Appendix 1

COMPETENCES FOR TRAINING IN PAEDIATRIC CLINICAL PHARMACOLOGY

Ethics of clinical trials in children

- Understand the principles of ethical research in children, the need to study medicines scientifically and the process by which this is ensured.
- Understand the differences between adults and children in relation to the use of healthy volunteers for clinical trials and pharmacokinetic studies
- Understand the consent and assent issues in children, including legal aspects and process of informed consent
- Understand the structure, function and process of Local Research Ethics Committees and Multi-centre Research Ethics Committees (LRECs and MRECs)
- Understand the use of a placebo in clinical trials in children
- Be able to evaluate the risk involved with a procedure/study i.e. minimal, low or high
- Be able to determine the nature and frequency of invasive procedures
- Be able to prepare and critically analyse a submission to an ethics committee of a clinical trial in children

Pharmacokinetic studies in children

- Understand and use the principles of pharmacokinetics, optimise drug administration and drug effect

- Understand the different analytical methods available for determining drug concentrations
- Understand routes of drug administration
- Know circulating blood volume, especially in neonates and infants
- Understand population pharmacokinetics
- Understand common methods of drug assays required for paediatric studies
- Know about non-invasive methods of studying drug metabolism
- Be able to design clinical pharmacokinetic studies
- Be able to calculate clinical pharmacokinetic parameters (clearance, half-life, volume of distribution)
- Be able to interpret drug concentrations in body fluids
- Be able to alter therapeutic regimens appropriately using understanding of pharmacokinetics of relevant drug
- Be able to design an appropriate study to investigate the clinical pharmacokinetics of a medicine in paediatric patients of different ages, utilising the existing information about the medicine in relation to its metabolism and elimination in adults

Drug action and effect in paediatric patients

- Understand the differences between paediatric patients and adults in relation to drug delivery, metabolism and action
- Understand the development of the major metabolic pathways in relation to age and pharmacogenetic profile from prematurity through puberty. This includes P450 enzyme activity, glucuronidation and sulphation
- Understand the impact of other developmental physiology (absorption, distribution, excretion) on drug disposition across age ranges of life

- Know about maternal drugs and neonates (placental transfer, drugs in breast-milk)
- Know about childhood diseases and drug disposition (e.g. cystic fibrosis, diarrhoea)
- Know about specific formulations and delivery devices for paediatric use
- Know about factors affecting concordance
- Understand the differences in paediatric patients of different ages in relation to pharmacodynamic response
- Know about developing age appropriate pharmacodynamic scales
- Be able to study pharmacodynamic effect in different ages
- Know about the extrapolation of PK-PD relationship from adults to children
- Understand dose response relationships
- Understand the determination of optimum dose range

Drug toxicity

- Be able to detect and manage adverse drug reactions (ADRs) in paediatric patients of different ages
- Be able to assess drug toxicity in paediatric patients
- Be able to manage and advise on cases of overdose or poisoning
- Understand the differences between drug toxicity in the developing child and adults
- Know about specific age related drug toxicity e.g. valproate hepatotoxicity, propofol metabolic acidosis and the grey baby syndrome due to chloramphenicol
- Know about the common clinical presentations of ADRs in children

- Know about ADR surveillance schemes in relation to children (pharmacovigilance)
- Know about teratogenicity in the developing fetus
- Know about toxicity-testing in animals in pre-clinical drug development
- Know about formulation toxicity
- Be able to assess drug toxicity: definition and reporting of "Adverse event", and assessment of causality with study medication

Socio-political and regulatory aspects of use of medicines

- Understand the role of the pharmaceutical industry in the development of new medicines
- Understand the factors behind the issues in relation to medicines in children
- Know about licensing of medicines for paediatric patients and unlicensed and off label use
- Know about the regulatory agencies and their roles: structure, function, and their focus on paediatric drug development
- Know about health belief illness behaviour and patient demographics

Rational and cost effective use of medicines

- Know how to evaluate the evidence base for the use of medicines in childhood
- Understand how to use drugs rationally and cost effectively in clinical practice and to contribute to the use of drugs in such a manner within organisations and institutions
- Understand the role of NICE and local prescribing drug policies
- Be able to critically approach the use of drugs. Choice of drugs based on efficacy, safety, acceptability and cost

- Be able to assist in formulary development and management (local and national)
- Be able to assist in medicines' management in hospital and GP settings and at the interface
- Be able to work with others on such committees

The practical challenge of conducting a clinical trial in paediatrics

- Know about types of trial design
- Know about Good Clinical Practice
- Know about ethics of research in children and the process of informed consent
- Know about recruitment and retention of paediatric patients in a trial
- Know about principles of randomisation and use of controls, placebos and blinding
- Know about sampling and measurement techniques
- Know about statistical methods including sample size
- Be able to plan a trial and create a study team (including nurses and paediatric pharmacists)
- Be able to design a clinical trial in children

Education

- Be able to critically evaluate scientific publications and to search the medical scientific literature using electronic databases
- Know about the criteria for judging papers including experimental design and analysis
- Understand the source of bias including conflicts of interest
- Understand the nature and ethics of peer review
- Be able to use electronic databases

- Be able to teach paediatric clinical pharmacology to undergraduate medical students
- Be able to teach paediatric clinical pharmacology to other health professionals and graduates of medicine