CRED: Understanding Clinical Development Programme
Day one

Time	Activity
08:30	**Registration online**
09:00	**Introduction to TOPRA**
09:05	**Welcome and Introduction** **Clinical Development in Context** • Target product profile • Use 10-year development diagram, say where everything fits in • Why are clinical data needed? • Relevance of preclinical data • Definitions of Phases I, II, III and IV. • Clinical development strategy and the Clinical Development Plan • Sources of advice and timing • Need for a PIP
09:20	**Clinical Pharmacokinetics** • Objective: To understand how the drug is handled in man • Objective: To understand the basic parameters used to describe the PK of a drug • Describe the different processes involved in Pharmacokinetics: absorption, distribution, metabolism and excretion • Define the PK parameters which describe each process, e.g. Cmax, t½ , AUC, Volume of distribution, Clearance, Bioavailablity etc, and their relevance • Discuss multiple dosing and non-linear kinetics • Understand the importance of metabolism including, ▪ Drug metabolising enzymes, ▪ Importance of ensuring main metabolites in man are similar to those produced by preclinical toxicology species • Discuss generation of PK data throughout the different phases of Drug development including ▪ Overview of studies performed in phase I, II and III ▪ Standard PK sampling employed in Phase I and II. ▪ Use of sparse sampling and population PK approaches in Phase III. • Discuss importance of validation of analytical methods – as a regulatory requirement.
09:50	**Tea/ coffee break**
10:00	**Clinical Pharmacodynamics** • First in human trials • guideline • Objectives of clinical pharmacodynamic studies • Mechanism/onset/duration of action • Examples of pharmacodynamic models

Time	Activity
	• Different study designs • Identification of sub-group differences e.g. disease-related, gender, age, race, geography (racial sub-populations) • Biomarkers • Practicalities of clinical pharmacodynamic studies
10:30	**Break**
10:45	**Optimal Study Design – Objectives and Issues Relating to Phase II studies** • Objectives of Phase II studies • "Proof of concept" • Design of Phase II studies • Definition of target patient population • Choice of end point(s) • Dose response • Initial identification of possible safety issues • Importance of keeping the target product profile in mind throughout • Adaptive design and accelerated development • Conditional approval • PRIME • Orphan drug designation
11:15	**Break**
11:30	**Paediatric Investigation Plans** • Legal framework • Why children are different • Preferred approaches to clinical development in children • Devising PIP strategy • Content and format of a PIP • PIP review process • Compliance Check
12:00	**Panel Discussion**
12:30	**Close**

CRED: Understanding Clinical Development Programme
Day two

Time	Activity
08:30	**Registration online**
08:55	**Introductory comments**
09:00	**Design of Clinical Trials to Support Proof of Efficacy (Phase III)** • Confirmation of efficacy in the target patient population • Considerations for trial design e.g. control groups, duration of treatment • Long term safety data (circumstances when needed) • Choice of comparator (placebo vs active comparator) • Statistical issues – stats plan, primary and secondary endpoints, exploratory endpoints • Enlargement of the safety data-base to support the safety sections of the SmPC • Inclusion of quality of life (QoL) and other pharmaco-economic end-points to support pricing/reimbursement • Master protocols
09:30	**Break**
09:45	**Safety** • Pharmacovigilance - aims and objectives • Definitions • Directive 2001/20 - day to day requirements, annual safety reports • Causality attribution • Risk management plans • PASS Studies • The SPC • Current EU Pharmacovigilance Legislation – mention Reference Safety Information (RSI) and new guidance
10:15	**Break**

10:30	**The Perspective of a Regulatory Authority Reviewer**
	• Specific examples of what regulatory agencies look for
	• Common problems with the clinical data in MAAs
	• Reasons for different views and decisions between regulatory authority reviewers
	• Obtaining regulatory agency input and appropriate timelines
	  ○ CHMP scientific advice versus national agency advice
	  ○ Implementation of advice received

11:00	**Panel discussion**
11:30	**Close**

CRED: Understanding Clinical Development Programme
Day three

Time	Activity
08:30	**Registration online**
09:00	**Case study outline**
09:15	**Case study**
10:00	**Case study feedback session**
10:30	**Summary**
11:00	**Close**

Delegates will be encouraged to ask questions throughout the day so as to ensure the meeting is as interactive as possible.