EPIRARE (European Platform for Rare Disease Registries)

<table>
<thead>
<tr>
<th><strong>EPIRARE general information</strong></th>
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<tr>
<td><strong>Building Consensus and Synergies</strong></td>
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<td><strong>European Platform for Rare Disease Registries</strong></td>
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<td><strong>EPIRARE</strong> is a project</td>
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<tr>
<td>funded by the EU Commission (DG SANCO)</td>
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<tr>
<th><strong>Starting date:</strong></th>
<th>April 2011</th>
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<td><strong>Duration:</strong></td>
<td>30 months (April 2011 – October 2013)</td>
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<td><strong>Funding modalities:</strong></td>
<td>cofinanced 60% of total cost by European Commission</td>
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<td><strong>Coordinator of the project:</strong></td>
<td>National Centre for Rare Diseases, Italian National Institute of Health – Rome, Italy</td>
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Partners

23 partners in
14 countries in
3 continents
Aims

• To prepare a **European Platform** for the Registration of Rare Diseases Patients
• To ensure the quality and best use of the registered data
Background

- More than 500 RD registries in the EU (Orphanet and other sources)
- No uniform standards for the storing and management of data
- Registries set up for 20% of rare diseases, more registries for the same RD
- Need to increase data sharing and exchange
- Need to harmonise existing regulations (EU, national and regional)

The EU Council Recommendation on Rare Diseases (adopted in June 2009) recommends, among other topics, the implementation of registers and databases for epidemiological purposes.

Therefore, many initiatives may appear in the coming years
EPIRARE activities

- Survey of registries - conditions and needs
- Survey of registries - data elements definitions and formats
- Survey of patients expectations
- Consultation/survey of industry expectations
- Informal Consultation/Information of national policy-makers
- Liaison with Countries with established or planned national registries (BE, BG, DE, ES, FR, IT)
- Liaison with US ORDR, RD-Connect (IRDiRC)
- Participation in EU initiatives and RD Committees
EPIRARE activities

- An analysis has been carried out on the current directive on Personal Data Protection and on the draft Regulation discussed in the EU Parliament

- A document has been prepared on the needs of research and public health for international RD registries

A “petition”, requesting amendments to the draft regulation, has been prepared for the attention of the MEPs, and supporting a request for an audit in the Parliament
addressed to all RD registers in Europe
(developed 2011, implemented 2012)

- 80% in favour of an EU platform
- 73% in favour of an EU portal

**Main services expected** (39% - 69%)

- **Technological tools**
  (IT tools, networking tools)
- **Specific expert advice**
  (legal, quality, privacy, ethics)
- **Resources**
  (model documents, quality control systems, access to useful data)
Needs of identified stakeholders’ groups

**Registry holders**
- Services reducing collateral workload of a registry
- Services facilitating patient management
- **Assistance to start and run a registry**
- Funding
- Motivation of professionals providing data
- Communication and visibility
- **Networking**

**Patients**
- **Improved care for RD patients**
- Information
- **Social inclusion**

**Pharmaceutical Industry**
- **One stop shop for accessing information on diseases**
- **Finding a disease specific registry**
- Recruitment of patients for clinical trials
<table>
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<tr>
<th>Register reality</th>
<th>Patient expectations</th>
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<tbody>
<tr>
<td>1. Epidemiological research</td>
<td>1. Healthcare/Social Services planning</td>
</tr>
<tr>
<td>2. Clinical research</td>
<td>2. Treatment evaluation (efficacy/safety)</td>
</tr>
<tr>
<td>3. Natural history of the disease</td>
<td>3. Natural history of the disease</td>
</tr>
<tr>
<td>4. Disease surveillance</td>
<td>4. Epidemiological research</td>
</tr>
<tr>
<td>5. Treatment evaluation (efficacy/safety)</td>
<td>5. Clinical research</td>
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The EPIRAE Platform concept

Institutions

Industry

Patients, public

Clinicians, Researchers

data
The EPIRARE Platform Data Repository - prerequisites

- Multidisease
- Multipurpose
- Multistakeholder
- Multisource
The EPIRARE platform – Sets of Common Data Elements

**PATIENT**
- Minimum Set CDE:
  - GUID elements
  - Name, surname, date of birth, city of birth, sex; National unique ID Code
  - Diagnosis
  - City (& country) of residence
  - Diagnosis centre ID (& city & country)
  - Treatment Centre ID (& city & country)
  - Patient willingness x CT and donations

**DETERMINANTS, SERVICES**
- Genetic variants
- Familial factors
- Living environment & lifestyle
- OD/ off label treatments
- Health services and procedures

**OUTCOMES, RECRUITMENT, COSTS**
- Age at death
- Disability profile
- Burden of disease index score
- Co-morbidity
- Costs
- Key Clinical parameters
- Natural history, HTA, HC Quality

Case finding → Practice patterns
Common Data Elements (CDEs) among RD Registries: results from the EPIRARE survey on Common Data Elements

Epirare project carried out a web-based survey to a list of regional, national and international RD and orphan drug registries.

The survey inquired on more than 50 data elements likely to be collected by registries:

- registry aims,
- patients' personal data,
- clinical and genetic disease data and comorbidity,
- data on: diagnostic and treating Centres, orphan and common drugs and other treatments
- patients' interest in clinical trials and biological donations
- transplantations,
- link to biobanks.
Common Data Elements (CDEs) among RD Registries: results from the EPIRARE survey on Common Data Elements

Results:

Registries may be able to make estimates on: incidence (52%) and prevalence (52%), life expectancy (59%), survival time (48%), diagnostic delay (45.5%), patient migration for diagnosis (52%) and for treatment (48%), patient willingness to be contacted for donating biological sample (38%) and participating in clinical trials (29%), link to biobanks (20%), disability (7%), quality of life (13%), orphan drug use (29%), its effectiveness (33%) and its safety (20%), current drugs effectiveness (27%), information in other types of treatments (58%), surgery (48%), cognitive (5%), physic (15%) and other rehabilitation (27%).

Conclusion: the survey show that most Registries currently collect data as proposed by the Epirare questionnaire and may be used in their current form to be shared within the platform to support public health policies and research.
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<th>Directorate-General Health and Consumers (DG SANCO)</th>
<th>Directorate-General Joint Research Centre (DG JRC)</th>
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<tr>
<td>To enable data analysis within and across many rare diseases and to facilitate clinical trials and other studies and research</td>
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Principal goal of the Platform
Main Objectives

1. Promote **interoperability** of existing registries
2. **Support for new registries**
3. Act as a **hub** providing access to all data collection in the field of RD
4. Provide **IT tools** to maintain already existing selected data collection
Activities will be developed

- Taking into account outcomes of the projects funded by the Health Programme and Framework Research Programmes
  EPIRARE, RD-CONNECT, PARENT JA, EUCERD JA, ORPHANET JA

- Ensuring collaboration with national registries

- Establishing collaboration with IRDiRC

- Establishing collaboration with the Global Rare Diseases Patient Registry and Data Repository (GRDR)

- Establishing collaboration with the Cancer Registries (ENCR)
THE INTERNATIONAL AND EUROPEAN CONTEXT FOR RARE DISEASE RESEARCH
European Union action in the field of Rare Diseases

- Adoption of national plans and strategies in rare diseases in all Member States before the end of 2013.
- **Strength dissemination and visibility of the rare diseases** database ORPHANET: description of 6000 diseases.
- Contribution to the **revision of ICD** (International Classification of Diseases) version 11, during 2015/2016 classifying and codifying the maximum number of rare diseases.
- Creation of the **European Platform on Rare Diseases Registration** located in Ispra (Italy) during 2014. More than 600 registers in the EU.
- **Creation of an ERIC** (European Research Infrastructure Consortium) to support the European development on rare diseases during 2014/2015
- **Improving accessibility to orphan medicinal products in the UE**
- **Supporting EURORDIS** to reinforce patient’s empowerment
- To analyse feasibility of a common approach on neonatal screening for some rare disorders.
- Creation of **IRDiRC** (International Rare Diseases Research Consortium) for transatlantic cooperation (EU, USA, Canada, Australia, South Korea, Japan, ...)
- Future Joint Action on Rare Tumours (2015-2017).
Instruments to implement these goals

- 3rd European Union Health Programme 2014-2019
- Research Programme Horizon 2020
- Structural Funds 2014-2019

- The European Union Committee of Experts on Rare Diseases (EUCERD)
Two main objectives by the year 2020:
- to deliver **200 new therapies** for rare diseases
- to **diagnose most rare diseases**.
A number of grand challenges are being addressed through collaborative actions to reach these **2020 goals**.
RD-CONNECT: An integrated platform connecting databases, registries, biobanks for rare disease research
Members are composed of funding body/organisation investing a minimum of $10 million US over 5 years in research projects/programmes contributing towards IRDiRC objectives

Small funders may form a group of funders
E-Rare
ERA-Net for Research Programmes on Rare Diseases

What is an ERA-Net?

ERA-Net = European Research Area Network
E-Rare Consortium (2010-2014)
ERA-Net for Research Programmes on Rare Diseases

13 European (or Associated) Member States
17 Research (funding) Agencies/Ministries
E-Rare (2010-2014)

**Coordination & Support**
- Harmonization of national research programmes on rare diseases
- Enlargment and Increase of international collaboration
- Development of common policies
- Implementation of transnational research activities (JTCs)
- Other joint activities

**Joint Transnational Calls**
- Yearly joint calls
- Two “general” joint calls
- Two “focused” joint calls
- Open to any funding body

* EC budget

* National agencies’ budget
Other EU Research Infrastructures

- **EATRIS** European Advanced Translational Research Infrastructure in Medicine
  Translational research

- **ECRIN** European Clinical Research Infrastructure Network
  Clinical studies and biotherapies

- **BBMRI** Biobanking and Biomolecular Resources Research Infrastructure
  Research Biobanks

*European Strategy Forum on Research Infrastructures*

ESFRI identified **48 projects** of new research infrastructures so far, ESFRI will more focus on their implementation for the next few years.
Development and Implementation of EU Research Infrastructures

- **ESFRI**
  - EU Research Infrastructures

  - **Preparatory Phase**

  - **Structural Phase**
    - European Research Infrastructure Consortium (ERIC)

- **EATRIS**
  - European Infrastructure for Translational Medicine

- **ECRIN**
  - European Clinical Research Infrastructures Network

- **BBMRI**
  - Biobanking and Biomolecular Resources Research Infrastructure

**European Funds**

**National Funds**

**Regional Funds**
RARE DISEASE REGISTRY PLATFORMS
The Office of Rare Diseases Research (ORDR)/NIH has launched a pilot program to establish a Global Rare Diseases Patient Registry and Data Repository (GRDR) to collect patient clinical information without personal identifiers for research.

The goal of GRDR is to enable analyses of data across many rare diseases and to facilitate clinical trials and other studies.

The GRDR will also develop the capability to link patients’ data and medical information to donated biospecimens by using a Voluntary Global Unique Patient Identifier (GUID). The identifier will enable the creation of an interface between the patient registries that are linked to biorepositories and the Rare Disease Human Biospecimens/Biorepositories (RD-HUB) [http://biospecimens.ordr.info.nih.gov/](http://biospecimens.ordr.info.nih.gov/).
Rare Diseases have no borders! They don’t affect individuals, they affect entire families

**GRDR**

1. Patients Provide health information and test results
2. A Global Unique Patient ID (GUID) is assigned and patient data is mapped to common data elements (CDE’s)
3. Patient data linked to biospecimens via the GUID interfacing with RD-HUB
4. GRDR aggregates de-identified patient clinical information and specimen data
5. De-identified registry data is available to researchers for studies and clinical trials
6. Researchers can identify potential study participants and submit a contact request to the original registry owner
7. Registry owners notify identified participants. Interested patients are directed to the study contact
The Spanish National Rare Diseases Registry

SpainRDR is a project financed by the Institute of Health Carlos III (ISCIII) within the scope of the IRDiRC. Coordination: Institute of rare diseases Research (IIER).

Aims to build the National Rare Diseases Registry in Spain based on the input of two different strategies:
- Patient registries addressed to patient outcome research
- Population-based registries addressed to epidemiological research and social and health systems planning
The system of French National Rare Diseases Registries BaMaRa-BNDMR and RaDiCo

Plan National Maladies Rares

**Axis A**

**IMPROVE THE QUALITY OF PATIENT´S CARE**

A1- Improve the access to diagnosis and care
A-1- 4 Coordinate the «rare diseases» structures with a shared information system

**BaMaRa** - Banque Nationale de Données Maladies Rares

**Axis B**

**DEVELOP RESEARCH ON RARE DISEASES**

B-1 Create a national structure to impulse research with public and private partners
B-1-1 Create a foundation dedicated to rare diseases

**RaDiCo** - Rare Diseases Cohorts
The French experience: a shared information system

BaMaRa
Public health
A Minimum data set for all patients
Cross sectional

1
23 Groups; Care pathways
131 centres of expertise

2

3

23

COE1
COE2
COE3
COE4

COE5
COE6
COE7
COE8
COE9
COE10

COE11
COE...

COE131

RaDiCo
Research Phenomics
Cohorts for a single disease or groups of diseases
Extensive longitudinal data collection

1
2
3

23
A joint information system for BaMaRa and RaDiCo

BaMaRa:
- National Rare Diseases Plan 2
- Ministry of Health
- DGOS -> APHP
- Public Health
- Paul Landais
- 0,5M€/y/5 years

RaDiCo:
- Grand emprunt
- Ministère of Research
- Inserm -> Foundation RD
- Research
- S.Amselem A.Clement P.Landais
- 0,95M€/y/10 years

Shared gestion

Shared resources

Joint Information System

I S y - r a r e
The Italian National Rare Diseases Registry

**Identity Card**

- **Name:** National Registry of Rare Diseases (NRRD)
- **Date of establishment:** 2001
- **Location:** National Center for Rare Diseases (Istituto Superiore di Sanità)
- **Funding support:** Public funds (Italian MoH, ISS)
- **Geographical coverage:** National (90% of Italian regions)

**National Registry of Rare Diseases: Objectives**

- **Planning and evaluating health care programmes** (services utilization, patients’ mobility...)
- **Diseases surveillance** (estimation of prevalence and incidence, geographical and temporal distribution of RD)

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**The Ministerial Decree 2001, n. 279 establishes:**

1) Italian National Network for RD for
   - Prevention
   - Surveillance
   - Diagnosis
   - Treatment
   The network is made of Centres for Rare Diseases where patients are diagnosed and treated completely free of charge

2) National Registry of Rare Diseases as an important tool for evaluating the impact of RD on health services and on general population

3) List of RD

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**Diagram:**

- Clinical Research
- Health care
- Public health surveillance
- Interoperability