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

Heidrun Hildebrand, Bayer AG, c4c Project co-lead
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 be transformative and to collectively address children’s needs for better medicines.

**Impact**

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

**Why IMI**

**Status & Value**

- Expert advice and patient/parent involvement
- Access to over 300 Clinical and methodological paediatric experts
- Inclusion of YPAGs, patients and parent groups in advice meetings
- Single contracting structure, coordination/organization of Expert advice meetings

- **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 open for all beneficiaries

- **Paediatric Data Dictionary & TAUG**
- 1st Pediatric Data Dictionary established to allow standardization of data collection across Paediatric studies

IMI impact on paediatric medicine; November 10, 2021
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

Innovative methodology experts
4.2
Clinical experts
4.3
Patient participation groups 4.4

White papers
Multistakeholder meetings
Tools for patient involvement

25 Expert Groups – over 300 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 Pediatric Investigational Plans (PIPs)*

**29 requests for advice**
(7 industry partners & 2 academic sponsors)

- 5 did not proceed
- 17 completed
- 6 ongoing

**7 include PPI**

**19 include one or more Clinical Expert Groups**

**11 include one or more Innovative Methodology Groups**

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

**12 advice requests provided on Pediatric development strategy**

**5 reports included in submissions to regulatory bodies**

IMI impact on paediatric medicine; November 10, 2021
Centralized contracting structure (CCS)

*Improving efficiency by accelerating contracting timelines*

- 128 master consultancy agreements with Experts signed to date
- 8 master service agreements in place with companies
- Facilitating the advice process by reducing number of contracts
19 National Hubs serving 21 countries across Europe
Providing access to over 250 clinical sites

- 19 paediatric national networks in 21 countries*
- 2 new paediatric national networks under negotiation

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

* Finland & Iceland and Norway & Denmark are joined networks
c4c Site Feasibility Services
Increased efficiency through unique CDA 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*

<table>
<thead>
<tr>
<th>Trial</th>
<th>Number of c4c sites identified</th>
</tr>
</thead>
<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 1 - Initial sites identified by c4c**

*Within 20 working days*

**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>
<td></td>
</tr>
</tbody>
</table>

- *Minimum time 2 days;
- *Maximum time 38 days
### c4c Service for Trial Feasibility

**Major reduction in time needed to finalize CDAs**

"The c4c team was amazing during the CDA process for site identification. Having the c4c team’s help during this process was invaluable and allowed for a more efficient process”  
*Sponsor trial team*

<table>
<thead>
<tr>
<th>Trial</th>
<th>Number of CDAs</th>
<th>Time to complete (working days)</th>
<th>Mean time to complete (working days)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor A</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sponsor to c4c</td>
<td>1</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>SPoC to NH</td>
<td>15</td>
<td>80% within 3</td>
<td>3</td>
</tr>
<tr>
<td>NH to site*</td>
<td>38</td>
<td>97% within 5</td>
<td>8</td>
</tr>
<tr>
<td>Sponsor C_a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sponsor to SPoC</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>SPoC to NH</td>
<td>18</td>
<td>78% within 3</td>
<td>3</td>
</tr>
<tr>
<td>NH to site*</td>
<td>91</td>
<td>68% within 5</td>
<td>7</td>
</tr>
<tr>
<td>Sponsor B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sponsor to SPoC</td>
<td>1</td>
<td>&lt; 1</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>SPoC to NH</td>
<td>19</td>
<td>79% within 3</td>
<td>2</td>
</tr>
<tr>
<td>NH to site*</td>
<td>111</td>
<td>82% within 5</td>
<td>9</td>
</tr>
</tbody>
</table>

*Minimum time 1 working day; *Maximum time 29 working days

IMI impact on paediatric medicine; November 10, 2021
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
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

**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 TAU
- 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
Impact design and planning of studies

IMI impact on paediatric medicine; November 10, 2021
Thank you!