華山醫院

Origin and Development of Chinese GCP and Challenges to Its Implementation

Huashan Hospital, Fudan University,

Shanghai, China

Hejian Zou

Nov 24, 2008

GCP is the “Bible” for the Clinical Trials in China

- The China GCP is formulated to ensure the clinical trial process standardized, the results scientific and credible, and to protect the rights, benefits and safety of trial subjects
- The China GCP is a standard regarding the whole process of clinical trials
- The clinical trials of all drugs, in various phases, human bioavailability or bioequivalence study must be performed according to the China GCP guidelines

Principle in drafting out Chinese GCP

- To comply with the internationally recognized principle: ensuring the ethical and scientific integrity in clinical trials
- To be compatible with existing national provisions.
- To be acceptable internationally
- To be essentially feasible and executable
- To take ICH4 and WHO-GCP guidelines as the source documents of reference.

The Development Process of GCP In China

1986-1992	Information collection and understanding. Attendance of the Consultation Meeting on Development of WHO GCP Guidelines.
1993	Translation of existing GCP Guidelines of different countries as source information. Foreign experts were invited to make some introduction.
1994	Preparing the draft of Chinese GCP Guidelines; Seminars on GCP organized by administrative authority.

The Development Process of GCP In China (continued)

1995	A drafting group consists of 5 professors was authorized
May	First draft
June	Second draft
August	First consultation meeting
September	Third draft
October	Second consultation meeting
November	Fourth draft

The Development Process of GCP In China (continued)

1996	Consulting for traditional medicine and legislation Fifth draft
1997	Revision after attendance of ICH4 Sixth draft
1998	Finalized and approved by MOH
1999	Authorized by SDA
2003	Revised by SFDA

China GCP Guidelines

- Chapter 1 General provisions
- Chapter 2 Preparations and prerequisites for a clinical trial
- Chapter 3 Protection of trial subjects' rights and benefits
- Chapter 4 The protocol
- Chapter 5 Responsibilities of the investigator

China GCP Guidelines (cont')

- Chapter 6 Responsibilities of the sponsor
- Chapter 7 Responsibilities of the monitor
- Chapter 8 Data Recording and reporting
- Chapter 9 Statistical analysis and data processing
- Chapter 10 Management of investigational products

China GCP Guidelines (cont')

- Chapter 11 Quality assurance
- Chapter 12 Multicenter clinical trial
- Chapter 13 Supplementary articles/additional rules

- Appendix 1 Declaration of Helsinki
- Appendix 2 The necessary documents of clinical trials and the location of preservation

Applicability of GCP

- Clinical trial for medicine
  - ➢Registration, new indication, post-market
- All kinds of biomedical researches
  - ➢Involving human participants

Watch Dog

- SFDA was established in 1998
- Department of Drug Safety and Inspections:

  promote and supervise the implementation of GCP

Watch Dog (cont')

- Promote the training of China GCP
- Recognition of legal clinical trial institutions (of medicine, every 3 years)
- Examine and approve of new clinical trials
- Inspection during clinical trials

Research Institutions

- Teaching hospitals
- Central hospitals
  - High professional standard
  - Good facilities
  - Clinical pharmacology laboratory
  - Phase I unit

华山醫院

药物临床试验机构资格认定证书

CERTIFICATE FOR MEDICAL INSTITUTION CONDUCTING CLINICAL TRIALS FOR HUMAN USED DRUG

证书编号：0216
Certificate No：

医疗机构：复旦大学附属华山医院
Institution:

地址：上海乌鲁木齐中路 12 号
Address:

认定专业：感染、心血管、内分泌、血液、神经内科、神经外科、皮肤、泌尿、医学影像(诊断、治疗、核医学)、普通外科。
Certified Therapy Area:

经审查，符合药物临床试验机构资格认定的要求。特发此证。
After review the above-mentioned medical institution is qualified to conduct clinical trials.

有效期至 2011 年 9 月 17 日
This certificate remains valid until

Date for Issuing 2008 年 9 月 17 日

国家食品药品监督管理局制
PRINTED BY STATE FOOD AND DRUG ADMINISTRATION

SHAN HOSPITAL

Investigators

- Qualified clinical experts
- being trained on clinical pharmacology and GCP
- Experience in clinical trials

Selection of Investigators

- **Sponsor should select appropriate investigators among the state-recognized clinical trial institutions to assure the quality of CT**

Independent Ethics Committee (IEC)

- The establishment of IEC should be reported to SFDA for the record
- The committee composed of at least five members including medical professionals, non-medical, legal expert, non-affiliated, both male and female

Independent Ethics Committee (IEC) (cont')

- Review materials: protocol, informed consent, investigator's brochure, revision of protocol, record of SAE, discontinuation of CT
- Elements of IEC Review: the qualification of PI, informed consent meet requirement, bias in selection of trial subjects, no pressure on trial subjects, rights of trial subjects well protected, confidentiality of personal information protected, justifiable risk benefit ratio

HIRB

Huashan Institutional Review Board

HIRB History

- Established in 1996 (7 members)

  One of the earliest ECs in China
- Members renewed and replaced in 2000 (7 members)
- Members renewed and replaced in 2005 (9 members)
- Members renewed and replaced in 2008 (15 members)

華山醫院

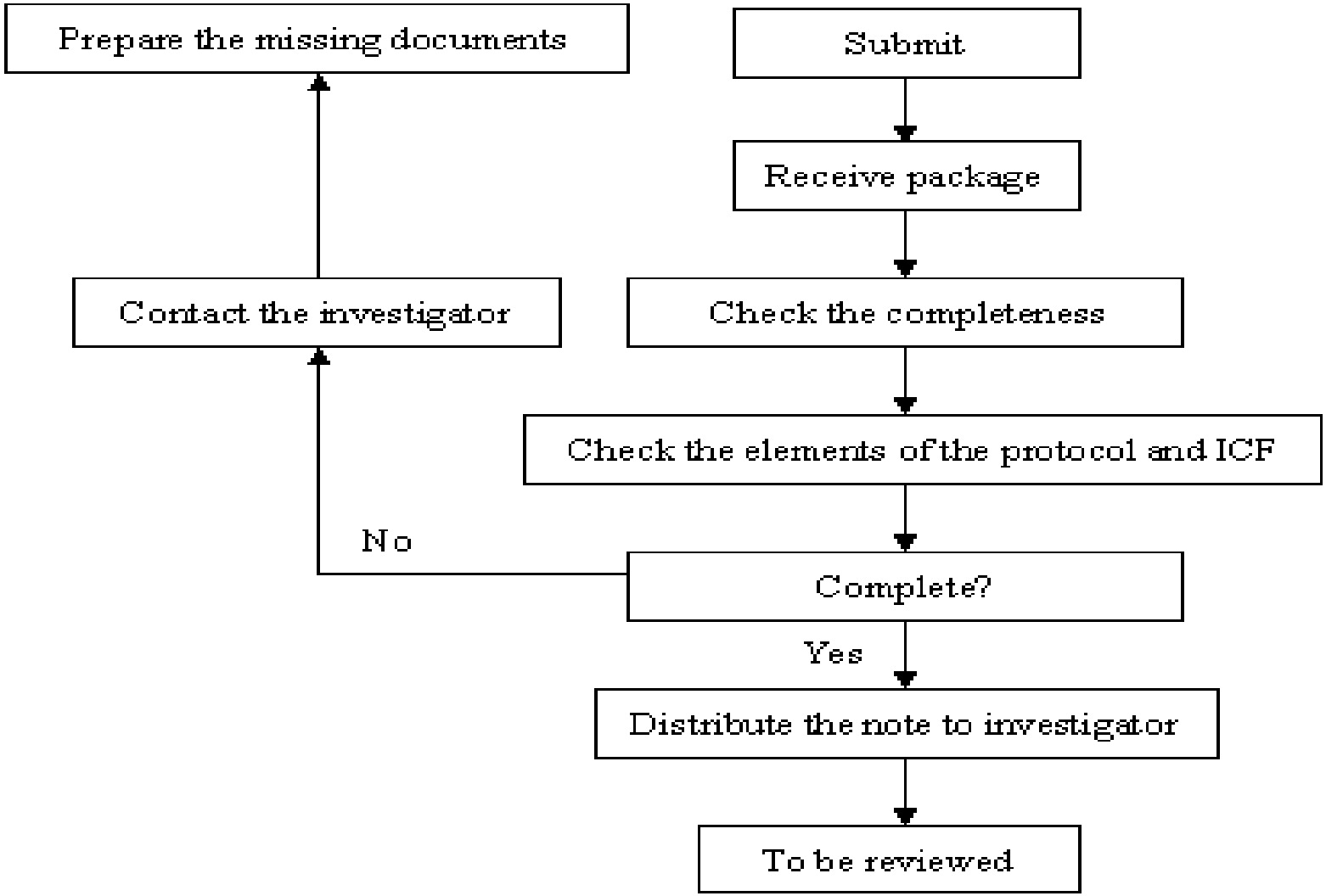
HIRB SOPs /01.1 Content

01 Preparation of Standard Operating Procedures (SOPs)
02 Constituting HIRB
03 Confidentiality Agreement and Conflict of Interest
04 Training HIRB Members and Personnel
05 Selection of Independent Consultant
06 Management of Protocol Submissions
07 Initial Review
08 Review of New Medical Device Studies
09 Ethical Review of Research Proposals for Government Funding
10 Expedited Review
11 Review of Resubmitted Protocols
12 Review of Protocol Amendments

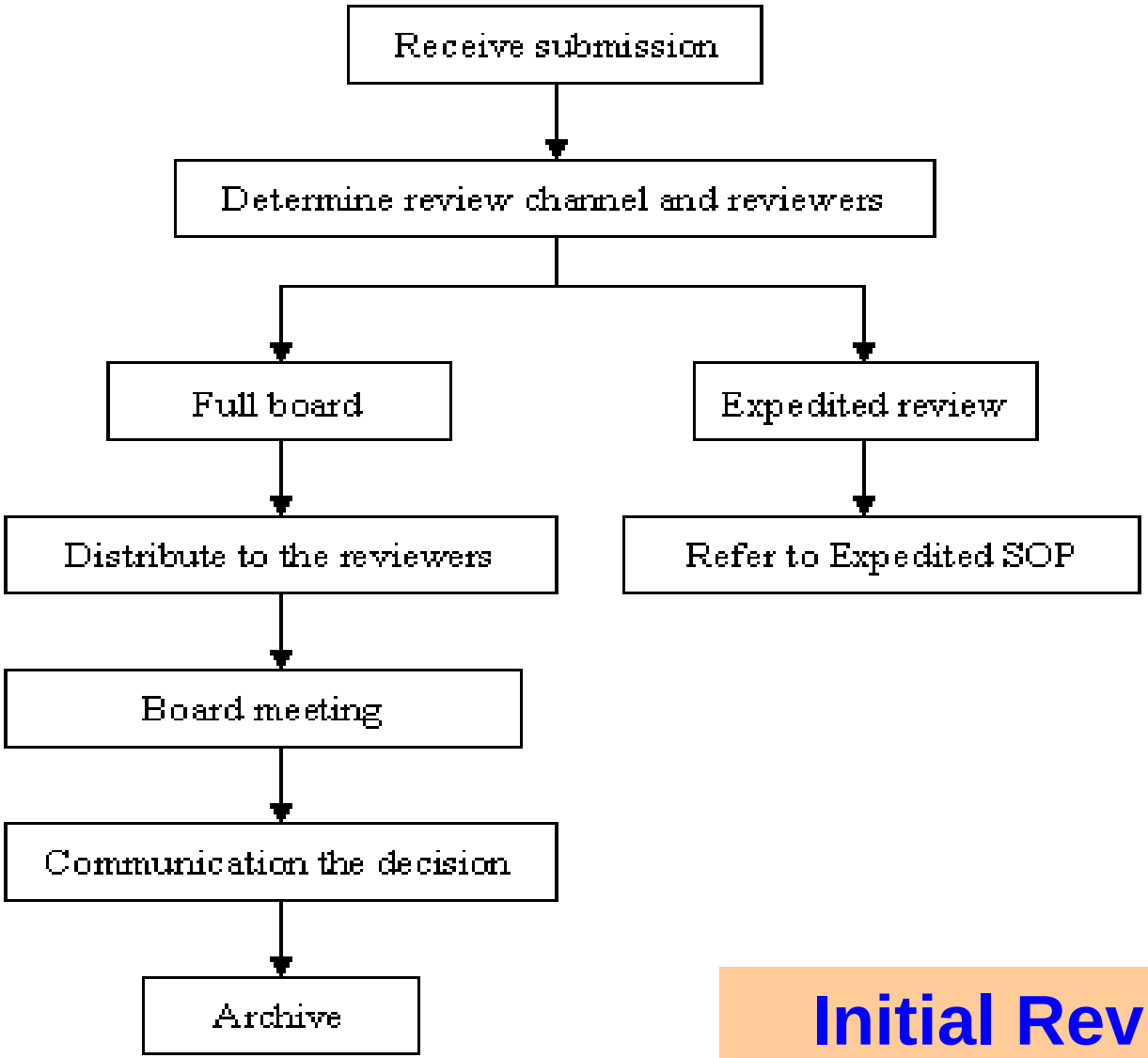
13 Continuing Review
14 Review of Final Reports
15 Non-Compliance/Protocol Violation
16 Response to Research Participants Requests
17 Management of Study Termination
18 Review of Adverse Events (SAE) Reports
19 Site Monitoring Visits
20 Preparation of Meeting Agenda and minutes
21 Emergency Meeting
22 Communication Records
23 Maintaining of Confidentiality
24 Maintenance of Active Study Files & Archive and Retrieval of Documents
25 Audit of the HIRB

Review Scope

- drug clinical trials
- medical device clinical trials
- biomedical researches involving human participants



Submission Flow Chart



Initial Review Flowchart

Overview of the HIRB's Decisions

Decisions	2006.1-12	2007.1-12	2008.1-9
▪Approve	7	30	10
▪Approved with recommendation	54	33	24
▪disapprove	2	0	0
▪Resubmission for re-review	4	6	11
▪Approve Rate(%)	91.04	91.30	75.56

Difficulties faced

- Investigator: should “keep the rule” anytime
- Sponsor: be responsible, Medical Department? Mornitor? Auditor?
- Multi-center CT: Communication among ECs, different quality of EC
- Authority of EC
- Self-protection of subjects
- Support enough from your hospital?

Insurance-- protection to subjects

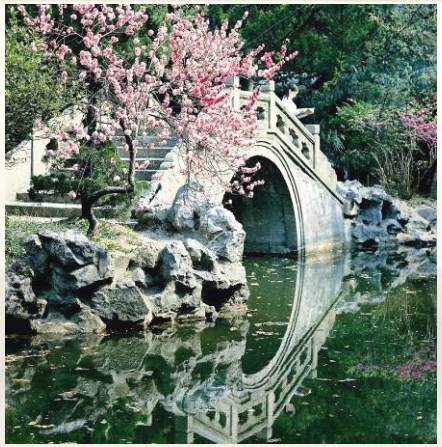
- Sponsor should provide financial assurance for trial subjects
- Sponsor pay for all therapeutic expenses due to trial-related harm or death of trial subjects and relevant financial reimbursement
- Lack of insurance for clinical trial

Both Challenge and Opportunity Exist!

- Self-improving & Capacity building
- Learning by doing! Step by Step!

華山醫院

A Harmonized Paradises



Thanks!

HUASHAN HOSPITAL

- http://www.hjzou.com/download/fercap.ppt