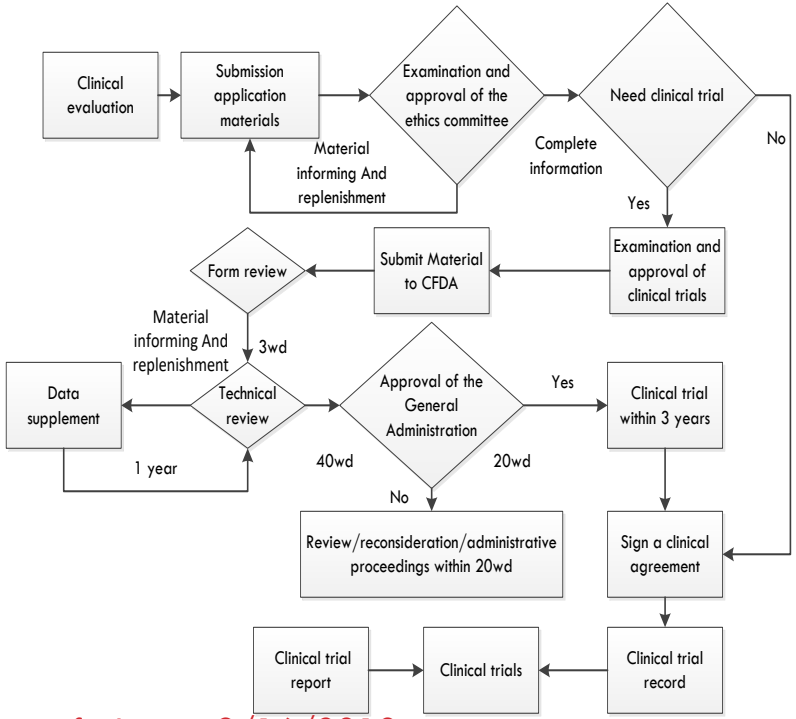
- Proof of registration in country of origin required
- Certificate of free sales(CFS) ;
- Certificate of foreign government (CFG);
- Certificate of manufacturer's qualification;
- Agency authorization letters.
- Such as:
- ISO 13485 certificate;
- American FDA , 510(k) with seal;
- Manufacturing license of Japan or Korea Companies.

CFDA Regulations

- Registration test
- Class I : Accept self inspection report
- Class II and class III devices;
- Provide relevant technical information , technical requirements , and samples.
- Medical device inspection organization:
- Qualification of medical equipment inspection
- Scope of inspection
- Pre evaluation
- Registration test passed , apply for clinical trial or apply for registration.

CFDA Regulations

- Clinical trials in China
  - Class II and class III devices;
  - Predicate device and substantial equivalence;
  - Combined with foreign and local test reports (comply with China Good Clinical Practice (GCP) / be applicable to the Chinese patient population/other requirements)
  - Medical device testing center CFDA by authorized;
  - Unless exemption



CFDA Regulations

- Submission of quality system certificates
- Technical review process;
- If necessary, The CFDA's quality management system inspection technical organization shall carry out the verification according to the relevant requirements;
- The technical review organization should participate in the verification when necessary.
- The time is not within the time limit for review

CFDA Regulations

Prepare Standard documents

- Class II and III devices need a comprehensive review (technical/administrative reviews);
- New and high-risk products may also require expert group meetings;
- Device classification determines the documentation required for your CFDA submission (technical review guide);
- China medical device assessment center websitehttp://www.cmde.org.cn/CL0001/
- Note:
- All documents must be submitted for CFDA examination in simplified Chinese;
- Submit the information catalogue, including the first and second level title;
- The data corresponding to each second level title should be compiled separately;
- Each technical review cycle is 60wds(class II) or 90 wds (class III);
- The time of expert group meetings shall not be counted within the time limit for review;

申报资料一级标题	申报资料二级标题
1.申请表	
2.证明性文件	
3.医疗器械安全有效基本要求清单	
4.综述资料	4.1 概述 4.2 产品描述 4.3 型号规格 4.4 包装说明 4.5 适用范围和禁忌症 4.6 参考的同类产品或前代产品的情况（如有） 4.7 其他需说明的内容
申报资料一级标题	申报资料二级标题
5.研究资料	5.1 产品性能研究 5.2 生物相容性评价研究 5.3 生物安全性研究 5.4 灭菌和消毒工艺研究 5.5 有效期和包装研究 5.6 动物研究 5.7 软件研究 5.8 其他
6.生产制造信息	6.1 无源产品/有源产品生产过程信息描述 6.2 生产场地
7.临床评价资料	
8.产品风险分析资料	
9.产品技术要求	
10.产品注册检验报告	10.1 注册检验报告 10.2 预评价意见
11.说明书和标签样稿	11.1 说明书 11.2 最小销售单元的标签样稿
12.符合性声明	

CFDA Regulations

- Submit CFDA application for Import Medical Device Registration Certificate (IMDRC)

- Class I :Prepare the technical documents (no submission fee);
- Class II and class III :Prepare registration documents, including test reports, agency authorization letters, 510 (k) / CFG, clinical assessment (if applicable) and other technical documents (with submission fee);
- Registration fee:
- Class II : 210900 yuan;
- Class III: 308800 yuan;
- CFDA issued the certificate of registration and published online.;
- The validity of the device certificate :
- Class I : permanently valid;
- Class II and class III: 5 years.;
- The CFDA license number must be placed on the device label, including IFU;
- At this point, medical equipment approval is sold in China.

CFDA Regulations

Change registration

- The class II and class III devices have been registered;
- Its design, raw materials, production technology, scope of application and use methods have changed substantially;
- May affect the safety and effectiveness of the medical devices;
- The registrant should apply to the original registration department for the change of registration procedures;
- If a non substantive change does not affect the safety and effectiveness of the medical device, it shall record the change to the original registration department.

Information on the change registration of medical devices

- Application
- Proof document
- A declaration of the registrant on the change
- Photocopy of the original medical device registration certificate and its appendix, and the registration changes of medical devices.
- Requirements for changing application items
- Safety risk management report related to product change
- Information on the impact of change on product safety and effectiveness
- Registration inspection report for changing parts of product technical requirements
- Conformance statement

CFDA Regulations

Continuation of registration

- The registration period of medical devices is valid for 5 years.;
- If a renewal is required at the expiration of the validity period, the application for renewal of registration shall be submitted to the original registration department **6 months** before the expiration of the validity period.
- Note:
- If the application for renewal of registration is not made **6 months** before the expiration of the validity period, the registration shall not be continued.

- **Information on the continued registration of medical devices**
- Application
- Proof document
- A statement about no change in the product
- Photocopy of the original medical device registration certificate and its appendix, and the registration changes of medical devices.
- Product analysis report in the validity period of the registration certificate
- Product inspection report
- Life verification report
- Conformance statement
- Other

CFDA Regulations

- Recall-《measures for the management of medical equipment recall》
- The main contents of the assessment of defective medical device products include:
- Whether the product meets the mandatory standard, registered or archival product technical requirements;
- Is there any malfunction or injury during the use of medical devices;
- Whether there will be any harm in the existing use environment, whether there are scientific literature, research, related tests or verification can explain the causes of injury;
- The area and the characteristics of the population involved in the injury;
- The degree of injury to the health of the human body;
- The probability of injury;The short-term and long-term consequences of injury;
- Other factors that may cause harm to the human body;
- According to the severity of defects in medical devices, the recall of medical devices is divided into:
- Level one recall: the use of the medical device may or has caused serious health hazards.
- Level two recall: the use of the medical device may or has caused temporary or reversible health hazards.
- Level three recall: the possibility of using this medical device to cause harm is small but still needs to be recalled.

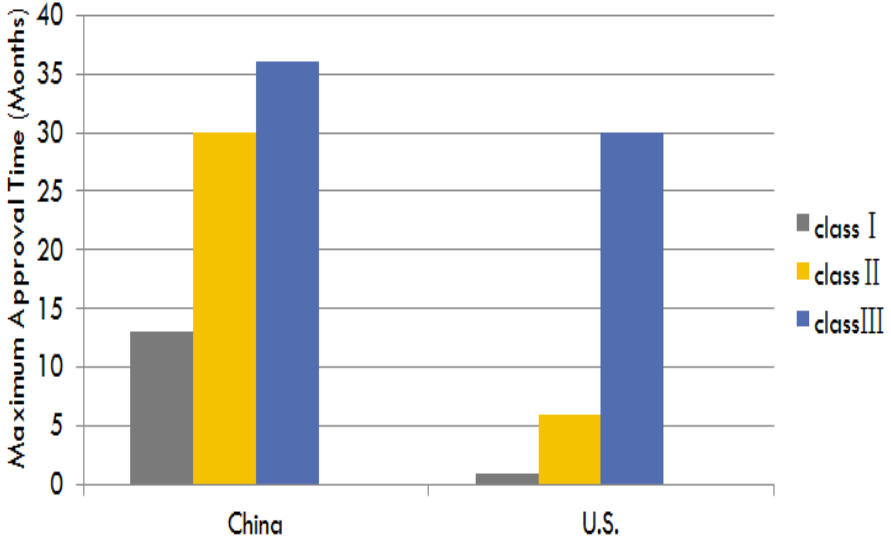
Compare with FDA

Compare with FDA

		CFDA	FDA
Classification		Ⅰ / Ⅱ / Ⅲ	Ⅰ / Ⅱ / Ⅲ
Registrant		Registered Agent (registration process, product quality / recall)	U.S. Agent (product registration)
Requirement	Class I (low risk)	Regular management	General Control
	Class II (medium risk)	Strict control +CER+GMP	PMN+GMP
	Class III (high risks)	Special measures +CER+GMP	PMA+CER+GMP
Quality system regulation		ISO 13485 YY 0287-2016	FDA_QSR 820
Proof documents		Yes(CFS/CFG)	No
Validity		Ⅰ (permanent)/ Ⅱ and Ⅲ (5 years)	permanent

Compare with FDA

- CFDA regulations are similar to FDA regulations;
- The Approval Time of CFDA is much longer than FDA;
- There are differences in classification;
- Example –Endoscope：
- FDA: class Ⅰ about 1 month
- CFDA: class Ⅱ about 30 months



Trends and FAQ

Trends

- The market share of medical devices in the world is increasing;
- Medical device market in China is in a stage of rapid expansion;
- CFDA regulations are becoming more and more perfect;
- The support of national policy.
- Example- medical device registrants
- Shanghai /Tianjin/Guangdong

Trends

- Implementation plan of pilot scheme for medical device registrants in China (Shanghai) free trade pilot area:
- The applicant may entrust the production sample of the enterprise with corresponding production conditions in the administrative area of Shanghai;
- The registered person has the corresponding production qualification and ability, which can be produced by itself, and can also entrust the Shanghai medical equipment production enterprise to produce the product;
- The registrant does not have the corresponding production qualification and ability, and can directly entrust the medical equipment production enterprise of Shanghai to produce the product;
- If the entrusted production enterprise does not have the corresponding production qualification, it may submit the medical device registration certificate of the registrant for the production license;
- A registered person can also commission a number of Shanghai medical device manufacturers to produce products at the same time.

FAQ

- Is in-country representation required for foreign manufacturers selling in China?

- Yes. In fact, you should be represented by the representative offices established within the territory of our country or the enterprise legal persons designated in the territory of our country.
- Liaison with CFDA and XXXXXX, collect information on medical device adverse events after the market and report to the corresponding registration management department, to recall the products that have problems after the medical device listed, and report to the corresponding food and drug supervision and management department. Truthfully and accurately convey relevant regulations and technical requirements to xxxxxx, and are jointly and severally liable for product quality and after sales service.

FAQ

- Do we need to include proof of home-country approval with our CFDA device submission?
- Yes. You are required to show proof of home country approval with a Certificate of Free Sale or Certificate to CFDA. Manufacturers are required to show Certificate of manufacturer's qualification.

- How long does the CFDA registration process take?
- It varies by device and classification. Please refer to the registration cycle diagram.

FAQ

- If a process is denied, can I submit an appeal?
  - Yes, the company has 20 days to submit the appeal to CFDA, provided there is grounds to appeal. This period is counted from the publication in the Official website.

- If a product undergoes a change is necessary a new registration?
  - It depends your changed project, if it affect the safety and effectiveness of the medical devices, you should apply to the original registration department for the change of registration procedures; If a non substantive change does not affect the safety and effectiveness of the medical device, it shall record the change to the original registration department.

Summary

Summary

- Our Services-CFDA
- Determining the classification of devices
- Harmonization of Chinese product testing
- Determine whether your equipment needs clinical trials
- Preparation of registration applications and technical requirements
- Submit to CFDA
- Follow up CFDA

Contributions

- Jianjie Wei
- Shelly Nie
- Huiqi Jiang

Sources

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