

Clinical Trials in paediatric population MPA perspective

Ingrid Wallenbeck
Medical Products Agency
Uppsala, Sweden

MPA, recent experience

May 2004 to October 2006: 10 paediatric studies ~ 4 per year

- 2 studies in premature newborns
 - 8 studies in children and adolescents (4-5 to 18 years)

 - 3 studies with unsaturated fatty acids or fish-oil
 - 2 studies in children with juvenile diabetes
- + enuresis-study, spastic muscles CP patients, immunoglobulin
Crohns disease.

Paediatric clinical trials; Issues for consideration

- Justification of the study
- Age group(s)
- Evidence of direct benefit for the child, or group
- Age appropriate scales or measures of endpoints
- Study risks, pain and discomfort
- Overall benefit risk relationship
- Age specific informed consent/assent

More to be considered

- Children are not small adults
- Differences to be expected for
 - pharmacokinetics
 - pharmacodynamics
 - adverse events
- Medical products to be tested in the least vulnerable population / age group

Children; Age groups

- neonates 0-27 days
- infants 1 to 23 months
- children 2-11 years
- adolescents 12-18 years

Subject Information and Consent

- Patient information
 - child level
 - parent/legal representative level
- Informed consent
 - Described in Läkemedelslagen (1992:859)

Ethical and Legal basis

- Ethical principles

Declaration of Helsinki

Convention on the Rights of Children (UNICEF)

- Legal basis

Directive 2001/20/EC

**Regulation of the European Parliament and the Council
on Medicinal Products for Paediatric Use (in progress)**

- agreed June 1, 2006, into force end of 2006

Relevant guidelines

Guideline ICH E11 (CPMP/2711/99/EN.pdf)

Guideline on the role of pharmacokinetics in the development of medicinal products for the paediatric population (EMEA/CHMP/EWP/147013/2004)

Guideline on Conduct of Pharmacovigilance for medicines used by the Paediatric Population (EMEA/CHMP/PhVWP/235910/2005)

Guideline on Clinical Trials in small Populations (CHMP/EWP/83561/2005)

Guideline on the ethics of clinical trials in children (EMEA/188775/2006)

+ Various Condition/Disease specific guidelines

+ Reflection paper on the use of pharmacogenetics in the pharmacokinetic evaluation of medicinal products (in progress) (EMEA/128517/2006)

Relevant ur Läkemedelsverkets författningssamling

LVFS 2003:6 & LVFS 2005:3

- motivera valet av tidpunkt för barnstudier
- beskriva planerad uppföljning av biverkningar
- specificera åldersgrupper
- minimera antal patienter och antal ingrepp
- lämplig och kompetent personal
- riskminimering
- system för snabbt avbrott

Design considerations for Paediatric Clinical trial

- Objective(s) & scientific questions to be answered
- Avoid any source of bias
- Avoid uncontrolled trials
- Avoid placebo when withholding effective treatment
- Consider rescue treatment and escape procedures
- Avoid pain and distress and minimise fear

Formulations

- Where they exist, paediatric formulations to be used
- Some excipients to be avoided
- Vaccines to be studied in target population, taking into consideration immune system maturation

Differences to be expected for adverse events

- Childhood diseases and disorders may be qualitatively and quantitatively different
- Rapid change of body mass, morphology and body composition
- Effects on CNS and growth/development

Risk/ Benefit assessment

- Assess in terms of probability, magnitude and duration
- Risks may be immediate or delayed
- Chronic/ lifelong treatment ?

Differences to be expected for pharmacokinetics

- Enzymes and transport proteins involved in the PK may differ from adults as a consequence of developmental gene expression

More to be considered

Consult MPA for scientific advice

EMEA/SAWP provides advice on paediatric developments