CRED: Understanding Clinical Development Programme
Day one

Time	Activity
09:20	**Registration and Coffee**
09:30	**Introduction to TOPRA**
09:35	**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
09:50	**Clinical Pharmacokinetics** • Objective a) to see how the drug is handled in man and b) to compare handling with that in animals in order to validate the animal studies. • May be necessary to generate additional data in animals if the differences are too great or the usual species is too sensitive e.g. use a different species, test a metabolite produced in man but not the animals species used. • Describe the different aspects that are investigated: absorption, distribution, metabolism and excretion and their relevance. • Definition and discussion of PK parameters, e.g. Cmax, t½ , AUC, tissue distribution, mean residence time etc. • Outline the types of studies. Importance of using sufficient numbers of subjects and of sampling times. • Discuss analytical methods and their validation, e.g. use of radiolabelled drug, analytical methods such as HPLC or ELISA. Discuss the pros and cons. • Dose relationships, e.g. linear vs non-linear. • Problems with proteins, peptides – but still need to be examined.
10:30	**Tea/ coffee break**
10:50	**Clinical Pharmacodynamics** • First in human trials • guideline • Objectives of clinical pharmacodynamic studies • Mechanism/onset/duration of action • Examples of pharmacodynamic models • Different study designs

Time	Activity
	• Identification of sub-group differences e.g. disease-related, gender, age, race, geography (racial sub-populations) • Biomarkers • Practicalities of clinical pharmacodynamic studies
11:30	**Panel Discussion**
12:00	**Lunch**
13:00	**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 – mention orphan drug designation
14:00	**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
14:35	**Case study and feedback session** *Tea to be taken in case study groups*
17:00	**Close**

CRED: Understanding Clinical Development Programme
Day two

Time	Activity
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
10:00	**Tea/ coffee break**
10:30	**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
11:30	**Panel discussion**
12:00	**Lunch**
13:00	**Case study and feedback session** *Tea to be taken in case study groups*

15:15	**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
	  o CHMP scientific advice versus national agency advice
	  o Implementation of advice received

16:00	**Summary**
16:30	**Close**

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