



DEFERIPRONE
EVALUATION IN
PAEDIATRICS

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Paediatric medicines and funds for paediatric research in EU

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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

Regional
National
European

Researchers
Universities
Research Organisations
Industry- SMEs
Citizens-Patients

Joint Programming Initiatives
Research Infrastructures
Knowledge Sharing
Investing in Research
International Cooperation



Main public initiatives for funding Health research in EU

- DG Research Programs

FP5-FP6 –Health Calls
FP7-HEALTH Calls
HORIZON 2020

- DG Sanco Programme

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).

A colorful illustration of several diverse children's heads and shoulders, including a girl with red pigtails, a girl with dark skin and braids, and a boy with brown hair, all smiling. They are positioned around a large orange speech bubble.

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

THEME	PROJECTS No	FUNDING
Off-patent paediatric drugs	20 projects	€ 98,6M
Rare diseases	19 projects	€ 90M
Brain and brain-related diseases	13 projects	€ 79M
Diabetes and obesity	9 projects	€ 38M
Cancer	4 projects	€ 29M
Potentially new & re-emerging epidemics	2 projects	€ 29M
Other chronic diseases	4 projects	€ 24M
Neglected infectious diseases	2 projects	€ 16M
HIV/AIDS, malaria and tuberculosis	5 projects	€ 19M
Promoting healthy behaviour in children and adolescents	5 projects	€ 13,5M
Adverse drug reaction research	4 projects	€ 12M
Large scale data gathering	1 project	€ 12M
Safety and efficacy of therapeutic vaccines	1 project	€ 6M
Impact and cost-effectiveness of existing major health programmes	2 projects	€ 5,8M
International network of excellence	1 project	€ 5,8M
Child and adolescent mental health	1 project	€ 5,8M
Identifying patients' needs in the clinical trial context	1 project	€ 1,4M

... and many, many other areas and projects

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) No1901/2006⁴⁷): 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:

www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000092.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac05800260a4&jsenabed=true



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

START YEAR	ACRONYM	FP7 HEALTH CALL
2008	Loulla & Philla	FP7-HEALTH-2007-B HEALTH.2007.4.2-1
2008	NeoOpioid	
2008	03K	
2008	Tinn	
2009	NEuroSIS	
2009	EPOC	HEALTH-2009-Single-Stage HEALTH.2009.4.2-1
2009	NEMO	
2010	NeoMero	
2010	PERS	HEALTH-2010-single-stage HEALTH.2010.4.2-1
2011	TINN 2	
2011	HIP trial	HEALTH-2011-single-stage HEALTH.2011.4.2-1
2011	DEEP	
2011	NEO-CIRC	FP7-HEALTH-2013-INNOVATION-1 HEALTH.2013.4.2-1
2011	TAIN	
2011	KIEKIDS	
2013	CloSed	FP7-HEALTH-2013-INNOVATION-1 HEALTH.2013.4.2-1
2013	GAPP	
2013	METFIZZ	
2013	LENA	
2014	NeoVanc	

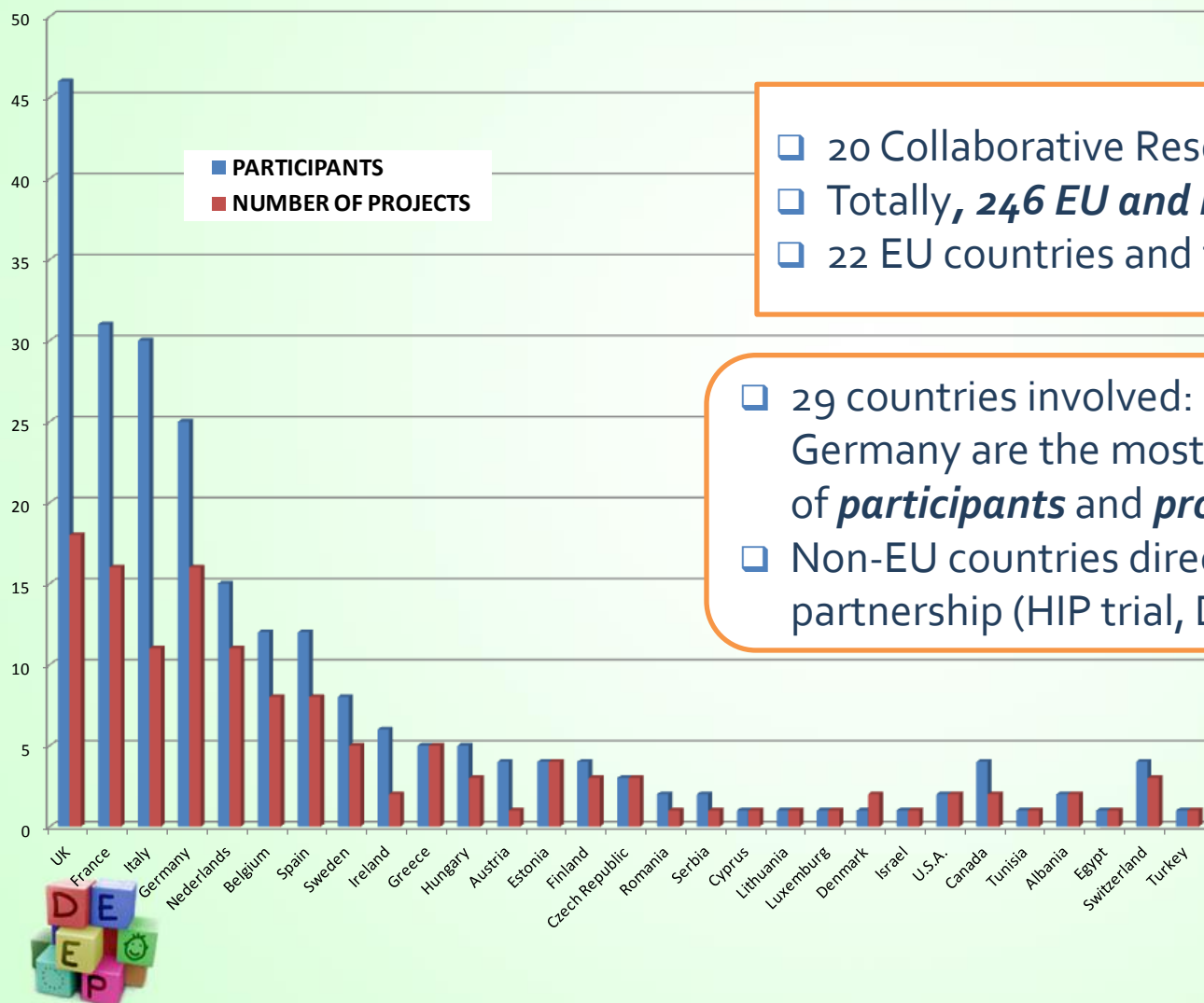
FP7-HEALTH Calls
Area 4.2: Responding to EU policy needs
Subprogramme area: HEALTH.4.2-1
Off-patent medicines for children

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



FP7 off-patent paediatric drugs : research consortia



- 20 Collaborative Research Consortia,
- Totally, **246 EU and non-EU institutions**
- 22 EU countries and 7 non-EU countries

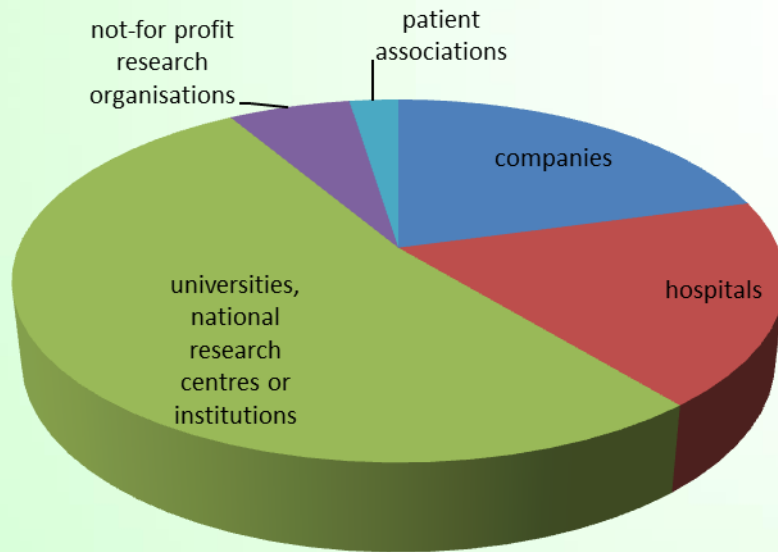
- 29 countries involved: UK, France, Italy and Germany are the most represented both in term of **participants** and **projects**
- Non-EU countries directly involved in 4 partnership (HIP trial, DEEP, NEO-CIRC, GAPP) s



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:

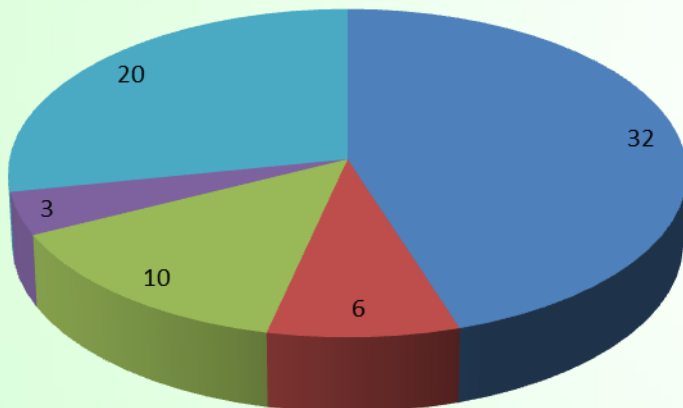
- ☐ 6/20 networks include a patient association
- ☐ 9/20 networks include a not-for-profit research organisation
- ☐ Globally involved 51 private companies: pharmaceutical companies (13), CROs, companies for the manufacturing and supply chain consultancy, companies for the knowledge transfer, trusts, etc



FP7 off-patent paediatric drugs: the studies

A total of 71 studies

Study type



■ Clinical Trials

■ Non-Interventional studies

■ in silico modeling studies

■ non-clinical studies in animals

■ forms/formulation 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

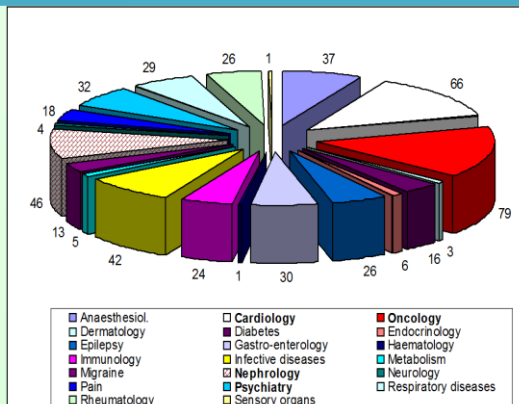
	Preterm newborns	Newborns 0-27 gg.	Infants 1 months- 2 years	Children 2-5 years	6-11 years	Adolescents 12-18 years
Loulla & Philla						
NeoOpioid						
03K						
Tinn						
NEuroSIS						
EPOC						
NEMO						
NeoMero						
PERS						
TINN 2						
HIP trial						
DEEP						
NEO-CIRC						
TAIN						
KIEKIDS						
CloSed						
GAPP						
METFIZZ						
LENA	NOT AVAILABLE					
NeoVanc						

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 approved 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

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

Tentative Proposal

To establish effectiveness and safety of combined DPF/DFO use in a large population versus all other comparators

(additional: PK, costs, HTA)



[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

DG Sanco Health Programme

- 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 ?**



Directive 2011/24/EU of patients' rights in cross-border healthcare



- Right to **choose and be reimbursed** for **healthcare provided** by public or private providers located in the EU

Networks of healthcare providers aiming at

Improving quality and safety and access to highly specialised healthcare

about their rights, treatment options
safety levels of healthcare providers

operation among Member States



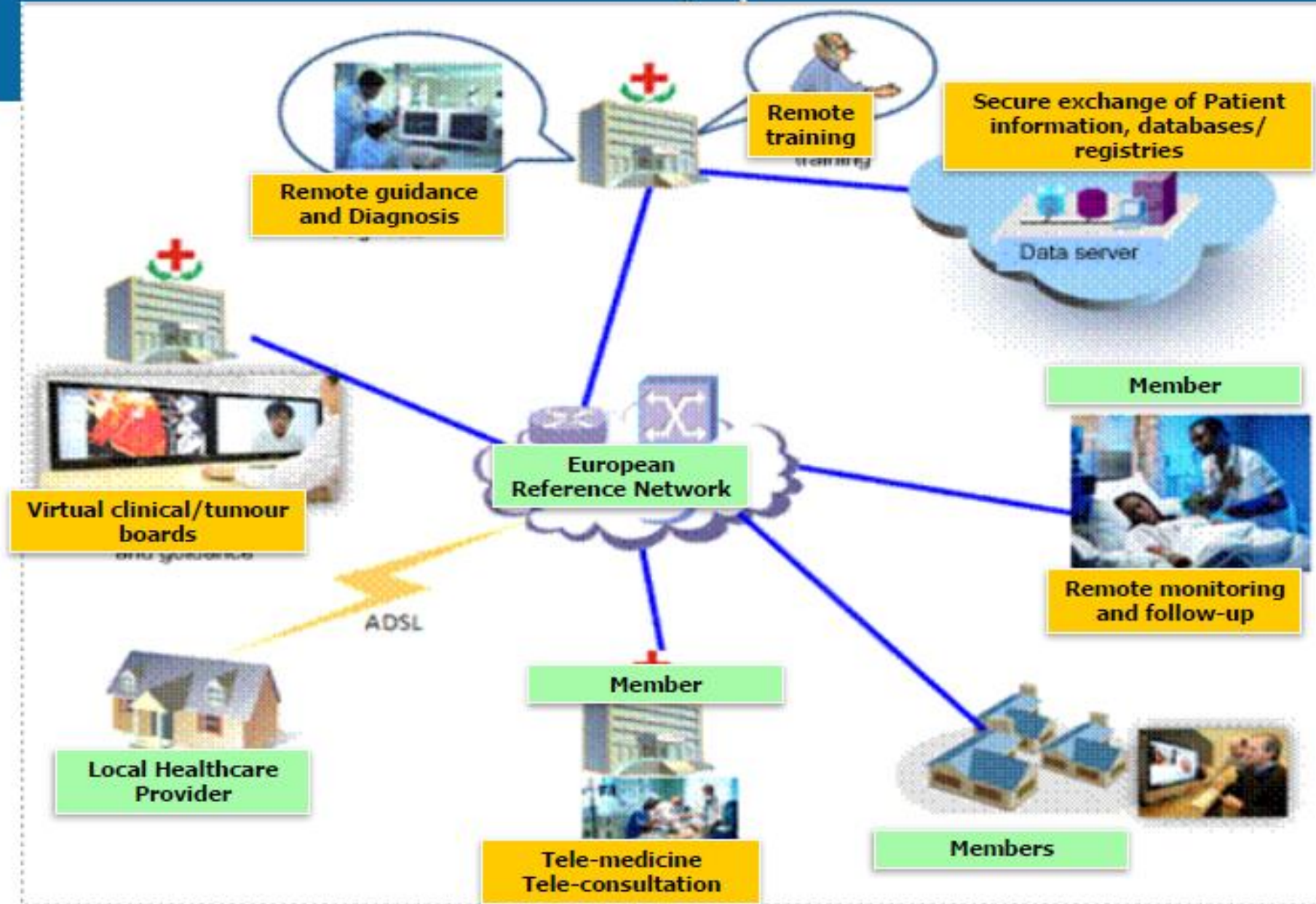
European Reference Networks awareness conference

Brussels 23 June 2014

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



European Reference Networks awareness conference

Brussels 23 June 2014



- 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

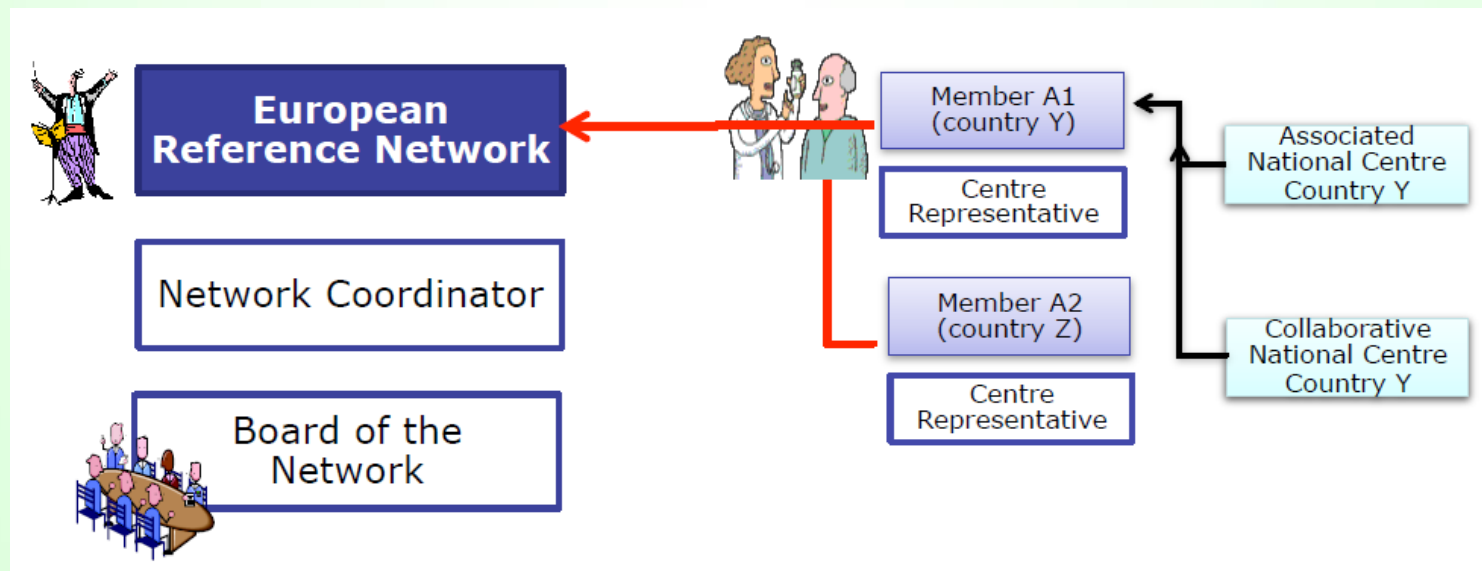


- a) patients empowerment and centred care**
- b) organisational, management and business continuity**
- c) research and training capacity**
- d) exchange of expertise, information systems and e-health tools**
- e) expertise, good practice, quality, patients safety and evaluation**

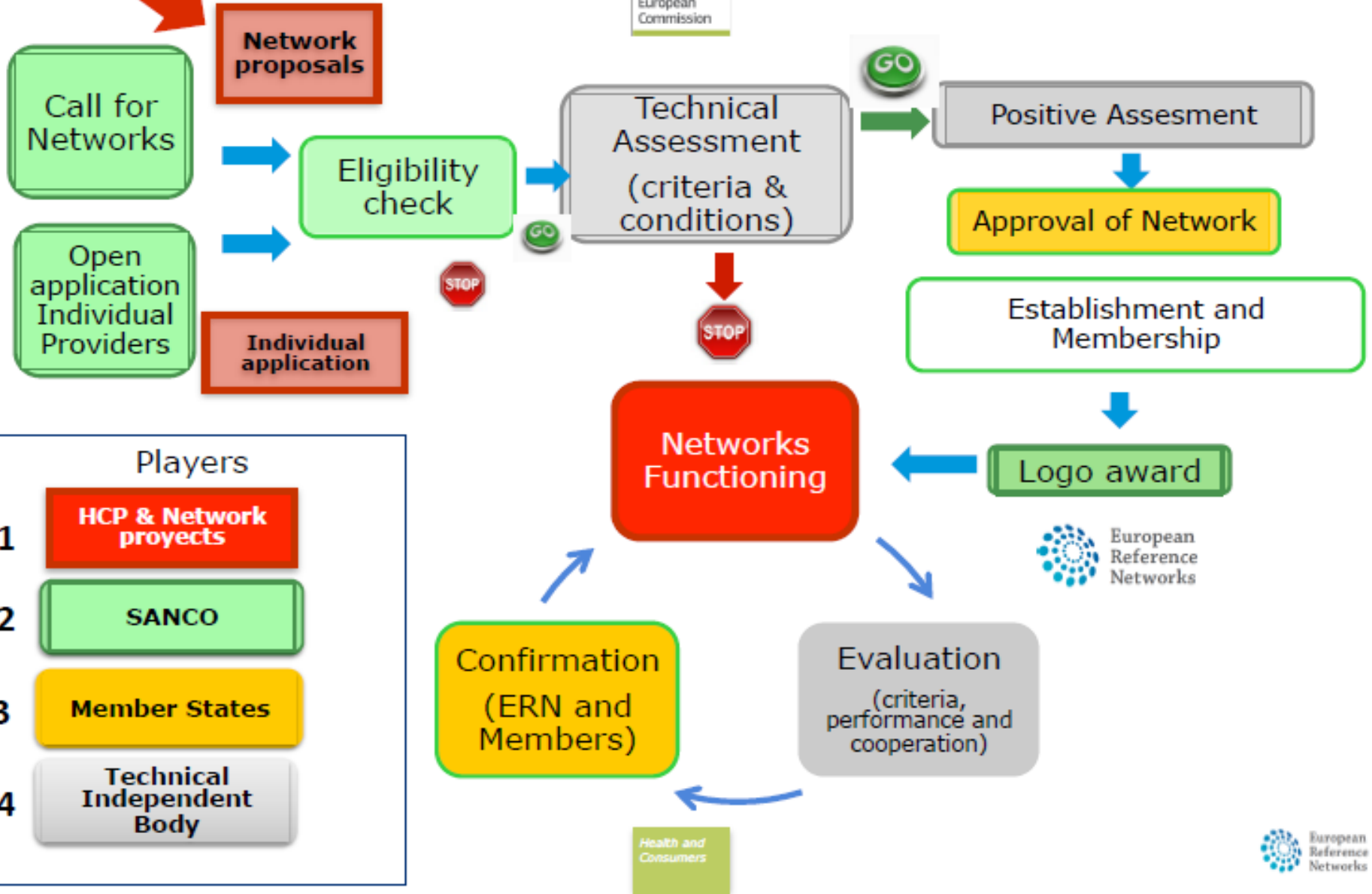


ERN-criteria for networks

- **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.



ERN Scenario



Players

- 1 **HCP & Network projects**
- 2 **SANCO**
- 3 **Member States**
- 4 **Technical Independent Body**

From DEEP to an European Reference Network: are we ready?

ERN tentative timeline & milestones



May
2014



**Entry into force
legal acts**

July
2014



**Call for
Assessment
Manual**

II quarter
2015



**Call for selection
independent
body(ies)**

IV quarter
2015



**Call for
Networks**

II quarter
2016



**Establishment
of Networks**

