Global Clinical Trials in Korea

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For APEC, OCT.13, 2006
Contents

- Regulatory changes relevant to Clinical Trials in Korea
- Current Status of Clinical Trials in Korea
- What we have learned
- Future plans
Major regulatory changes in Korea since 1999

- Jan 2001: Total revision of KGCP according to ICH GCP
- June 2001: Adoption of the Bridging Concept
  - Diverse bridging strategies were required
  - Effective since 2001 for NDA
- Dec 2002: Separation of IND from NDA
  - Participation in international study enabled
Regulatory Hierarchy

Regulations for Clinical Trials

- Pharmaceutical Affairs Law
- Enforcement regulation of Pharmaceutical Affairs Law
- Korea GCP Guideline
- CTA Guideline
- Guideline for Accredited Clinical Institutes
Essential Elements in a Clinical Trials

- Protocol approved by KFDA
- Only at the accredited sites
- Qualified investigator
- Protect the right and safety of subjects
- Informed consent before enrollment of subjects
- Investigational drugs

defined in the Enforcement regulation of PAL
History of KGCP

- Established as of December 28, 1987
- Enforced since October 1, 1995
- Revised as of January 4, 2000
- Legislation of IND system August, 2001
- Preparation of detailed regulations for IND system December, 2002

Harmonize with ICH guideline E6
Clarify the responsibility of investigator
Reinforce the function of IRB
Protect the rights and safety of subjects
Evaluation on Foreign Clinical Data and Bridging data in Korea

New Product Candidate

Foreign Clinical Data

Clinical Data in Koreans (Inside or Outside Korea)

7 waiver categories

Bridging Study Exemption

Bridging Study in KOREAN

Bridging Data Waiver

Bridging Data
Bridging Waiver Categories

- Orphan drugs or drugs used as orphan drugs
- Drugs for AIDS
- Drugs for Life-threatening Disease
- Anticancer drugs of the following:
  - No standard therapy
  - Therapy followed by a failure in a standard therapy
- Diagnostics or Radioactive drugs
- Topical drugs with no systemic effect
- No ethnic differences
Introduction of IND

- Separation between developmental clinical stage and commercial product approval, such as IND and NDA
  - Effective since December 2002
  - Different submission requirement according to the drug developmental stage
  - Shortening of review period (30 days)
  - Encouragement to participate in multinational clinical trials
  - Activation of Pre-IND consultation programs
  - Flexible regulation on manufacturing/importing of clinical supplies
  - Alleviation of qualifications for IND applicant

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Guidance of Accredited Clinical Institutes

Purpose

– To assure the quality of clinical study and institutes

What are Essential to Accredit?

– Appropriate facilities and equipments
– Pool of personnel to support the clinical study
– Activities of IRB
– Education program of GCP
– Structures and activities to manage the clinical study
Qualified Institutional Pool

Number of accredited clinical institutes

<table>
<thead>
<tr>
<th>Class</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
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<tbody>
<tr>
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<tr>
<td>Dental Hospital</td>
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(by 2006. 8.)
Clinical Trial Approval Process

**KFDA Process**

- **Pre-IND Consultation**
  - Optional Consultation

- **Submission**
  - Protocol
  - CMC
  - Preclinical
  - IB

- **Review**

- **Approval**
  - Timeline: 30 days

**IRB Process**
Parallel review with KFDA process

- **Submission**
  - Protocol, ICF
  - IB, CRF, CV

- **Review**

- **Approval**

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Increased Number of Clinical Trials

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<table>
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<tr>
<th>Year</th>
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Status of Clinical Trials by Study Phase

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Course of CTA average Review Time

**Graph**
- **Y-axis**: Days
- **X-axis**: Year (1998 to 2005)
- **Title**: KFDA database

**Legend**
- Orange line: KFDA database

**Data Points**
- 1998: 20 days
- 1999: 40 days
- 2000: 60 days
- 2001: 80 days
- 2002: 100 days
- 2003: 120 days
- 2004: 140 days
- 2005: 160 days

**Note**
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Reinforcement inspection system

- Inspection for IRB management system
- Inspection for Investigator (on-going C/T)
- Systematic Inspection for clinical trials
  - Regular report on the status of on-going clinical trial
  - Notification on the completion of clinical trial
  - Sponsor, CRO, IRB, Investigator etc.
- Develop and disseminate check-list for Inspection to facilities
Good Regulation Practice in Clinical Trials of KFDA

- Amendment of Regulations
- Good Review Practice
  - Assurance consistency, clarity, transparency
  - Promotion and application of Guidelines for Clinical Evaluation by indications
  - Development of Training program for the reviewers
  - Meeting within KFDA and sharing the review experiences
  - Activation the consultations by formal meetings with sponsors
- Disclosure of Review Summary
- Dialogues between customers and the KFDA
- Restructure KFDA to functional team for review quality and efficiency

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Amendment of Regulations

- Task Force Team
  - Regulator, experts from industries and academia
- Draft regulations
- Open to the public for hearing the opinion
- Evaluation for unnecessary restriction by regulatory reform committee
- Amendment of Regulations
What we have learned:

- Qualification of Investigator
- Importance of IRB review
- Importance of SOP
- Need for Clinical Research Resources
- Need for Regulatory Service from Authorities
- Need for communication and harmonization with Foreign Authorities
Improvement in Clinical Study Institutes

**Hospital**

**Improvement in hardware**
- Increased number of accredited hospital
- Major hospitals have specialized clinical trial centers and laboratories

**IRB**

**Improvement in software**
- IRBs are well-organized and well-operated in accordance with the KGCP requirements
- IRBs hold regular training as to KGCP and ICH-GCP for the investigators, pharmacists, CRC and other medical staffs
Improvement in Clinical Trials Staff

Investigator

Improvement in qualification
• Increased opportunities to participate in global study since 2001 and good awareness of GCP
• Enthusiastic to join in early development stages of new drugs
• Proficiency in strict regulatory inspection

Clinical Research Coordinator

Improvement in qualification
• Increased number of research nurses with clinical expertise
• Major hospitals are able to utilize CRC pools in and out of the hospitals
• Well-organized and qualified annual trainings for CRCs are available
**Future Plan**

- IRB management
- Resource management
  - Support the training course for investigators, CRC, CRA, IRB members
  - Develop the training program for reviewers
  - Keep the transparency of review process
- Supporting plan for Clinical Centers by MOHW
  - 9 Regional centers designated in 2004-2006
  - Support for Facilities, Operation systems, R&D etc.
  - $0.5 ~ 1 million/center/yr for 5 years
- Revise the regulations to harmonize with international ICH guidelines
- Encouragement the industries to participate in multinational clinical trial
Thank you very much
for your attention!!

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