conect 4children
COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

Overview of c4c project: vision & mission, key objectives and output

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Tartu 12° June 12° 2018

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Overview

- Vision and Mission
- Context
  - We can't do everything, start with useful steps
  - Need to be aware of different contexts
- Project
- Key objectives

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Vision: Better medicines for babies, children and young people through a pan-European clinical trial network.

Estonian Contributions

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, June 2007, p. 1995–2000 Vol. 51, No. 6
0066-4804/07/$08.00+0 doi:10.1128/AAC.01506-06

Pharmacokinetics of Penicillin G in Very-Low-Birth-Weight Neonates[▽]

Tuuli Metsvaht,[1]* Kersti Oselin,[2] Mari-Liis Ilmoja,[3] Kaili Anier,[4] and Irja Lutsar[5]

Pediatric and Neonatal Intensive Care Unit, Clinic of Anesthesiology and Intensive Care, Tartu University Clinics,[1] Institute of Pharmacology, Tartu University,[2] Pediatric and Neonatal Intensive Care Unit, Tallinn Children's Hospital,[3] Institute of Pharmacology, Tartu University,[4] and Institute of Microbiology, Tartu University,[5] Tartu, Estonia

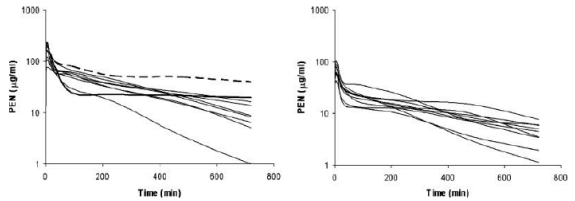

FIG. 1. Individual time-concentration curves of intravenous PEN in VLBW infants receiving PEN doses of 50,000 IU/kg (left) and 25,000 IU/kg (right). Dotted line, the patient accidentally received PEN at a dose of 83,300 IU (50 mg)/kg; the data for this patient were excluded from calculations of the PK parameter values for group 1; bold line, an infant born at the 26th week of gestation with a BW of 700 g had clinical edema and a PEN $t_{1/2}$ of 35.1 h; the data for this patient were included in the calculations of the PK parameter values for group 1.

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c4c Mission

- Europe will use a coordinated approach to deliver high quality "regulatory grade" clinical trials in
  - Multiple countries
  - Multiple sites
  - All paediatric age groups
- By supporting
  - Trial implementation using resources shared between studies
  - Trial design through a combination of information about natural history, feasibility, appropriate innovation, and expert opinion
  - Education and awareness within and beyond the network

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High level resource for:

- Industry Sponsors
- Investigator Initiated Studies
- Publically-funded studies

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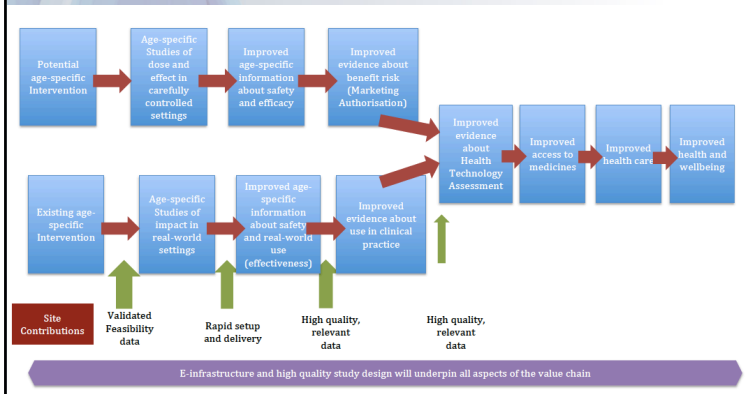
Context

- Policy
- Opportunities
- Difficulties
- IMI2 process
- Global setting
- Different perspectives
  - Language / culture
  - Drivers

Context: pharmaceutical value chain



Planning, set-up & conduct of a Paediatric Development Program

A multifaceted challenge…

Defining the medical need	Right indication and population	Preparing and agreeing a Paediatric Development Plan	Small patient populations – competing developments
Use/acceptance of innovative study designs	Insufficient trial infrastructure	Divergent view of Ethic Committees	Contradictory local regulations
Diverse standard of care across Europe	Impact on daily lives of patients and families	Dose, route of administration, application device	Acceptance of Paediatric research in society

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Challenges when conducting paediatric trials

Lack of experience in designing & conducting Paediatric studies by (industry) sponsor

Assessment of site capability, patient availability, and feasibility of trials is often inaccurate

Most new paediatric trials require a new network of sites to be built

Most sites negotiate their own CDAs, contracts, budget templates, and IRBs/EC approvals to prepare for studies

Many sites are inexperienced, poorly trained, and under-resourced

Poor study design
Poor feasibility
Poor site engagement
Inefficiency

→ Poor/delayed study delivery

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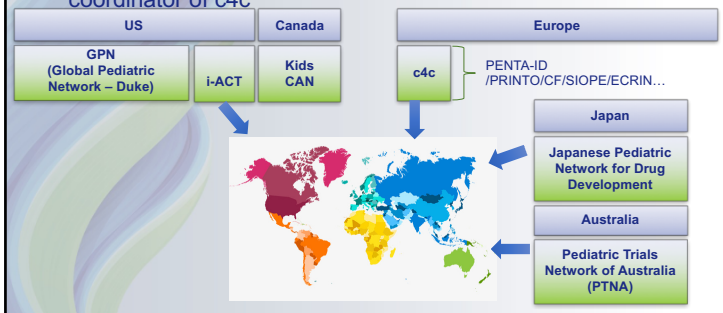
Global Paediatric clinical trial networks

- The **c4c** network will collaborate with other existing networks
- Working contacts are already established via the scientific coordinator of c4c



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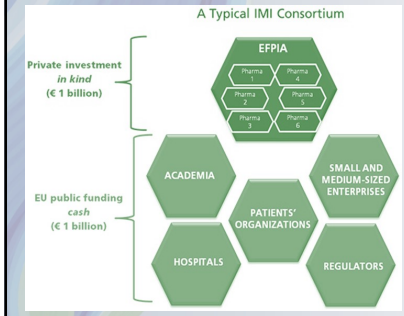
pan-EU Paediatric Clinical Trials Network

A project under the EU Innovative Medicines Initiative (IMI)



- **Improve the current drug development process**
- **efficacy, safety & quality** of health products.
- **Reduce time to clinical proof of concept**
- Develop **new therapies** for diseases with **high unmet need** & **limited market incentives**
- Allow engagement in a cross-sector, multi-disciplinary consortium at the forefront of cutting-edge research

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Project Concept

1. Use resources and funding of the IMI project to setup the network and its processes
   1. National
   2. International
2. Demonstrate the value of the network approach with selected
   1. Studies
   2. Sites
3. Generalise from the demonstration projects to the broader network

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3. Gene
   to the broader network jects

From
- **Specific**
- **Selected**

To
- **Generalised**
- **Sustainable**

2019

2024

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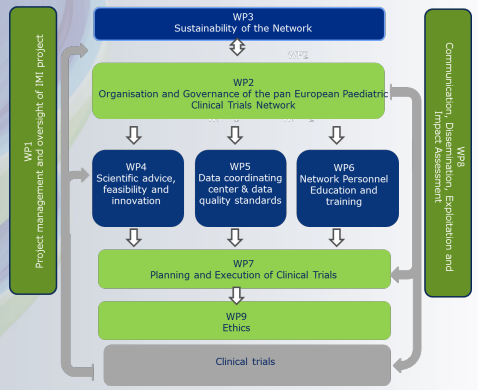
c4c-Project overview



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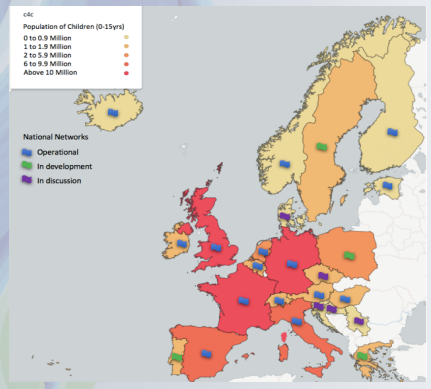
c4c consortium members



- 10 EFPIA companies
- 18 pediatric national networks
- 2 large patient advocacy groups
- 8 EU Multinational sub-specialty Networks,
- 2 large children's hospitals

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New consortium – experienced partners

Internationally recognized public partners such as:

PRINTO
Paediatric Rheumatology INternational Trials Organisation (PRINTO)

PENTA-ID Network

Karolinska Institute

The European Society for Paediatric Oncology

The European Cystic Fibrosis Society

EURORDIS RARE DISEASES EUROPE
European Organisation for Rare Diseases Association

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c4c and contributors to paediatric research

Sponsor

Sites

Specialty networks

Clinical experts

Investigators

Methodological experts

Children, Young People and Families

Examples of Estonian networks

Pediatr Drugs
DOI 10.1007/s40272-016-0173-5

CrossMark

ORIGINAL RESEARCH ARTICLE

Product Substitution as a Way Forward in Avoiding Potentially Harmful Excipients in Neonates

Georgi Nellis[1,2] · Tuuli Metsvaht[1,3] · Heili Varendi[2] · Jana Lass[4] · Jennifer Duncan[5] · Anthony J. Nunn[5] · Mark A. Turner[6,7] · Irja Lutsar[1]

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Examples of Estonian networks

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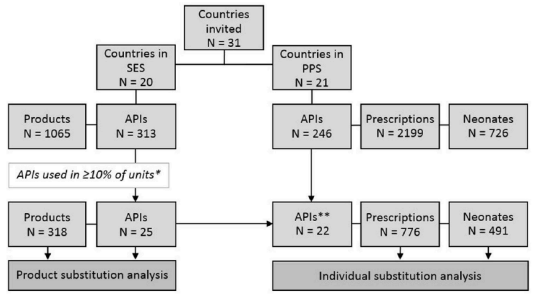
ORIGINAL RESEARCH ARTICLE

Product Substitution as a Way Forward in Avoiding Potentially Harmful Excipients in Neonates

Fig. 1 Flowchart of SES and PPS methods and selection of APIs for substitution analysis. * excluding multivitamins, topical products and APIs with no EOI; ** common in SES and PPS. *API* active pharmaceutical ingredient, *PPS* point prevalence study, *SES* service evaluation survey



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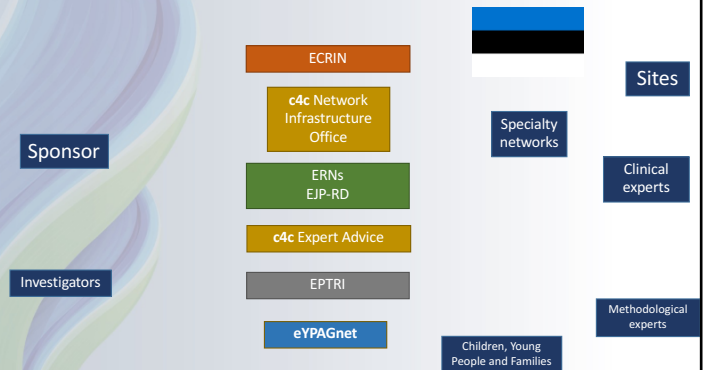
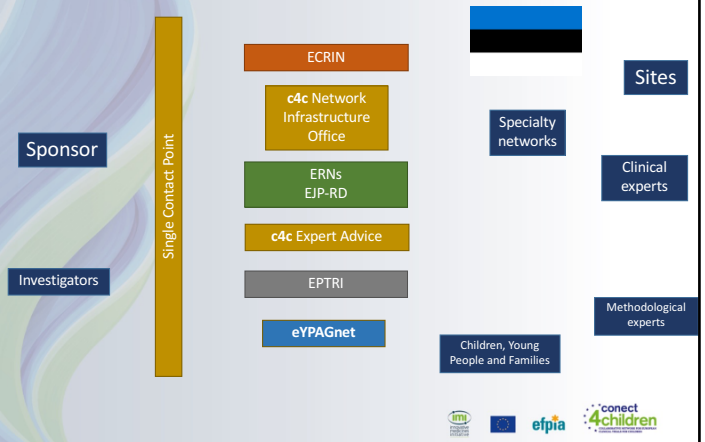
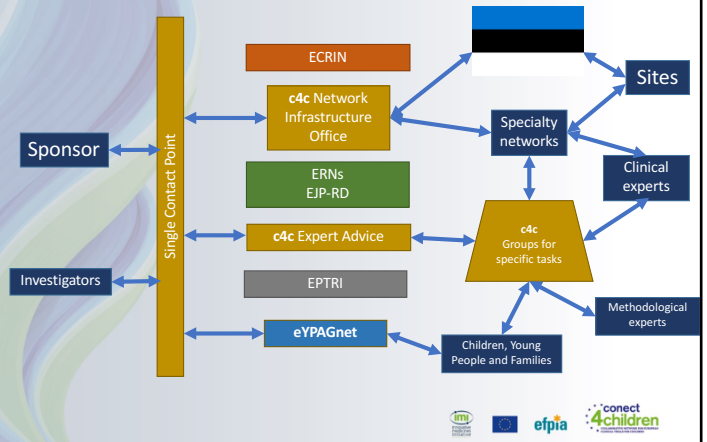
One-stop shops

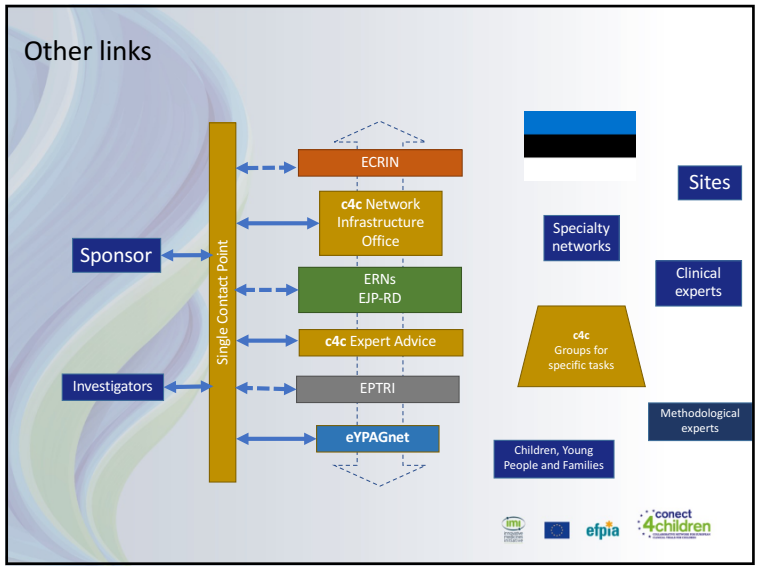


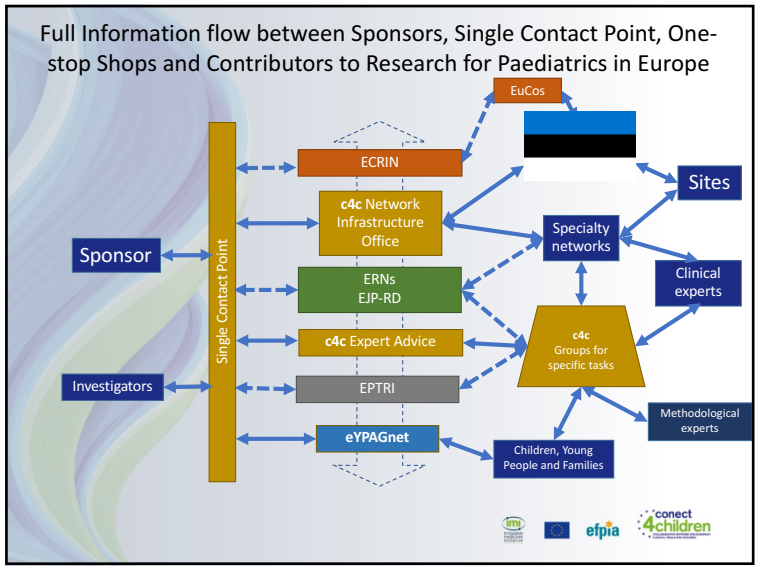
Position of c4c single contact point



c4c Information flow between Sponsors, Single Contact Point, One-stop Shops and Contributors to Research for Paediatrics in Europe







Benefits for sponsors of placing a study with c4c

- High quality input to study design and preparation through rigorous strategic and **operational feasibility** assessment
- **Efficient implementation** by adopting consistent approaches, aligned quality standards and coordination of sites at national and international level
- A **single point of contact** for all sponsors, sites and investigators
- Collaboration with/access to EU pediatric specialty networks

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Benefits to the paediatric community

- **Harmonized, streamlined procedures** across the trial lifecycle
- Opportunities to **build economies of scale** at site and national level
  - Reducing barriers to entry and so making paediatric research more attractive and competitive
- **Access to a wide range of study sponsors** through a **transparent**, evidence-based, network-wide vetting procedure
- **Input from relevant specialty networks and methodologists** on study design, implementation and assessment.

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Key Objectives

- Trials
  - Setup through national hubs and qualified sites
  - Implementation
- Input
  - Pilot advisory groups and other fora
- Supporting activities
  - Education
  - Data
- Sustainability
  - Business case(s)

Key activities

- A single point of contact
- Efficient implementation of trials
- Adopting consistent SOPs
- International network with lean central coordination
- Multi- KEY stakeholder collaboration
- Strategic and operational feasibility assessment
- Experts to develop innovative trial designs and methodology

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Industry viability trials:
selection, funding and purpose

- **Final selection** of industry-sponsored studies **once the network is established** based on the then current portfolio development.
- The selected studies will target a **variety of indications.**
- All industry studies are directed at yielding **data and information** that will be placed in the **drug label (SmPC and/or USPI) and/or have a Pediatric Plan** agreed with major Health Authorities
- Studies **sponsored and 100% funded by the respective company**
- Studies will be used to **test the viability of the network** by selecting and comparing metrics about study stet-up and conduct

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Non-industry-sponsored proof of viability studies

- Call to be launched in 2Q2018
- Call open outside **c4c** network but sponsor will be one **c4c** Beneficiary
- Selection process via NetCom and based on:
  - Utility to the consortium (to test processes and systems)
  - Scientific value
    (to respond to relevant clinical need and promote innovation)
  - Complementarity to industry studies
  - Feasibility
  - Patient's acceptability (to test patients advocacy involvement in design)
  - Likelihood of completing recruitment within 3 years of FPFV
  - Sponsor's commitment to report on trial processes and experiences
    (to facilitate dissemination and knowledge sharing within the network)

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Expert advice

Comment on studies, as early as possible

Children and Young People are experts at being children and young people

Scope “multistakeholder meetings”

Education

Support clinical trials

- GCP
- Site training

Promote clinical trials

- Hospital managers
- Society

Scope of c4c (by 2024)

Type of study	Industry/non-industry
Intervention	Drug, biologics, devices; non-interventional
Geography	Europe
Phase of study	Ph 1- 4; observational, registry studies
Endpoints	PK/PD, efficacy, safety
Responsibilities	The c4c network will provide some central services for trials, for example, trial feasibility, pharmacovigilance activities and commissioning of trial supplies. c4c is not a CRO

Expected long term impact of c4c

- **Access to new experimental therapies** for children in well-designed clinical trials
- **Better training** for research personnel and **improved trial**

“Better medicines for babies, children and young people through a pan-European clinical trial network”

- **Enhanced role** of **clinicians and patient/parent advocacy groups** in planning and designing studies
- **Broadening the access of academic medical centers and clinical faculty** across Europe to new experimental therapies

c4c Values

Making a difference
Accountability
Dependability
Loyalty
Collaboration

Ways of working

Scope
Gather information
Draft proposals
Comment on proposals
Pilot
Implement

Clear time windows for contributions

"Respond to consultations, or, don't complain later"

Contracts, templates and systems

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Conclusions

We have a once in a lifetime opportunity to make a difference

We have all the right people with the right skills

We can succeed if we:

- Work to deadlines
- Focus and coordinate
- Respond to consultations
- Share and respect needs