How to meet the CFDA requirements for Phase 1 clinical trials

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OBJECTIVES

- Future reforms in China's regulatory environment
- Accreditation for Phase 1 Facilities
- Supervision of Phase 1 Clinical Trials
- Common criticisms from CFDA
- Operations of the Phase 1 Clinical Trials Centre

Current Situation

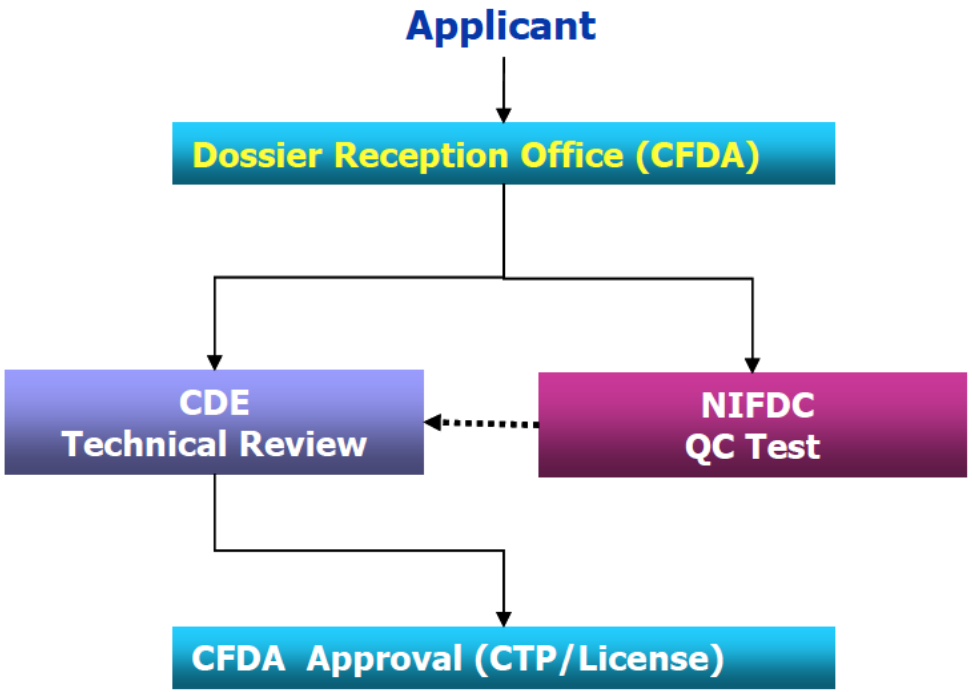
Exemption from China-specific trials if previous trials included large groups of Asian patients

Current Situation

- Use China as part of international multi-center trials
  - But wait until in Phase II or Phase III clinical study OR
  - Received market authorization elsewhere

POTENTIALLY BEGINNING WITH PHASE I STUDY

Current Situation



Approval Timeline for Chemical drug (based on RDPAC survey)

- **IDL-CTA: 36±4 m**
- **IDL-NDA: 29±4 m**
- **IMCT-CTA: 13±2 m**
- **IMCT-NDA: 36±4 m**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Future Reforms in China

- Clinical trial approval vs. 60 working day response
- Allow pharmaceutical companies to run first in human Phase 1 trials in China
- Allow the use of multi-regional clinical trial data to support new drug applications in China
- Expansion of China's fast track pathway

Future Reforms in China

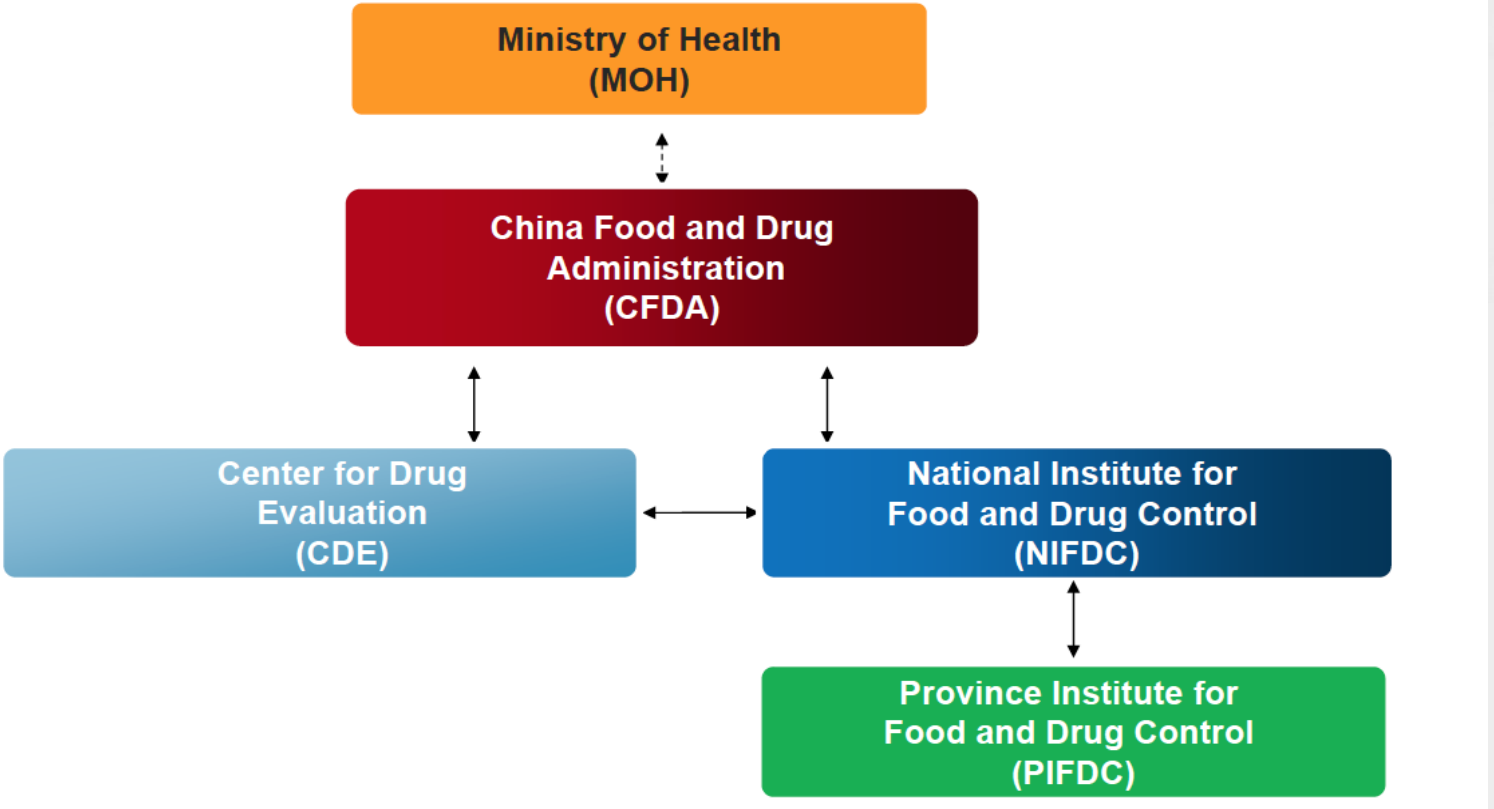
第四章 提交境外临床试验数据的基本技术要求

第十五条 临床药理学，主要包括药代动力学和药效学。鼓励药品上市许可持有人从区域和人种等多角度进行种族敏感性分析，为有效性和安全性评价提供支持。

Future Reforms in China

- Boost the supply of Phase 1 facilities
- Shift the focus from pre-approval supervision to day-to-day operational supervision
  - More rigorous and regular inspections

China Food and Drug Administration



Affiliated Organizations of CFDA

- National Institutes for Food and Drug Control
- Centre for Drug Evaluation
- Centre for Food and Drug Inspection
- National Committee on the assessment of the Protected Traditional Chinese Medical Products
- Centre for Drug Re-evaluation
- Centre for medical Device Evaluation
- Administrative Service and Complaint Centre
- Internal Service Centre
- Information Centre of CFDA
- Institute of Executive Development
- Certification Centre for Licensed Pharmacist of SFDA
- China Pharmaceutical Newspaper
- China Medico-pharmaceutical Science & Technology Publishing House
- China Centre for Food and Drug International Exchange
- Southern Medicine Economic Research Institute of CFDA
- Chinese Pharmaceutical Association

China Food and Drug Inspection

Supervision of Clinical Trials in China

- Certification of Drug Clinical Research Institutions
- On-site inspection of drug registration
- Triggered inspection
- Routine inspection of drug clinical research institutions

Accreditation for Phase 1 Facilities

- In 2003, CFDA initiated mandatory certification of clinical research institution
- Ensure all clinical trials to be conducted in qualified institutions with well trained investigators
- Re-certification every 3 years

Accreditation for Phase 1 Facilities

- Time: 2-3 days
- Inspector: 3-5 inspectors from CFDA and invited experts
- Procedure: Facility tour; review of equipment, SOPs, investigator interview and data audit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现场检查玛丽医院
陈志峰教授

Accreditation for Phase 1 Facilities

- Investigator interview (qualification, experience, personnel, GCP training)
- Phase 1 facility (equipment and medical emergency management)
- SOPs
- Bio-analysis laboratory
- Institutional Review Board
- Study audit of completed clinical trials

Key elements of Bio-analysis Inspection

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

Inspection of Phase 1 Clinical Trials

- On-site inspection for drug registration
- Triggered inspection
- Routine inspection of drug clinical research institutions

On-site Inspection

- Comparison of data submitted by sponsor to source record on site
- Inspection of pharmacological analysis, clinical trial
- Inspection conducted by PFDA or CFDI
- Inspection outcome: data accepted/ data not accepted/ conditional accepted

Triggered Inspection

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

Routine Inspection

- Conducted by PFDA
- Annual inspection plan
- No less than 2 facility inspections to each certified institutions in 1 year
- No less than 15% study audit of all clinical trials in the province in 1 year

Common Criticisms

- AE determination and management
- Lack of equipment
- Subject identification
- Subject recruitment and selection
- Documentation and signing of informed consent form
- Medical history documentation

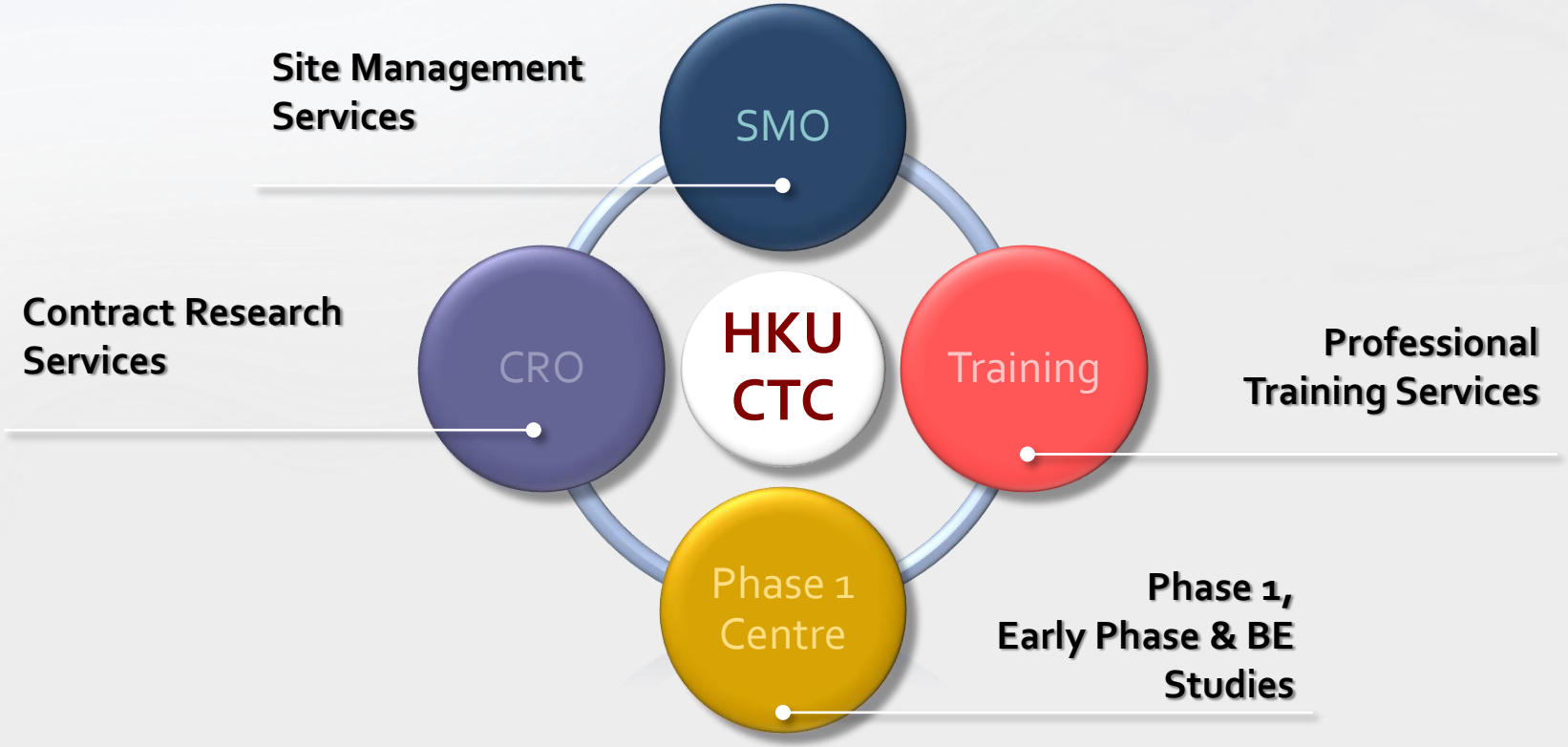
Common Criticisms

- IMP dosage, route of administration and timing
- IMP importation, transportation and storage documentation
- Biological samples schedule determination
- Biological samples transfer log
- Biological samples storage condition monitoring

Common Criticisms

- Inadequate documentation
- Inadequate or violation of SOPs
- Inadequate reserve samples
- Inadequate calibration of instruments
- Inconsistent manual integration
- Suboptimal maintenance of computer system

Operations of the Phase 1 Clinical Trials Centre



Risk Group		Risk Factors *(See notes overleaf)*	Yes	No
Human Subjects	1	Recruitment of human subjects [***see notes of completion***]	☐ →2	☐ →B
Medical Products	2	Use of any medical product that is not needed or used for the Subjects' normal clinical care [***see notes of completion***]	☐ →3	☐ →8
	3	Each medical product used is registered or permitted to be marketed in Hong Kong	☐ →4	☐ →5
	4	Use of each medical product is within the labeled use in Hong Kong [***see notes of completion***]	☐ →8	☐ →5
	5	Any medical product used is a chemical or biological drug that is to be tested in humans for the first time	☐ →C	☐ →6
Study Designs	6	The study is a phase 1 clinical trial on a chemical or biological drug as designated on its study protocol	☐ →C	☐ →7
	7	The study only has human pharmacology, tolerability and/or safety (but not efficacy) of the chemical or biological drug as its primary objective(s) as specified on its study protocol	☐ →C	☐ →A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7


6
7


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Clinical Trials Centre
The University of Hong Kong

Announcements

- HKU-CTC's new article is available in the Health Action Magazine (Jan 2016 Issue)
  12th Jan, 2016 NEW
- HKU-CTC's new article is available in the Health Action Magazine (Dec 2015 Issue)
  8th Dec, 2015
- The 2nd International Conference on Phase 1 and Early Phase Clinical Trials (ICPOEP 2015) was successfully held on 20 - 21 November, 2015.
  27th Nov, 2015
- HKU-CTC' Biennial Report 2013/2014 is available.
  27th Nov, 2015
- HKU-CTC's new article is available in the Health


Search Investigators


EDC Solutions

SUSAR Reporting

HKU Clinical Trials Registry

Public Corner 公眾資訊

臨床試驗是藥物研發的必經階段，旨在通過一系列有系統的測試，把有潛質的新藥由實驗室帶到臨床應用。

我們的使命

THANK YOU !

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