Paediatric medicines and funds for paediatric research in EU

Adriana Ceci
ERA – European Research Area

AN OPEN SPACE FOR KNOWLEDGE
The European Research Area is composed of all research and development activities, programmes and policies in Europe which involve a transnational perspective.

ERA consists of activities, programmes and policies which are designed and operated at all levels and for all the interested people

<table>
<thead>
<tr>
<th>Regional</th>
<th>Researchers</th>
<th>Joint Programming Initiatives</th>
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</thead>
<tbody>
<tr>
<td>National</td>
<td>Universities</td>
<td>Research Infrastructures</td>
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<td>European</td>
<td>Research Organisations</td>
<td>Knowledge Sharing</td>
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<td></td>
<td>Industry-SMEs</td>
<td>Investing in Research</td>
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<td>Citizens-Patients</td>
<td>International Cooperation</td>
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Main public initiatives for funding Health research in EU

• DG Research Programs

• DG Sanco Programme

**FP5-FP6 – Health Calls**

**FP7-HEALTH Calls**

**HORIZON 2020**

**DG Sanco Health Programme**
The health theme in the FP7: main achievements

Health theme:
• €6 billion EU investment
• 1,000 projects
• 11,000 teams
• 3,500 organisations
• 130 countries

Source: Research priorities and Networks, Norstedt I and Cupers P, Health Directorate, Research & Innovation DG, European Commission
The paediatric initiative in the FP7

Child health has been addressed:

- throughout all work programme topics, where appropriate
- through specific topics:
  - Responding to EU policy needs: Adapting off-patent medicines to the specific needs of paediatric populations (Max. €6m).

From 2007 to 2013 funded 140 paediatric projects, for a total of 665 million Euro.

Source: Costescu A “Off-patent Paediatric Medicines-7th call Overview of FP7-Funding HORIZON 2020 state of play” VI Foresight Training Course, 2013
The paediatric initiative in the FP7

<table>
<thead>
<tr>
<th>THEME</th>
<th>PROJECTS No</th>
<th>FUNDING</th>
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<tbody>
<tr>
<td>Off-patent paediatric drugs</td>
<td>20 projects</td>
<td>€ 98,6M</td>
</tr>
<tr>
<td>Rare diseases</td>
<td>19 projects</td>
<td>€ 90M</td>
</tr>
<tr>
<td>Brain and brain-related diseases</td>
<td>13 projects</td>
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<tr>
<td>Diabetes and obesity</td>
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<td>Cancer</td>
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<tr>
<td>Other chronic diseases</td>
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<tr>
<td>Neglected infectious diseases</td>
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<tr>
<td>HIV/AIDS, malaria and tuberculosis</td>
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<td>€ 19M</td>
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<tr>
<td>Promoting healthy behaviour in children and adolescents</td>
<td>5 projects</td>
<td>€ 13,5M</td>
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<tr>
<td>Adverse drug reaction research</td>
<td>4 projects</td>
<td>€ 12M</td>
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<tr>
<td>Large scale data gathering</td>
<td>1 project</td>
<td>€ 12M</td>
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<tr>
<td>Safety and efficacy of therapeutic vaccines</td>
<td>1 project</td>
<td>€ 6M</td>
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<tr>
<td>Impact and cost-effectiveness of existing major health programmes</td>
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<td>International network of excellence</td>
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<td>Child and adolescent mental health</td>
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<tr>
<td>Identifying patients’ needs in the clinical trial context</td>
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<td>€ 1,4M</td>
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</tbody>
</table>

Source: Costescu A “Off-patent Paediatric Medicines-7th call Overview of FP7-Funding HORIZON 2020 state of play” VI Foresight Training Course, 2013
Paediatric needs and the EU funding initiative

• Specific funds have been addressed to the group of medicines included in the Priority List

**FP7-HEALTH Calls**

*Area 4.2: Responding to EU policy needs*

*Subprogramme area: HEALTH.4.2-1*

**Off-patent medicines for children**

**HEALTH.2013.4.2-1:** Investigator-driven clinical trials for off-patent medicines using innovative, age-appropriate formulations and/or delivery systems. FP7-HEALTH-2013-INNOVATION-1. Proposals will address one of the options below:

A) for use in children (Regulation (EC) No1901/2006): Projects are expected to contribute to expanding the availability of medicines for children. Particular attention will be paid to age-appropriate formulations and of specific delivery systems for children. Projects will conduct appropriate clinical trials in children, respecting the current legislation and considering the ethical aspects and the particular needs of children and their families. Patient advocacy groups should be involved where possible and appropriate. The aim is to conduct clinical trials with the view of obtaining a PUMA (Paediatric Use Marketing Authorisation). Priority will be given to following areas, as mentioned in the EMA list of priorities for paediatric medicines:

The paediatric initiative in the FP7: off-patent paediatric drugs

20 projects aimed to investigate 24 active substances in the paediatric population:
- to provide evidence for a better use of medicinal products
- to use the acquired knowledge for new Paediatric Use Marketing Authorisations

<table>
<thead>
<tr>
<th>START YEAR</th>
<th>ACRONYM</th>
<th>FP7 HEALTH CALL</th>
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<tbody>
<tr>
<td>2008</td>
<td>Loulla &amp; Phill</td>
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<td>2008</td>
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<td>TINN 2</td>
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<td>2011</td>
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<td>2013</td>
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<td>2013</td>
<td>GAPP</td>
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<td>2013</td>
<td>METFIZZ</td>
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<td>2013</td>
<td>LENA</td>
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<td>2014</td>
<td>NeoVanc</td>
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20 Collaborative Research Consortia,
Totally, **246 EU and non-EU institutions**
22 EU countries and 7 non-EU countries

29 countries involved: UK, France, Italy and Germany are the most represented both in term of **participants** and **projects**
Non-EU countries directly involved in 4 partnership (HIP trial, DEEP, NEO-CIRC, GAPP) s
FP7 off-patent paediatric drugs: research consortia

**PROJECT COORDINATORS:**
- 12 universities and other public research centres institutions
- 2 companies
- 2 not-for-profit research organisations

**PROJECT PARTICIPANTS:**
- 6/20 networks include a patient association
- 9/20 networks include a not-for-profit research organisation
- Globally involved 51 private companies: pharmaceutical companies (13), CROs, companies for the manufacturing and supply chain consultancy, companies for the knowledge transfer, trusts, etc
FP7 off-patent paediatric drugs: the studies

A total of 71 studies

32 Clinical Trials:
- 29 paediatric clinical trials and 3 study in healthy adult volunteers
- 8 PK/PD/dose finding, 10 efficacy and safety trials and 12 PK/PD/efficacy/safety trials
- 387 investigational sites in EU or non-EU countries
- More than 7000 paediatric patients globally planned to be enrolled...

23% of all paediatric patients involved in CTs from 2008 to 2011 (EudraCT, Five-year report EMA-PDCO)
FP7 off-patent paediatric drugs: the paediatric population

All the paediatric subgroups are represented in the studies

Newborns and preterm newborns
- included in 14 CTs
- A neonatal condition is specifically addressed by the projects NeoOpioid, NeuroSIS, NEMO, TINN2, HIPtrial, NeoCirc and NeoVanc
The lesson learnt from these projects

- Still few drugs studied (18% of the AS included in the Priority List)
- Some therapeutic areas have not been addressed at all
- PIP implementation: the approved PIPs are different from the applied projects
- Most of the PIPs have generated delays in the timeline of the projects and/or the need for amendments to the approved projects (without changes in the funds)
- PUMA? The completion date of the first group of PIPs is foreseen in 2015. Maybe it’s too early to judge but more incentives are needed for Industries.

136 active substances are included in the EMA-PDCO Priority Lists from 18 therapeutic classes
FP7 outcomes...

• Despite the difficulties, the projects represent a positive example in the paediatric research scenario. New initiatives aimed to consolidate the acquired results are needed.

• Updated funding programmes should be available as stated in the Paediatric Regulation art. 40.
From FP7 ... to Horizon 2020

Which calls for paediatric research?
The launch of Horizon 2020

- A single programme bringing together 3 different initiatives
- Coupling research to innovation
- Focus on societal challenges facing EU society
- Simplified access for all companies, universities, institutes in all EU countries and beyond

(from Alessandra Martini presentation, EU Commission, December 3rd 2013)
Horizon 2020 calls of interest in the field of paediatrics

- PHC-18-2015 Establishing effectiveness of healthcare intervention in the paediatric population
- PHC-14-2015 New therapies for rare diseases
- PHC-13-2014 New therapies for chronic non-communicable diseases
- HCO-10-2014 ERA NET rare disease research implementing IRDiRC objectives
Horizon 2020 call:
Establishing effectiveness of healthcare intervention in the paediatric population

• Proposals should focus on clinical research approaches providing a deeper understanding of effectiveness, efficacy and safety of healthcare interventions and the use of HTA methods in the paediatric population → a detailed programme based on CTs and/or real world data addressing clinical, therapeutic (including PD and PK properties) and safety aspects of healthcare interventions → to identify and assess benefits and risks

Tentative Proposal

To establish effectiveness and safety of combined DPF/DFO use in a large population versus all other comparators
(Additional: PK, costs, HTA)

⇒ Drugs and other interventions
⇒ All phases. Interventional/non interventional.
⇒ Clinical and economic (including HTA)
⇒ All therapeutic area.

**PHC-18-2015**
Deadlines: Stage 1 → 2014-10-14, Stage 2 → 2015-02-24
Horizon 2020 call: New therapies for rare diseases

1. development of new or improved therapeutic approaches, for repurposing of existing therapies
2. preclinical research, animal model development, GMP production
   • The proposed CT design must take into account recommendations from protocol assistance given by EMA
   • The medicinal product must have been granted the EU orphan designation
   • A concise feasibility assessment justified by available published and preliminary results and supporting data shall be provided

To advance the development of new therapeutic options for rare disease patients
To contribute to reaching the IRDiRC objective to deliver 200 new therapies for rare diseases by 2020

**PHC-14-2015**

**Deadlines:** Stage 1 → 2014-10-14; Stage 2 → 2015-02-24
The Health Programme is the European Commission’s main instrument for implementing the EU health strategy. The programme aims, through projects and other actions it funds, to improve the level of physical and mental health and well-being of EU citizens and reduce health inequalities throughout the Community. A new opportunity?
Criteria related with the scope of ERN and the targeted diseases or conditions:

• **Highly specialised healthcare**
  - Complexity of diagnosis and treatment
  - High cost of treatment and resources
  - Need of advanced/highly specialized medical equipment or infrastructures

• **Need of a particular concentration of expertise and resources**
  - Rare expertise/need of concentration of cases
  - Low prevalence/incidence/number of cases
  - Evaluated experiences of Member States
Networking elements, communication and eHealth solutions
• 6 Sets of criteria for networks
• 5 Sets of general criteria for members
• 2 Sets of specific criteria for members
ERN-Members’ general criteria

1. Set of horizontal criteria and conditions to be fulfilled by all healthcare providers regardless of the field of expertise

   5 groups
   22 criteria

   a) patients empowerment and centred care
   b) organisational, management and business continuity
   c) research and training capacity
   d) exchange of expertise, information systems and e-health tools
   e) expertise, good practice, quality, patients safety and evaluation
ERN-criteria for networks

- **Networks can be flexible** & have different architectures and internal relations but there are key organizational features.
- All Members in an ERN **must have in common the expertise** they specialise in certain treatment/s offered or disease/s or health condition/s they focus on.
From DEEP to an European Reference Network: are we ready?