GRADUATE CERTIFICATE IN PHARMACEUTICAL REGULATION

GMS5101 Clinical Trial Design and Data Analysis

8 July 2019 – 12 July 2019

Duke-NUS Medical School

DRAFT WORKSHOP PROGRAMME

Learning outcomes

- Describe the design and operational attributes of different phases of clinical trials
- Apply relevant regulatory guidelines in marketing authorization of pharmaceutical products
- Explain basic principles of pharmacokinetic and statistical analyses as relevant to assessing benefit-risk ratio and regulatory decision-making for approval of pharmaceutical products.
- Explain the ethical, legal and regulatory aspects of design and conduct of clinical trials.
- Distinguish clinical trial design and statistical analysis between multi-regional clinical trials and domestic clinical trials.

Graduate Certificate in Pharmaceutical Regulation

GMS5101: Clinical Trial Design and Data Analysis

8 – 12 July 2019

Day 1 – 8 July, Mon

	Topic	Speaker/ Organisation
8.30am	**Registration**	
Session 1: Introduction to Clinical Trials		
9.00am	**Opening of Graduate Certificate Programme**	**Prof John Lim** Executive Director Centre of Regulatory Excellence (CoRE) Duke-NUS Medical School
9.10am	**Workshop Briefing**	**Dr Uttara Soumyanarayanan** Associate II CoRE Duke-NUS Medical School
9.30am	**Overview of Clinical Trials (Local)** • Legal Framework • Clinical Trial Registers • PI-initiated vs pharma initiated development trials • Roles & responsibilities of different stakeholders	**Mr Foo Yang Tong** Director Regulatory Legislation Group Director's Office Health Sciences Authority
10.00am	**Evolving Trends in Clinical Trial Landscape** • Limitations of conventional RCTs • Adaptive trials • Pragmatic trials • Quality by design trials	**Dr Uttara Soumyanarayanan** CoRE
10.30am	**Break**	
10.50am	**Oncology vs Non-Oncology Drug Development** • Clinical endpoints, surrogate markers, biomarkers • Single arm studies • Stratification variables • Case examples of recent approvals that have interesting learning points • Drug development expedited approval pathways	**Dr Brian Booth** Deputy Director Division of Clinical Pharmacology V Office of Clinical Pharmacology Center for Drug Evaluation and Research U.S. Food and Drug Administration (FDA) (Video presentation)
Session 2: Clinical Trial Design & Operations		
11.30am	**Ethical and Legal Aspects** • IRB, Informed Consent • Impact of HBRA guidance reforms on informed consent forms • Use of Placebo • Patient Safety	**Dr Yeo Jing Ping** Director Research Integrity, Compliance and Ethics Singapore Health Services Ptd Ltd (SingHealth)

12.15pm	**Group Activity:** Review Patient Information Sheet and Informed Consent Form to find deficiencies	**Dr Yeo Jing Ping** SingHealth **Dr. Andrew Green** Associate Consultant CoRE Duke-NUS Medical School
1.00pm	**Lunch**	
2.00pm	**Clinical Trial Operations** • 5 project phases of clinical trials • Key functions and process in CTOs • The site Perspective & the Patient Perspective • Clinical Trials 2.0	**Mr Robert Kerle** Head R&D Solutions Southeast Asia IQVIA
3.00pm	**Practicum I: Phase I Clinical Trials** • Dose-escalation study • Phase I study design • Complete flowcharts with timelines for different studies, inclusion exclusion criteria.	**Dr. Andrew Green** CoRE **Adj A/Prof Cynthia Sung** Visiting Expert, CoRE Duke-NUS Medical School
4.00pm	**Break**	
4.30pm	**Practicum I: Phase I Clinical Trials** Continued.	
5.30pm	**End**	

Day 2 – 9 July, Tue

	Topic	Speaker/ Organisation
8.30am	Individual and group assessment I	
Session 3:	**Safety in Clinical Trials**	
9.30am	**Safety data analysis and reporting in Clinical Trials** • Influence of nonclinical data on safety assessment plan • Safety analysis plan • Common AE templates/tools • Severity, AEs, safety parameters measured • Analysis: Safety monitoring and reporting	**Prof Hervé LeLouet** President CIOMS
10.15am	**Break**	
10.45am	**Current practice and Innovations in safety monitoring** • PV in clinical trials • Data Safety Monitoring Board (DSMB) • Reporting timelines • Phase IV commitments • Post-market registries	**Prof Hervé LeLouet** CIOMS
11.30am	**GCP Inspections in Singapore** • Quality of clinical trials • GCP Inspection Framework in Singapore • How to prepare for GCP Inspections	**Ms Sumitra Sachidanandan** Regulatory Consultant Innovation Office and Clinical Trials Branch Health Products Regulation Group Health Sciences Authority
12.30pm	**Lunch**	
Session 4:	**PK/PD in Clinical Trials**	
1.30pm	**Utility of PK/PD Across Different Clinical Trial Phases** • Dosing regimen • Time to steady state • Bioequivalence studies (Bridging Formulations, Generics) • Clinical Pharmacology (Food effect, DDI) • Clinical Trial Simulation	**Adj A/Prof Cynthia Sung** Visiting Expert, CoRE Duke-NUS Medical School
2.30pm	**Introduction to PK Visualizer** • Hands-on exercise PK/PD	**Prof Edmund Lee** Department of Pharmacology Yong Yoo Lin School of Medicine (YYLSoM)
3.30pm	**Break**	
4.00pm	**Practicum II: Phase 2 trials** • Analysis of safety and efficacy data of Phase 2a • Design criteria for Phase 2b trials	**Facilitators:** Adj A/Prof Cynthia Sung, CoRE Dr. Andrew Green, CoRE Prof Edmund Lee, NUS
5.30pm	**End**	

Day 3 – 10 July, Wed

	Topic	Speaker/ Organisation
8.45am	Individual and group assessment II	
Session 5: Statistical Analysis Plan (SAP)		
10.00am	**Biostatistics Part I** • Concepts for analysing trial data: p-value, CI, sample size, power. • Case examples	**Dr. Andrew Green** CoRE
10.45am	**Break**	
11.15am	**Biostatistics & SAP Part II** • Handling Outliers and Missing Data • Coherence and validation of primary endpoints • Interim Analysis • Judgement – Clinical Relevance and alignment to practice guidelines	**Dr Daphne Lin** Deputy Director Division of Biometrics IV Office of Biostatistic Center for Drug Evaluation and Research U.S. Food and Drug Administration (US FDA)
12.30pm	**Lunch**	
1.20pm	**Considerations in regulatory decision-making of CTA** • Documents to consider • ICH E8 guideline • Review of clinical trial protocol	**Dr Carole Légaré** Director Office of Clinical Trials Therapeutic Products Directorate Health Canada
2.00pm	**Practicum III: Phase 3 design and data analysis** • Phase 3 trials: design, choosing endpoints, powering the trial • Phase 3 trials: Review of safety data • Regulatory decision-making	**Lead facilitator:** Adj A/Prof Cynthia Sung CoRE **Assisted by:** Dr Carole Légaré, Health Canada Dr Daphne Lin, US FDA
3.00pm	**Break**	
3.30pm	**Practicum III:** Continued	
5.30pm	**End**	

Day 4 – 11 July, Thurs

	Topic	Speaker/ Organisation
8.30am	**Registration**	
9.00am	**Welcome MRCT workshop participants**	**A/Prof Silke Vogel** Deputy Director CoRE Duke-NUS Medical School
9.15am	**MRCT Introduction** • Introduction to multi-regional CT • Global progress and update on MRCTs • APEC Harmonization and Convergence	**Asst Prof James Leong** Head, Pharmaceutical Regulatory Science Programme, CoRE Duke-NUS Medical School
9.40am	**Fundamentals of MRCT** • ICH E17 Guideline for MRCT • **G**lobal drug development: Industry perspective • CTD and region-specific Information • Resolving conflicts between MRCT and domestic drug development	**Dr Yeo Jing Ping** SingHealth
10.15am	**Break**	
10.45am	**Selection of Primary/Secondary Endpoints** • Standardization of endpoints across cultures • Regional variations in "standard of care" • ICH E5 guideline: Impact of Ethnic Factors **Geographic Considerations** • Selection of Suitable Regions	**Dr Carole Légaré** Health Canada
11.30am	**Statistical Analysis Plan of an MRCT** • ICH E3, E5, E9 • Statistical complexities of an MRCT • Identifying co-variates • Subgroup analysis • Minimising noise	**Dr Daphne Lin** US FDA
12.15pm	**Lunch and Photograph Taking**	
1.15pm	**Dose Optimization and Adjustment** • Approaches to dose-finding in drug development • Interindividual variability • Ethnic Factors and genomic variation • Bridging studies to new populations **Special populations** • Elderly (ICH E7) • Children (ICH E11) • Renal/hepatic impairment	**Adj A/Prof Cynthia Sung** CoRE
2.15pm	**Pharmacogenetics and Ethnicity** • Case Examples	**Prof Edmund Lee** YYLSoM
3.00pm	**Break**	

3.30pm	**Breakout Session I** *Team based hands-on learning approach applied using mock dossier*	**Lead facilitator:** **A/Prof Cynthia Sung,** CoRE **Assisted by:** Dr. Andrew Green, CoRE Dr Daphne Lin, US FDA Prof Edmund Lee, YYLSoM
5.00pm	**End**	

Day 5 – 12 July, Fri

	Topic	Speaker/ Organisation
8.30am	End of the course assessment for Graduate Certificate students	**CoRE**
9.30am	**Role of clinical data-sharing in MRCTs** • Important considerations: resources involved, ethics • Good practice documents and principles • Platforms and initiatives • Case examples	**Dr. Rebecca Li** Executive Director Vivli (Video Presentation)
10.00am	Break	
10.30am	**Planning of Global Clinical Trials** • When and why? • Stepwise expansion approach • Selection of countries • Key challenges	**Liza Huang** Deputy Head of Clinical Operations Boehringer Ingelheim
11.15am	**Clinical Trial Operations in MRCT** • Planning: site qualification and initiation • Conduct: patient enrolment and data integrity • Future trends for clinical trial operations	**Liza Huang** Deputy Head of Clinical Operations Boehringer Ingelheim
12.00pm	**Lunch**	
1.00pm	**Regulatory decision-making of MRCTs** • Clinical Data Analysis • Benefit-Risk Evaluation and Decision-Making	**Asst Prof James Leong** CoRE
2.00pm	**Breakout Session II** *Team based hands-on learning approach applied using mock dossier*	**Lead facilitator:** Asst Prof James Leong, CoRE **Assisted by:** Dr. Andrew Green, CoRE A/Prof Cynthia Sung, CoRE Dr Carole Légaré, Health Canada Dr Daphne Lin, US FDA
3.30pm	**Tea Break**	
4.00pm	**Panel discussion:** • New trial design, new clinical endpoints • Patient centric approach: PROs, patient engagement and education • Role of big data in post approval phase and RWE	**Moderator:** **Prof John Lim** CoRE **Panelists:** Dr Carole Légaré Adj A/Prof Cynthia Sung
5.00pm	**APEC MRCT workshop conclusion**	**Prof Silke Vogel** CoRE
5.15pm	**End**	