Clinical trial Regulatory Environment in China

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Three levels Regulatory system

- **Laws**
- **Related Regulations**
- **Series of detailed Provisions**

- **Peoples’ Congress**
- **State Council**
- **SFDA**
Levels of Authority

Ministry of Health

SFDA

Provincial DA

City Level DA

County Level DA
SFDA Organizational Chart

Commissioner

- General Office (Finance & Planning Dep.)
- Policy & Regulation Dep.
- Food Safety & Coordination Dep.
- Food Safety & Supervision Dep.
- Drug Registration Dep.
- Medical Device Dep.
- Drug Safety & Inspection Dep.
- Drug Market Compliance Bureau
- Personnel & Education Dep.
- International Cooperation Dep.
- Others: Retired, Discipline, …
Affiliated Organizations to SFDA

SFDA

- Center for Drug Evaluation (CDE)
- National Institute for the Control of Pharmaceutical and Biological Product (NICPBP)
- Chinese Pharmacopoeia Commission (ChPC)
- Certification Committee for Drugs (CCD)
- Center for Health Food Evaluation
- Center for Drug Reevaluation (CDR)
- China Center For Pharmaceutical International Exchange (CCPIE)
- Center for Information
- Center for Training
Clinical Trial Approval Procedure

Applicant → Dossier Required

Receiving office

CDE
- Technical Evaluation

Assessment Report → SFDA

CT Approved

Ethics Committee

CT Commencement
Application Dossiers

Part I: General data and Administrative Documents
Part II: Chemical, Pharmaceutical and Biological Data
Part III: Pharmacological and Toxicological data
Part IV: Clinical Data
Application Dossiers

PART I

1. Name of the drug
2. Document for attestation
3. Aim and justification of the selected project
4. Summary and review of the study results
5. Sample of package inserts, drafting description and reference materials
6. Sample of package and label
PART II

7. Review of the pharmaceutical study.
8. Manufacturing process and literatures for API; the formulation, manufacturing process and literatures for pharmaceutical preparation.
9. Identification data and literatures for chemical structure or components,
10. Quality study data and literatures
13. The origin and specifications of the excipients.
14. Stability data and literatures
15. Immediate packaging materials selection, and its specifications
Application Dossiers

PART III

16. Review of the pharmacological and toxicological study data.
17. The main pharmacodynamics data and literatures
18. General pharmacology data and literatures
19. Acute toxicity data and literatures.
20. Long term toxicity data and literatures
21. Special toxicity data and literatures related to topical and systematic administration, such as hypersensitivity (topical, systematic and photosensitive toxicity), hemolysis and topical (blood vessel, skin, membrane muscle, etc.) irritation, etc.
22. Interaction data and literatures of efficacy, toxicity and pharmacodynamics for multiple components.
23. Mutagenicity data and literatures.
24. Reproductive toxicity data and literatures
25. Carcinogenicity data and literatures
26. Drug dependence data and literatures
27. Animal pharmacokynetics data and literatures
PART IV
28. Overview of related clinical study literatures.
29. Clinical study protocol and plan.
31. The copy of Informed Consent and ethics committee approval.
Evaluation and Approval Timelines

1. Dossier Receiving: **5 days**
2. Provincial DA Primary Evaluation: **30 days** (Local product)
3. QC lab’s tests: **60 days**; Bio-product: **90 days**
4. CDE technical Evaluation for CTA: **90 days**
   (Special Procedure: **80 days**)  
5. SFDA administrative approval: **30 days**
   (Special Procedure: **20 days**)
Special Procedure

1. TCM derived from Herbal, animal, and mineral that have never been previously used as therapeutics
2. New chemical entity (NCE)
3. Anti-HIV/AIDS products (treatment, prevention, Diagnosis)
4. Products for malignant tumor
5. Products for rare diseases (orphan drugs)
6. Products for the diseases that efficacious treatment are not available yet
Patient Number Requirements

For NCE
1. Statistically meaningful
2. The minimum patient number requirements:
   - Phase I: 20-30 patients
   - Phase II: 100 patients
   - Phase III: 300 patients
   - Phase IV: 2000 patients

For first importation application:
1. PK study
2. 100 pairs of patients, controlled, randomized, study
3. At least 60 patients for each indication
CT Applicant Requirements

- Chinese nationality
- Domestic Law person: pharmaceutical company, organization, institute, not individual
- For multi-center international trial, applicant is foreigners, but, an Chinese representative has to be authorized, as the agent. The agent should be a law person
**Investigator Requirements**

- Qualified hospitals are pre-selected and designated by SFDA and MOH, according to standardized procedure and requirements for personnel qualification, equipment, etc.
- Around 300 hospitals now, called “National CT Base Hospital”
- “National CT Base Hospital” are inspected by SFDA and MOH jointly
Control of Samples

- Manufactured in GMP facilities
- Adequate scale-up
- Freely provided to subjects
- Sales not allowed
- “For Clinical Trial Only” must be placed on the label
Chinese GCP

- Published in 1998, amended in 1999, latest reversion Aug. 6, 2003
- Protecting subjects is the utmost purpose
- Helsinki Declaration as fundamental
- ICH, WHO guidelines as bases
Characteristics of Chinese CT System

- Clinical Trials must be approved by SFDA prior to ethics committee approval
- Trials must be conducted by designated hospitals
- Designated hospitals are pre-selected by SFDA, as Clinical Bases
- Good Clinical Practice (GCP) works as guideline
- Large part trials for Generics
International Clinical Trial Pre-conditions

- At least three countries involved, with PI in abroad and same protocol.
- Drug already marketed abroad, or at least Phase II trial or Phase III trial has already commenced abroad
- No any trials for vaccines without marketing authorization abroad
Utilization of International Multi-center Trial Result

- For drug importation application, after the marketing approval by original countries or regions
- For domestic manufacturing application
- For ICH region marketing application
Rules for International Multi-Center Trial

- Phase I study again among Chinese population for some trials
- Report all adverse event of the whole trial, not only those found in China
- Inform SFDA of the ending of a trial, by preparing a Clinical Trial Report
- Only way to utilize the result is by submitting the whole set of data from the whole multi-center trials
Prospected Benefits from International CT

- Learn more international experiences
- Better GCP compliance by rigid monitoring, auditing and inspection
- More qualified investigator through the training and practice of international trials
- Less money required from government budget for GCP training, and more objectives can be achieved
- Possibly early access to new products, beneficial to public health
Something we realized as problematic

- Huge CT approved and less CT Base Hospitals comparatively
- Investigators are less trained than required
- Lack of experiences in international trials
- Small and separated Ethics Committee by each hospitals
- Investigators more decidable or dominative than sponsors
- Lack of insurance policy for both investigators and subjects
- Relatively longer approval time than benchmark
Regulatory Improvement needs

- Differentiation between IND and NDA
- Differentiation between technical requirements for IND and NDA, especially CMC
- Differentiation between approaches to technical evaluation for IND and NDA
- Reduction of large number of CT application for none-innovative product - waste of CT resources
New Moves Concerned

- China-Korea-Japan, tri-party on CT will bring new input to regional cooperation
- 2007 Provisions for Drug Registration, cut CT sample tests requirement, accept CDT dossier, approval time shortening
- Special Procedure provides pre-consultation with CDE
- RMB 800 billion ($120 billion) government funds for health reform, some goes to CT for improvement.
- Government Initiative to encourage innovation by providing RMB 6.9 billion ($1.0 billion)
- Big R&D center built in China
Dealing with new situation

- Continuing regulatory improvement to support domestic need in innovation, attract more international multi-center CT
- Close connection with international community to utilize new achievement of ICH, APEC LSIF, and tri-party
THANK YOU for your attention.

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