MRCT-GCP inspection Regulatory Science Center of Excellence
Core curriculum

Basics of MRCT
1) Introductory session: how a regulatory decision is made
2) Trend of Clinical Development for Medicinal Product
3) Expectation on MRCT
   - Industry’s view point
   - Regulator’s view point
4) Essential information for MRCT
   - Disease prevalence (Epidemiological Data)
   - Healthcare System and Medical Practice
   - Medical needs
   - Utilization of IT
5) Regulatory Requirements
   - Difference between MRCT and Domestic Study
   - How to meet different regional requirements
6) Relevant ICH Guidelines for MRCT
   - E2A, E2F, E5(R1), E6(R1, R2), E8, E9, E10, E17

Development Strategy
1) Current issues on product approval
   - Industry’s view point
   - Regulator’s view point
2) MRCT or Domestic Development?
   - MRCT for all trials?
   - Stepwise Expansion of Regions?

Protocol Design and Statistical Analysis Plan
1) Selection of Geographical Regions to include
2) Number of Patients in Each Region
   - Method of Dynamic Enrollment of Subjects
3) Primary/Secondary Endpoint?
4) Statistical Analysis Plan
5) Determination of standard drug as comparator
   - How to determine a comparator in a trial, such as when to use the placebo as an adequate comparator or how to choose a standard drug as comparator.
6) Determination of efficacy parameters
   - How to determine whether the parameters used in a trial are adequate to assess the efficacy of a drug.

**Finding Optimal Dosage**

1) For Next Stage/Trial
   - The possibility to test the optimal dosage in phase III trial which is not covered yet in phase II trial.
2) For Special Population
   - Population with renal or hepatic impairment: How to determine adequate number of subjects for the trial.
   - Pediatric and elderly population: How to determine the appropriateness of extrapolating adult dosage to pediatric/elderly dosage
3) Ethnic Difference / Genomic Difference
   - Type of drugs that will need specific studies among Asian population, such as due to different kinds of enzymes in Asian population.
4) For rare disease indication
   - Number of subject adequate for rare disease indication and the possibility to assess the efficacy from only phase II trial.

**Clinical Data Analysis**

1) Difference between Statistical Significant and Clinical Significant
2) How to set sub-set for Sub-population Analysis?
3) Signal detection
4) How to determine the need to conduct the sub-group analysis
5) The use of sub-group analysis data for the indication extension
   - Will it be permitted to use sub-group analysis data for the extension of an indication, and how far the sub-group analysis data can be used to claim
the extension of an indication?

**Handling of ADR report**
1) ADR Report timeline
2) How to evaluate ADR report so that the Regulatory can take an action to the clinical trial conduct

**Assessment of Mock Marketing Authorization Application**
1) Assessment by Attendees (Small groups), Presentation and Discussion

**Risk Management Plan (RMP)**
1) Development Stage
   - To avoid failure in development
   - Safety signal management
2) RMP for Market Authorization Application

**GCP inspection in the review of MRCT data**
1) Lecture on real world GCP inspection by PMDA and EMA (30 min x 2 sessions = 1hr)
2) Presentation from ThaiFDA (20 min)
3) Workshop: How to assess the findings of GCP inspection, which are significant/grave deviation and which are not? (60 min)
   For example, unexpected report, deviations, etc
4) Presentation on outcome of discussion (40 min)
5) Wrap-up (5min)

Potential Discussion topics in Session of GCP inspection in the review of MRCT data
- Difficult Areas: *Computer system, Lab/Test procedure, Grading of Observation*
- New, specific, and advance Knowledge / Technology
- To become Trainer on Basic GCP inspection, for other NRAs
- Inspection of BE study
- Inspection of Pharmacogenomic study
- Electronic record keeping system