c4c aims to enhance the development of Better Medicines for babies, children and young people through a pan-European clinical trial network

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How things have developed...

Since the first implementation of the Paediatric Regulation, we have seen...

❖ An ever-increasing number of Paediatric Investigation Plans
❖ Continuous increase in Paediatric clinical trials and the number of children to be involved
❖ A growing number of new treatment options being approved for use in children

But also:
❖ About 40% of PIPs are not completed as planned
❖ Increased competition between studies about shared resources (Investigators, sites, patients)

Nordic Paediatric Medicines Conference Sept 2022
### A multi-faceted challenge...

<table>
<thead>
<tr>
<th>Topic</th>
<th>Description</th>
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<tbody>
<tr>
<td>Finding the right indication and population</td>
<td>Lack of sufficient trial infrastructure</td>
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<tr>
<td>Use/acceptance of innovative study designs</td>
<td>Impact on daily lives of patients and families</td>
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<tr>
<td>Lack of appreciation of need for clinical research in children in society</td>
<td>Divergent Ethical standards</td>
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<tr>
<td>Contradictory local regulations</td>
<td>Small patient populations – competing developments</td>
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A pan-EU Paediatric Clinical Trial Network

A project under the EU Innovative Medicines Initiative (IMI2)

- Ensure **efficacy, safety & quality** of health products
- **Reduce time** to clinical proof of concept
- Improve the current **drug development process**
- 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
CONECT4CHILDREN

COLLABORATIVE NETWORK FOR EUROPEAN CLINICAL TRIALS FOR CHILDREN

**Why PPP**

The paediatric clinical trial infrastructure in the EU is fragmented and not sufficiently developed. A broad multidisciplinary public-private collaboration is required to meet the challenges and to collectively address children’s needs for better medicines.

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**Impact**

- Improved paediatric development plans and study designs
- More efficient implementation and conduct of Paediatric clinical trials
- Improved data quality, better trial feasibility and faster enrollment

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**Status & Value**

- Expert advice and patient/parent involvement
- Access to over 400 Clinical and methodological paediatric experts
- Inclusion of YPAGs, patients and parent groups in advice meetings; Single contracting structure, coordination of Expert Advice
- Single Point of Contact
- Access to local networks in 21 European countries and over 250 clinical sites
- Aligned processes across the entire network increase efficiency and quality
- c4c Training Academy
- Providing standardized training to all study sites and site personal, Master courses on Pediatric Drug Development
- Paediatric Data Dictionary & CDISC TAUG
- 1st Pediatric Data Dictionary established to allow standardization of data collection across Paediatric studies

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The paediatric clinical trial infrastructure in the EU is fragmented and not sufficiently developed. A broad multidisciplinary public-private collaboration is required to meet the challenges and to collectively address children’s needs for better medicines.
c4c makes a difference
Areas of highest impact

**Design and planning of studies**
Advice requests
- Outcomes directly impacting studies designed and conduct
- Reports supporting discussion with Regulatory authorities

**Trial feasibility & opening sites**
Significant decrease in time to sign CDAs
Increase in number of high quality sites available for site selection and feasibility

**Data standards**
Cross-Cutting Paediatric Data Dictionary as basis for CDISC TAUG
- Supporting sharing and interoperability of data

**Education**
Multiple short courses
Advanced Course in Paediatric Clinical Trials and Drug Development is in progress

**Patient and Public Involvement (PPI)**
Improving PPI plan’s of sponsors, ensuring systematic involvement
Impact design and planning of studies
Strategic Feasibility Advice

Improving the way paediatric studies are planned and designed

Coordinated by Secretariat
Create Charter (4.5); Definition of operations and selection of expert members

Strategic feasibility groups
4.1

Advice
Single/multiple PIP development
Clinical Methodology Feasibility assessment

Requests

25 Expert Groups – over 400 registered experts

Adolescent Medicine
Neuromuscular diseases

Cardiology
Neuroscience & Epilepsy

Endocrinology & Diabetes
Oncology (incl. haematology)

Developmental pharmacology
Pharmacogenomics and other Omics technologies

Ethics
Pharmacometrics

Formulations
Pharmacovigilance

Gastroenterology & Hepatology
PPI (carers, parents, patients, patient organisations, YPAGS)

Health Technology Assessment
Psychiatry

Infectious diseases & Vaccinology
Respiratory

Intensive care
Rheumatology & Autoimmune diseases

Metabolic diseases
RSV

Neonatology
Study design & Clinical trial methodology

Nephrology
Implementation of the advice
Impacting the design of Paediatric Investigational Plans (PIPs)

As of 17 Aug 2022

34 scoping interviews
(7 industry partners & 3 academic sponsors)

7 did not proceed 25 completed 2 ongoing

11 include PPI

23 include one or more Clinical Expert Groups

14 include one or more Innovative Methodology Groups

# advice requests per group:
- Adolescent medicine (4)
- Cardiology (2)
- Developmental Pharmacology (3)
- Ethics (7)
- Formulations (2)
- HTA (1)
- Infectious diseases & Vaccinology (3)
- Intensive Care (2)
- Neonatology (3)
- Nephrology (3)
- Neuroscience & Epilepsy (4)
- Oncology/Haematology (4)
- Pharmacogenomics (2)
- Pharmacovigilance (1)
- Psychiatry (2)
- Respiratory (5)
- RSV (1)
- Study design and Clinical trial methodology (8)
- Other; dermatology (1)

Advice Reports support Regulatory discussions & submissions
Master Consultancy Agreements in place to allow easy contracting
### 1\textsuperscript{st} MSM: Paediatric Inflammatory Bowel Disease

- Virtual event held 14-15 April 2021 with more than 100 participants representing academia, patients and advocates, regulators (EMA, PDCO, FDA) and industry
- Very positive post-meeting feedback
- Publication in scientific journal accepted
- A multi-stakeholder approach enables the identification of solutions to accelerate drug development in paediatrics
- Initiative fully endorsed by EMA* and FDA

*2020 progress report on Joint EMA/EC action plan on paediatrics

### 2\textsuperscript{nd} MSM: Atopic Dermatitis

- 1-2 March 2022 (Virtual)
- participants representing academia, patients and advocates, regulators (EMA, PDCO, FDA) and industry
- Publication in scientific journal planned
20 National Hubs serving 21 countries across Europe
Providing access to over 250 clinical sites

c4c established
• 20 paediatric national networks in 21 countries*

Closely cooperating with
• 8 European multinational specialty networks
• 3 global research networks

* Finland & Iceland is a joint network
c4c Site Feasibility Services

*Increased efficiency through unique CDA cascade process*

**Stage 1**
- database search; Initial c4c Site identification
- **20 working days**
  - National Hub (NH) review and recommendation of sites

**Innovative CDA cascade process and templates**
- Sponsor to c4c Single Point of Contact (SPoC*)
- c4c to National Hub (NH)
- NH to Site
- **72 hours each**

**Stage 2**
- Protocol Specific Feasibility
- Sponsor submitted questions
- NH review for completeness and quality
- And NH recommendation

Sponsor informs c4c of Country/ Sites progressing to Protocol Feasibility
Sponsor informs c4c of Country/ Sites selected
Sponsor feedback to sites and NH
c4c Site Identification and Feasibility Service

*Fast identification of high number of high quality sites*

Stage 1 - Initial sites identified by c4c

*Within 20 working days*

<table>
<thead>
<tr>
<th>Trial</th>
<th>Number of c4c sites identified</th>
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<tbody>
<tr>
<td>Sponsor A</td>
<td>101</td>
</tr>
<tr>
<td>Sponsor B</td>
<td>142</td>
</tr>
<tr>
<td>Sponsor C_a</td>
<td>161</td>
</tr>
<tr>
<td>Sponsor C_b</td>
<td>160</td>
</tr>
<tr>
<td>Sponsor D</td>
<td>171</td>
</tr>
</tbody>
</table>

Stage 2 - Protocol specific feasibility

<table>
<thead>
<tr>
<th>Trial</th>
<th>Number of sites</th>
<th>Mean Time to complete*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor A</td>
<td>8</td>
<td>15 days</td>
</tr>
<tr>
<td>Sponsor B</td>
<td>74</td>
<td>9 days</td>
</tr>
<tr>
<td>Sponsor C_a</td>
<td>65</td>
<td>16 days</td>
</tr>
<tr>
<td>Sponsor C_b</td>
<td>ongoing</td>
<td></td>
</tr>
<tr>
<td>Sponsor D</td>
<td>ongoing</td>
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- *Minimum time 2 days;
- *Maximum time 38 days
c4c work supporting Data Harmonisation and standardisation
Paving the way for better data quality and re-usability

Cross Cutting Paediatric Data Dictionary

**IMPACT:** More harmonised paediatric data = More efficient and effective trials

Data Recommendations

**IMPACT:** Higher quality more interoperable data = increased scientific knowledge

Therapeutic Area User Guide (TAUG)

**IMPACT:** c4c is influencing standards development on a global level = potential to de-risk paediatric trials
Training and Education

- **c4c Paediatric Medicine Academy**
  - Teachers from Academic and Pharma Partners

- **Students/Users**
  - Trainings addressing different professionals roles

- **c4c Academy Management Secretariat**
  - Administrative management of the courses

- **Integrated educational program**
  - to address best practice in paediatric clinical trials and paediatric medicine development

- **c4c Academy Platform**
  - Virtual Learning Environment hosting courses

- **Education Board (EB)**
  - To provide quality oversight and address educational needs
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 readiness** at all participating sites
- **Improved efficiency** in executing trials (faster, cheaper)
- **Improved data quality** for labelling of next generation medicines for children
- 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
Route to sustainability
*To make our vision a reality c4c needs to:*

• Transition the c4c network into an independent organization that can function at the end of the IMI funding
• Co-ordinated by a not-for-profit legal entity, likely based in the Netherlands
Thank you!