Domenica Taruscio
Director
National Centre for Rare Diseases
Istituto Superiore di Sanità
Rome, Italy
domenica.taruscio@iss.it
EPIRARE is a project funded by the EU Commission in 2010 (2011-2013)

Duration: 30 months

Starting date: April 2011

Funding modalities: cofinanced 60% of total cost by European Commission

Coordinator of the project:
National Centre for Rare Diseases, Italian National Institute of Health – Rome, Italy
Justification

• There is a great interest of researchers in registries for rare diseases; in fact, there are many registries, mainly promoted by academicians.

• 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 will appear.

  *Moreover, we should keep in mind that:*

• There are several difficulties for EU data collection and exchange from the Regulation on personal data protection.

• On the other hand, a wide population base is especially necessary in the case of RD patients.

• Therefore, we presented to the EU Commission the application for the EPIRARE project.
1. **To define the needs of the EU registries and databases on rare diseases (status of art)**
   Description: Define the features of the current registries with reference, e.g. to legal basis; organizational and IT measures used; data collected; informed consent; personal data protection regulation; quality assurance, operational and financial support.

2. **To identify key issues to prepare a legal basis**
   Description: Assess the most suitable EU legal instrument in order to allow the registration of individual subjects’ health data in compliance with the EU Directive 45/96 and in coherence with other relevant provisions.

3. **To agree on the Register and Platform Scope, Governance and long-term sustainability**
   Description: Define the scope and a governance model representing the interests of relevant stakeholders in strategic decisions and ensuring long-term sustainability of the platform.
4. To agree on a Common data set, disease-specific data collection and data validation

**Description:** Define a common data set, which is independent of the registered rare disease, provides information consistent with the agreed scope of the registers and/or the underlying platform, is useful for public health actions.

5. To identify tools and other facilities supporting the operation of the platform users

**Description:** To define the services and contents which help in performing activities of interest of the platform users. Moreover, such tools will ensure quality of data, quality procedures and data protection.
25 partners in
15 countries in
3 continents
The project is organised in 8 Workpackages:

**WP1 - Coordination of the project**
*WP Leader: Domenica Taruscio*
National Centre for Rare Diseases, Istituto Superiore di Sanità, Rome (Italy)

**WP2 - Dissemination of the project**
*WP Leaders: Domenica Taruscio, Fabiola Gnessi*
National Centre for Rare Diseases, Istituto Superiore di Sanità (Italy)

**WP3 - Evaluation of the project**
*WP Leaders: Rumen Stefanov, Information Centre for Rare Diseases and Orphan Drugs, BAPES (Bulgaria); Franco Cavallo, University of Turin (Italy)*

**WP4 - Legal basis**
*WP Leader: Tobias Schulte - University of Maastricht (Netherlands)*
The 8 Workpackages: WP5 – WP8

WP5 - Policy scenarios on scope, aims, governance and long-term sustainability
WP Leader: Yann Le Cam - EURORDIS (France)

WP6 - Common data set and disease-specific data collection
WP Leader: Fabrizio Bianchi - National Council of Research Pisa (Italy)

WP7 - Data quality, validation and data sources integration
WP Leader: Manuel Posada de la Paz - Istituto de Salud Carlos III (Spain)

WP8 - Current needs of existing registries on rare diseases
WP Leader: Sabina Gainotti - National Centre for Rare Diseases, Istituto Superiore di Sanità (Italy)

Steering Committee
Advisory Board
Associated Partners (by Country) (a)

Coordinating Team
Domenica Taruscio, Luciano Vittozzi, Sabina Gainotti, Yllka Kodra,
Fabiola Gnessi, Tania Lopez, Pierpaolo Mincarone
National Centre for Rare Diseases, Istituto Superiore di Sanità (Italy)

Van Oyen Herman, Jansen Herwing
Public Health and Surveillance – Institut Scientifick de Santé Publique (Belgium)

Rumen Stefanov
Information Centre for Rare Diseases and Orphan Drugs-BAPES (Bulgaria)

Tzala Sophia
Hellenic Centre for Disease Control and Prevention (Greece)

Filippo Palumbo, Maria Elena Congiu, Silvia Arcà, Cristina Tamburini
Ministry of Health (Italy)
Associated Partners (by Contry)(b)

Fabrizio Bianchi, Anna Pierini, Michele Lipucci
National Council of Research (Italy)

Tobias Schulte, Angela Brand
Institute for Public Health Genomics, University of Maastricht (Netherland)

Manuel Posada de la Paz, Manuel Hens
Istituto de Salud Carlos III (Spain)

Pilar Solar Crespo
Ministerio de Sanidad y Política Social (Spain)

Yann Le Cam, Fabrizia Bignami, Monica Ensini
EURORDIS
Collaborating partners (by Country) (a)

Li Dingguo
Rare Diseases Society – Shanghai Medical Association (China)

Ingeborg Barisic
EUROCAT Steering Committee, University of Zagreb (Croatia)

Karaman Pagava
Tbilisi State Medical University (Georgia)

Holm Graessner
University of Tübingen (Germany)

Sandor Janos
Pécs University, Institute of Applied Health Science (Hungary)

Paola Facchin
Coordinator of Italian Interregional Group on Rare Diseases, Coordinator of Veneto Registry of Rare Diseases, Università di Padova (Italy)
Collaborating partners (by Country) (b)

**Carlo Francescutti**  
WHO Collaborating Centre (Italy)

**Monica Pace**  
Italian Institute of Statistics (Italy)

**Dorica Dan, Simona Dimitriu**  
Romanian National Alliance for Rare Diseases (Romania)

**Anil Mehta**  
University of Dundee (UK)

**Edmund Jessop**  
National Commissioning Group, London Strategic Health Authority (UK)

**Stephen Groft**  
Office for Rare Diseases Research – NIH (USA)

**Wills Huges-Wilson**  
Joint EBE-EuropaBio Task Force on Rare Diseases and Orphan Drugs
The development of guiding reports, including the legal and organizational framework, for the registration of RD patients is strategic to build up an evidence base for Community, public health policies, health service management, clinical research and the assessment of orphan drugs effectiveness and appropriateness of use.
Expected Outputs (1)

1. State of art: to describe the current situation, the challenges and the expectations on Patients Registries and Databases

2. To reach consensus on best practice model of a legal instrument for a European Platform of patients RD Registries

3. Possible policy scenarios on Scope, Common data set, Governance and Sustainability of the Platform

4. Guidelines for data sources and quality of RD Registries in Europe

5. Identification and characterization of services and facilities of a European Platform of EU RD Registries
6. Promotional **material, website, and activities intended for dissemination** at conferences and distributed to stakeholders

7. European Workshops with stakeholders to discuss the possible **policy scenarios**

8. Capacity building **workshops** with Patients’ Associations

9. **Reports**
In Europe a disease is considered rare when it affects no more than 5 individuals among 10,000 persons.
Informed Consent for Rare Diseases Patient Registries Linked to Biorepositories

Washington, DC (USA), December 13-14, 2010
National Registry of Rare Diseases: the Italian experience
MILESTONES ABOUT:

- National Health Plans ‘98-00; 2003-05; 2006; 2010
- Rare diseases as a specific topic;
- Regional Health Plans
- Ministerial Decree 279/2001:
  National Network for Rare Diseases
- Agreements between the
  Ministry of Health and Regions (2002; 2007)
- Ministerial Decree 15th April 2008: Inter-regional Centres for rare diseases
Regulatory Framework:
MINISTERIAL DECREE 18 May 2001, n. 279

“Regulation for the institution of the National Network for the prevention, surveillance, diagnosis and therapy of rare diseases and the exemption from patients’ participation in the costs of the relevant healthcare”
THE MINISTERIAL DECREE 18 MAY 2001, n. 279:

- Defines the National Network:
  - Centres identified by Regions
  - Regional and Interregional Coordination Centres

- Establishes the National Registry of Rare Diseases at the Istituto Superiore di Sanità (Rome)

- Regulates the exemption from patients’ participation to the costs for diagnosis and treatment of rare diseases, listed in the Annex of the decree (284 diseases and 47 rare diseases’ group; 331 code which include a larger number of rare diseases).
SOME EXAMPLES
OF REGIONAL
AND INTER-REGIONAL
NETWORKS + REGISTRIES
(alphabetic order by Region)
REGIONAL Network
an example: LOMBARDIA

http://malattierare.marionegri.it/
Informed Consent for Rare Diseases Patient Registries Linked to Biorepositories

Washington, DC (USA), December 13-14, 2010
Informed Consent for Rare Diseases Patient Registries Linked to Biorepositories

Washington, DC (USA), December 13-14, 2010

www.regione.toscana.it/salute/malattierare
Coordinamento Regionale per le Malattie Rare - Regione Veneto
Rare diseases centre - Venetian Region - Italy

Benvenuti nel sito del Registro delle malattie rare
Welcome to rare diseases register web page

Regione Veneto
Venetian Region

Dipartimento di Pediatria di Padova
Paediatrics Department

Università di Padova
University of Padua

Azienda Ospedaliera Padova
Padua Hospital

http://malattierare.regione.veneto.it/
NATIONAL REGISTRY OF RARE DISEASES: main objectives

• Planning and evaluating health care programmes (services utilization, patients’ mobility, etc.)

• Diseases surveillance (estimation of prevalence and incidence, geographical and temporal distribution of RD)
Informed Consent for Rare Diseases Patient Registries Linked to Biorepositories

Washington, DC (USA), December 13-14, 2010

EPIDEMIOLOGICAL FLOW: Regional and National Level

NATIONAL REGISTRY OF RARE DISEASES

EACH AUTHORIZED HOSPITAL IN A GIVEN REGION

COORDINATOR CENTRE OF THE REGIONAL REGISTRY

AGREED DATA SET (EVERY 6 MONTHS)
In Lombardia there are
a) 1 coordination centre
b) 31 Center for RD, which have been established by regional regulatory N. 7328/2001

EXAMPLE OF LOMBARDIA

Informed Consent for Rare Diseases Patient Registries Linked to Biorepositories
Washington, DC (USA), December 13-14, 2010
AGREEMENT BETWEEN CENTRAL STATE AND REGIONS (2002, 2007)

AGREED DATA SET
TO BE SENT BY REGIONAL REGISTRIES TO THE NATIONAL REGISTRY AT THE ISS
(EVERY 6 MONTHS)

- IDENTIFICATION CODE OF PATIENT
- LIVE–DEADH (DATE)
- DIAGNOSIS OF RARE DISEASE
- REGION, HOSPITAL WHICH MADE THE DIAGNOSIS
- DATE OF THE DIAGNOSIS
- ORPHAN DRUG USED
### Exemption code (national) (331 different code)

### List of rare diseases and/or their groups

### Examples of rare disorders included in each specific group

### Synonymous

**ICD**

- Infectious diseases
- Syndromes with cancer
- Diseases of the endocrine system, metabolism and immune system
- Diseases of the blood and of hematopoietic organs
- Diseases of the nervous system
- Diseases of the cardiovascular system
- Diseases of the digestive system
- Diseases of kidney and urinary system
- Diseases of the skin and subcutaneous tissue
- Diseases of the connective tissue
- Congenital malformations
- Some conditions of perinatal origin
- Some symptoms, signs and disorders not otherwise specified
Up to now 485 rare diseases are collected in the NRRD

<table>
<thead>
<tr>
<th>ICD Groups</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diseases of the nervous system</td>
<td>19535</td>
<td>21,05</td>
</tr>
<tr>
<td>Diseases of the blood and blood-forming organs</td>
<td>19126</td>
<td>20,60</td>
</tr>
<tr>
<td>Endocrine, nutritional and metabolic diseases</td>
<td>17594</td>
<td>18,95</td>
</tr>
<tr>
<td>Congenital malformations, deformations and chromosomal abnormalities</td>
<td>13963</td>
<td>15,04</td>
</tr>
<tr>
<td>Diseases of the musculoskeletal system and connective tissue</td>
<td>8798</td>
<td>9,48</td>
</tr>
<tr>
<td>Neoplasms (Cod. ICD-9-CM da 239)</td>
<td>4082</td>
<td>4,40</td>
</tr>
<tr>
<td>Diseases of the circulatory system</td>
<td>3976</td>
<td>4,28</td>
</tr>
<tr>
<td>Diseases of the skin and subcutaneous tissue</td>
<td>3183</td>
<td>3,43</td>
</tr>
<tr>
<td>Diseases of the digestive system</td>
<td>1229</td>
<td>1,32</td>
</tr>
<tr>
<td>Certain infectious and parasitic diseases</td>
<td>558</td>
<td>0,60</td>
</tr>
<tr>
<td>Diseases of the genitourinary system</td>
<td>552</td>
<td>0,59</td>
</tr>
<tr>
<td>Certain conditions originating in the perinatal period</td>
<td>219</td>
<td>0,24</td>
</tr>
<tr>
<td>Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified</td>
<td>9</td>
<td>0,01</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>92824</strong></td>
<td><strong>100,0</strong></td>
</tr>
</tbody>
</table>
SURVEILLANCE OF RARE DISEASES IN ITALY

- HEALTH OPERATORS CENTRES OF HOSPITALS (COLLECT DATES)
  - EXPERTS
  - ITALIAN DRUG AGENCY
  - NATIONAL REGISTRY FOR RARE DISEASES (ISS)
  - MINISTRY OF HEALTH
  - RESPONSABLES OF REGIONAL REGISTRIES

Informed Consent for Rare Diseases Patient Registries Linked to Biorepositories
Washington, DC (USA), December 13-14, 2010
List of Hospital Centres dedicated to rare diseases and Regional Registries

National Helpline on Rare Diseases and Orphan Drugs

Newsletters
The EPIRARE brochure

Background

The EU Council Recommendation on rare diseases (2002/376/EC) recommends support of registries and databases for epidemiological purposes, by adopting a strategy in the field of innovative research for the exploration of rare diseases, pursuant to the new framework for quality, governance and long-term sustainability.

25 partners in 15 countries in 3 continents

ITALIAN NATIONAL CENTRE FOR RARE DISEASES

Institute of Health, Viale Regina Elena, 299
00161 Rome, Italy
Tel. +39 06 4990 0016
epirare@fin.ist
www.epirare.eu

Informed Consent for Rare Diseases Patient Registries Linked to Biorepositories
Washington, DC (USA), December 13-14, 2010
MAIN OBJECTIVE

To inform patients, health and social operators on:
- rare diseases and orphan drugs
- centres for prevention, diagnosis, treatment and surveillance (present at regional, national and international level)
Informed Consent for Rare Diseases Patient Registries Linked to Biorepositories

Washington, DC (USA), December 13-14, 2010

HOW WE SPREAD THE INFORMATION

Newsletters
Thanks for your attention

www.epirare.eu

domenica.taruscio@iss.it