Regulatory issues for academic-led multinational trials in Asia: Who takes responsibility?

Commentary :

Kaori Shinagawa, MD, PhD
Senior Scientist for Clinical Medicine
Pharmaceuticals and Medical Devices Agency
Visiting Lecturer, Keio University School of Medicine

Multi Regional clinical trials (MRCTs)

Trends of New Drug Application approvals

- The number of approved drugs based on Multi Regional clinical trials (MRCTs) has increased in Japan
  - ✓ 100 applications were approved based on GCT as of March 31, 2015

Advantage of MRCTs

- Efficient drug/ medical device development in shorter time period
- Enhance the scientific knowledge about ethnic difference

Regulatory Issues for MRCTs: Regional difference

- Difference in regulation related to protection of safety of human subject
  - ✓ Informed consent, compliance to protocol, adverse event reporting
- Difference in regulation for trial conduct
  - ✓ The application of ICH GCP to practice may differ among regions
- Difference in regulation for Investigational New Drug (IND) or Investigational Device Exemption (IDE)
  - ✓ Laws related to Clinical Trial Notification in Japan
- Difference of composition and review methods of Institutional Review Board (IRB)
- Compensation to subjects
  - ✓ Difference in health care insurance system

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

- ICH: bring together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration
  - Founding Regulatory Members : EC(Europe), FDA(US), MHLW/PMDA (Japan)
  - Founding Industry Members: EFPIA, JPMA, PhRMA
  - Standing Regulatory Members: Health Canada(Canada), Swissmedic (Switzerland)
  - Regulatory Members : ANVISA(Brazil), CFDA(China), HAS(Singapore), MFDS(Republic of Korea), TFDA(Chinese Taipei)
- ICH's mission is to achieve greater harmonisation worldwide to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner.

ICH guidelines contribute to efficient conduction of MRCTs

ICH E6: Guideline for Good Clinical Practice (R2) 2016.11.9

- The application of ICH GCP to practice might be different among regions.
- It is needed to comply with the regulatory rules in each regions.

Japanese circumstances for MRCTs and Academic-led clinical trials

Laws and regulations

- The Pharmaceuticals and Medical Devices Act (Nov 25, 2014)
- Ministerial Ordinance on Good Clinical Practice for Drugs (Mar 27, 1997, as last amended Dec 28, 2012)

Japanese-GCP

Clinical Trial In-Country Representative

- Responsibility: To take the necessary measures to prevent health hazards due to investigational products
- A sponsor of a clinical trial that resides outside Japan shall appoint an eligible person residing in Japan
  - ✓ will be responsible for all aspects of sponsoring the clinical trial; conducts all the procedures in relation to regulatory authority, medical institutions, etc

    ex: Submitting a Clinical Trial Notification (CTN)

    Reporting adverse drug reactions to the regulatory authority

Japanese circumstances for Academic-led clinical trials

Academic-led clinical trials

Sponsor-investigator (non-industry sponsored investigator)

- An investigator who has submitted a clinical trial notification in order to conduct a clinical trial at the medical institution to which the investigator belongs.
- Coordinating investigator who has submitted a clinical trial notification at more than one medical institution
- Responsibility
  - ✓ as a principal investigator
  - ✓ as a sponsor

Responsibilities of sponsor-investigator

- Responsible for medical care of subjects
  - ✓ Responsible for taking the necessary measures to prevent health hazards due to investigational products
- Responsible for reporting safety information to PMDA

Japanese Sponsor-investigator is responsible for all aspects of regulatory issues in Academic-led MRCTs.

Comments on Academic-led multinational trials in Asia

- MRCTs conducted in Japan must follow Japanese GCP.
  - Implementation of ICH GCP may differ across regions.
- It is important to understand requirements of each regulatory agency among regions that take part in MRCTs.
- To ensure patient safety, Academic-led MRCTs must be kept to the same standards as trials sponsored by industry.
- Japanese Sponsor-investigator is responsible for all aspects of regulatory issues in Academic-led MRCTs that include Japan.
- PMDA is interested in learning more about Academic-led MRCTs in Asia
- ICH guidelines contribute to efficient conduction of MRCTs. Continued discussion among regulators will achieve enhanced harmonization of regulatory environments related to MRCTs.