PAED-Net – the German Network

Clinical Research in Paediatrics
2nd Symposium of the Swiss Clinical Trial Organisation

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Introductory Remarks concerning Infrastructures for Clinical Trials in Germany

- **KKS (Coordination Centres for Clinical Trials)**
  - 12 out of 36 Medical Schools, competitive application
  - Initiated in 1999
  - Funded over 6 years with 30 Mio €
  - **Goals:**
    - education
    - methodology (biostatistics, data management, IT)
    - clinical operations
    - quality, clinical monitoring
    - clinical conduct, educated study nurses and investigators
    - regulatory and pharmacovigilance
Challenges led to PAED-Net Germany

- In 2000, German paediatricians established the concept for a Clinical Trial Network - PAED-Net

- In 2002, the application to the BMBF supported by the Coordination Centre for Clinical Trials (KKS) and many Children Hospitals, resulted in funding of
  - 6 PAED-Net Units (staffed with 1 MD and 1 study nurse each)
  - Coordinating office University Mainz (staffed with 2MDs/PhDs)
  - Initiation of a “Demonstration” trial

- In 2005, successful second application to BMBF, resulting in the continuation of funding up to 2008

- Overall funding 2002 – 2008: 5.5 Mio EURO
PAED-Net Moduls serve as a link between

- Pediatric Hospitals and Organisations involved in clinical trials
  and

- KKS (Study-Logistics and -Methodologies, Quality– and Data-Management, Professional Clinical Pharmacology, ...)

PAED-Net: Concept
PAED-Net: 6 Centers
Coordinating Center in MAINZ

KKS: 6 + 6 Centers

Cooperating Teaching Hospitals

> 100 General practitioners throughout Germany

www.paed-net.org
Paediatric Network and the KKS-Structure

Children's Hospital Privat Praxis

KKS-Mainz

PAED-Net-Modul

KKS-Heidelberg

PAED-Net-Modul

KKS-Freiburg

PAED-Net-Modul

KKS-Leipzig

PAED-Net-Modul

KKS-Münster

PAED-Net-Modul

KKS-Köln

PAED-Net-Modul

KKS-Berlin

PAED-Net-Modul

KKS-Dresden

PAED-Net-Modul

KKS-Düsseldorf

PAED-Net-Modul

KKS-Marburg

PAED-Net-Modul

KKS-Tübingen

PAED-Net-Modul

KKS-Halle

PAED-Net-Coordinating Center

KKS-Mainz

PAED-Net

Planning and Realization of multicenter trials in child populations
PAED-Net Objectives

- Developing excellence in drug research & development as well as conduct of clinical trials in the paediatric population
- Building a national network with infrastructure as platform for multicentre clinical trials
Tasks of PAED-Net with support of KKS

- Consulting/Advice; Feasibility
- Study conduct
- Investigator Recruitment
- Study Coordination and Project Management
- Pharmacovigilance
- Monitoring
- Data Management
- Biostatistics
- Tools, Templates, SOP
- Training courses
Achievements of PAED-Net (1)

- PAED-Net / KKS Staff: Paediatricians, MDs, Clinical Pharmacologists, Biostatisticians and IT Scientists, Clinical Data Manager, Clinical Epidemiologists, Study Nurses, Monitors
- 4 Network trials: Intensive Care, Gastroenterology, Epidemiology, Oncology
- Since 2002, about 150 clinical trials: Allergology, Metabolic Diseases, Cardiology, Nephrology, Diabetes, Pulmonology, Dermatology, Neurology, Infectious Diseases, Oncology, Psychiatric Disorders, Vaccination-Trials
- Harmonised SOPs in cooperation with KKS
- Trial data base (for network partners)
Achievements of PAED-Net (2)

- Education and training:
  - certified training programs for paediatric investigators, study nurses, monitors, scientists
  - workshops on EU Paediatric Regulation and its implementation in Germany
  - seminars on pharmacovigilance in the paediatric population
  - regular workshops on ICH-GCP standards
  - training concerning medical device studies

- Standardised essential study documents, e.g. patient and parent information, informed consent, documents for assent

- Public relation:
  - flyer; homepage; interviews (German TV, professional journals); talks on paediatric trials issues in conferences; publications in scientific and medical journals
Curriculum of GCP training course for investigators, study nurses, scientists

- Drug therapy in children, off-label use, need for paediatric trials
- Drug development in industry, Paediatric Regulation, PIP, ICH E11
- Principles of paediatric trials (e.g. ethical standards, population, methods, trial medication, assurance)
- Ethical and regulatory requirements, application for approval
- Writing a study protocol
- Study design and biostatistics
- Informed consent/assent
- Clinical conduct according to GCP, responsibilities, recruiting strategies
- Data documentation, monitoring, audits
- Pharmacovigilance
- Study report, publication
Prospective, multicentre, randomised, double-blind, placebo controlled scientific driven clinical trial to evaluate efficacy and safety of clonidine as concomitant medication for analgesia and sedation in 200 long-term ventilated neonatal patients

**Primary endpoint**

Reduction of analgetic and sedative agents by continuous infusion of clonidine

**Start:** August 2003
Lessons Learned
Complex Trial Organisation

Coordination Center Köln

- Principal Investigator
- Monitoring Coordination
- Data Management

DMSC

Köln

Münster

Freiburg

Mannheim

Mainz

Leipzig

HZ Leipzig

DHZ Berlin

DHZ München

München Hauner

Siegen

Essen

Köln (Uni)]
Köln (Riehl)
Lessons Learned
Recruitment and Randomisation

![Graph showing recruitment and randomisation progress over time. The graph includes two lines: one for planned recruitment and one for randomised recruitment. The x-axis represents time, and the y-axis represents the number of participants. The graph shows the number of participants recruited and randomised at different points in time.]
Summary of Experiences in Trials

Requirements:
- Extensive human resources and intensive training
- Close cooperation between PI and trial centres
- Clearly defined communication procedures
- Experience in complex contract negotiations
- Acceptance that complex study designs may demand procedures different from those previously established in participating hospitals – teaching again !!!!
- Nothing happens as predicted, in particular with concepts for subject recruitment
Summary of Experiences in Networking

- TRUST and CONFIDENCE
- Communication
- Transparency of mission, goals and intentions
- Commitment to the goals/shared goals and aims
- Corporate identity instead of „self-realisation“
- Collaboration spirit and willing to work and win as a team
- Ownership and responsibility for the network and its members
- Sticking to the agreed rules
- Commitment to the trials
- Continuity of members and staff, their qualification & experience
Experiences after Paediatric Regulation came into force

- More requests for consultancy/feasibility by industry
  - Paediatric-clinical questions
  - Paediatric trial designs
  - Population and clinical methods are of main interest
  - Few requests for PIP (Paediatric Investigational Plan)
  - Despite of 201 approved PIPs (incl. potential deferrals) in 2010 no relevant increase in clinical trial applications in Germany
Conclusions

- Networking is challenging and requires – besides paediatric and trial excellence - team spirit, shared goals, confidence and trust

- Funding of PAED-Net was not continued despite of the requests of the Paediatric Regulation concerning national networks in the EU-MS

- Therefore collaboration between the previous PAED-Net members today is based primarily on shared clinical and scientific interests
Consultancy, Advisory Tasks

- Epidemiology, paediatric medicine
  - Standard therapy, best care
  - Population at risk
  - Concomitant diseases
  - Affected age groups
  - Incidence, Prevalence

- Ethical aspects
  - Minimal burden, minimal risk
  - Pregnancy tests, sexual abstinence
  - Blood volume, venous punctures
  - Number of visits, physical examinations

- Study design
  - Endpoints (different from adults)
  - non-invasive variables

- Feasibility
  - Number of patients
  - Realization of trials in EU which have been designed in US