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

Commentary:

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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
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)

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.
• 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.