European
Reference
Networks

THE EUROPEAN REFERENCE NETWORKS: A VISION FROM INSIDE

MAURIZIO SCARPA

CHAIR,

EUROPEAN REFERENCE NETWORK

COORDINATORS GROUP

COORDINATOR,

EUROPEAN REFERENCE NETWORK

HEREDITARY METABOLIC DISEASES

THE ORIGIN OF THE ERNS

European Commission

The road to ERNs

2002
Free movement of patients

2005
Commission's High Level Group on Health Services and Medical Care
Centres of Reference report

2006
RD Task Force Working Group on centres of reference
Updated report CoR
Public Health Programme
First pilot networks proyects

2011
Directive application of patients' rights in cross-border healthcare
Article 12 ERN

2013
Eucerd Recommendations European Reference Networks (Rd Erns)

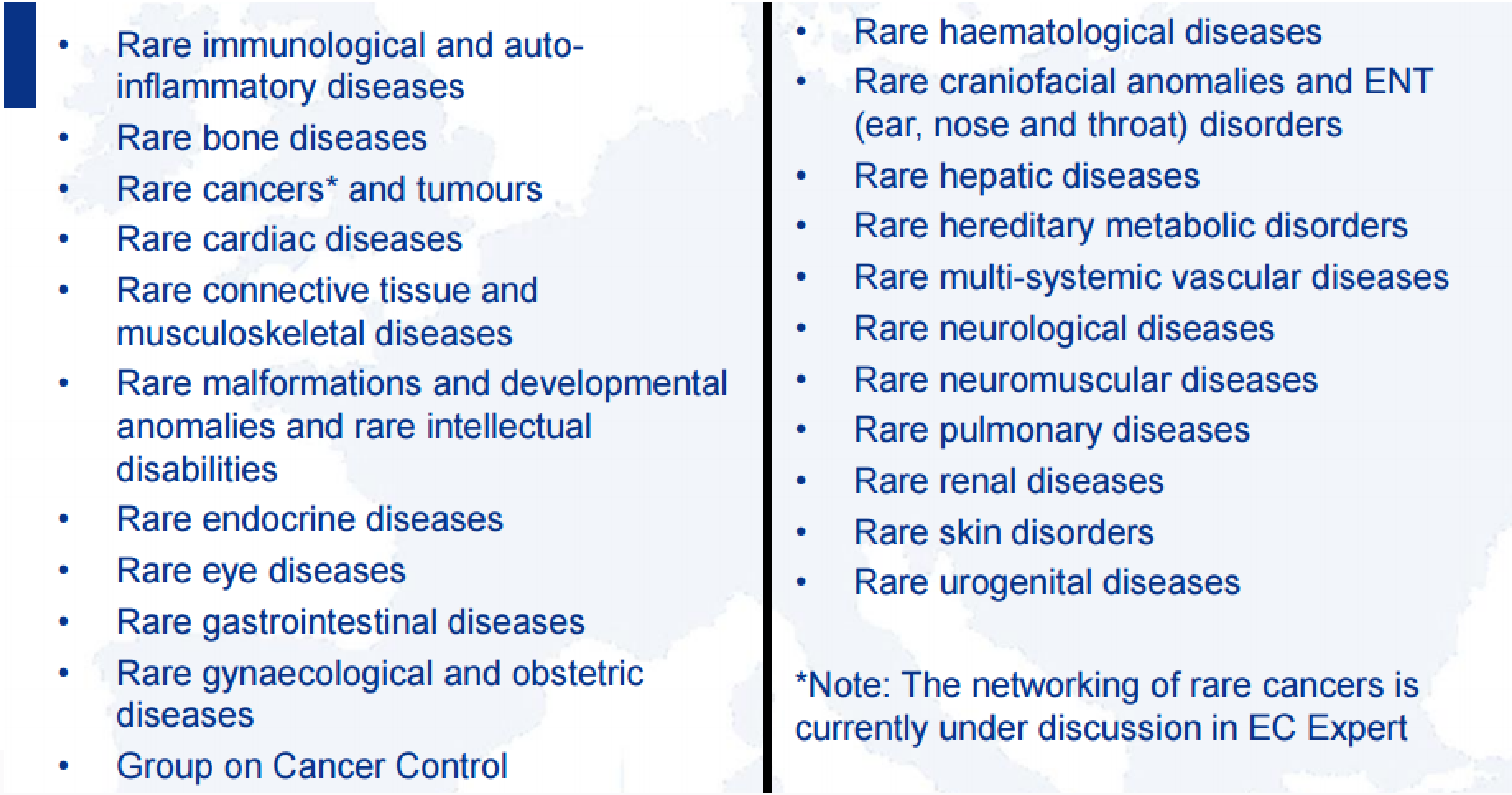
2014
Commission Decisions on ERN

Health and Consumers

European Reference Networks

Slide kindly provided by Enrique Terol, EU Commission

Grouping Rare Diseases In Thematic Networks

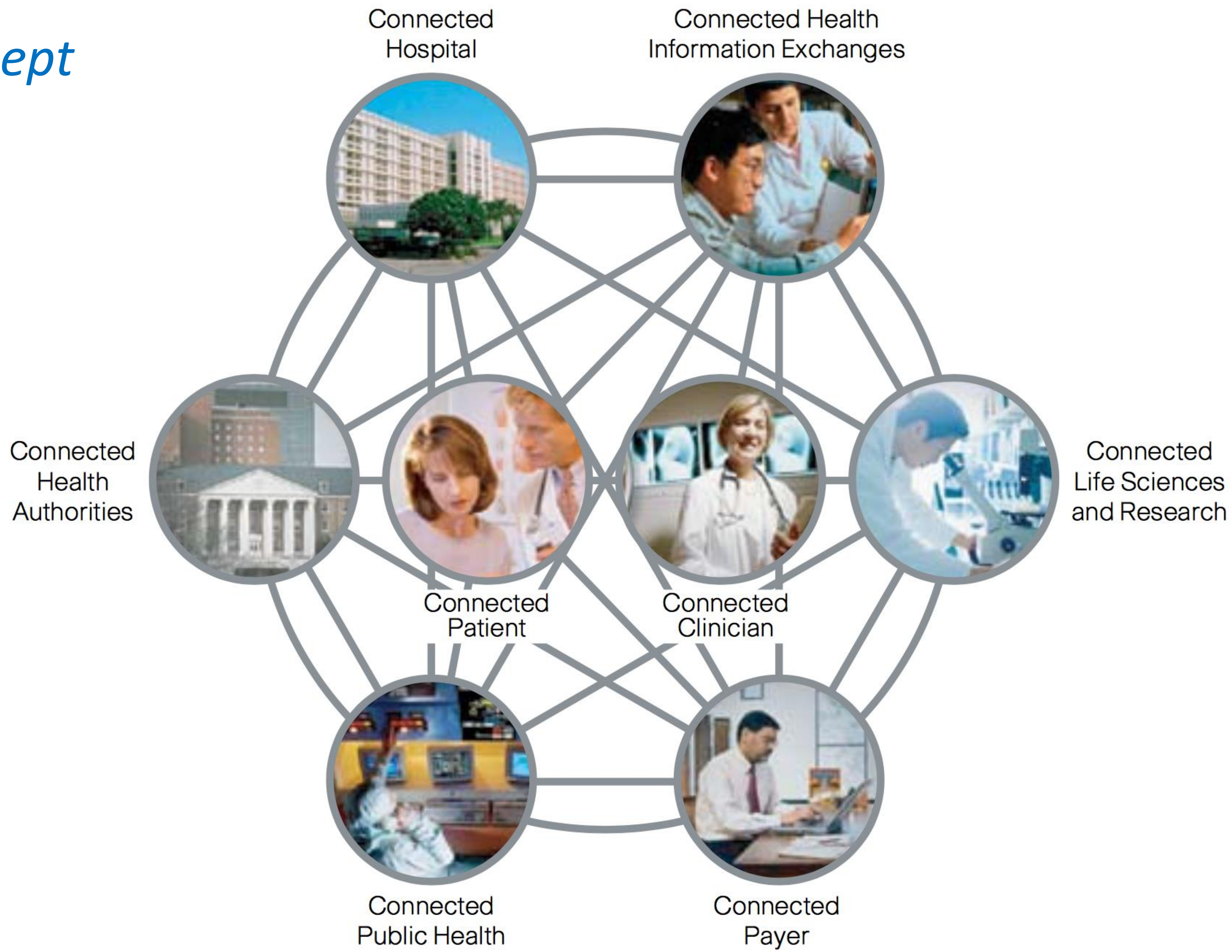


- Rare immunological and auto-inflammatory diseases
- Rare bone diseases
- Rare cancers* and tumours
- Rare cardiac diseases
- Rare connective tissue and musculoskeletal diseases
- Rare malformations and developmental anomalies and rare intellectual disabilities
- Rare endocrine diseases
- Rare eye diseases
- Rare gastrointestinal diseases
- Rare gynaecological and obstetric diseases
- Group on Cancer Control
- Rare haematological diseases
- Rare craniofacial anomalies and ENT (ear, nose and throat) disorders
- Rare hepatic diseases
- Rare hereditary metabolic disorders
- Rare multi-systemic vascular diseases
- Rare neurological diseases
- Rare neuromuscular diseases
- Rare pulmonary diseases
- Rare renal diseases
- Rare skin disorders
- Rare urogenital diseases

*Note: The networking of rare cancers is currently under discussion in EC Expert

European Reference Networks

The ERN Concept



Approved ERNs

European
Reference
Networks

1. ERN BOND	European Reference Network on Rare Bone Disorders
2. ERN CRANIO	European Reference Network on Rare craniofacial anomalies and ENT disorders
3. Endo-ERN	European Reference Network on Rare Endocrine Conditions
4. ERN EpiCARE	European Reference Network on Rare and Complex Epilepsies
5. ERKNet	European Rare Kidney Diseases Reference Network
6. ERN RND	European Reference Network on Rare Neurological Diseases
7. ERNICA	European Reference Network on Rare inherited and congenital anomalies
8. ERN LUNG	European Reference Network on Rare Respiratory Diseases
9. ERN Skin	European Reference Network on Rare and Undiagnosed Skin Disorders
10. ERN EURACAN	European Reference Network on Rare Adult Cancers (solid tumours)
11. ERN EuroBloodNet	European Reference Network on Rare Haematological Diseases
12. ERN EURO-NMD	European Reference Network for Rare Neuromuscular Diseases
13. ERN EYE	European Reference Network on Rare Eye Diseases
14. ERN GENTURIS	European Reference Network on Genetic Tumour Risk Syndromes
15. ERN GUARD-HEART	European Reference Network on Uncommon And Rare Diseases of the HEART
16. ERN ITHACA	European Reference Network on Rare Congenital Malformations and Rare Intellectual Disability
17. MetabERN	European Reference Network for Rare Hereditary Metabolic Disorders
18. ERN PaedCan	European Reference Network for Paediatric Cancer (haemato-oncology)
19. ERN RARE-LIVER	European Reference Network on Rare Hepatological Diseases
20. ERN ReCONNET	Rare Connective Tissue and Musculoskeletal Diseases Network
21. ERN RITA	Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases Network
22. ERN TRANSPLANT-CHILD	European Reference Network on Transplantation in Children
23. VASCERN	European Reference Network on Rare Multisystemic Vascular Diseases
24. ERN eUROGEN	European Reference Network on Rare and Complex Urogenital Diseases and Conditions

EUROPEAN REFERENCE NETWORKS

European
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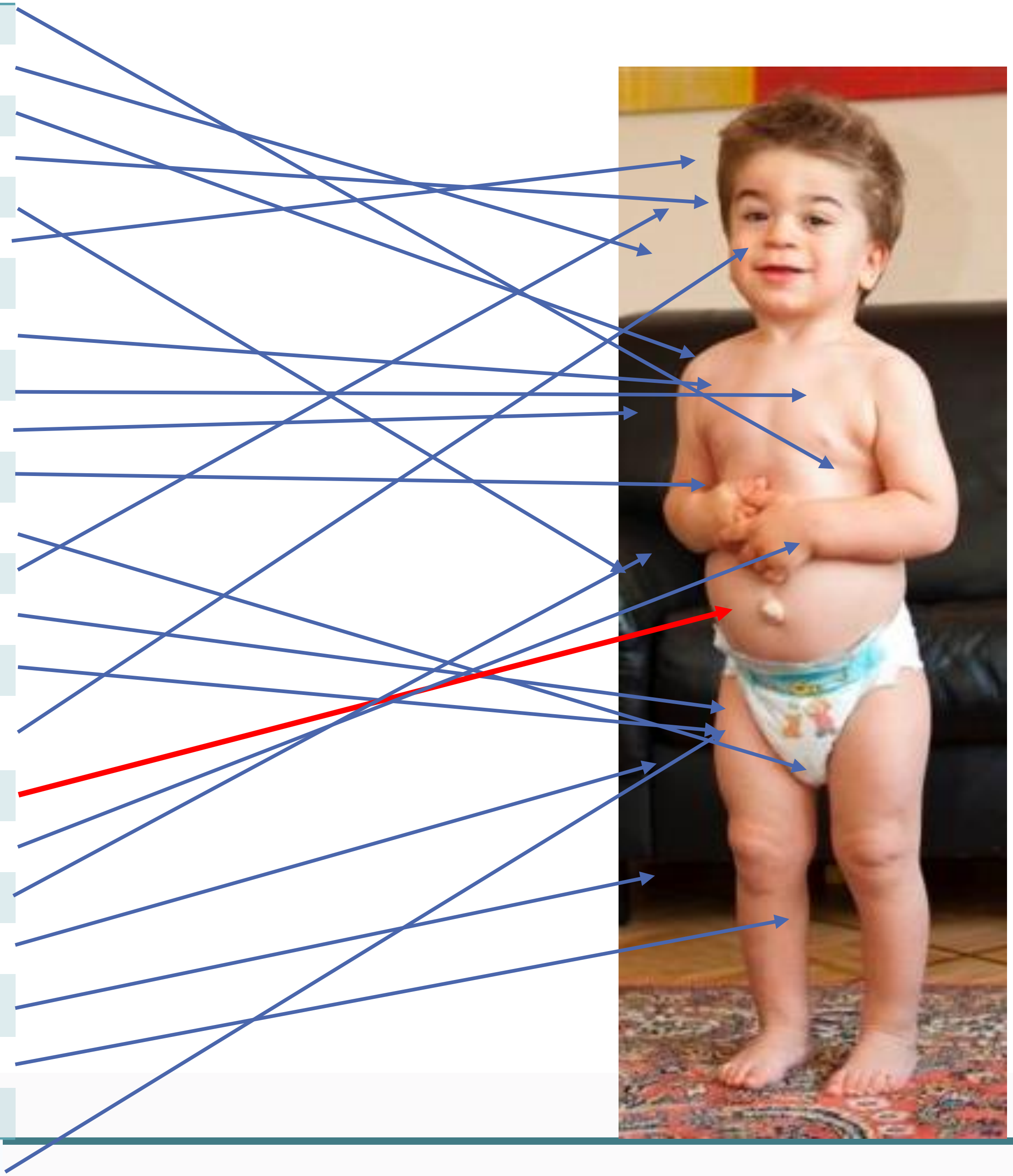
Networks



1. ERN BOND
2. ERN CRANIO
3. Endo-ERN
4. ERN EpiCARE
5. ERKNet
6. ERN RND
7. ERNICA
8. ERN LUNG
9. ERN Skin
10. ERN EURACAN
11. ERN EuroBloodNet
12. ERN EURO-NMD
13. ERN EYE
14. ERN GENTURIS
15. ERN GUARD-HEART
16. ERN ITHACA
17. MetabERN
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20. ERN ReCONNET
21. ERN RITA
22. ERN TRANSPLANT-CHILD
23. VASCERN
24. ERN eUROGEN

Wraith JE, Clarke JTR. In: *Physician's Guide to the Treatment and Follow-up of Metabolic Diseases*. 2006:203.

European Reference Networks Conference

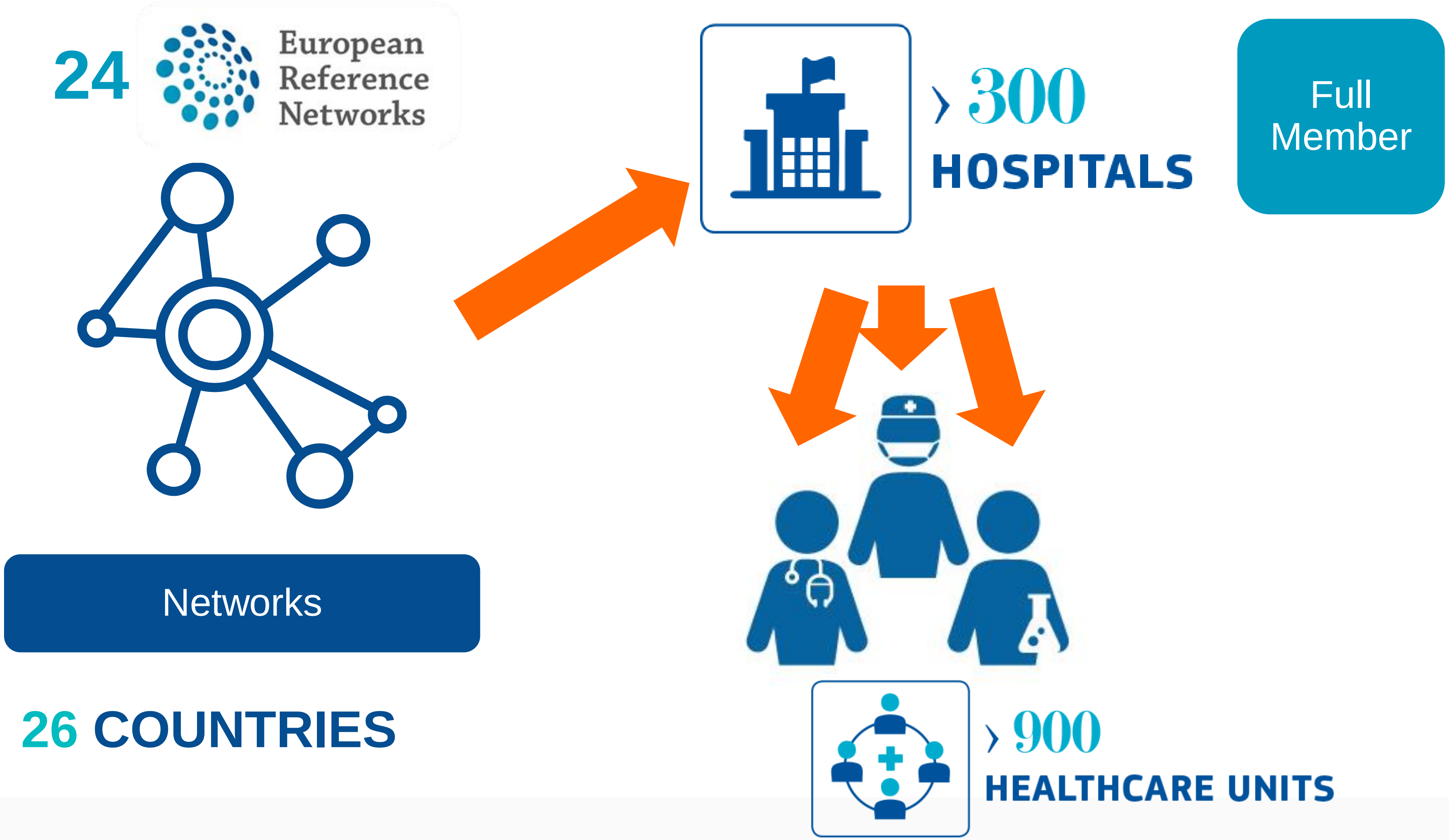
& ERN Kick-off meeting

Vilnius, Lithuania, 9-10 March 2017

EUROPEAN REFERENCE NETWORKS

VILNIUS: EUROPEAN REFERENCE NETWORK AWARD

Coordination is important since ...



24 European Reference Networks

Networks

26 COUNTRIES

› 300
HOSPITALS

Full Member

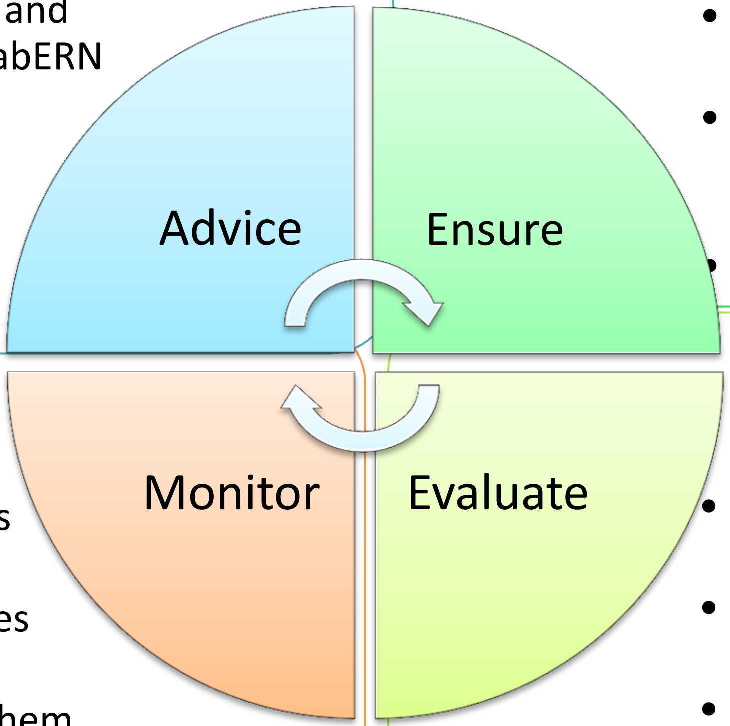
› 900
HEALTHCARE UNITS

Kindly from E. Terol

European
Reference
Networks

MEMBER STATES	No. ERNS	No. HOSPITALS	No. HCP	MEMBER STATES	No. ERNS	No. HOSPITALS	NUMBER HCP
ITALY	23	66	186	**BULGARIA**	6	6	7
FRANCE	ALL	38	111	**ROMANIA**	6	6	7
GERMANY	23	42	121	**SLOVENIA**	9	3	9
UK	22	35	112	**ESTONIA**	3	2	3
NETHERLANDS	ALL	13	90	**CROATIA**	2	1	2
BELGIUM	19	10	36	**AUSTRIA**	2	1	2
SPAIN	19	16	42	**NORWAY**	3	2	3
CZECH REPUBLIC	18	8	28	**IRELAND**	3	1	3
SWEDEN	20	6	30	**LATVIA**	2	1	2
PORTUGAL	16	8	29	**LUXEMBOURG**	1	1	1
POLAND	17	12	21	**CYPRUS**	2	1	2
DENMARK	11	4	20	**MALTA**	-	-	-
FINLAND	12	4	14	**GREECE**	-	-	-
HUNGARY	10	4	12	**SLOVAK REP.**	-	-	-
LITHUANIA	12	2	12	**TOTAL**		293	905

Involvement of Patients



- care is patient-centred
- transparency in quality of care, safety standards, clinical outcomes and treatment options
- planning, assessment and evaluation of the MetabERN

- All ethical issues & concerns for patients are in place
- the performance of the MetabERN.
- Provision of patient perspective
- Methods for feedback and evaluation of patient experience,
- transparency in quality of care, safety standards, CO and treatment options
- Clear planning, assessment and evaluation of the MetabERN

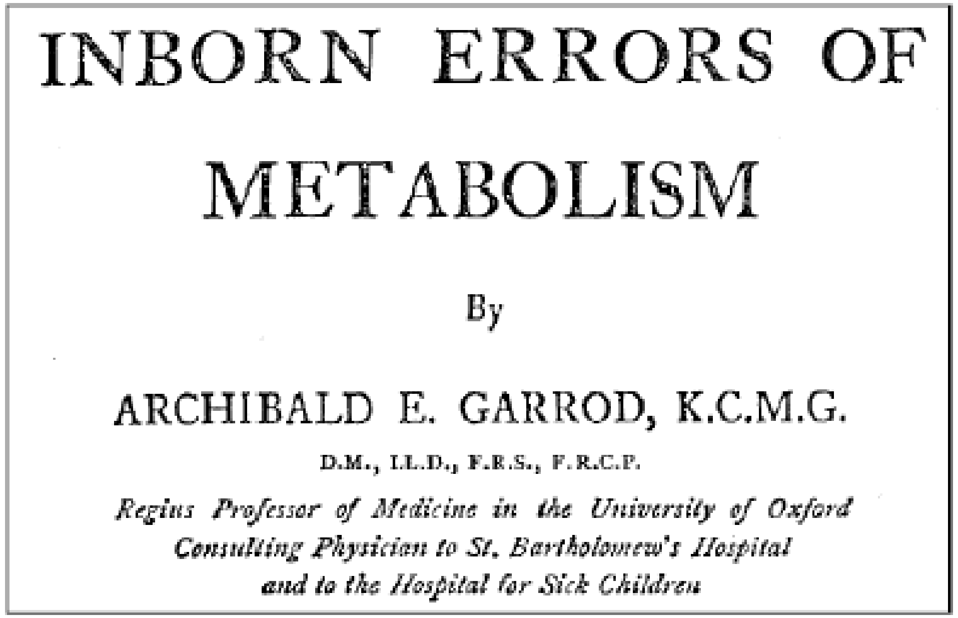
- Patients involvement is ongoing
- patients representatives are equal participant
- Results and act upon them to implement changes and amelioration of the achievements

- Review involvement mechanism regularly
- Incorporate patienst feedback to implement improvements
- Involve patients in the addressing of their specific needs, preferences, priorities (Survey, feedback systems, etc)

The European Reference Network for Hereditary Metabolic Diseases, MetabERN, as an example of a typical ERN.

INBORN ERRORS OF METABOLISM

- Name proposed by Sir ARCHIBALD GARROD in 1908
- Observations about 4 disorders, with recurrence in families:
  Alcaptonuria, Pentosuria, Cystinuria and Albinism
- Investigated urine chemistry as a reflection of systemic metabolism and disease
- In 1923 he wrote his best known work:
  „INBORN ERRORS OF METABOLISM“



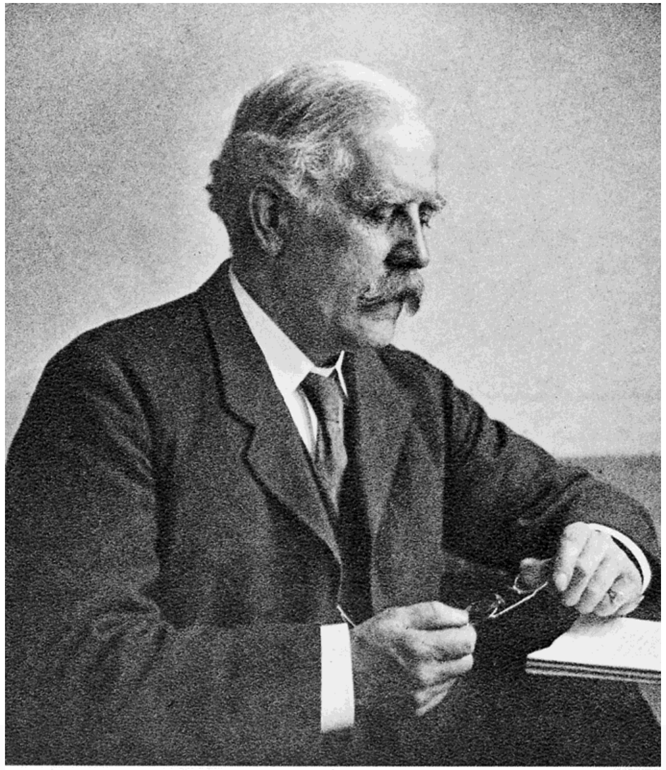
INBORN ERRORS OF
METABOLISM

By

ARCHIBALD E. GARROD, K.C.M.G.

D.M., LL.D., F.R.S., F.R.C.P.

Regius Professor of Medicine in the University of Oxford
Consulting Physician to St. Bartholomew's Hospital
and to the Hospital for Sick Children

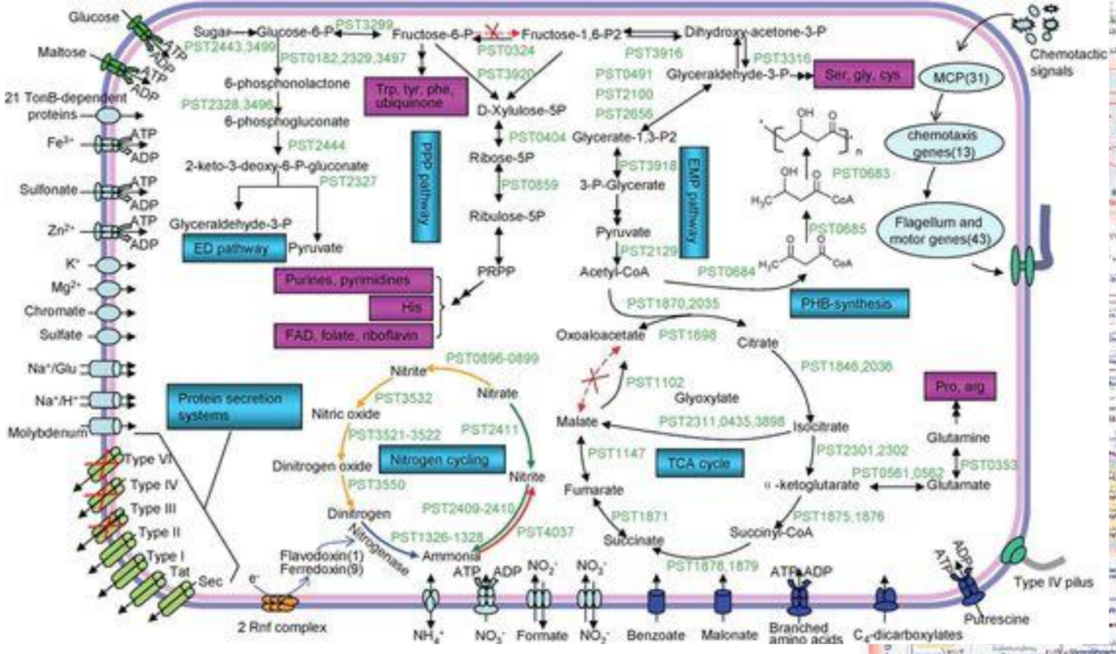


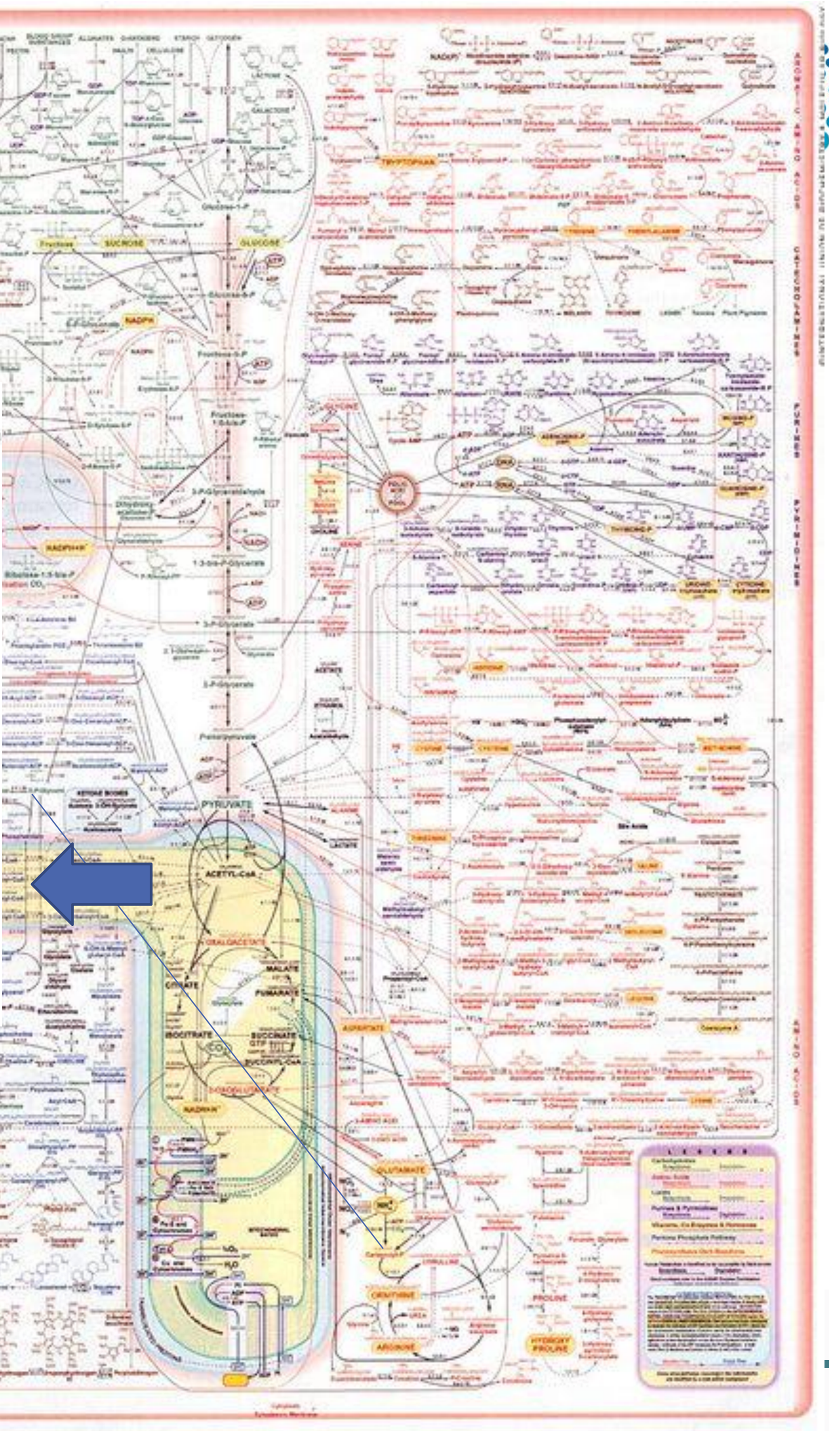
(1856-1937)

A.E. Garrod.

European
Reference
Networks

METABOLISM TODAY
>700 diseases





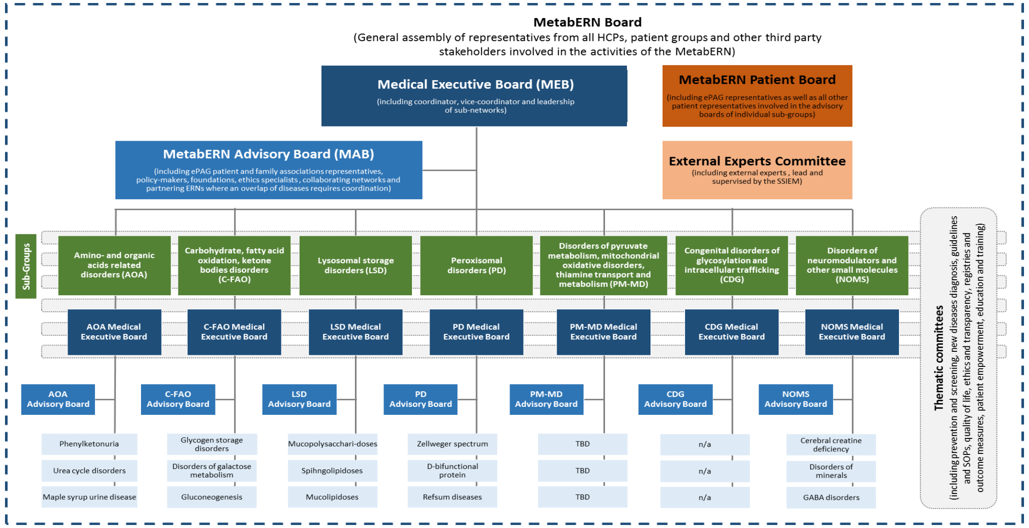
About 60%: CNS involvement/epilepsy
About 30%: Skeletal problems
About 30%: Liver Involvement
About 30%: Cardiological problems
About 25%: Kidney problems

MetabERN: ERN on HEREDITARY METABOLIC DISEASES

Coordinator

Prof. Maurizio Scarpa MD PhD

Helios Dr. Horst Schmidt Kliniken Wiesbaden,



MetabERN Board
(General assembly of representatives from all HCPs, patient groups and other third party stakeholders involved in the activities of the MetabERN)

Medical Executive Board (MEB)
(including coordinator, vice-coordinator and leadership of sub-networks)

MetabERN Patient Board
(including ePAG representatives as well as all other patient representatives involved in the advisory boards of individual sub-groups)

MetabERN Advisory Board (MAB)
(including ePAG patient and family associations representatives, policy-makers, foundations, ethics specialists , collaborating networks and partnering ERNs where an overlap of diseases requires coordination)

External Experts Committee
(including external experts , lead and supervised by the SSIEM)

Sub-Groups

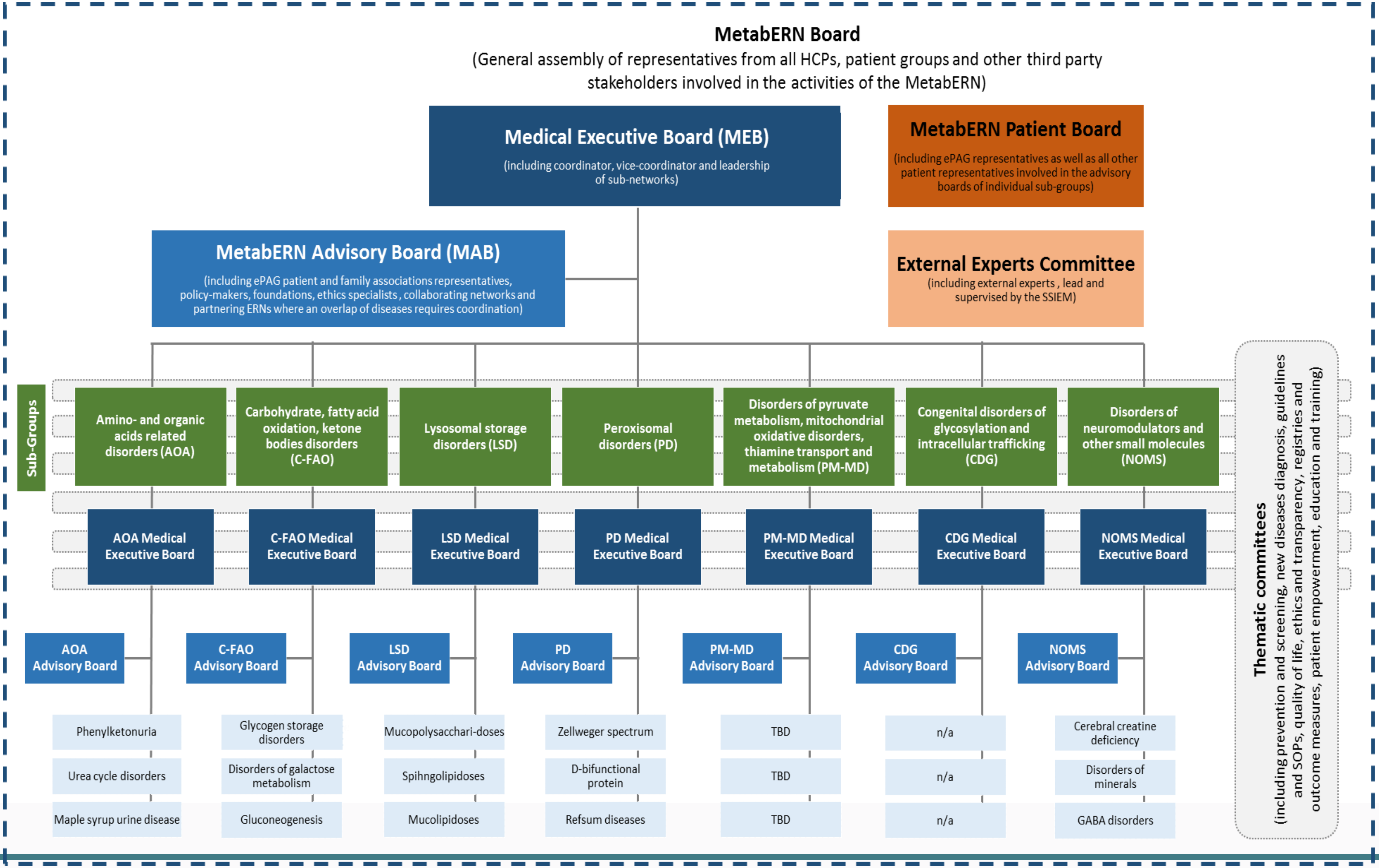
Amino- and organic acids related disorders (AOA)	Carbohydrate, fatty acid oxidation, ketone bodies disorders (C-FAO)	Lysosomal storage disorders (LSD)	Peroxisomal disorders (PD)	Disorders of pyruvate metabolism, mitochondrial oxidative disorders, thiamine transport and metabolism (PM-MD)	Congenital disorders of glycosylation and intracellular trafficking (CDG)	Disorders of neuromodulators and other small molecules (NOMS)
AOA Medical Executive Board	C-FAO Medical Executive Board	LSD Medical Executive Board	PD Medical Executive Board	PM-MD Medical Executive Board	CDG Medical Executive Board	NOMS Medical Executive Board
AOA Advisory Board	C-FAO Advisory Board	LSD Advisory Board	PD Advisory Board	PM-MD Advisory Board	CDG Advisory Board	NOMS Advisory Board
Phenylketonuria	Glycogen storage disorders	Mucopolysacchari-doses	Zellweger spectrum	TBD	n/a	Cerebral creatine deficiency
Urea cycle disorders	Disorders of galactose metabolism	Spihngolipidoses	D-bifunctional protein	TBD	n/a	Disorders of minerals
Maple syrup urine disease	Gluconeogenesis	Mucolipidoses	Refsum diseases	TBD	n/a	GABA disorders

Thematic committees
(including prevention and screening, new diseases diagnosis, guidelines and SOPs, quality of life, ethics and transparency, registries and outcome measures, patient empowerment, education and training)

1) ***Aminoacid and organic acids related disorders***
2) ***Disorders of pyruvate metabolism, Krebs cycle defects, mitochondria oxidative phosphorylation disorders, disorders of thiamine transport an metabolism***
3) ***Charbohydrate, fatty acid oxidation and ketone bodies disorders***
4) ***Lysosomal disorders***
5) ***Peroxisomal and lipid related disorders)***
6) ***Congenital disorders of glycosylation and disorders of intracellular trafficking***
7) ***Disorders of Neuromodulators and Small Moleculel***

BE	BG	CZ	DE	DK	ES	FR	HR	HU	IT	LT	NL	NO	PL	PT	SE	SI	UK
6	1	1	10	1	5	9	1	1	11	1	5	2	1	5	2	1	6

MetabERN Structure



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- AOA Advisory Board
- Phenylketonuria
- Urea cycle disorders
- Maple syrup urine disease

Carbohydrate, fatty acid oxidation, ketone bodies disorders (C-FAO)
- C-FAO Medical Executive Board
- C-FAO Advisory Board
- Glycogen storage disorders
- Disorders of galactose metabolism
- Gluconeogenesis

Lysosomal storage disorders (LSD)
- LSD Medical Executive Board
- LSD Advisory Board
- Mucopolysacchari-doses
- Spihngolipidoses
- Mucolipidoses

Peroxisomal disorders (PD)
- PD Medical Executive Board
- PD Advisory Board
- Zellweger spectrum
- D-bifunctional protein
- Refsum diseases

Disorders of pyruvate metabolism, mitochondrial oxidative disorders, thiamine transport and metabolism (PM-MD)
- PM-MD Medical Executive Board
- PM-MD Advisory Board
- TBD
- TBD
- TBD

Congenital disorders of glycosylation and intracellular trafficking (CDG)
- CDG Medical Executive Board
- CDG Advisory Board
- n/a
- n/a
- n/a

Disorders of neuromodulators and other small molecules (NOMS)
- NOMS Medical Executive Board
- NOMS Advisory Board
- Cerebral creatine deficiency
- Disorders of minerals
- GABA disorders

Thematic committees

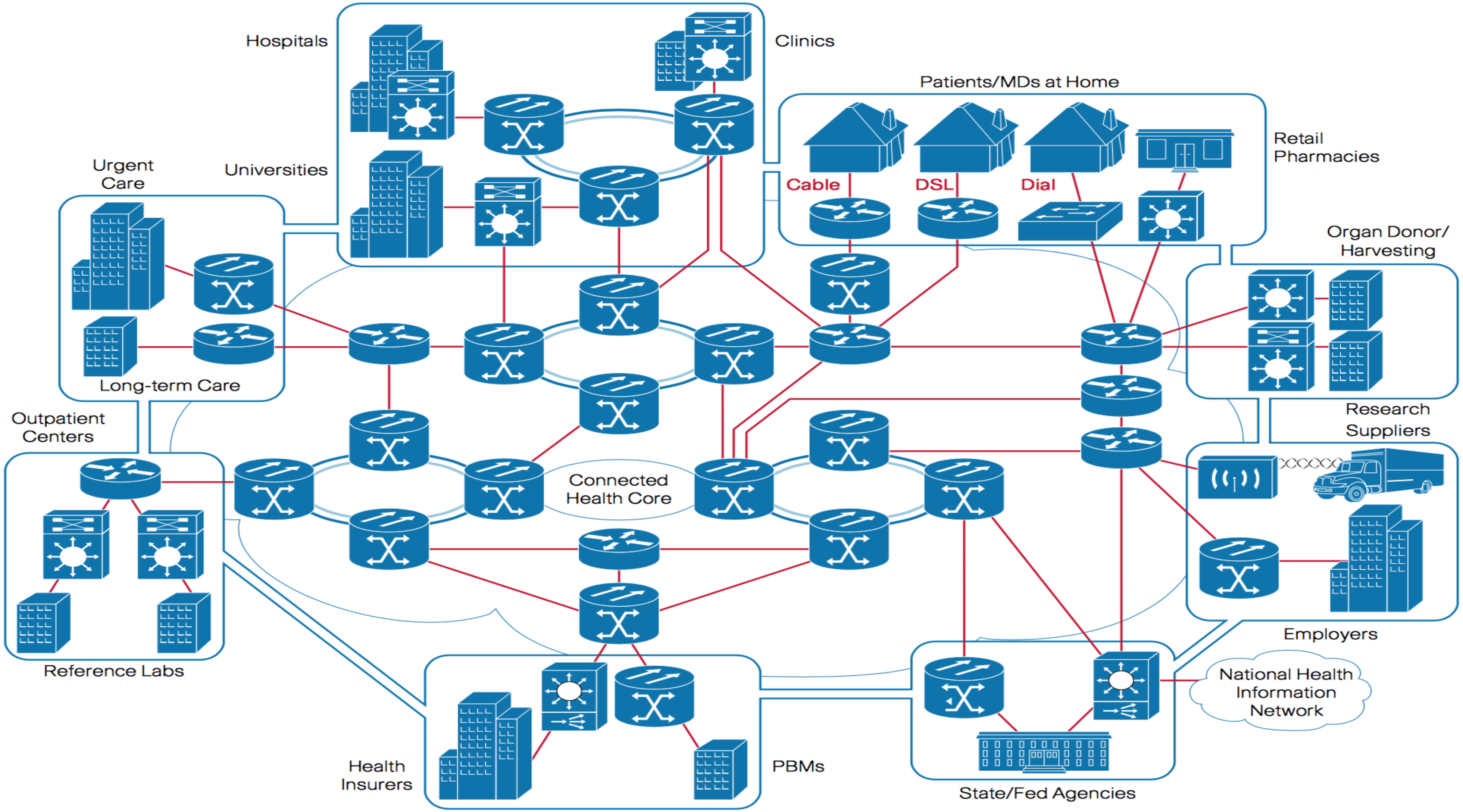
(including prevention and screening, new diseases diagnosis, guidelines and SOPs, quality of life, ethics and transparency, registries and outcome measures, patient empowerment, education and training)

ERN ACTIVITIES

- Prevention and Screening
- Diagnosis/New Diseases Diagnosis
- Epidemiology/Registries and Outcome
- Management/Quality of Life and Transition Guidelines and Pathways
- Virtual Counselling
- Education and Training
- Patient Empowerment
- Clinical Trials
- Research
- Dissemination/Stakeholders Relations

European Reference Networks

One Of The Secrets For Success Of The ERN Crosslinking : The IT Platform



CPMS ACTIVITY

NUMBER OF USERS REGISTERED			
this month	64	Total	786

NUMBER OF ACTIVE USERS			
This month	174	Total	891

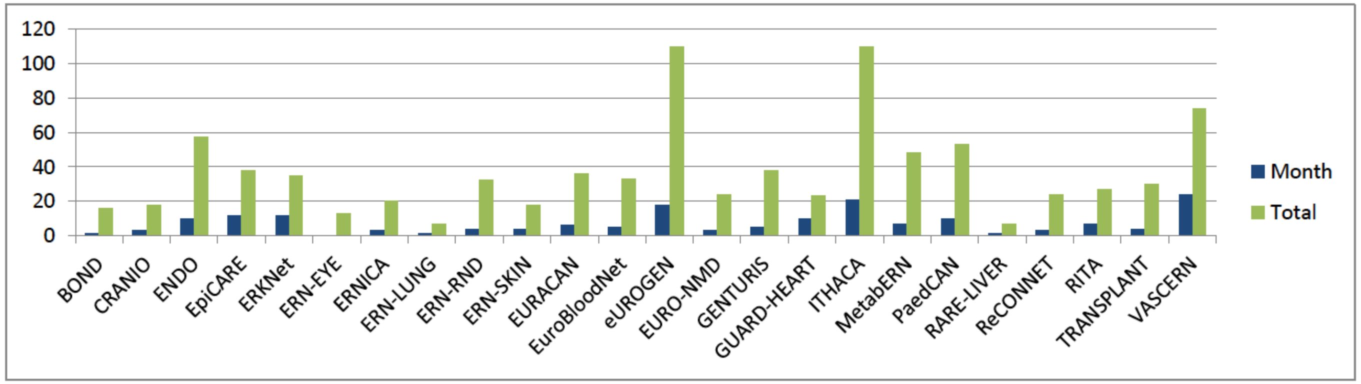
*Total Active users = Sum of active users/Month

NUMBER OF CREATED PANELS*			
This month	16	Total	127

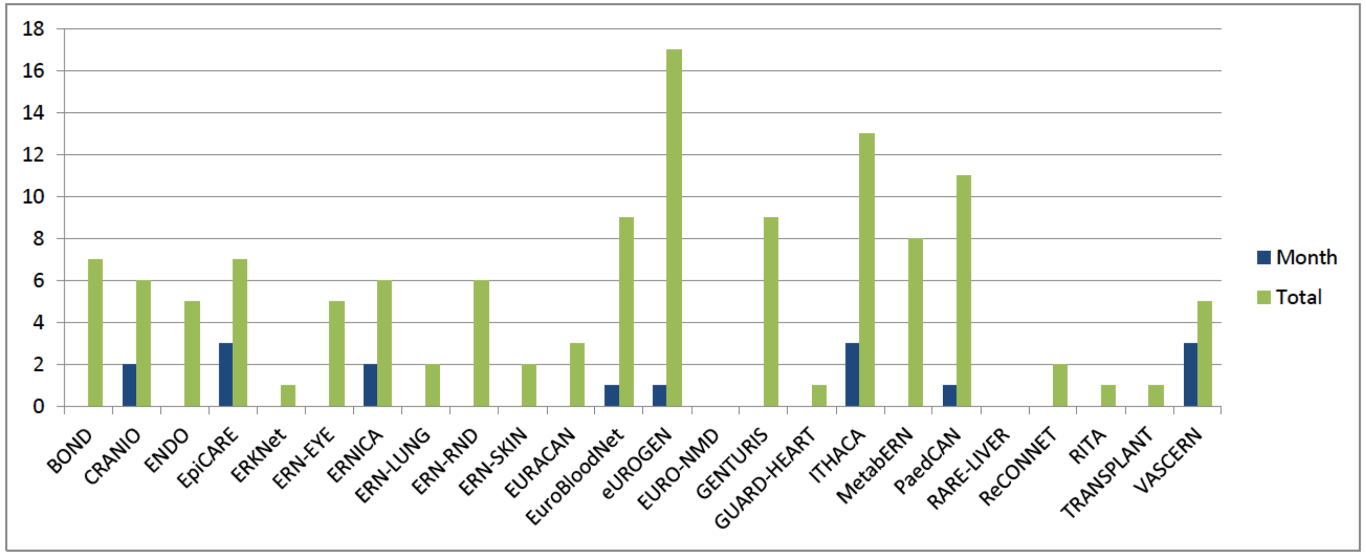
*at various phases of aborted, open, panel selection, assessment, sign-off, closed and archived

NUMBER OF PANELS CLOSED/ARCHIVED			
This month	4	Total	17

ACTIVE USERS/ ERN



PANELS /ERN



European Reference Networks

The ERN Coordinators Group

Chair: Maurizio Scarpa, MetabERN
Vice-Chair: Franz Schäfer, ERKNET
Board: WG Coordinators

WG	LEADERSHIP
IT & DATA-SHARING	Ruth Ladenstein, ERNPaedcan
RESEARCH	Eduardo López Granados, ERN TransplantChild
LEGAL ASPECTS, DATA PROTECTION & ETHICS	Nicoline Hoogerbrugge, GENTURIS
CROSS-BORDER HEALTHCARE AND BUSINESS CONTINUITY	Holm Graessner, ERN-RND; Kate Bushby, EURO NMD
MONITORING & ASSESSMENT	Christopher Chapple, EUROGEN
GUIDELINES, EDUCATION, TRAINING	Paolo Casali, ERN EURACAN
SPECIAL PROJECTS: NHS INTEGRATION SUSTAINABILITY	Maurizio Scarpa, MetabERN

European
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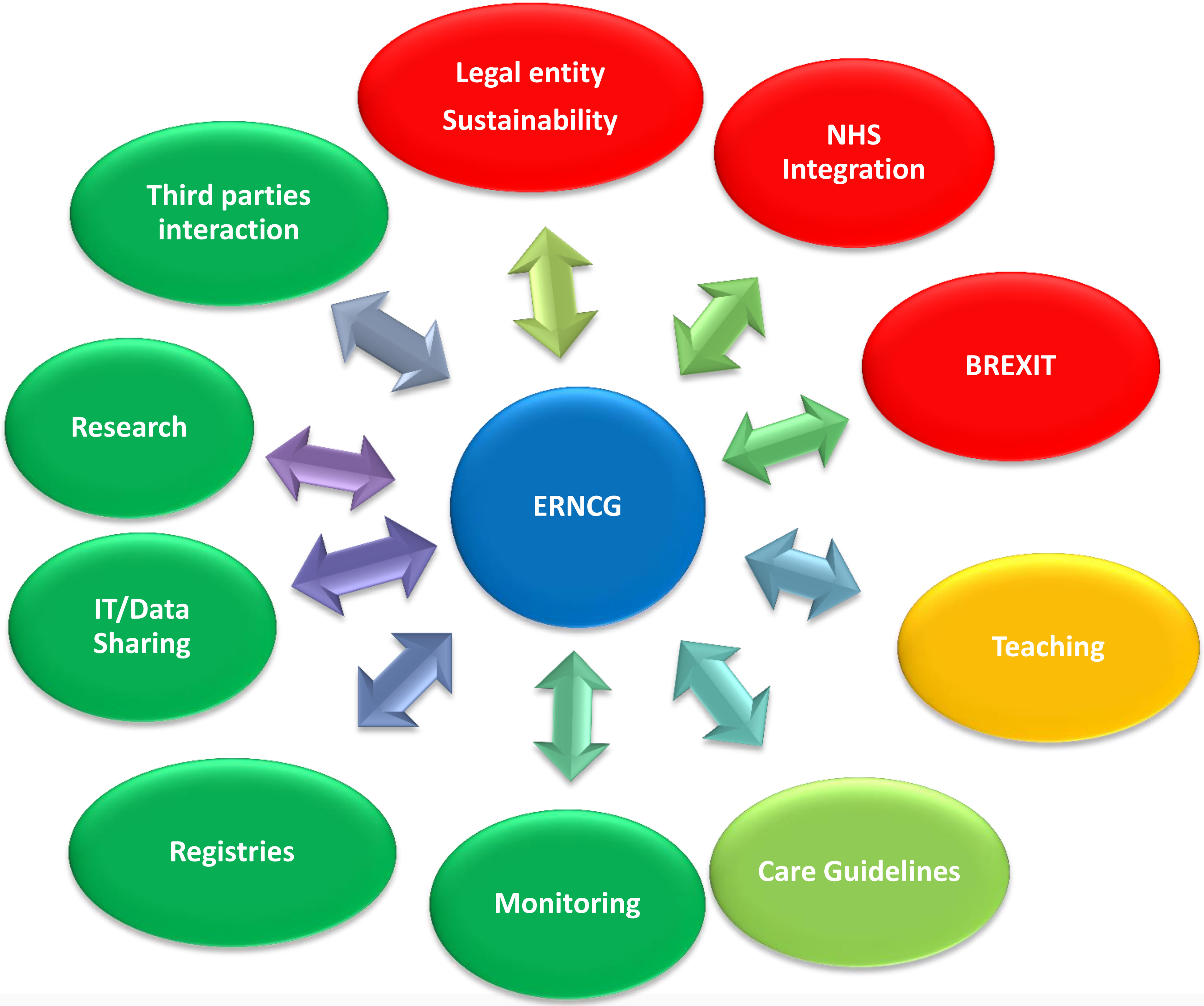
Achievements



Legal entity

Sustainability

NHS Integration

BREXIT

Teaching

Care Guidelines

Monitoring

Registries

IT/Data Sharing

Research

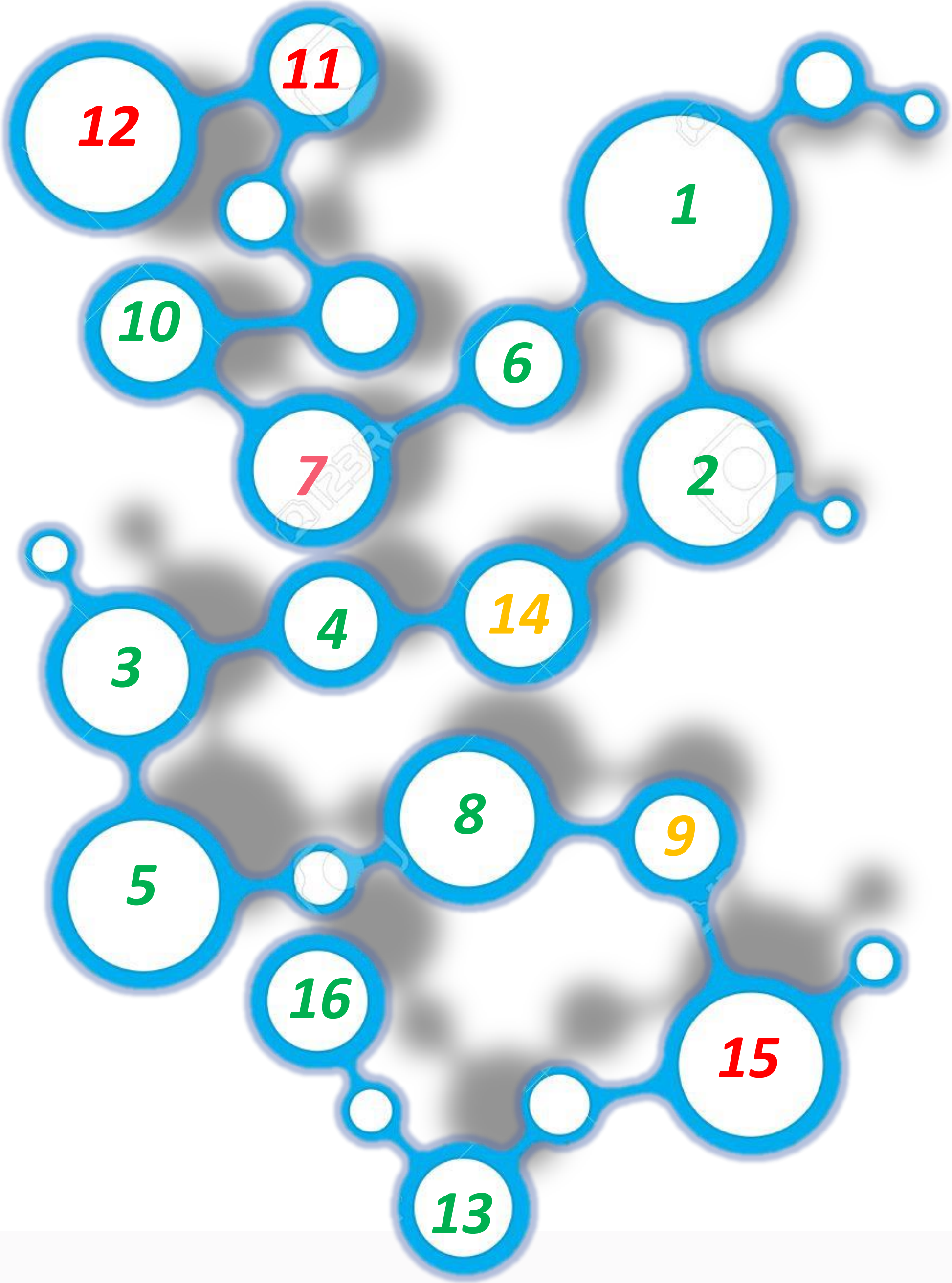
Third parties interaction

ERNCG

European Reference Networks

The ERN Interactome: Coordination of the Activities

1. ERNs COORDINATION
2. PATIENT COMMITMENT
3. DISEASE IDENTIFICATION
4. REGISTRY
5. DATA SHARING
6. COMUNICATION/AWARENESS
7. EDUCATION
8. **SHARED VIRTUAL COUNSELLING**
9. NETWORK OF SPECIALISTS
10. INSTITUTIONAL STAKEHOLDERS
11. PAYERS
12. NATIONAL HEALTH SYSTEMS/NPRD
13. RESEARCH COORDINATION
14. GUIDELINES/PATIENT PATHWAYS
15. STANDARD OPERATING PROCEDURES
16. QUALITY INDICATORS



THE ERN INTERACTOME 2016

1. ERNs COORDINATION
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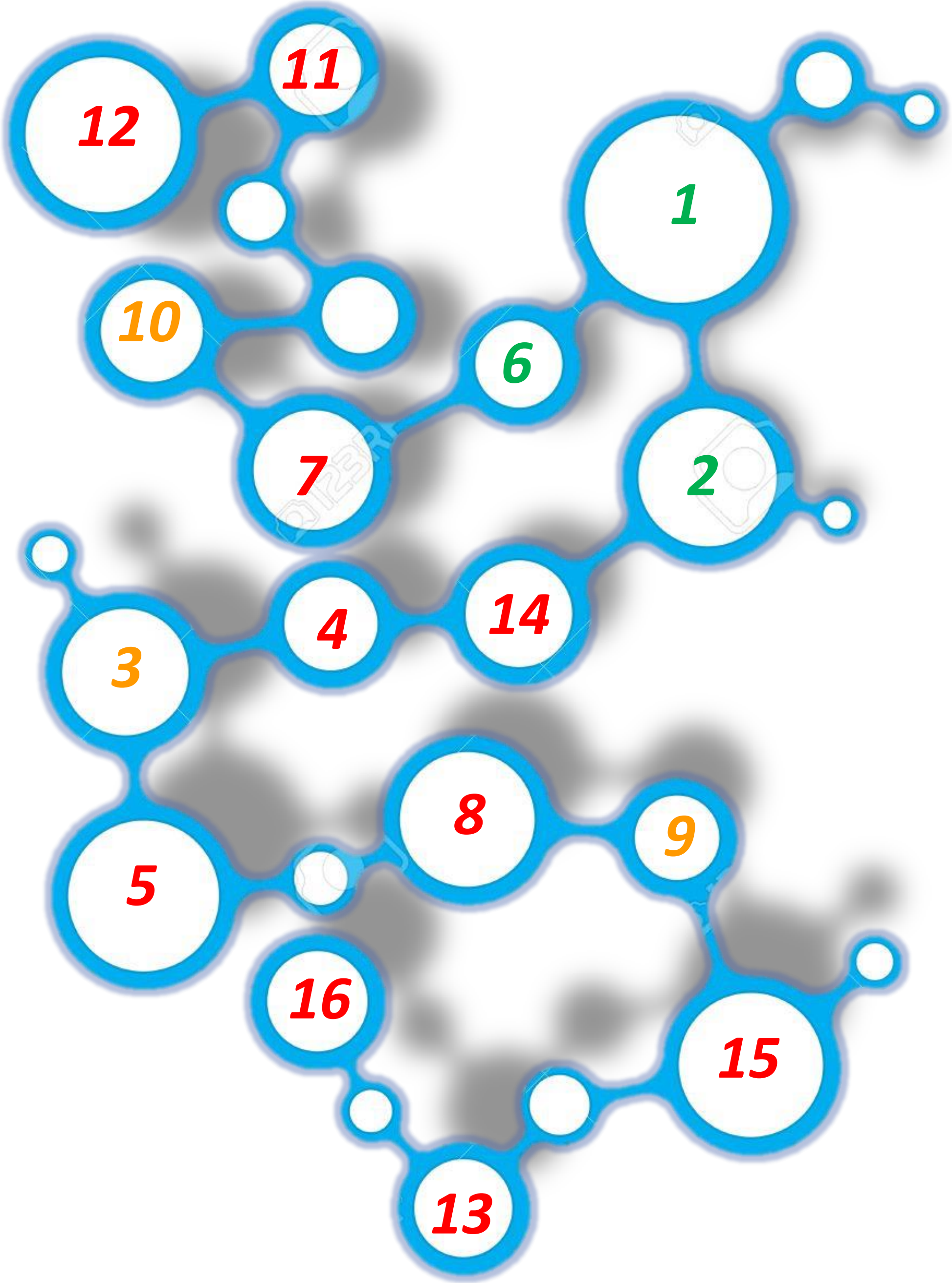
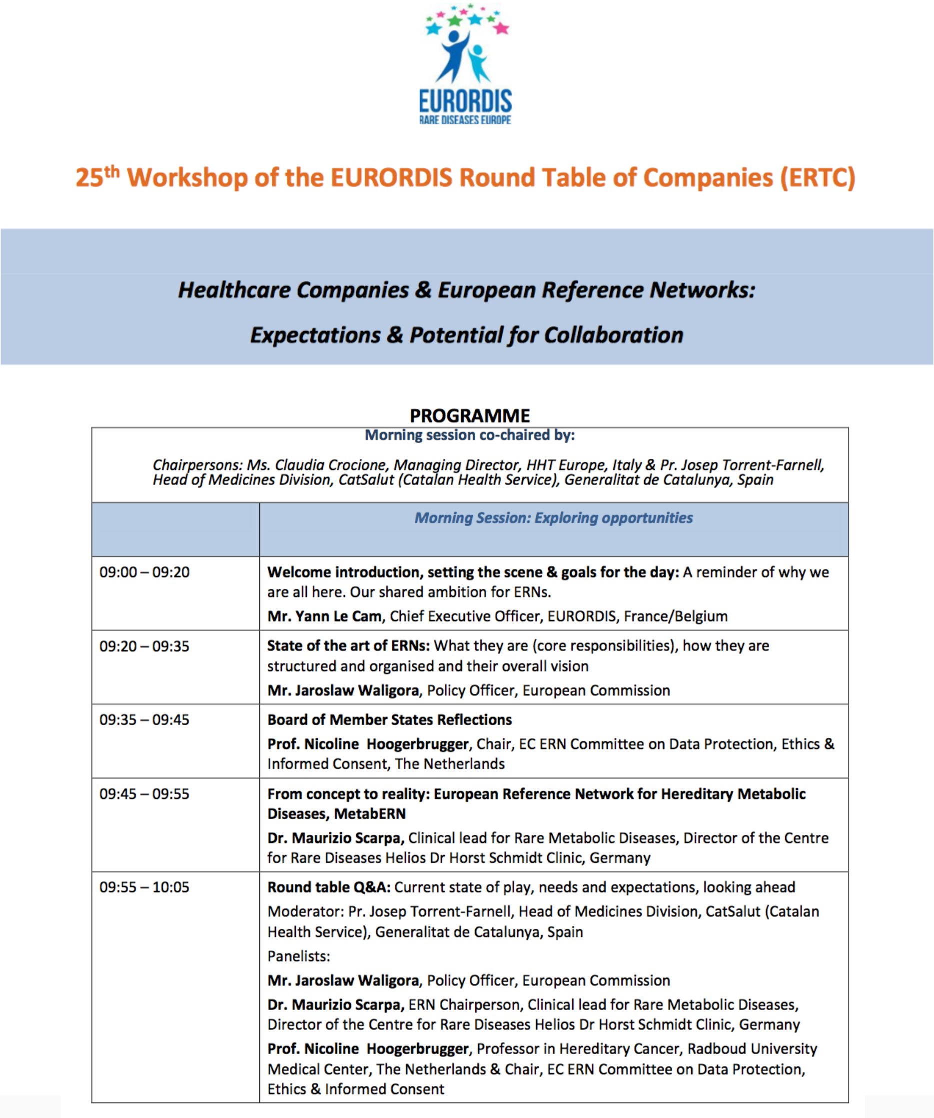


Work in Progress for the Coordinators

- Continuous collaboration with the BoMS Representatives
- Sustainability of the ERNs
- Integration into the National Health Systems
- Legal entity of the ERNs
- Reimbursement of the ERN activities
- Liability of Coordinators/ recognition of the Coordinator role

EUROPEAN REFERENCE NETWORKS

European Reference Networks



EURORDIS
RARE DISEASES EUROPE

25th Workshop of the EURORDIS Round Table of Companies (ERTC)

Healthcare Companies & European Reference Networks:

Expectations & Potential for Collaboration

PROGRAMME

Morning session co-chaired by:

Chairpersons: Ms. Claudia Crocione, Managing Director, HHT Europe, Italy & Pr. Josep Torrent-Farnell, Head of Medicines Division, CatSalut (Catalan Health Service), Generalitat de Catalunya, Spain

	Morning Session: Exploring opportunities
09:00 – 09:20	**Welcome introduction, setting the scene & goals for the day:** A reminder of why we are all here. Our shared ambition for ERNs. **Mr. Yann Le Cam**, Chief Executive Officer, EURORDIS, France/Belgium
09:20 – 09:35	**State of the art of ERNs:** What they are (core responsibilities), how they are structured and organised and their overall vision **Mr. Jaroslaw Waligora**, Policy Officer, European Commission
09:35 – 09:45	**Board of Member States Reflections** **Prof. Nicoline Hoogerbrugger**, Chair, EC ERN Committee on Data Protection, Ethics & Informed Consent, The Netherlands
09:45 – 09:55	**From concept to reality: European Reference Network for Hereditary Metabolic Diseases, MetabERN** **Dr. Maurizio Scarpa,** Clinical lead for Rare Metabolic Diseases, Director of the Centre for Rare Diseases Helios Dr Horst Schmidt Clinic, Germany
09:55 – 10:05	**Round table Q&A:** Current state of play, needs and expectations, looking ahead Moderator: Pr. Josep Torrent-Farnell, Head of Medicines Division, CatSalut (Catalan Health Service), Generalitat de Catalunya, Spain Panelists: **Mr. Jaroslaw Waligora**, Policy Officer, European Commission **Dr. Maurizio Scarpa,** ERN Chairperson, Clinical lead for Rare Metabolic Diseases, Director of the Centre for Rare Diseases Helios Dr Horst Schmidt Clinic, Germany **Prof. Nicoline Hoogerbrugger**, Professor in Hereditary Cancer, Radboud University Medical Center, The Netherlands & Chair, EC ERN Committee on Data Protection, Ethics & Informed Consent

European Reference Networks

EUROPEAN HEALTH FORUM GASTEIN

20TH
European Health Forum
Gastein

Health in All Politics –
a better future for Europe

1) WORKSHOP ON PERSONALISED MEDICINE AND RD
2) WORKHOP ON SUSTAINABILITY OF ORPHAN DRUGS
3) WORKSHOP ON BIG DATA
4) MEETING WITH THE COMMISSIONER:
    - LEGAL ENTITY
    - SUSTAINIBILITY

EUROPEAN REFERENCE NETWORKS

SAVE THE DATE

FEB 28 2018

On the occasion of *Rare Diseases Day* on 28 February 2018, the **European Reference Network for Rare Bone Disorders (ERN-BOND)**, together with MEP Elena Gentile, are delighted to invite you to a European Parliamentary Meeting entitled:

European Reference Networks

S&D

EUROPEAN REFERENCE NETWORKS ACCELERATING AND IMPROVING DIAGNOSIS FOR RARE DISEASES PATIENTS

An ERN-BOND White paper on Diagnosis

Keynote speaker: Vytenis Andriukaitis, Commissioner for Health and Food Safety

European Parliament, Brussels
Room A3G2
Wednesday, February 28 2018
13:00 - 15:00

ERNs Are Not A Project But A New New Concept Of Medicine

Rare disease research: European reference networks are off to a good start

Written by **Vytenis Andriukaitis** on 20 February 2018 in **Opinion**

One year on from their launch, the European reference networks are helping patients access treatment and research from across the EU, writes Vytenis Andriukaitis.

Vytenis Andriukaitis | ***Photo credit: Natalie Hill***

THE PARLIAMENT
POLITICS, POLICY AND PEOPLE MAGAZINE

- This way it is the medical knowledge that travels, meaning there is no need for patients to undertake exhausting trips between regions and countries as was often the case in the past.
- In the longer term, I hope to see the ERN model extended to other diseases. I am positive that as we reach a critical mass of patients being analysed, diagnosed and treated, the ERNs will generate more and more research on rare diseases, improving the quality of life of children

European
Reference
Networks

In summary, ERNs represent a major opportunities for ….

Patients

- Optimization of care pathways for patients with rare disease: diagnosis, management access to therapy
- Creation of databases/registries/natural histories of patients in a coordinated way
- Close interaction with family associations which may help logistical challenges associated with conducting trials for small patient population
- Counselling the patients in the understanding the value of the clinical trials
- Possibility of generating studies also for rare patients due to the availability of numbers of patients in a coordinated way
- More effective clinical trial designs that consider the very special and unique circumstances of rare disease research
- Close interaction among ERNs to integrate expertise needed for clinical trials
- Protection of patients from not well designed clinical trials

National Health Systems

- Close contact with regulatory authorities, key opinion leaders, patient advocacy organizations. and non-traditional players, like technology companies, to create a new coordinated way to manage patients affected by rare diseases and optimize access to diagnosis and therapy.
- Impact on the National Health System to spare resources, optimize services and avoid waste of expertise
- Impact on the awareness for rare diseases. Creation of an European epidemiology on rare diseases, common registries, databases, research projects.
- Impact on the awareness for cost of rare diseases. Creation of EU HTAs for the calculation of the cost of the management of patients with rare diseases and prediction of sustainability.
- Impact on the discussion on the sustainability of orphan drugs.
- Interaction with National Health Istitute and Drug agency for postmarketing analysis.

European Reference Networks

Conclusions

- ✓ ERNs are NOT a project or a program, they are a CONCEPT and represent the major achievement of the European spirit of collaboration, sharing and health investement in the field of rare diseases
- ✓ ERNs group the most acknowledged centers of excellence in Europe, all sharing the same level of commitment and interest for rare diseases
- ✓ ERNs are NOT single networks, but rather a critical mass of about 300 hospitals and over 1000 specialised units, cross feeding each other to meet the needs of our patients.
- ✓ Crosslinking is in the nature of the ERNs due to multidisciplinarity implications of the cared diseases.
- ✓ The ERNs´ integration inside the MS National Health Systems/National Plans for Rare Diseases will represent a major achievement for the Cross Border Care
- ✓ The ERNs´/MS National Health Systems/National Plans for Rare Diseases integration is instrumental to define strategies to optimize the cost of management of patients of rare diseases
- ✓ The ERN Coordinators Group is an outstanding instrument for the EC/ National Health Systems/National Plans for Rare Diseases to define a uniform pan-European plan for rare diseases.