IVD Regulations in China

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Topics

1. Regulation Overview
2. CFDA
3. Registration Requirements
4. Trends

IVD Definitions

"Reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from human body." **21CFR 809.3**

"In vitro diagnosis reagents" as defined in current Measures refer to the in vitro diagnosis reagents administrated as medical devices, they include any reagents, reagent cartridge, calibration product (substance) and quality control product (substance) etc. for in vitro determination of human samples (various body fluid, cells and tissue samples, etc.) during the revention and control, diagnosis, treatment monitoring and observation of disease, evaluation of health as well as the prediction on hereditary disease, whether used alone or in combination with instruments, apparatus, equipment or systems.

CFDA 2007 ***Provisions for the Registration of In Vitro Diagnostic Reagents (Trial)***

BD Products

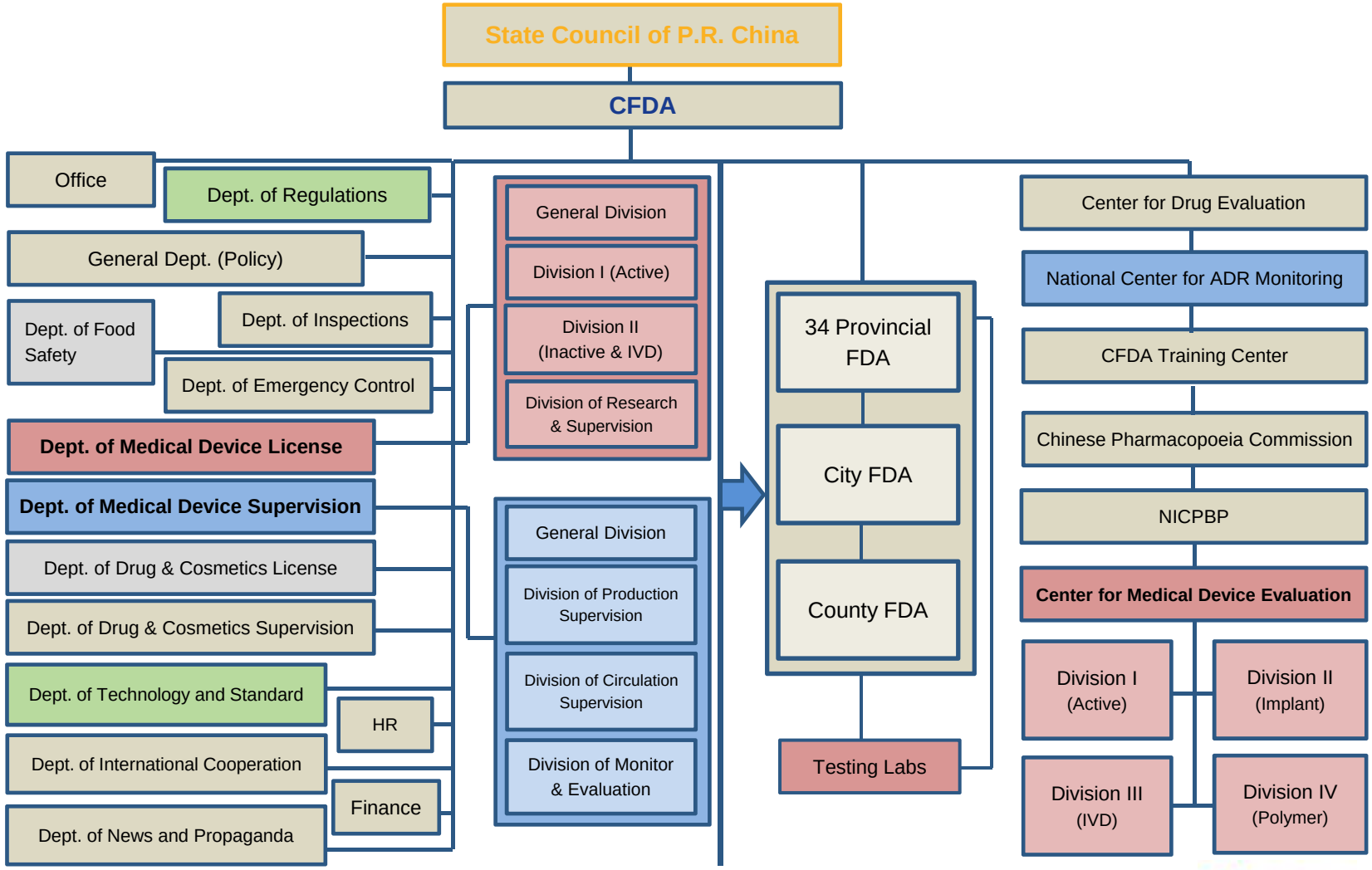
Regulation Overview

1. Regulator:
   - China Food and Drug Administration
   - Provincial FDA
   - City FDA
2. Classification: class I, II and III
3. Premarket approval is required for Class II and III medical devices and IVDs. Class I – more like notification.
4. Product testing by CFDA approved labs, and clinical trials in China are required for Class II and III IVDs

Regulation Overview

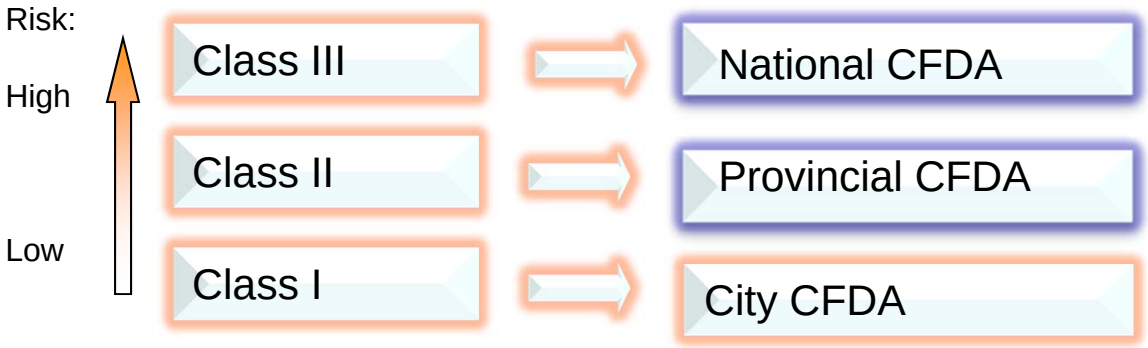
- **Regulations on Supervision and Management of Medical Device** State Order 276, Jan. 4, 2000
- Premarket Regulations
  - Measures for the Administration of Medical Device Registration, Decree of CFDA No. 16, August 9, 2004
  - In Vitro Diagnosis Reagent Registration and Management Method (Interim), CFDA [2007] #229, April 19, 2007
  - Requirements for the Format of Application Documents in IVD Reagent Registration, CFDA[2007]#609, Sept. 30, 2007
  - In Vitro Diagnosis Reagent Clinical Study Technical Guidance, CFDA [2007] #240, April 28, 2007
  - In Vitro Diagnosis Reagent User's Manual Drafting Guidance, CFDA [2007] #240, April 28, 2007
- Post-market Regulations:
  - CFDA Order〔2007〕239 Appendix 1 Provisions on the Examination and Evaluation of Quality Management System of In Vitro Diagnostic Reagents (Trial)
  - Adverse Event Reporting CFDA Order〔2011〕425
  - Measures for Administration on Medical Device Recall (for trial implementation) MOH Order No. 82 [2011]
- Total 68 registration guidelines

CFDA

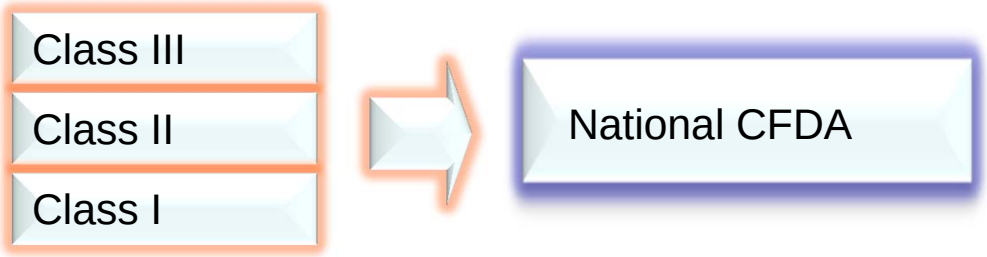

State Council of P.R. China
CFDA
Office
Dept. of Regulations
General Dept. (Policy)
Dept. of Food Safety
Dept. of Inspections
Dept. of Emergency Control
Dept. of Medical Device License
Dept. of Medical Device Supervision
Dept. of Drug & Cosmetics License
Dept. of Drug & Cosmetics Supervision
Dept. of Technology and Standard
HR
Dept. of International Cooperation
Finance
Dept. of News and Propaganda
General Division
Division I (Active)
Division II (Inactive & IVD)
Division of Research & Supervision
General Division
Division of Production Supervision
Division of Circulation Supervision
Division of Monitor & Evaluation
34 Provincial FDA
City FDA
County FDA
Testing Labs
Center for Drug Evaluation
National Center for ADR Monitoring
CFDA Training Center
Chinese Pharmacopoeia Commission
NICPBP
Center for Medical Device Evaluation
Division I (Active)
Division II (Implant)
Division III (IVD)
Division IV (Polymer)

Product Classification and Approval Agency in China

- Domestic products:

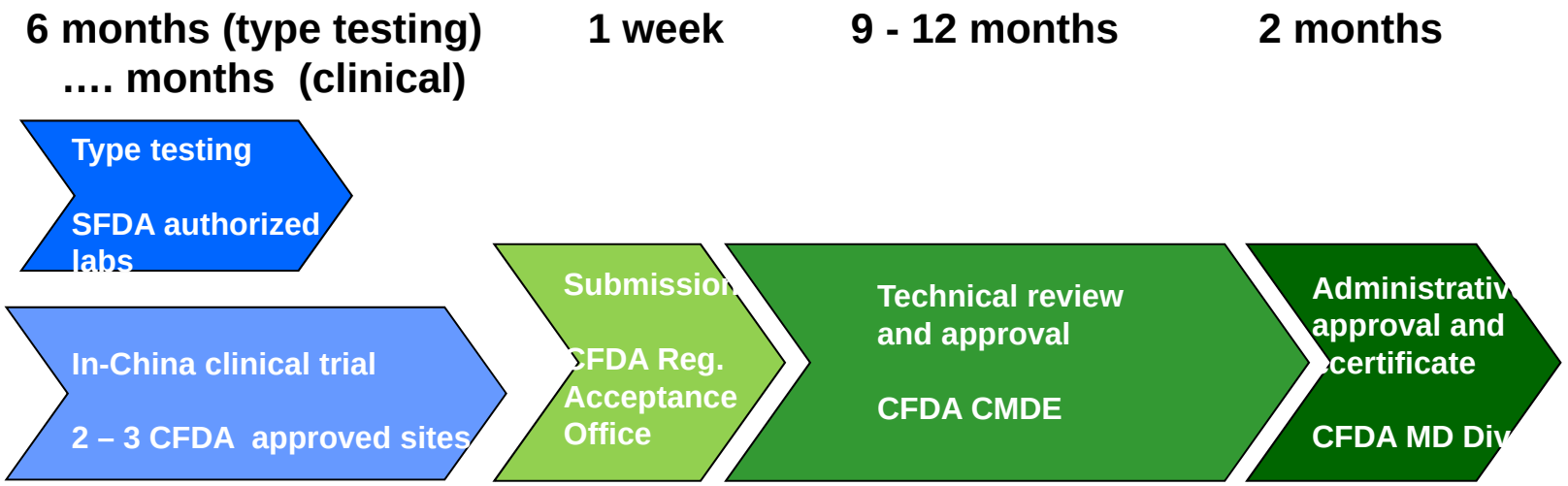


- Imported products:



Of the 240 IVD products classified in China as class III, more than 140 are class II in the United States.

Imported IVD Registration Process & Timeline



Type testing:

Class II, III

Chinese national and industry Standards

Product Registration Standard

Clinical trial:

Class II, III IVD

N>=1,000*

Full dossier:

Company info

Product Registration Standard

Technical info

Certificates

…

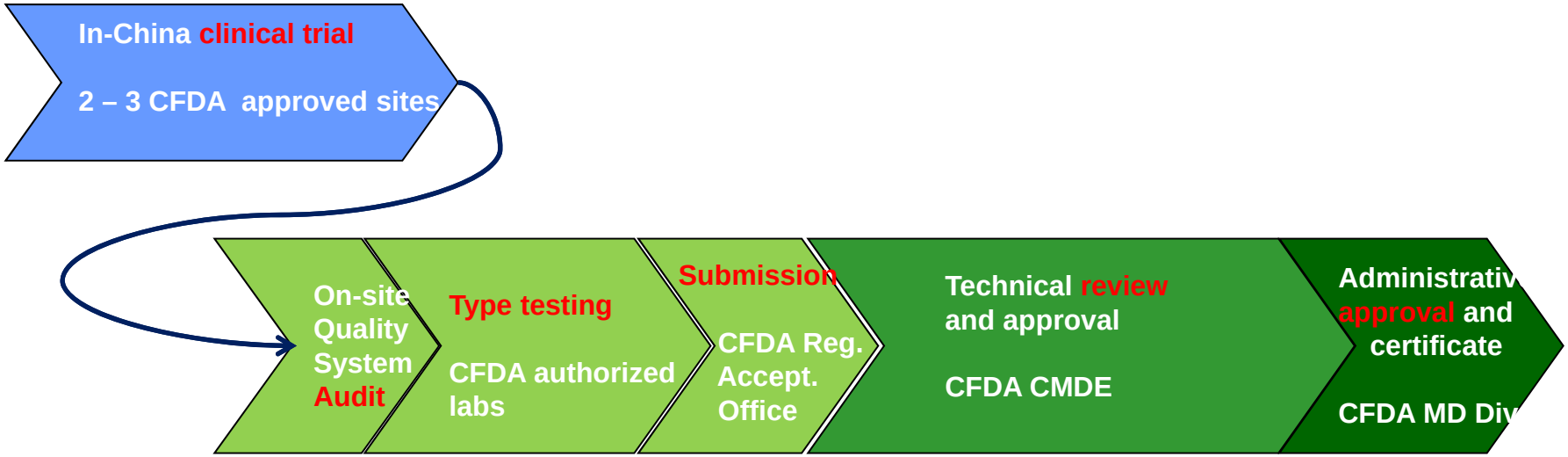
Q&A

Additional Testing

Additional Info

Domestic IVD Registration Process & Timeline

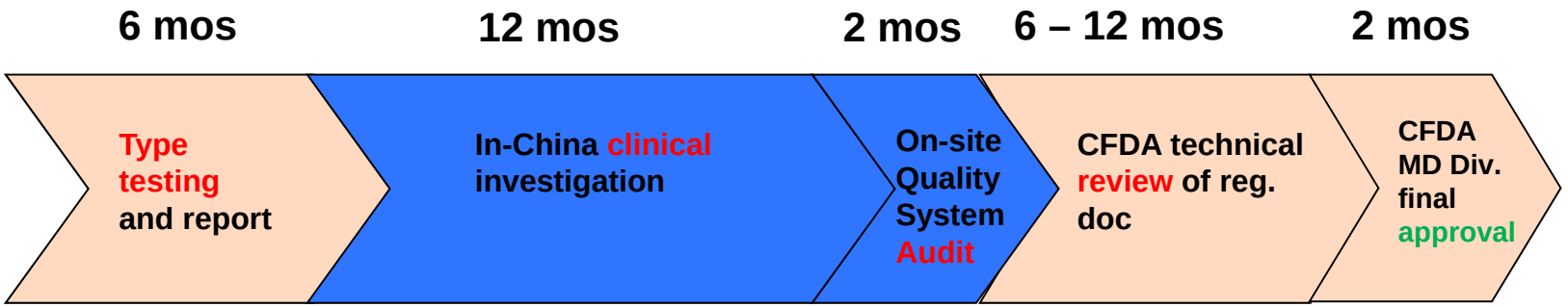
…. months (clinical)



Domestic product approval process should take longer

MD Registration Process

Domestic class II and III



Imported class II and III

CFDA Registration Documents List – IVD Reagents

No.	Documentations		Requirements
1	Application Form of registration		Original with signature from both manufacturer and agent
2	Manufacturer Qualification Certificate		Original, or notarized copy
3	Overseas Pre-market Approval		Original, or notarized copy
4	ISO13485 certificate		Original, or notarized copy
5			
6			
7	registration agency		Stamp
8	Letter of Authenticity		Original with notarization
9	Product Summary		Signature with notarization
10	Instructions for use		Notarized and signature
11	Instruction for Use in Chinese(SFDA Format)		2 copies with original stamp
12	Statement of conformity of 2 IFUs		Stamp
13	Letter of Authorization for drafting PRS		Original with notarization
14	Statement of conformity of 2 PRSs		Stamp

1. Ensure product name is consistent in all documents (CFG, product labeling, DoC, etc.)
2. Ensure manufacturer name and address are consistent in all documents

CFDA Registration Documents List – IVD Reagents

15	Product Registration Standard (PRS)		English PPS from manufacture, signature with notarization, Chinese PRS, 2 copies with stamp
16	The Statement for Typical Product Used for Testing in China		Original and notarized
17	Test report issued by CFDA test center (3 lots)		Original
18	Study report of key raw materials		Signature with notarization
19	Study report of production technics & reaction system		Signature with notarization
20	Documents of Performance Evaluation		Signature with notarization
21	Study report of the reference value (range) determination		Signature with notarization
22	Stability Data and Documents (real time)		Signature with notarization
23	Clinical Report (contains overseas study report and in-China clinical trial report)		Signature with notarization (Overseas) Original and stamp (China local evaluation)
24	Batch record of three consecutive batches of products		Signature with notarization
25	Package and Labeling		Signature with notarization; (Overseas), stamp (China version)
26	Invitation Letter for Quality Audit		Signature with notarization

Registration Documents for 4 Reagents

16 Big Binders for 4 Reagents Registrations

13

Product Registration Standard (PRS)

1. Product information (description, Model, Configuration, Components, Raw material, Product Sketch, etc.)
2. References (regulations, guidelines, standards)
3. Product specifications (must meet GB/YY Standards) (Physical, Chemical, Biological, etc.)
4. Detailed test methods for each specification
5. Labeling contents
6. Sterilization, storage, shelf life information
7. Rational, principle and rule for the specs and requirements in PRS (rational must be provided for the requirements in GB/YY standards that are not applicable for the product to be registered)

Why Is PRS (YZB) Important ?

YZB

医 疗 器 械 注 册 产 品 标 准

ZB/BDM 006–2006

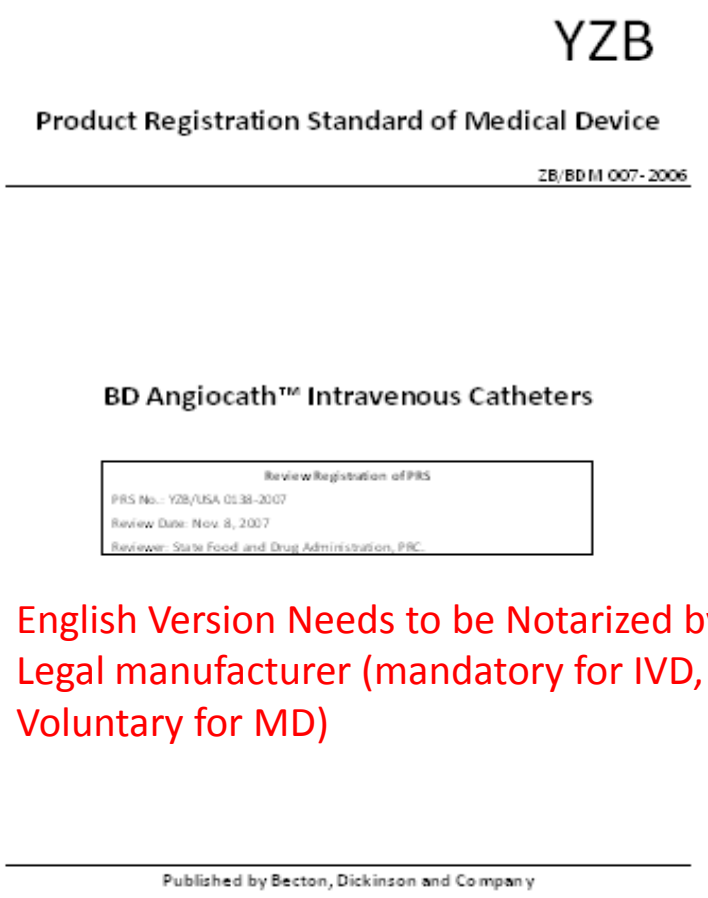
静脉留置针

BD Insyte ™ Intravenous Catheters

医疗器械注册产品标准复核章
注册产品标准编号: YZB / USA 0128-2007
复 核 日 期: 2007年 1月 8日
复 核 部 门: 国家食品药品监督管理局

BD China Legal Stamp →

美国 BD 公司 发布



YZB

Product Registration Standard of Medical Device

ZB/BDM 007-2006

BD Angiocath™ Intravenous Catheters

Review Registration of PRS
PRS No.: YZB/USA 0138-2007
Review Date: Nov. 8, 2007
Reviewer: State Food and Drug Administration, PRC

Published by Becton, Dickinson and Company

English Version Needs to be Notarized by Legal manufacturer (mandatory for IVD, Voluntary for MD)

1. Approval of an IVD by CFDA = approval of an IVD described in PRS (YZB)
2. Changes to CFDA Approved YZB (PRS) Will Result in Re-registration

Changes That Require Change Registration - IVD

- Manufacturer name and address
- Product agent or registration agency
- intended use/indications for use
- key raw materials, e.g. Ag and Ab
- testing conditions and reference value (or reference range), etc.
- product specifications, parameters and testing method
- instruction for use, e.g. add packing specification, add applicable model of instrument etc,
- storage conditions and/or shelf life
- manufacturing site (substantial change of manufacturing site)
  - Moving manufacturing sites outside of China
  - Moving manufacturing into/out of China
- Other changes which may affect the safety and efficiency of the product

Requirements That Make Reagent (IVD) Registration Challenging

1. IVDs not approved at the country of legal manufacturer cannot be registered in China (since 2007)
   - CE marked IVD reagents cannot be registered anymore for legal manufacturer that is not in Europe

2. Technical Documents
   - Huge amount of information required
   - Consistency among documents (product name, mfg name, etc.)
   - Concern for confidential documents

3. Product Testing
   - 3 batches to be tested by an CFDA authorized lab:
     - Time consuming to collect samples from 3 batches
     - Products with short shelf life
4. Clinical
   - N= 1000* cases total at 3 clinical sites in China (class III)
   - Comparison study: compare new product to approved product
   - Clinical sites must be CFDA approved hospitals
   - Difficulties in enrollment for rare diseases
   - Lack of expertise and resources externally
   - Cost is increasing rapidly

Changes in 2013

- 18 registration guidelines were released in 2013: Dialysis, etc.
- Elimination of 3C certificate
- Change registration review/approval by provincial FDA from CFDA
- Fast track approval for innovative products
- Simplified re-registration processes
- Down-classification (ultrasound, X-ray, X-ray accessories, X-ray protection products, e-system)
- Etc.

Trends – massive changes will take place at a faster pace

1. Order 276 and resulting changes to regulations, guidelines, standards
   - Expected to be released before the end of this year.
2. Perennial issues: country of origin, clinical trials, re-registration, IVD classification and registration requirements, etc.
3. Emerging challenges
   - UDI
   - EMC testing/certification – Jan. 2014 & Jan. 2015
   - Software testing/certification
   - Tighter registration control: registration rejected if supplements are not submitted within 60 working days
   - Postmarket surveillance

Suggestions

- AdvaMed
- US Dept. of Commerce
- EUCCC
- China Association of Medical Device Industry (CAMDI)
- Standards Committees
  - National Institutes For Food and Drug Control (NIFDC)
    - **Institute for Medical Device Standardization Administration**
  - http://www.nifdc.org.cn/qxbgzx/CL0482/

Thank You

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