Global registries for rare diseases: challenges and solutions

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ORPHAN EUROPE
RECORDATI GROUP

Personal « registry » background

- EuroWilson clinical database to design randomised clinical trials for Wilson's disease
- European registry for intoxication type metabolic diseases
- European registry for homocystinurias and methylation defects
- European cystinosis registry
- Development of post marketing surveillance registries for Orphan Europe: homocystinuria, cystinosis…

Presentation contents

- What is a rare disease? What is a registry?
- Registries in rare diseases
  - Current situation and issues
  - Best scenarios for rare disease registries
  - National, European and global initiatives
- Case study for good rare disease registry collaboration

What is a rare disease?

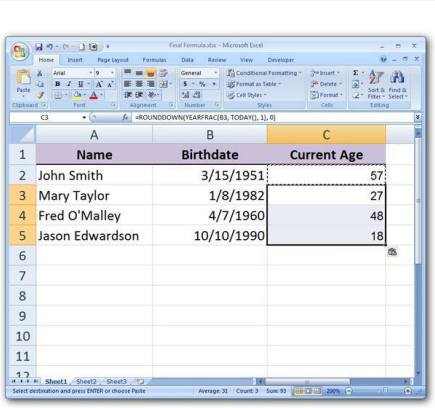
- Definitions (orphan drug regulation)
  - EU: 5 in 10,000, and life-theatening or chronically debilitating
  - US: <200,000
  - Japan, Taiwan, Australia, S.Korea…
- Approximately 7-8000 different rare diseases
- Over 50 million people affected worldwide
- Diagnosis is often delayed
- 75% of rare diseases affect children
- There are certain challenges that all patients and families affected by rare disease share

Research and drug development challenges

- A European orphan drug legislation that is working with 1184 orphan drug designations of which 82 have received Market Authorisation.
- But still thousands of rare diseases with no or inadequate treatment
- Small dispersed patient populations
- Patients are rare – experts are rare
- Variable disease phenotyping
- Limited knowledge, natural history data…
- Wide variation in infrastructures in Europe:
  - access to diagnosis
  - newborn screening programmes
  - clinical practice
  - Treatment

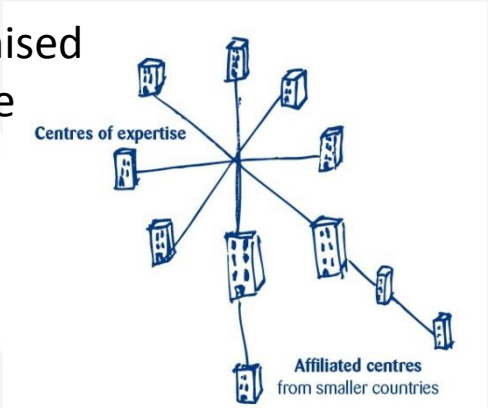
Registry definition

- An organised system that uses observational study methods to collect uniform data (clinical and other)
- Evaluates specified outcomes for a population defined by a particular disease, condition or exposure
- Serves one or more pre-determined scientific, clinical or policy purposes



	A	B	C
1	Name	Birthdate	Current Age
2	John Smith	3/15/1951	57
3	Mary Taylor	1/8/1982	27
4	Fred O'Malley	4/7/1960	48
5	Jason Edwardson	10/10/1990	18

Or an organised multi-centre network



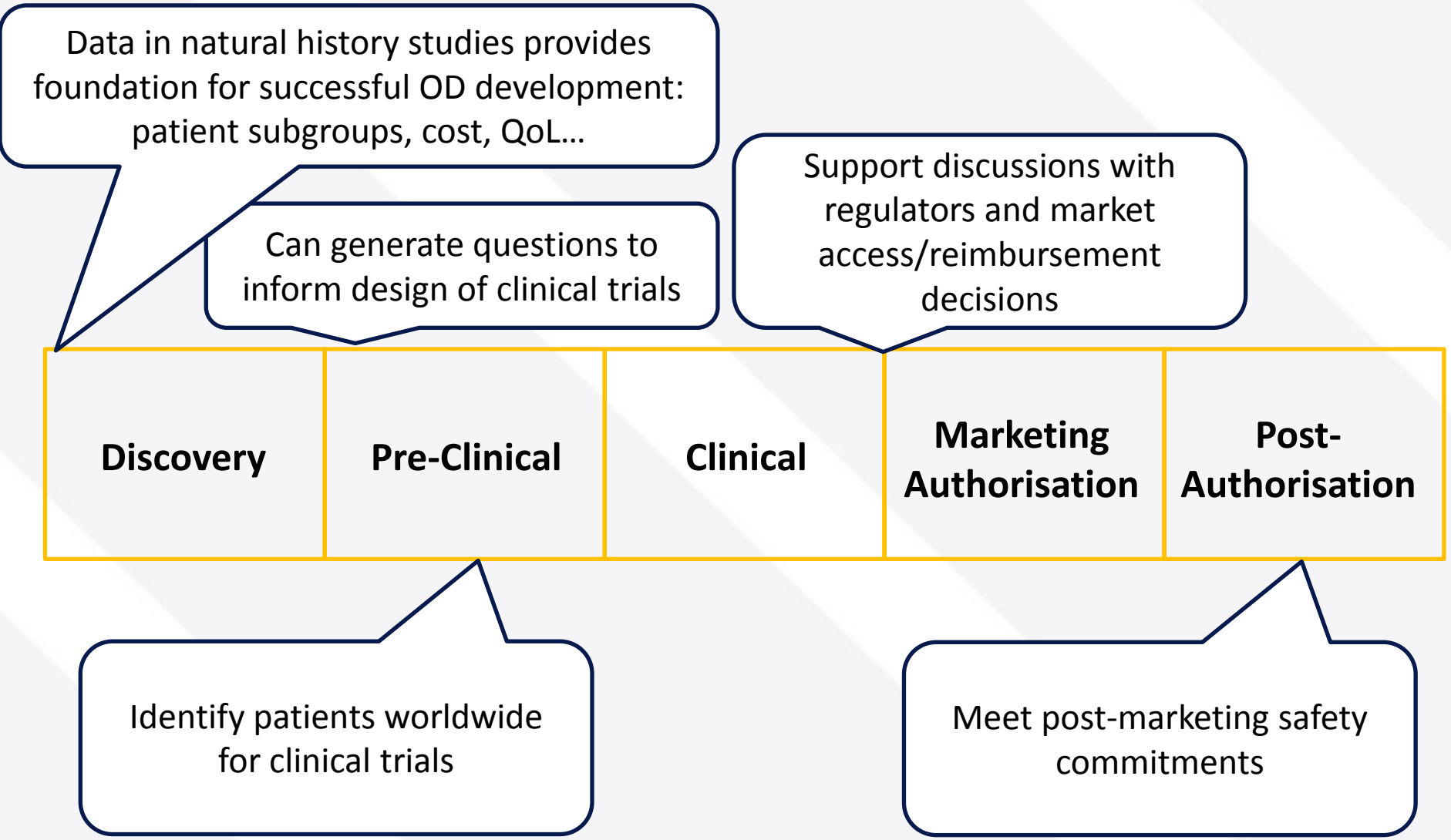
Can be one person with a laptop and no hypothesis

* Adapted from Gliklich RE, Dreyer NA: Registries for Evaluating Patient Outcomes: A User's Guide (2007)

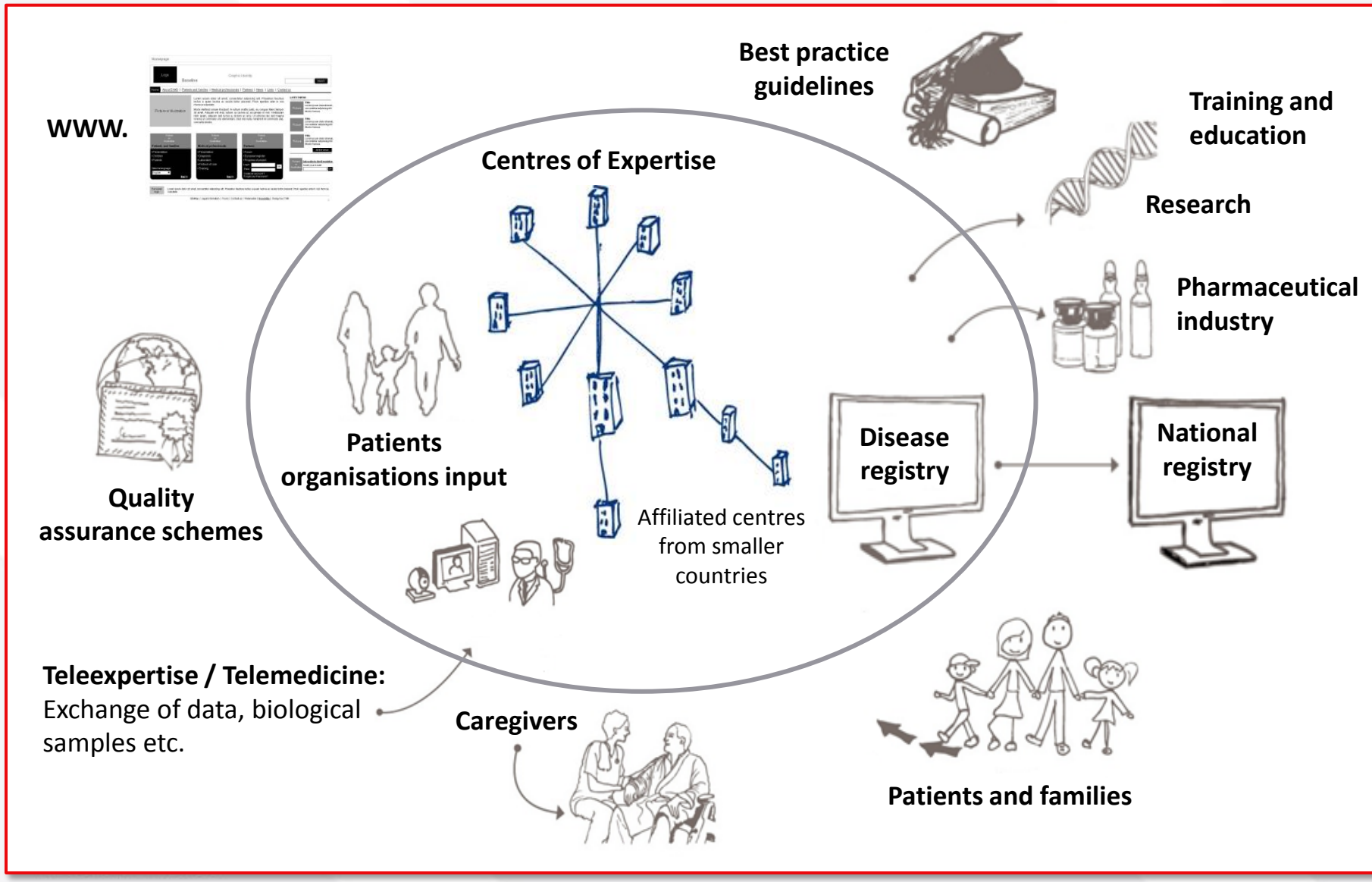
Comparison with Randomised Controlled Trials (RCTs)

	RCT	Registry
Purpose	Controlled experiment	Real world practice and outcomes
Duration	Finite	Often indefinite
Inclusion criteria	Specific	Few inclusion/exclusion criterea
Visits	Per Protocol	HCP Practice
Site visits	Yes	Variable
Patient consent	Yes	Usually
Site honorarium	Substantial	Minimal
Analytic methods	Standard methods	Broader epidemiological methods
Disease characteristics	Homogenous Per Protocol	Heterogeneous, study subpopulations
Treatment Outcomes	Efficacy	Effectiveness

Interest for a registry in each step of the orphan drug pathway

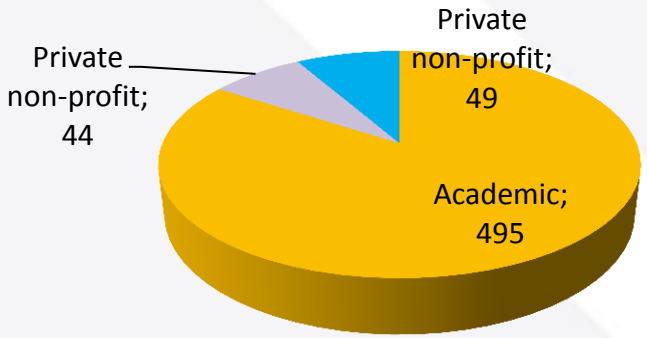


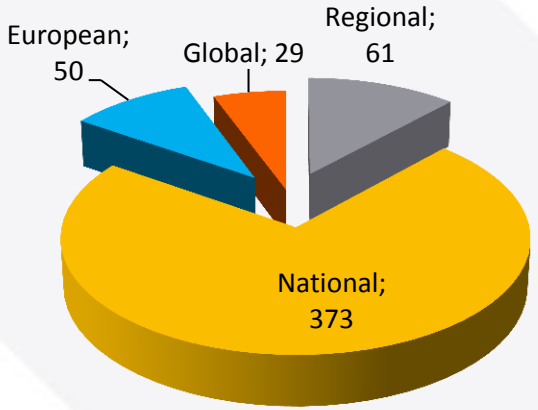
For building a collaborative community of expert physicians

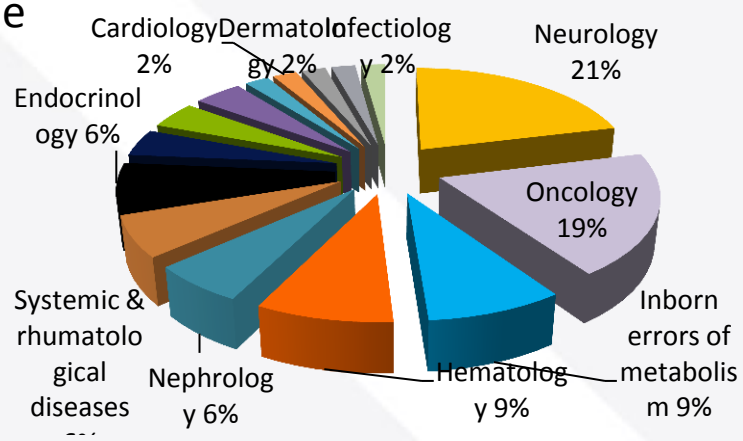


Gowing use of patient registries for rare diseases

- 500 + registries
- Different platforms: no uniform standards
- Work in isolation in different disease areas
- Variable quality of data
- Country specific registries capture different data points in different languages complicating data consolidation
- 40% orphan drugs (ODs) are granted under exceptional circumstances
- Duplication of registries: particularly when multiple ODS
- DG Sanco & DG research have funded 16 & 27 projects for RD including registries
- Non-sustainable funding







Registry priority area in the field of rare diseases and orphan medicines

- Commission communication on Rare Diseases: Europe's challenges (2008)
- Council Recommendation on an action in the field of rare diseases (2009/C 151/02) adopted on 8 June 2009
- Cross-Border Healthcare Directive 2011/24/EU: Personal data exchange
- EUCERD recommendations on rare disease patient registration and data collection
- Collection of data/registries included in national rare disease plans or strategies
- Eurordis, NORD and CORD joint policy paper on registries
- Position paper for multistakeholder, multipurpose RD registries from the EBE-EuropaBio TF on RD and OMP

Share, merge

Compare, research

Across borders

Two levels of data: public health & research

For all rare diseases

Priority to collect national minimum data sets / core data elements

- Measure the **same thing**
  the same way
  across all **rare diseases**
- Requires a **national agreement** to collect uniform data and to supply it as part of the national plan or strategy.

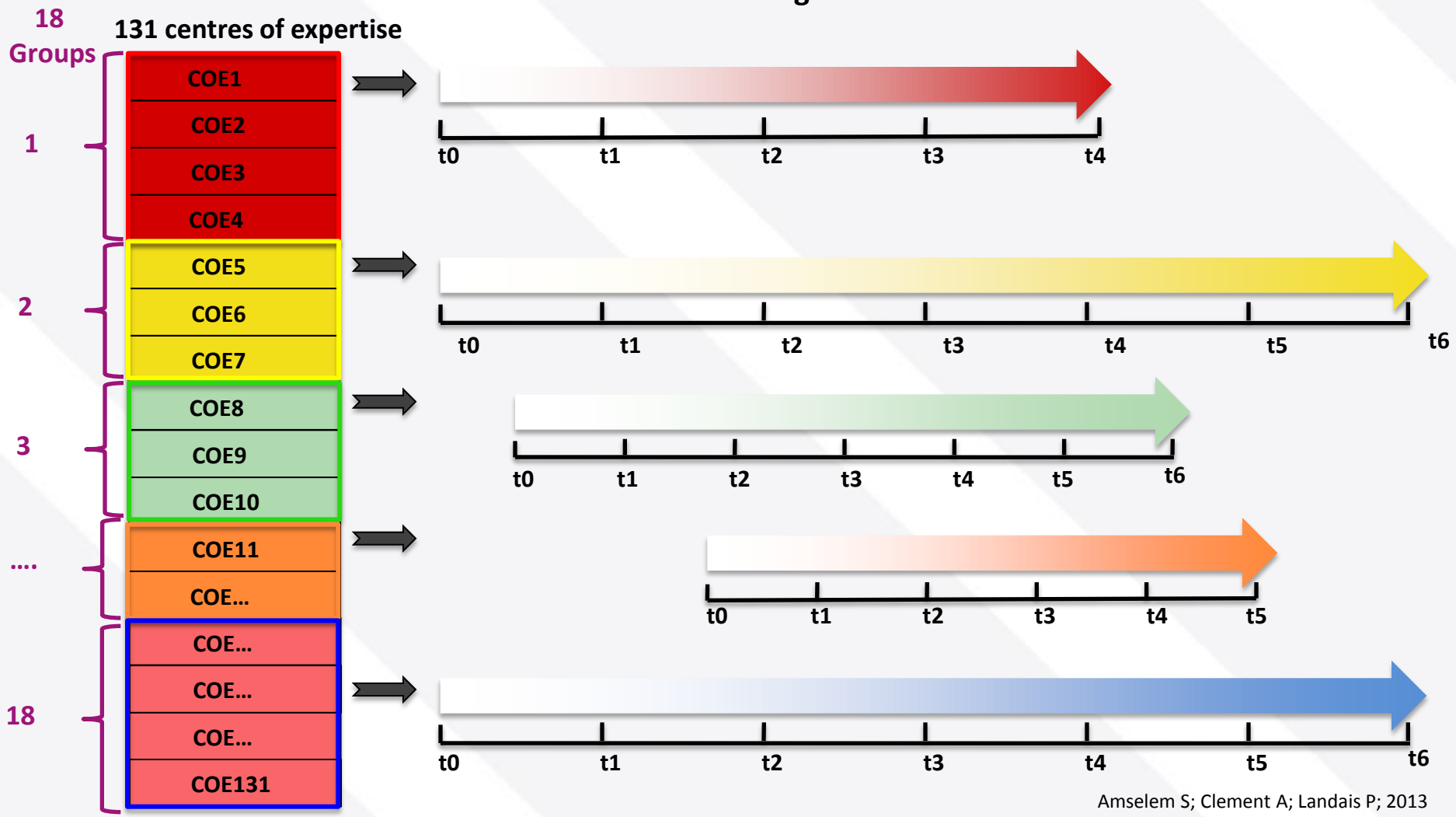
For single diseases and disease groups

Need for individual datasets to address specific research questions

The French experience: a shared information system

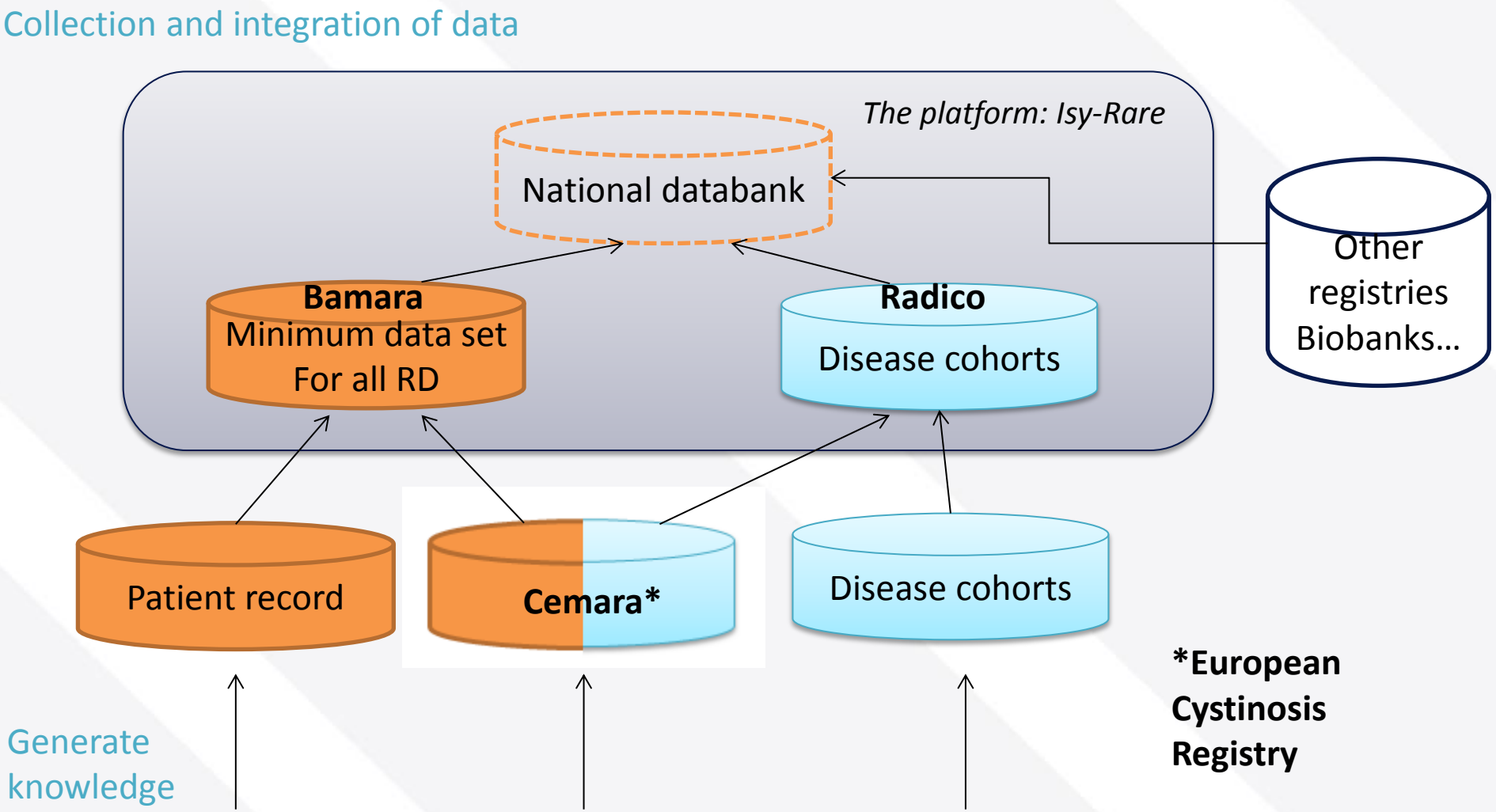
BaMaRa
Public health
Minimum data set for all patients

RaDiCo
Research
Cohorts for single or groups of diseases; longitudinal data collection



Amselem S; Clement A; Landais P; 2013

The French experience: A shared information system



Other national initiatives

- Switzerland: Build up gradually from the funded project Radiz : pilot phase in metabolic diseases. Registry to be included into federal law; example cancers
- USA
- Spain
- Italy
- Bulgaria

European platform for registries

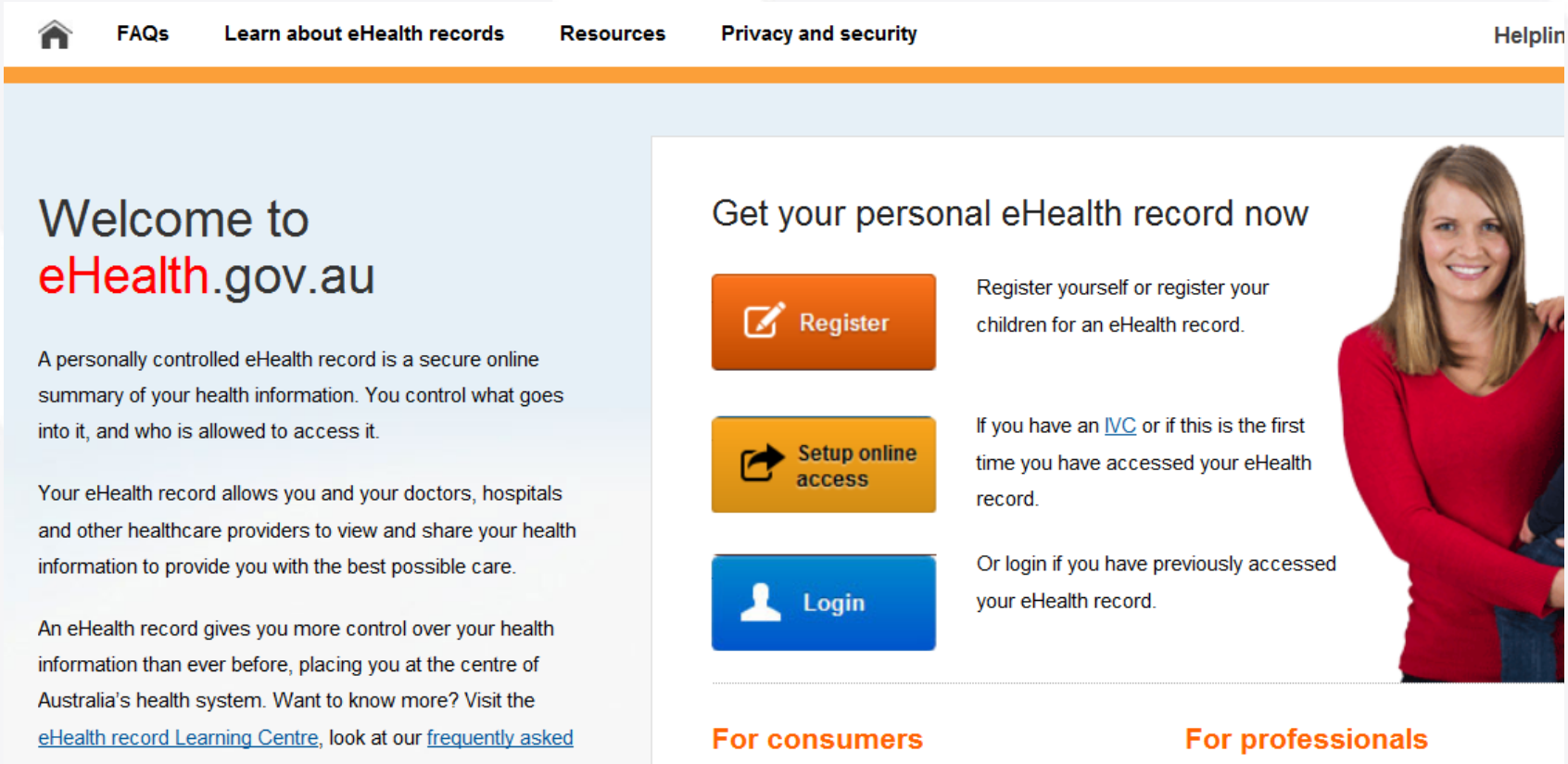
- Hosted by the Joint Research Committee (JRC) and funded by the European Commission DG Sanco

- National minimum datasets → Federation of national platforms
- Platform to support registration
- Platform to direct to sources of data
- Platform of services to registries

- Will not replace the primary sources
  - Except may be for very rare diseases if there is an option for establishing primary data collection
- Will not decrease the cost of data collection and exploitation at primary sources

Electronic health/medical records, big data

- N=all (rather than a biopsy of the system)
- Useful for:
  - Detecting rare side-effects
  - Identify segments of populations that may benefit from drugs…



IRDiRC

INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

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NEW THERAPIES

Objective 2020: 200 new therapies

Disclaimer: the numbers do not reflect IRDiRC initiatives only

IRDiRC registry policy: to support and encourage rare disease research and development of drugs

DECIPHER - a valuable database for researchers and clinicians: Q&A with Dr. Helen Firth

OrphaNews Europe: What was the aim of developing DECIPHER? What were the factors that helped in creating this database? Dr. Helen Firth: The DECIPHER project was conceived as a clinical and research tool to: • Aid in the interpretation of data from genome-wide analyses eg. Differentiation...

Full Article →

IRDiRC delivers a successful and inspiring conference: a common goal emphasised

The first IRDiRC conference was held on April 16-17 2013 in the charming city of Dublin, Ireland. Thought leaders from all over

IRDiRC policies and guidelines refer to the principles that the IRDiRC members agree to follow as well as the recommendations from the Scientific Committees.

The first IRDiRC conference report and speakers PowerPoint presentations are available online.

Read more about IRDiRC policy and guidelines

Read more about the first IRDiRC conference

The FP7 projects

One infrastructure platform

RD Connect

- Contribution to the IRDiRC objectives of delivering 200 new therapies for rare diseases and means to diagnose most rare diseases by the year 2020
- Development of an integrated, quality-assured and comprehensive hub/platform in which complete clinical profiles are combined with -omics data and sample availability for rare disease research, in particular IRDiRC-funded research.

Two « omics » science projects

EURenOmics

- European Consortium for High-Throughput Research in Rare Kidney Diseases (Franz Schaefer, Universitätsklinikum Heidelberg, Germany)

NeurOmics

- Integrated European Project on Omics Research of Rare Neuromuscular and Neurodegenerative Diseases (Olaf Riess, Institute of Human Genetics, University of Tübingen)

Successful registry case study

European Registry and Network for Intoxciation type Metabolic Diseases (E-IMD)

European registry and network for intoxication type metabolic disorders

- European commission funding 2011-2013
- Platform for 11 different RD
- 60 clinical partners from 24 countries
- Pharmaceutical industry

- Patient organisations
- Societies for inherited metabolic diseases
- Scientific consortia
  - UCDC
  - J-UCD

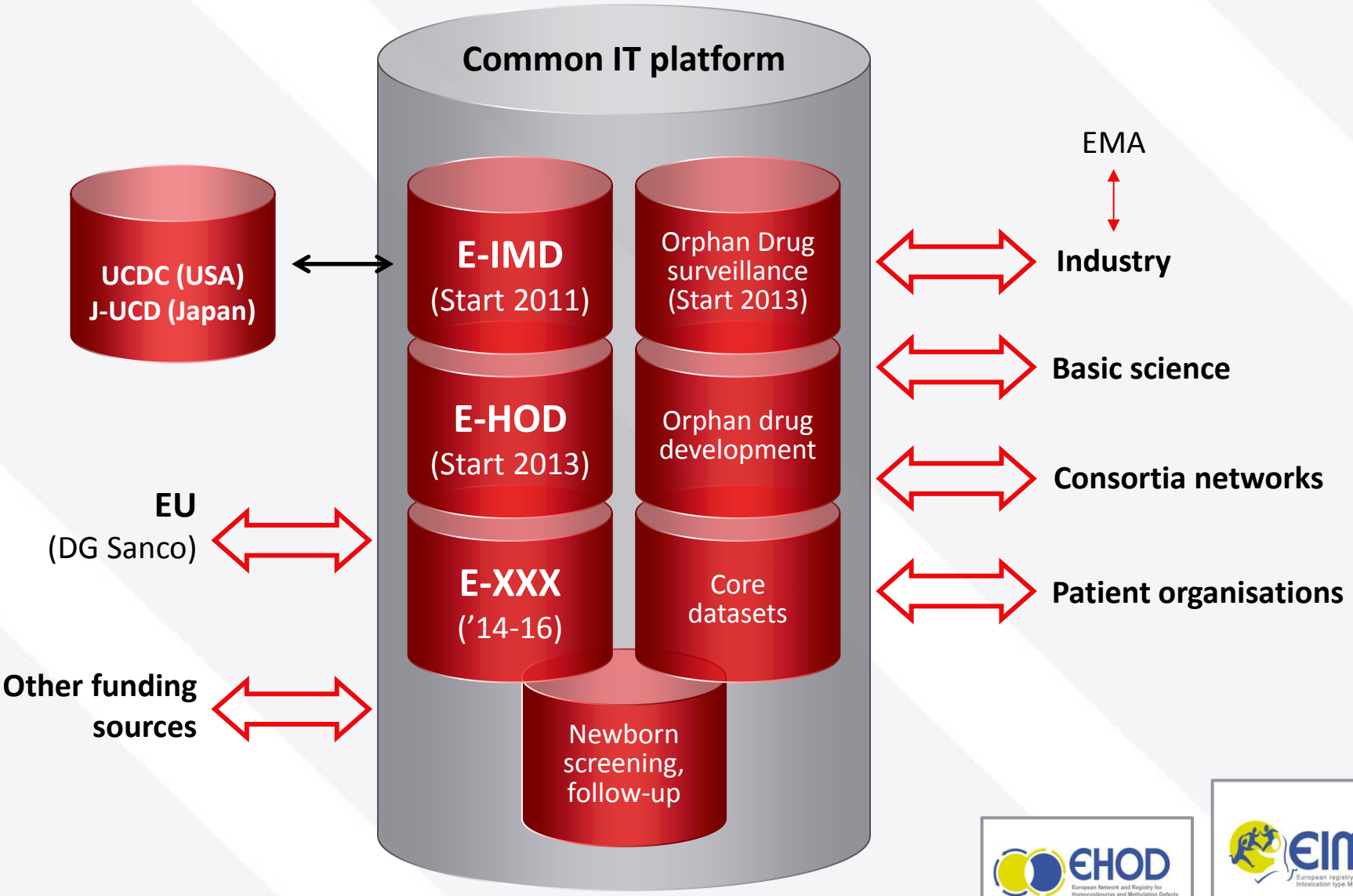
EIMD
European registry and network for Intoxication type Metabolic Diseases

Expanding disease panel

Further expand the registry and network to new IMD

European funding	***European funding***	***Private funding***
2011	**2012**	**2014**
Urea cycle defects	***Homocystinurias***	23 other intoxication type metabolic diseases
NAGs	• CBS	20 co-factor associated diseases affecting the brain
CPS1	• MTHFR	
OTC	• CblC	
ASS	• CblD	
ASL	• CblE	
ARG1	• CblF	
HHH	• CblG	
Organic acidurias	• CblJ	
PA	***Methylation defects***	
MMA	• MAT	
IVA	• GNMT	
GA-1	• SAHH	
	• ADK	
	Folate defects	
	• MTHFD	
	• GFT	
	• FTCD	

Towards an international regsitry and network for IMD



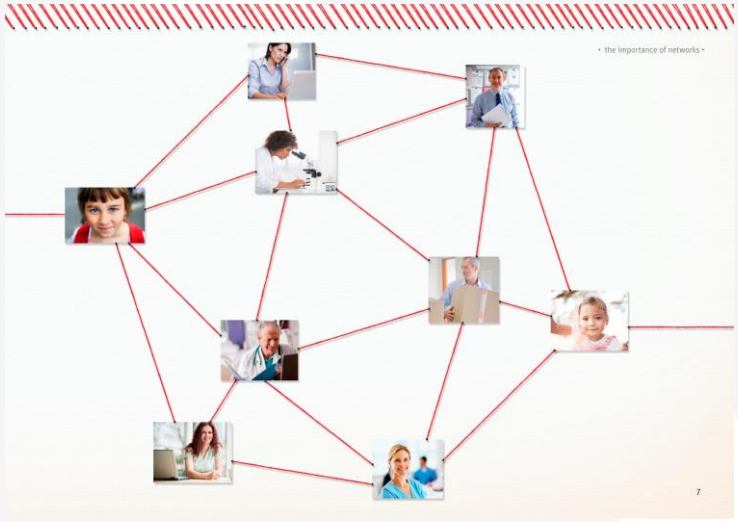
Challenges throughout the registry development

Planning a registry	Database development	Initial data collection	Follow-up data	Continuation or termination
1. Purpose 2. Governance agreement 3. Budget & length of study 4. Database content	6. Terms and language 7. Choice of IT 8. Research ethics committees/ data protection	9. Data quality and cleaning 10. Clinician co-operation and team working	11. Data analysis and interpretation 12. Access to the data 13. Publications 14. Sustainability	15. Sustainability 16. Partnerships

Gliklich RE, Dreyer NA: Registries for Evaluating Patient Outcomes: A User's Guide (2007)

Ensuring success

- Registries provide critical disease knowledge which makes diseases easier to study, increasing the probability a treatment can be developed.
- Registries should be recognised as a global priority
- Should encompass the widest geographic scope possible
- Should be centred on a disease or group of diseases rather than a therapeutic intervention
- Harmonisation of data so that databases and registries can be linked: Common Data Elements should be consistently used
- RD registries should involve patients and/or representatives in all aspects of the research
- Public-Private Partnerships should be encouraged to ensure sustainability
- The nature of RD requires that data should be collected on a long-term basis. Therefore registries need long-term funding.



Thank you