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