Regulatory oversight of drug clinical trial in China

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Outline

- Brief introduction of CFDA/CFDI
- Relevant laws and regulations
- Supervision of drug clinical trials
- Common findings of bioanalysis inspection

Brief introduction of CFDA/CFDI

History of CFDA

1998
Establishment of SDA for Centralized drug supervision

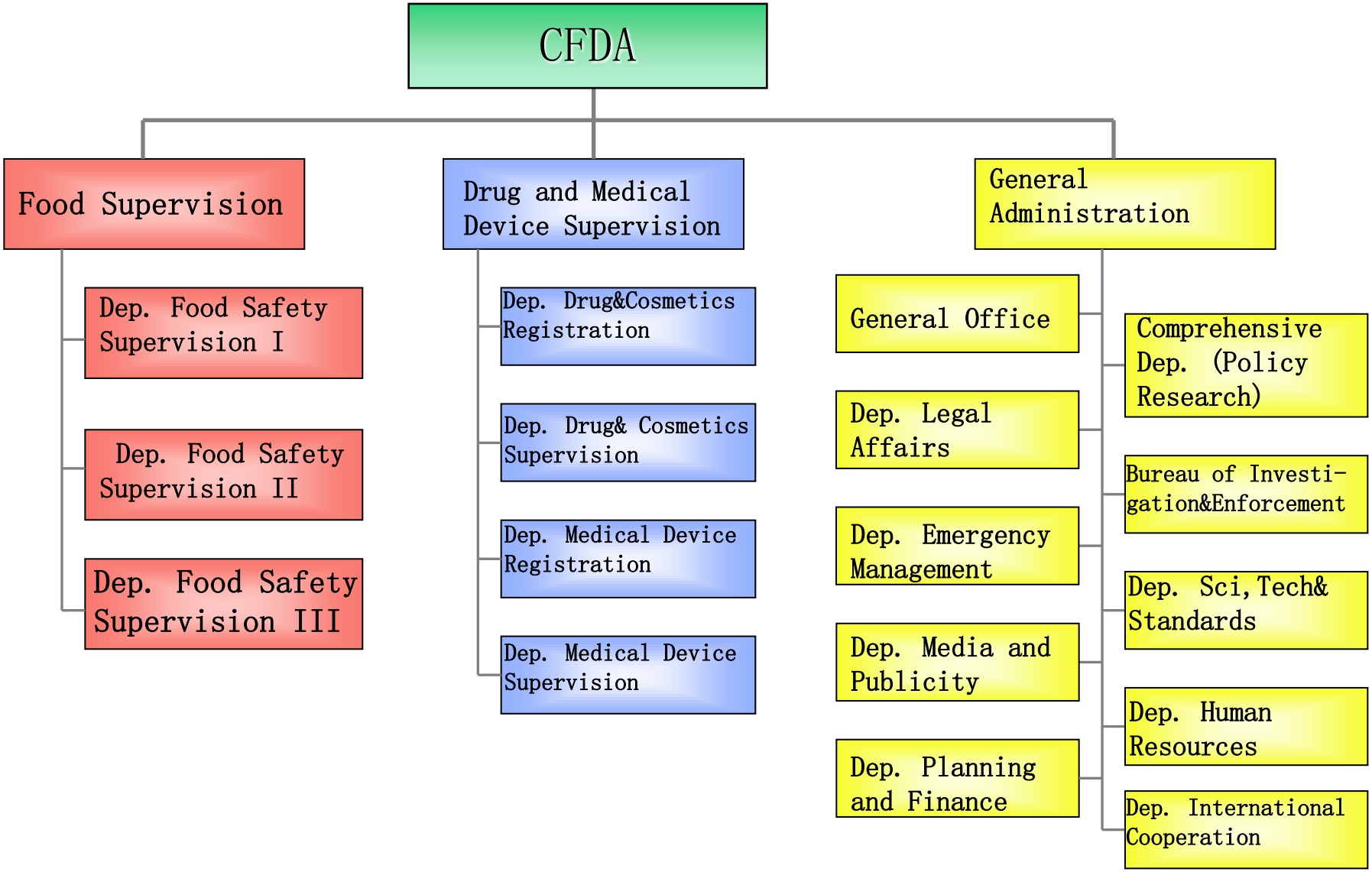
2003
 Establishment of SFDA with additional function of comprehensive food supervision as well as administration of health food and cosmetics

2008
Restructuring and functional adjustment

2013
Integration of food supervision duties from AQSIQ, SAIC and former SFDA

Main responsibilities of CFDA

- Draft laws, regulations and rules and policy plans on the administration and supervision of food (including food additives and health food) safety, drugs ,medical devices and cosmetics, formulate normative documents.
- Formulate the regulations on food administrative licensing and supervise their implementation.
- Formulate drug , medical device and food standards.
- Undertake drug and medical device registration, supervision and inspection.
- Formulate the investigation and enforcement system for food, drugs, medical devices and cosmetics, and organize their implementation.
- Give guidance to local food and drug administration.


CFDA
Food Supervision
Dep. Food Safety Supervision I
Dep. Food Safety Supervision II
Dep. Food Safety Supervision III
Drug and Medical Device Supervision
Dep. Drug&Cosmetics Registration
Dep. Drug& Cosmetics Supervision
Dep. Medical Device Registration
Dep. Medical Device Supervision
General Administration
General Office
Dep. Legal Affairs
Dep. Emergency Management
Dep. Media and Publicity
Dep. Planning and Finance
Comprehensive Dep. (Policy Research)
Bureau of Investi-gation&Enforcement
Dep. Sci,Tech& Standards
Dep. Human Resources
Dep. International Cooperation

Affiliated Organizations of CFDA

- National Institutes for Food and Drug Control
- State Pharmacopoeia Commission
- Center for Drug Evaluation
- Center for Food and Drug Inspection
- National Committee on the Assessment of the Protected Traditional Chinese Medical Products (Center for Health Food Evaluation)
- Center for Drug Reevaluation(National Center for ADR Monitoring)
- Center for Medical Device Evaluation
- Administrative Service and Complaint Center

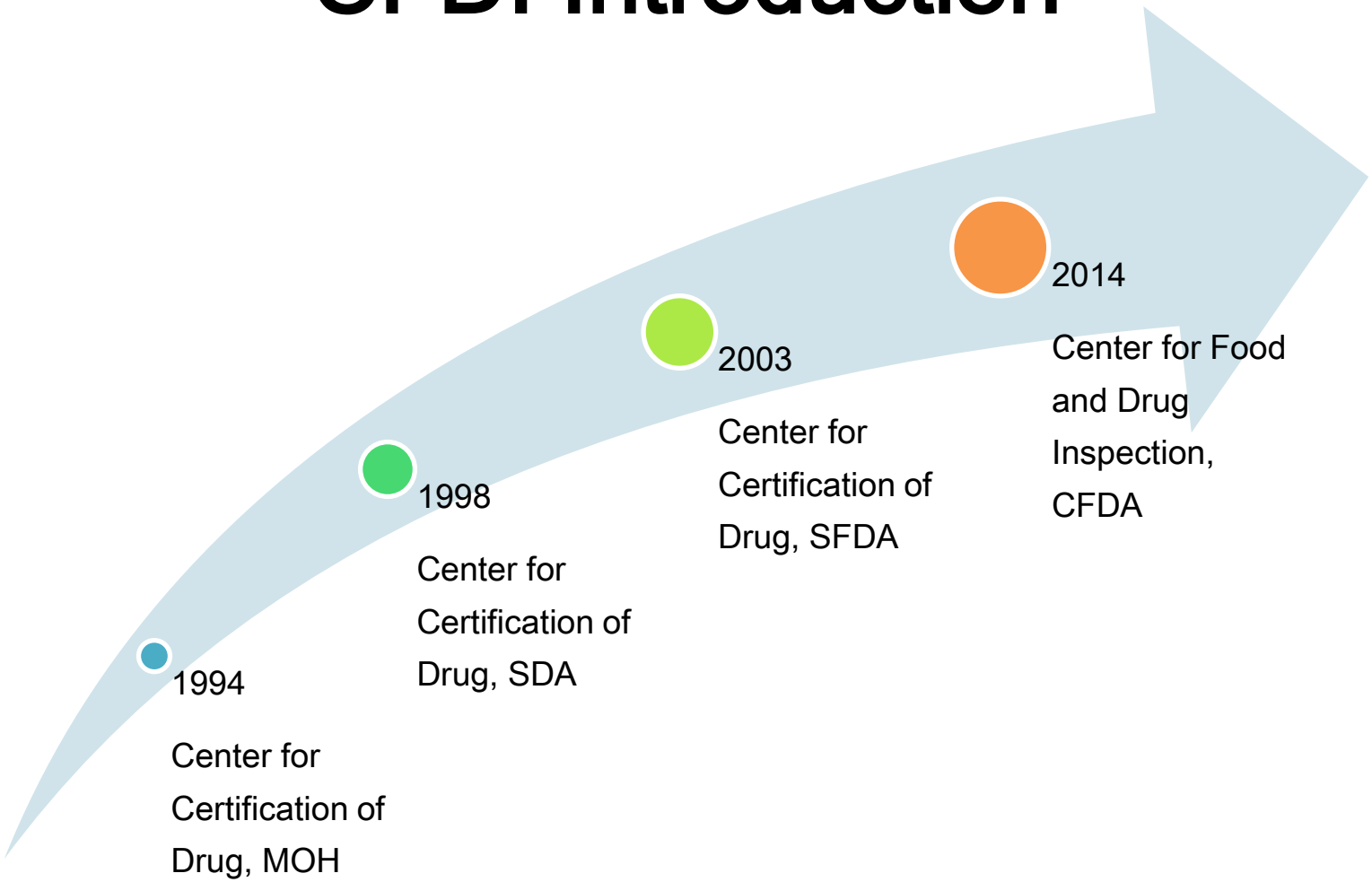
Affiliated Organizations of CFDA(cont)

- Internal Service Center
- Information Center of CFDA
- Institute of Executive Development, CFDA
- Certification Center for Licensed Pharmacist of SFDA
- China Pharmaceutical News paper
- China Medico-Pharmaceutical Science & Technology Publishing House
- China Center for Food and Drug International Exchange
- Southern Medicine Economic Research Institute of CFDA
- 146 warehouse
- Chinese Pharmaceutical Association

Local Food and Drug Administration

- CFDA
- Provincial FDA: 31
- Municipal &City-level FDA
- County-level FDA

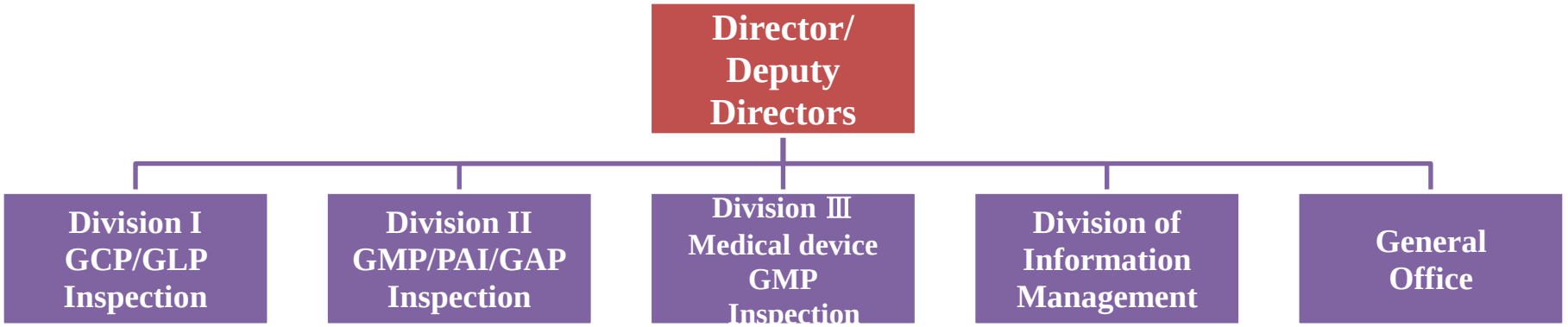
CFDI Introduction



Main Responsibility

- To carry out certification of clinical trial institution
- To carry out GLP inspection of nonclinical study facility
- To carry out inspection of vaccine clinical trial submitted for registration
- To carry out GMP inspection of drug manufacturing company
- To carry out overseas GMP inspection
- To carry out GAP inspection of TCM agriculture
- To carry out Pre-approval Inspection
- To carry out medical device GMP inspection of medical device manufacturing company
- Inspector management
- Undertake other work assigned by CFDA

CFDI Structure



Relevant Laws and Regulations

Legal Basis

Law

- Drug Administration Law (2001)

Regulation

- Regulations for Implementation of the Drug Administration Law (2002)

Legal Basis

Normative Documents

- Provisions for Drug Registration (2007)
- Provisions for Drug Import(2004)
- Good Clinical Practice (2003)
- Provisions for Certification of Drug Clinical Research Institutions (interim) (2004)
- Provisions for On-site Inspections for Drug Registration (2008)
- Notification on Re-certification of Drug Clinical Research Institutions (2009)

Legal Basis

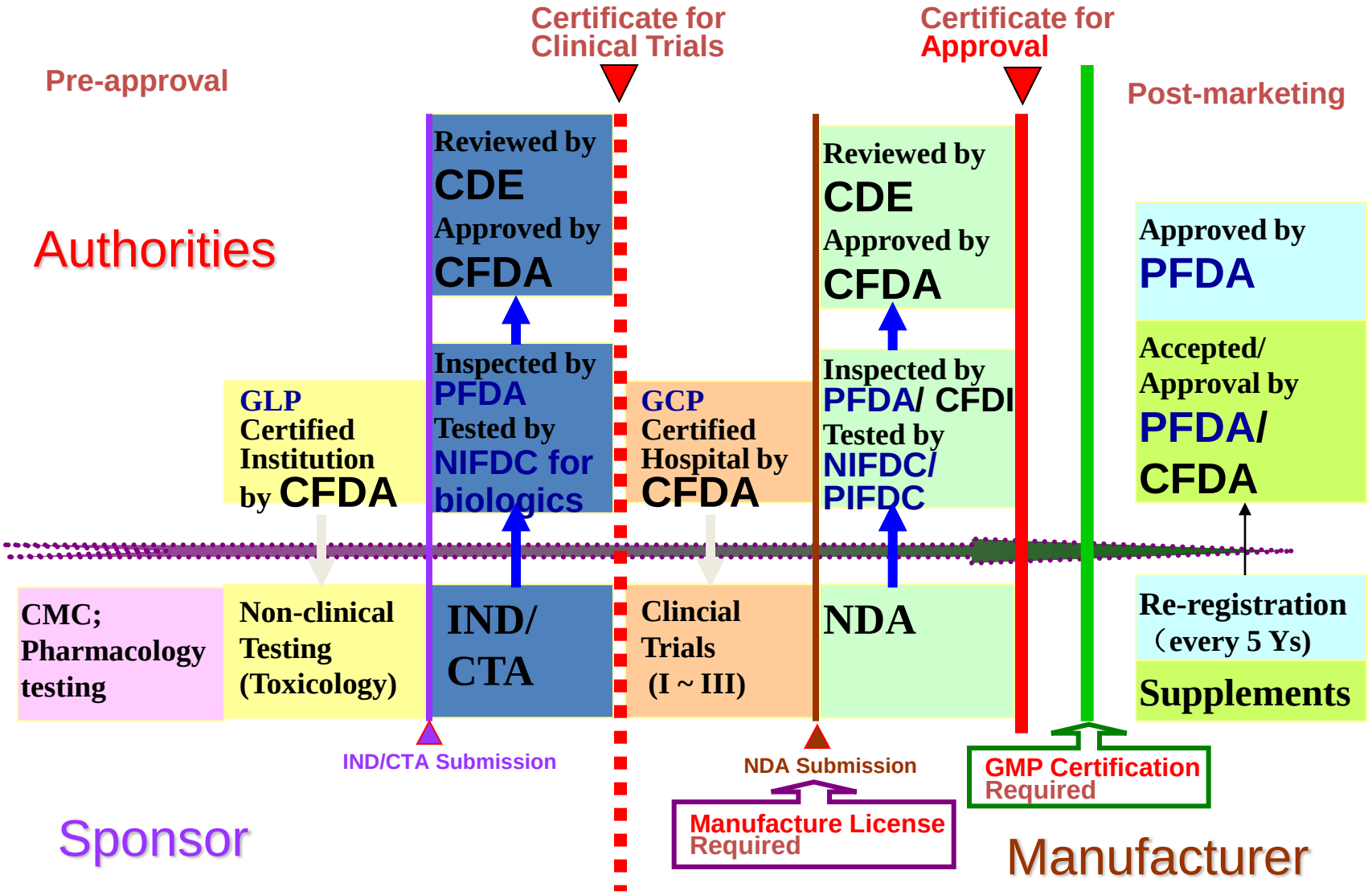
Guidance

- Guidance for ethical review of clinical trials by IRB (2010)
- Guideline for Phase I Clinical Trial Management(2011)
- Guideline for the management of Bioanalytical Lab in drug clinical trial (2011)
- Guideline for Clinical Trial Data Management (2012)
- Notice on Clinical Trial Database (2013)

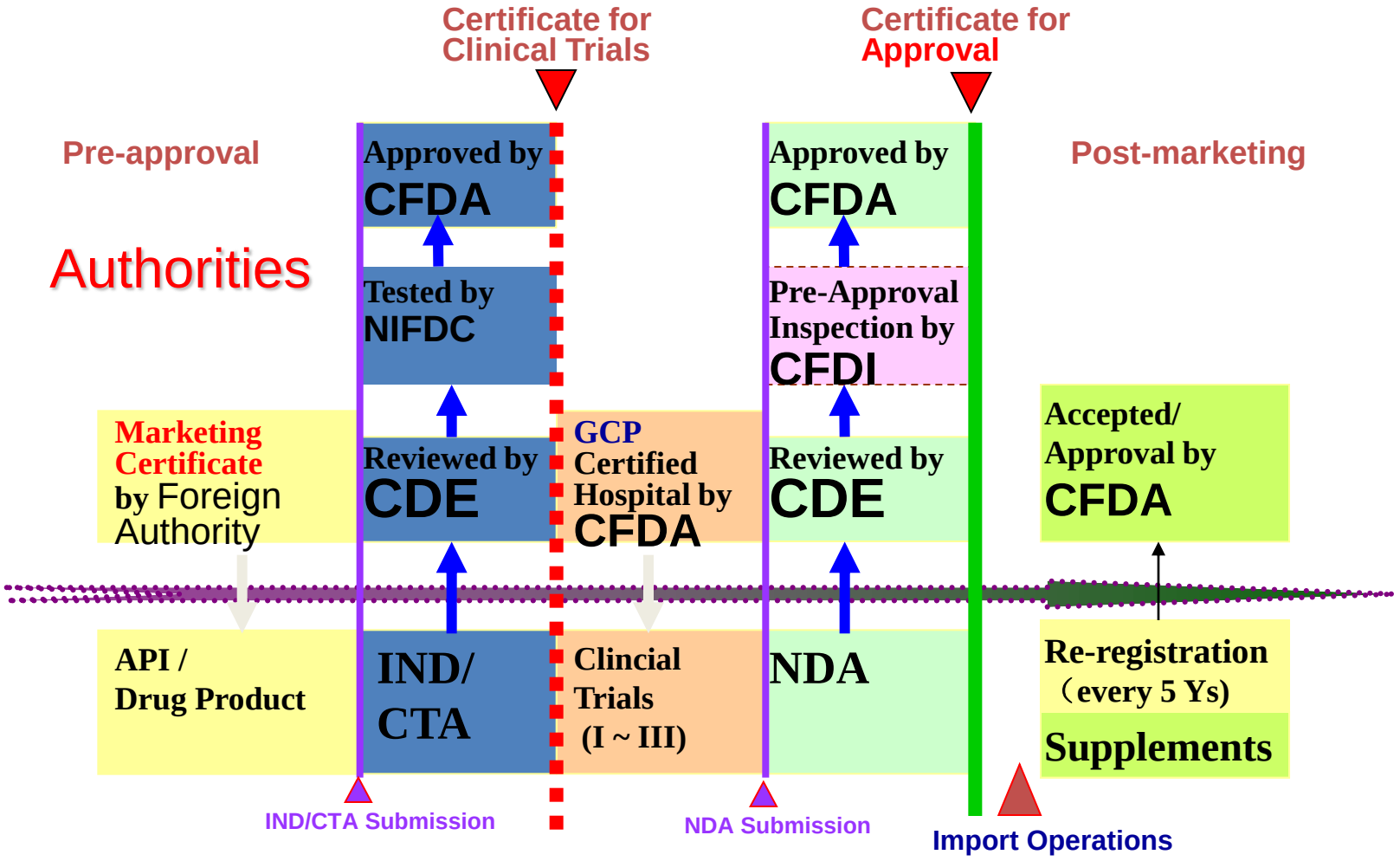
Guideline for the management of Bioanalytical Lab in drug clinical trial(2011)

- General principles
- Organization and personnel
- Premises
- Equipment and material
- Contract management
- SOPs
- Performance of the study
- Data management
- Quality assurance

Domestic New Drug Registration Process



Import Drug Registration Process



Supervision of drug clinical trials

Supervision of Clinical Trials in China

- Certification of Drug Clinical Research Institutions - CFDA/NHFPC/CFDI
- On-site inspection for drug registration – PFDA/CFDI
- Triggered inspection – CFDA/CFDI/PFDA
- Routine inspection of drug clinical research institutions – PFDA

Certification System

- In 2003, CFDA/NHFPC initiated certification of drug clinical research institution, mandatory requirement
- Overall evaluation of the hospital and clinical departments
- Ensure all clinical trials be conducted in qualified hospitals with well-trained investigators
- Re-certification every 3 years
- Till Sep2014, more than 400 hospitals with relevant clinical departments have been certified (Public announcement: www.sfda.gov.cn/WS01/CL0069)

Certification Process

- Time: 2-3 day
- Inspector: 3-5 inspectors, including inspectors from CFDI/PFDA, and outside experts
- Inspection method: facility tour/equipment and instrument/SOPs/investigator interview/data audit
- Inspection report submitted to CFDA/NHFPC for approval
- Inspection outcome: pass/correction action needed/fail

Certification criteria

- Clinical site management
- Phase I Unit
- Clinical department
- IRB

Certification Criteria-Clinical Site management

- facility management
- infrastructure (office, archives, fax, etc)
- SOPs

Certification Criteria –Phase I Unit

- Investigator interview (qualification, experience, personnel, GCP training)
- phase I ward (facility, equipment, especially emergency equipment)
- Bioanalysis lab (facility and equipment)
- SOPs
- Study audit of previous trials

Key elements of Bioanalysis inspection

- Storage condition
- Sample handling
- Assay validation
- Sample reanalysis
- Data comparison
- Audit trail
- Data quality

Certification Criteria –Clinical department

- Investigator (qualification, experience, training, etc)
- Medical level (bed, disease variety, patient number, etc)
- Medical equipment
- SOPs
- Study audit of previous trials

Certification Criteria –IRB

- Composition
- Qualification and training
- SOPs
- Review document
- archive

On-site inspection for drug registration

- Initiated on a trial basis in 2007 and formally initiated in 2008.
- Comparison of data submitted by sponsor to source records on site
- Inspection of pharmaceutical test, pharmacological test, toxicological test, clinical trial and PAI for each drug application.
- Inspection conducted by PFDA or CFDI.
- Inspection outcome: data accepted/data not accepted/conditional accepted

Triggered Inspection

- Study audit conducted by CFDI or PFDA
- Triggered by complaints or requests from CDE/CFDA
- To Investigator, CRO, laboratories
- To verify compliance with GCP
- 30-50 cases each year

Routine Inspection

- Conducted by PFDA
- Annual inspection plan
- No less than two facility inspections to each certified institutions in a year
- No less than 15% study audit of all clinical trials in the province in a year

Common findings of bioanalysis inspection

- Inadequate documentation (QCs and calibrators preparation, sample handling, weighing)
- SOPs absent or not followed
- Reserve samples not retained or inadequate number
- Calibration of instrument not adequate
- Inconsistent manual integration
- Poor management of Computer system

Conclusion

- With the restructuring of CFDA and revision of drug-related laws and regulation, clinical trial supervision will be enhanced.
- Risk-based inspection method will be adopted.
- Increasing collaboration with WHO and other drug regulatory agency.


Thank you!