

conect4children:

Collaborative Network for European Clinical Trials for Children

**Proposal for an Applicant Consortium to
IMI2 Call 10 Topic 4**

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The story so far...

- Current state
- The consortium
- The concept
- Global interoperability



Innovation

State of the Art

Many industry studies

Poor delivery

Poor design

Fragmentation

Inefficiency

Poor engagement

Poor feasibility

Opportunities

Precision
Medicine

Repurposed
medicines

Biologics

Big data

Methods

PK/PD

Design

Extrapolation

Devices

Apps

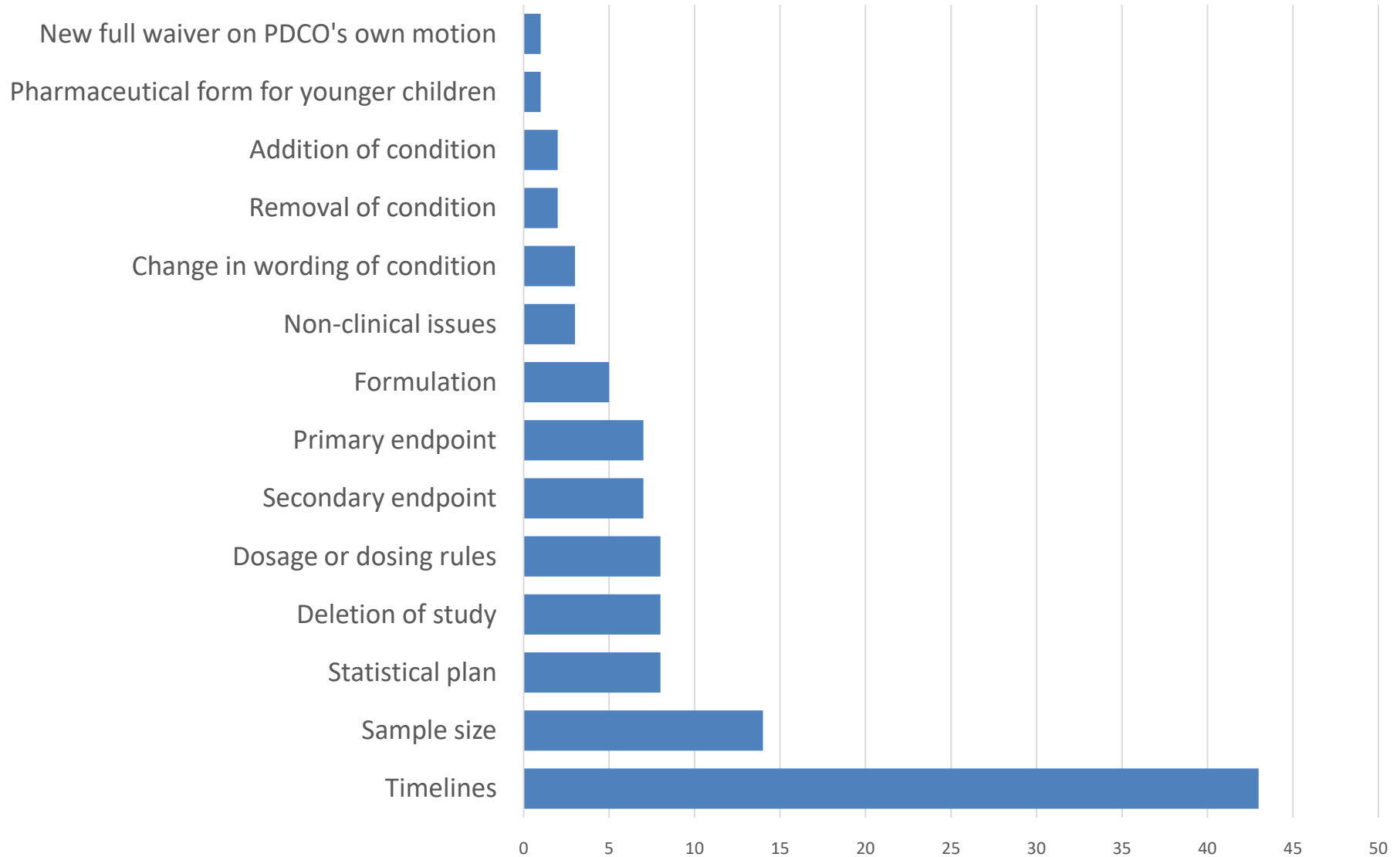
Global
Development

Integrated regulatory /
HTA assessments

Number of children planned to be enrolled in clinical trials,
by age by year of authorisation of the trial
(or, if not available, by year of protocol upload into EudraCT).

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Preterm neonates	0	0	0	327	82	2,527	1,552	3,634	4,997	1,979
Term neonates	0	98	5	184	169	1,353	2,283	1,488	2,168	1,749
Infants and toddlers	530	119	20	54,715	2,224	13,318	62,226	17,772	39,095	122,295
Children	2,683	706	270	5783	2,771	21,665	30,831	27,994	65,824	48,358
Adolescents	435	36,458	285	5801	4,869	20,206	22,680	17,628	45,717	36,921
Total	3,648	37,381	580	66,810	10,115	59,069	119,516	68,516	157,261	211,302

Causes of PIP amendments



Low numbers of participants per site

Active substance	Study	# of Patients in protocol (# of enrolled patients)	Number of sites/ Countries	Approximate recruitment rate pts/site/month
Riociguat	Ongoing: OL, dose titration, safety, tol, PK	20 (3)	36/13	0.03
Tadalafil	Ongoing: Pbc controlled, safety and efficacy (TTCW/6MWD)	134 (29)	59/17	0.01
Tadalafil	Ongoing: PK, safety	At least 15	21/6	0.01
Ambrisentan	Ongoing: OL, 2 dose, safety, efficacy	66 (35 EEA)	34/?	0.03
Macitentan	OL, AC, event driven efficacy safety, PK	300	Unknown	0.04
Completed studies for comparison:				
Bosentan	Completed: OL, PK, tol, safety, efficacy	64	48	0.06
Sildenafil	Completed: Pcb-controlled, dose ranging	234	41	0.1
Sildenafil	Completed: Long-term, open-label ext.	220	31	NA

Courtesy of James Strait, MSD

Current state


Network	Topic	Sites	Central contracts	Industry Liaison	Clinical Trials
NIHR-CRN	UK	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
	Finland	✓ <input type="checkbox"/>		✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
	Switzerland	✓ <input type="checkbox"/>		✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
	Austria	✓ <input type="checkbox"/>		✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
	Netherlands	✓ <input type="checkbox"/>		✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
	France	✓ <input type="checkbox"/>			
	Spain	✓ <input type="checkbox"/>			
	Italy	✓ <input type="checkbox"/>			
	13 others				

Current state

Network	Topic	Registries	Harmonised procedures	Industry Liaison	Clinical Trials
SIOPE	Oncology	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
PENTA-ID	HIV-ID	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
PRINTO	Rheumatic diseases	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
ECFS-CTN	Cystic fibrosis	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
TREAT-NMD		✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>	✓ <input type="checkbox"/>
....					
	PICU	✓ <input type="checkbox"/>			
	Cardiology				
	23 others				

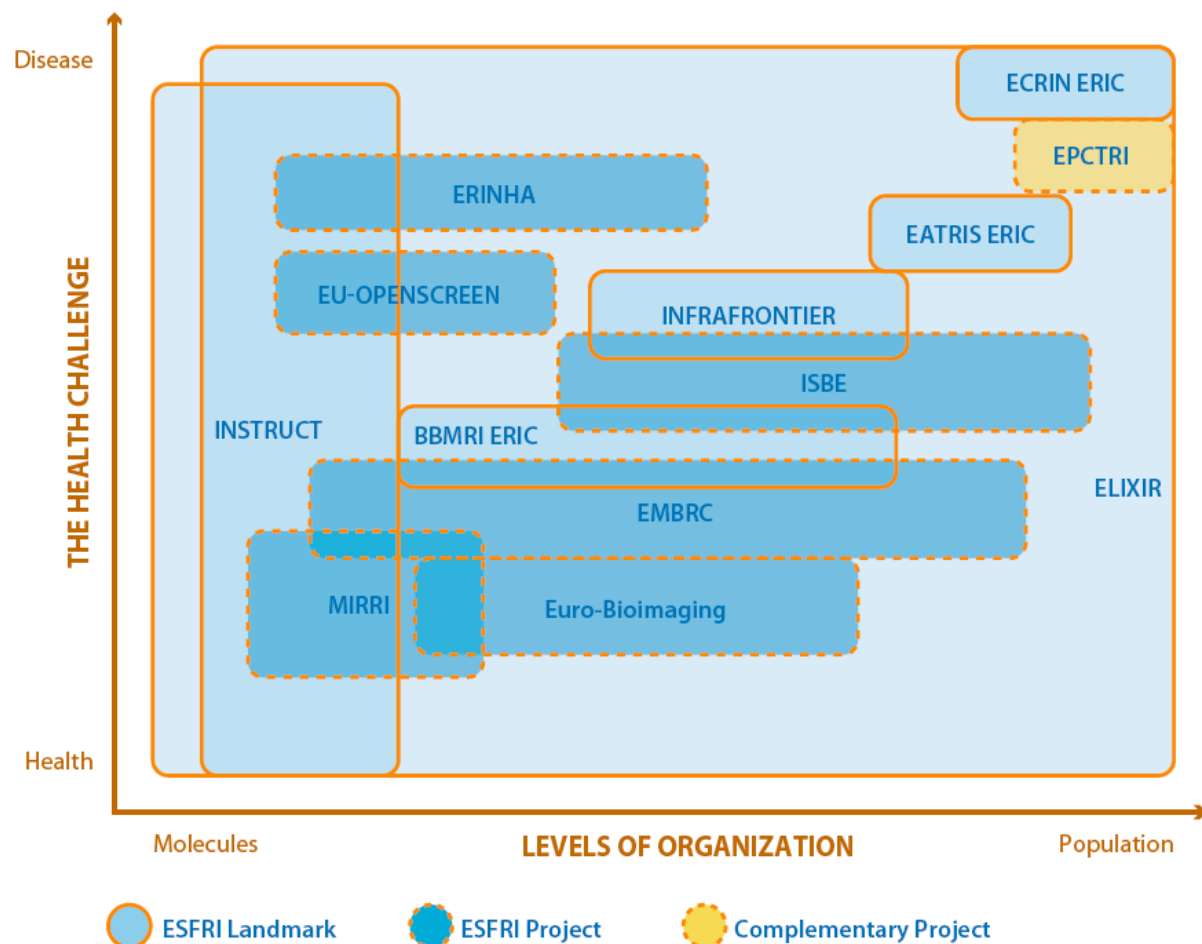
Breakdown of networks by type and category

National	Oncology/ Haematologic Malignancies	Diabetes/ Endocrinology/ metabolic disorders/ Gynaecology	Gastroenterolog y/ Hepatology	Allergology/ Immunology/ Rheumatology	Stem Cell /Organ Transplantation/ Haematology/Ha emostaseology	Respiratory diseases /Cystic Fibrosis	
DCRI	ITCC			PRINTO	EBMT	ECFS-CTN	
NIHR-CRN	Newcastle-CLLG		PEDDCReN				
ScotCRN	IBFMSG		EPLTN	JSWG of PRES			
FinPedMed							
PEDMED--NL	CLG- of EORTC						
MICYRN	CEPOETA						
CICPed	Category 1: Networks fulfilling all minimum criteria for membership of Enpr-EMA. Category 2: Networks potentially fulfilling all minimum criteria – but needing to clarify some issues before becoming a member of Enpr-EMA. Category 3: Networks currently not yet fulfilling minimum criteria. Category 4: Networks not performing clinical trials; e.g. methodology, infrastructure, etc.						Unable to fill self-assessment report
RIPPS							
OKids							
RECLIP							
Red SAMID							
MCRN-Hungary							
IPCRN							
Futurenest CR							
SwissPedNet							
NorPedMed	SPECIAL ACTIVITIES / AGE GROUPS						
NCCHD-Japan							
Cardiovascular diseases/ Nephrology	Psychiatry/ Neurology	Infectious diseases/ Vaccinolog y	Intensive Care/Pain/ Anaesthesiolog y/ Surgery	European neonatal network	European paediatric pharmacists	special activities (Phv, long term follow up, community paediatricians)	Expertise in clinical trial methodology
	EUNETHYDIS	PENTA-ID		GNN		FIMP-MCRN	TEDDY
	ECAPN	UKPVG		INFANT		NETSTAP e.V.	EYPAG Net
		ESPNIC		Neo-circulation			ECRIN
		RITIP		ESDPPP			EAPRASnet
		ReSViNet					



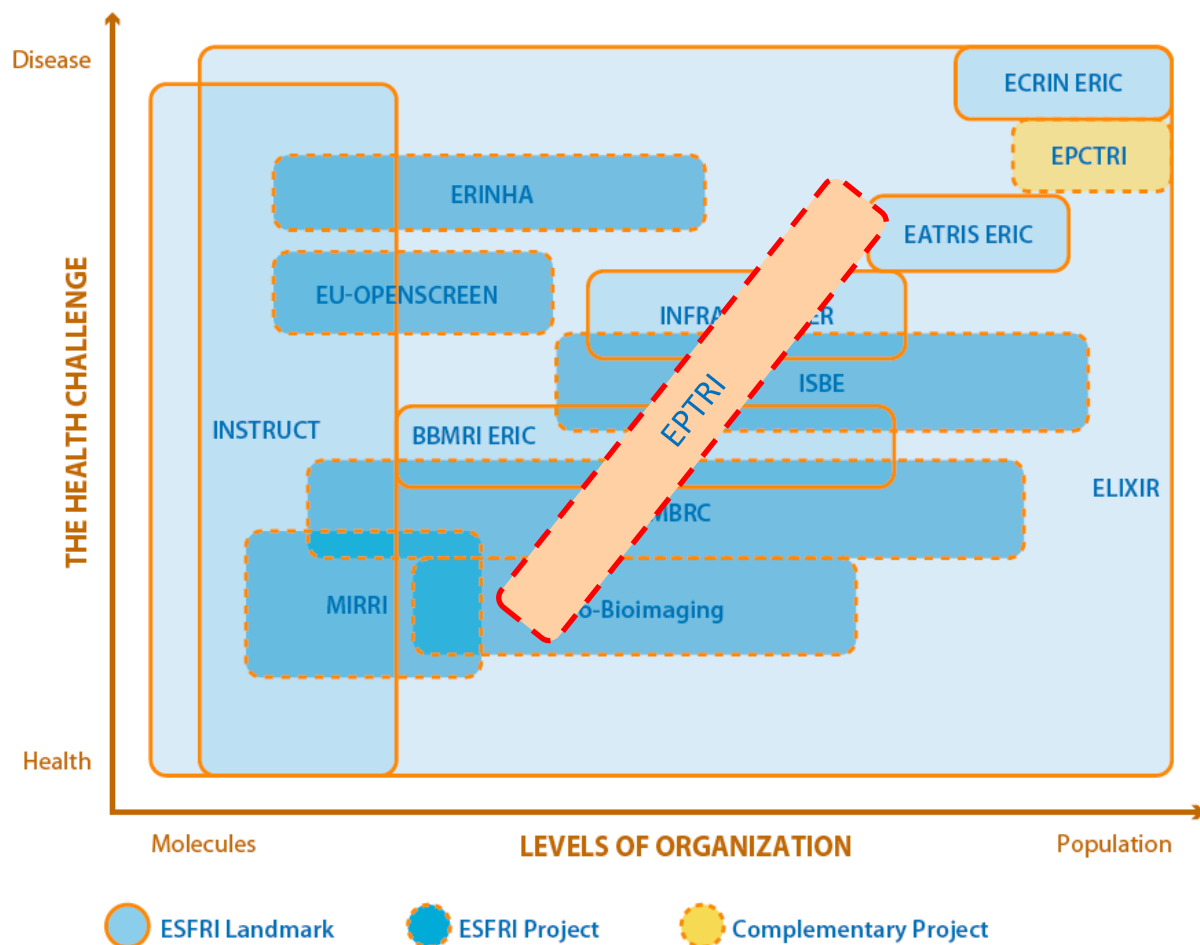
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Figure 3: the indicative position of ESFRI RIs relative to the different levels of organisation in the Health domain.



Existing infrastructures such as the ESFRI Landmarks ECRIN, BBMRI, EATRIS and others could connect in a "meta-structure" aiming at providing a full pipeline for drug development.

Figure 3: the indicative position of ESFRI RIs relative to the different levels of organisation in the Health domain.



Existing infrastructures such as the ESFRI Landmarks ECRIN, BBMRI, EATRIS and others could connect in a "meta-structure" aiming at providing a full pipeline for drug development.

Network Vision

Europe will use a coordinated approach to deliver high quality “regulatory grade” clinical trials in

- Multiple countries
- Multiple sites
- All paediatric age groups
- All paediatric disease groups
- Innovation

Network Mission

Improve availability of information about medicines used by children

Promote the delivery of high quality innovative trials of medicines for children by supporting:

- Trial implementation using resources shared between studies
- Trial design through a combination of information about natural history, feasibility and expert opinion
- Public- and industry-funded studies

Project Concept

1. Use resources from the IMI2 project to setup the network and its processes
 - National
 - International
2. Demonstrate the value of the network approach with selected
 - Studies
 - Sites
3. Generalise from the demonstration projects to the broader network

Sustainability

“Generalise from the demonstration projects to the broader network”

This involves:

- Persuading funders to invest in sites, national networks and international networks (including expert advisory groups)
- Demonstrating financial, economic and social value of the network
 - Capturing value that sites and networks create
- Proof-of-viability: inclusion or exclusion in the demonstration projects does not affect involvement in the definitive network

Engagement with existing and new networks

- Identify key contact
 - Triangulation to find right people
 - Engage with stakeholders
- Preliminary discussions with
 - Key contact
 - Stakeholders
- Face-to-face meeting
- Follow-up
- Implementation led by country

Countries so far:

Italy
France
Spain
Germany
Poland
Hungary
Denmark
Sweden
Belgium
Albania

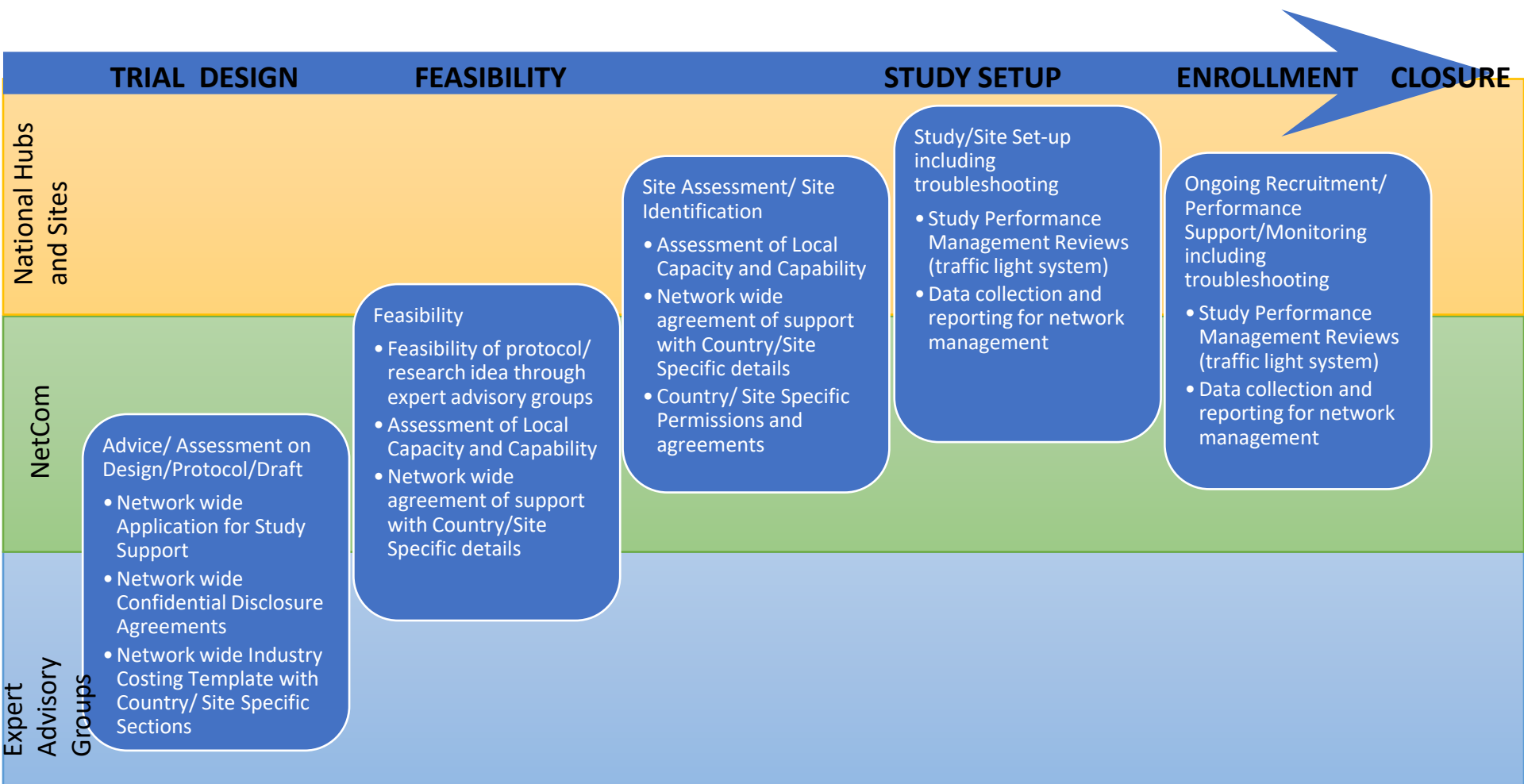
Croatia
Slovenia
Serbia

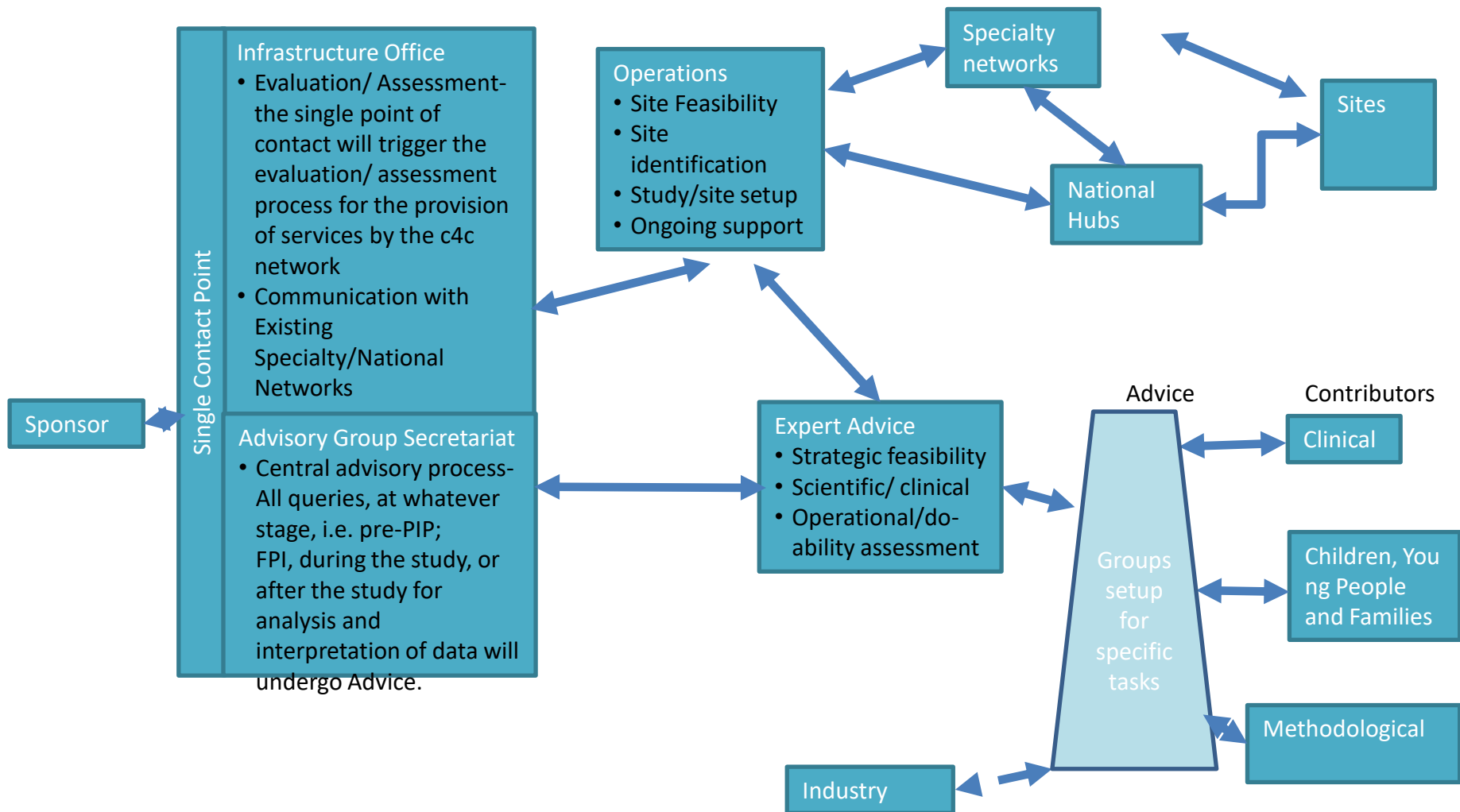
Consortium Members

National networks		Emerging networks
UK	Finland	<i>Poland</i>
Spain	Norway	<i>Portugal</i>
France	Estonia	<i>Sweden</i>
Italy	Austria	<i>Denmark</i>
Switzerland	Ireland	<i>Greece</i>
Belgium	Hungary	<i>Serbia</i>
Netherlands		<i>Croatia</i>
Germany		<i>Slovenia</i>

Consortium Members

Specialty	ERNs	Others
PENTA-ID	MetabERN	European Young People's Advisory Group Network
PRINTO	Renal	
CF	Rare epilepsies	EURORDIS
SIOPE	Paediatric Oncology	ECRIN
Treat-NMD		EUREC
<i>INNODIA</i>		TEDDY
<i>Other speciality Networks</i>		Other IMI2 projects (e.g. RESCEU)





Change Management

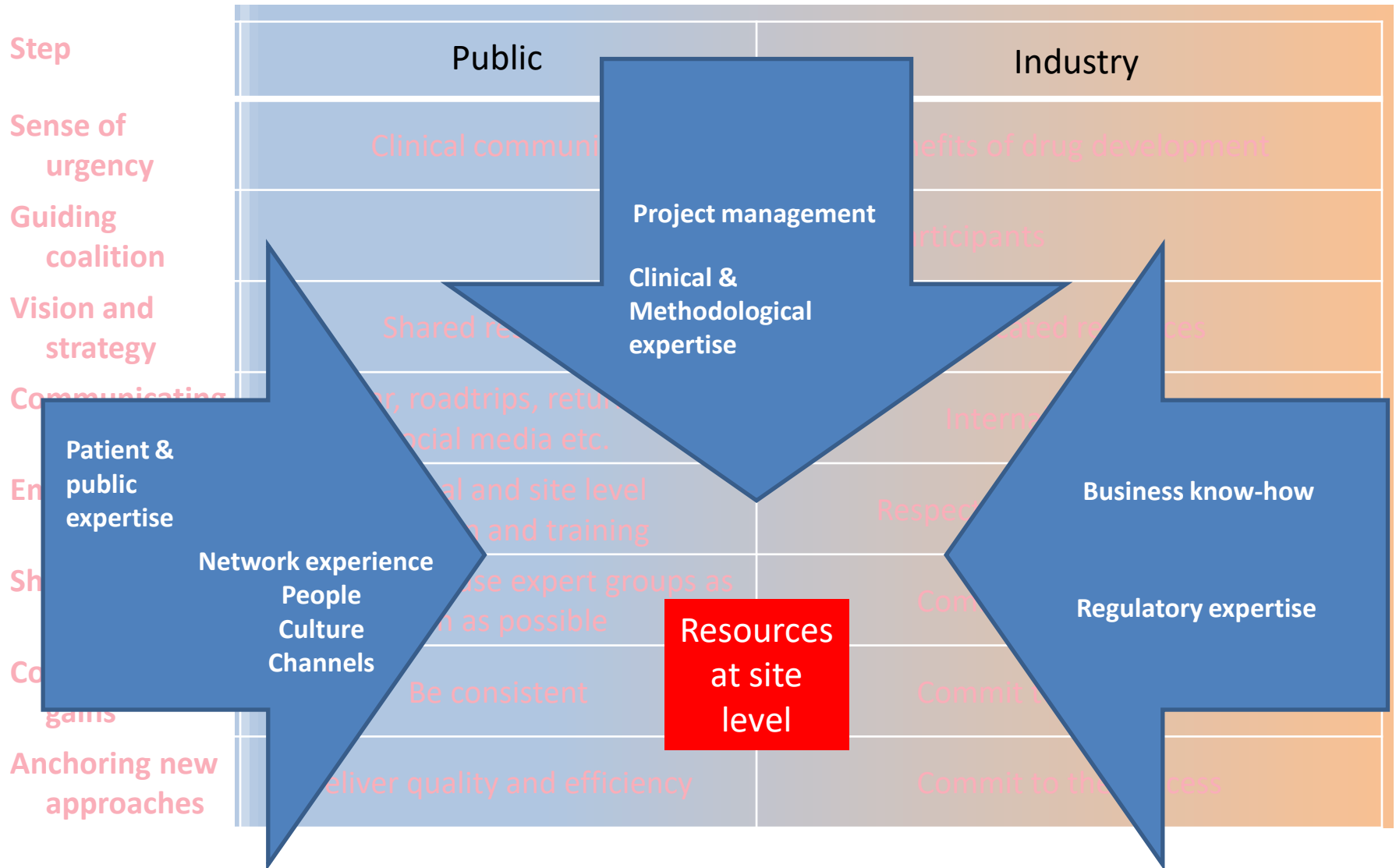
Step	Public	Industry
Sense of urgency	Clinical community	Benefits of drug development
Guiding coalition	Today, and all participants	
Vision and strategy	Shared resources	Dedicated resources
Communicating the vision	Webinar, roadtrips, return visits, social media etc.	Internal marketing
Empowering employees	National and site level Education and training	Respect network procedures
Short-term wins	Run trials and use expert groups as soon as possible	Commit to the process
Consolidating gains	Be consistent	Commit to the process
Anchoring new approaches	Deliver quality and efficiency	Commit to the process

Change Management

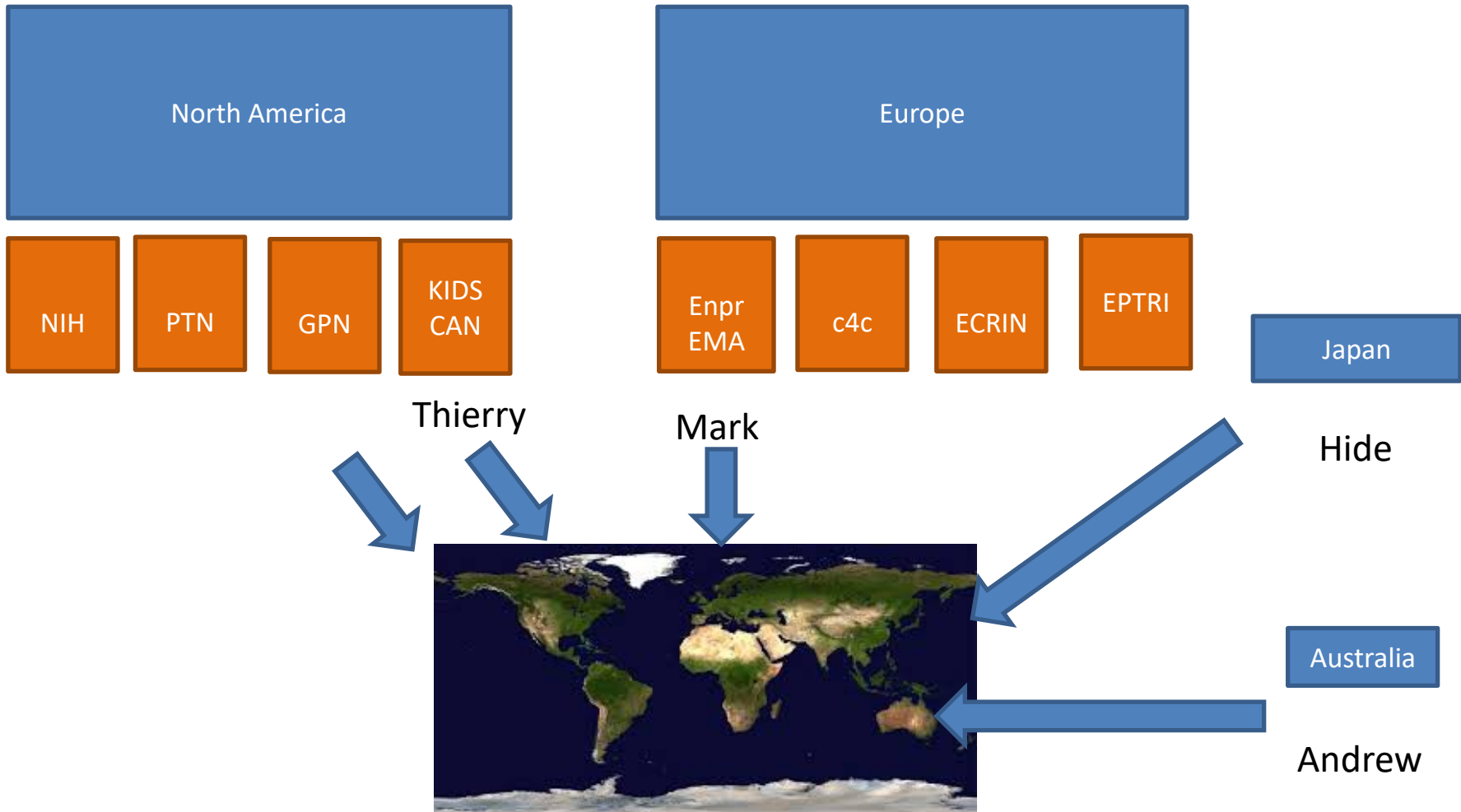
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Resources
at site
level

Change Management



Global Interoperability



Conclusion

Many challenges

Many opportunities

Need public private collaboration

Need national and continental integration

Important roles for an integrated Spanish trials network