Invitation Letter

APEC Pilot Center of Excellence Training
Multi-Regional Clinical Trials and Good Clinical Practice
10-13 April 2018
Harvard University, Cambridge, Massachusetts, USA

Dear Colleagues,

The Multi-Regional Clinical Trial Center of Brigham and Women's Hospital and Harvard (MRCT Center) and the APEC Harmonization Center (AHC) are pleased to invite you to join the **APEC Pilot Center of Excellence (CoE) Training on Multi-Regional Clinical Trials (MRCT) and Good Clinical Practice (GCP)**, focusing on ICH E17 and ICH E6(R2) guidelines. The program will be held **10-13 April, 2018,** at Harvard Faculty Club in Cambridge, Massachusetts, USA.

The training aims to enhance regulatory cooperation in the APEC region on the evaluation and regulation of MRCTs, increase the acceptability of MRCT data by multiple regulatory authorities, describe the concepts of MRCTs and MRCT design, and demonstrate practical approaches to GCP. A draft training program outline is attached.

We are pleased to invite regulators (reviewers and inspectors) with priority to those from emerging economies, and academic and industry representatives, as space allows. Training participants should involved with MRCTs and/or GCP inspection and have at least 2 years of regulatory experience and/or working with clinical trials.

Financial support is available from the AHC for one (1) participant from each of following APEC travel-eligible economies: Chiles, China, Indonesia, Malaysia, Mexico, Papua New Guinea, Peru, The Philippines, Russia, Thailand, and Viet Nam. If eligible, please contact AHC Secretariat directly at ahckorea@kpbma.or.kr for further information and process.

For other participants, please apply through the following online site by no later than March 10, 2018: http://survey.constantcontact.com/survey/a07ef0fb1ewjc6gy59y/start

If you need assistance of have any questions related to this Pilot CoE Training, please contact the MRCT Center at mrct@bwh.harvard.edu.

We look forward to welcoming you to Boston.

Michelle Limoli, PharmD
Co-Chair APEC RHSC

Toshiyoshi Tomiaga, PhD
Co-Chair APEC RHSC

Sunhee Lee
APEC Harmonization Center Director

Barbara Bierer, MD
MRCT Center Faculty Director

Draft Training Program Outline

Day 1 – April 10

Topics
Welcome & Introduction of trainers and participants APEC Harmonization Center remarks
Session 1: Basics of MRCT & Development Strategy 1) Introductory session: how a regulatory decision is made (overview) 2) Trend of Clinical Development for Medicinal Product 3) Expectation on MRCT & Current Issues on product approval 4) Regulatory Requirements / MRCT or Domestic Development? 5) Essential information for MRCT 6) Relevant ICH Guidelines for MRCT – Overview Discussion
Session 2: Protocol Design and Statistical Analysis Plan Basic principles when planning and designing MRCT (ICH E17) 1) Regional variability: Selection of Geographical Regions to include 2) Sample Size and Subject selection: Number of Patients in Each Region 3) Choice of Endpoints: Primary/Secondary Endpoint? 4) Statistical Analysis Plan 5) Selection of comparators: Determination of standard drug as comparator 6) Collecting and handling of efficacy and safety information: Determination of efficacy parameters
Walking Tour of Harvard University Welcome Reception

Day 2 – April 11

Session 3: Selection of doses: Finding Optimal Dosage 1) For Next Stage/Trial 2) For Special Population 3) Ethnic Difference / Genomic Difference
Session 4: Clinical Data Analysis 1) Difference between Statistical Significant and Clinical Significant – how to interpret variation in treatment effects in subgroups 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

Session 5: Handling of Adverse Drug Reaction (ADR) report 1) ADR Report timeline 2) How do regulatory authority / sponsor evaluate ADR report so that the Regulatory can take an action to the clinical trial conduct
Site visit Takeda

Day 3 – April 12

Session 6: Assessment of Mock Marketing Authorization Application 1) Assessment by Attendees (Small groups), Presentation and Discussion
Session 7: Risk Management Plan (RMP) 1) Development Stage 2) RMP for Market Authorization Application 3) Post-market safety evaluation of approved drugs based on MRCT
Q&A Session with Regulators
Session 8: GCP inspection in the review of MRCT data 1) Lecture on real world GCP inspection 2) Presentation on ICH E6(R2)

Day 4 (1/2 day) – April 13

Session 8: GCP inspection (continued): 3) Interactive Workshop: How to assess the findings of GCP inspection? 4) Discussion topics 5) Presentation on outcome of discussion
Q&A with faculty and facilitators Closing ceremony with distribution of participation certificates, post-evaluation survey