Public Health Impact of the Orphan Drug Regulation

Ségolène Aymé
Director of research at INSERM, Director of Orphanet
Former-chair of the Rare Disease Task Force of the European Commission
Chair of the WHO Topic Advisory Group on Rare Diseases
Paris, France

segolene.ayme@inserm.fr

Indicators of public health impact

- Process indicators
  - Other regulations, policy documents, programmes or strategies
  - At EU and national level
- Outcome indicators
  - Development of a community of stakeholders
    - ✓ Meetings, workshops
  - Development of infrastructures
    - ✓ Patient registries
    - ✓ Expert networks
  - Increased number of clinical trials

Impact on EU policy development

- In the field of Orphan Drugs:
  - 26 January 2007: Regulation on Medicinal Products for Paediatric Use
  - 31 May 2007 : Regulation on Advanced Therapies

- In the field of Rare Diseases:
  - 1st Community action programme on Public Health (1999-2007)
    - ✓ Rare diseases as one of the priorities
    - ✓ Target: improving knowledge and facilitating access to information
    - ✓ Orphanet Europe
  - 2nd Community action programme on rare diseases (2008-2013)
    - ✓ Exchange of information via existing networks
    - ✓ Strategies and mechanisms to encourage transnational cooperation: European Reference networks of Centres of Expertise

EU policy development in Public Health

January 2004

- **Rare Disease Task Force** at www.rdtf.org
  - Working party on Coding and Classification
  - Working party on Indicators
  - Working party on Standards of Care
  - OrphaNews Europe: 12,000 readers every two weeks

11 November 2008

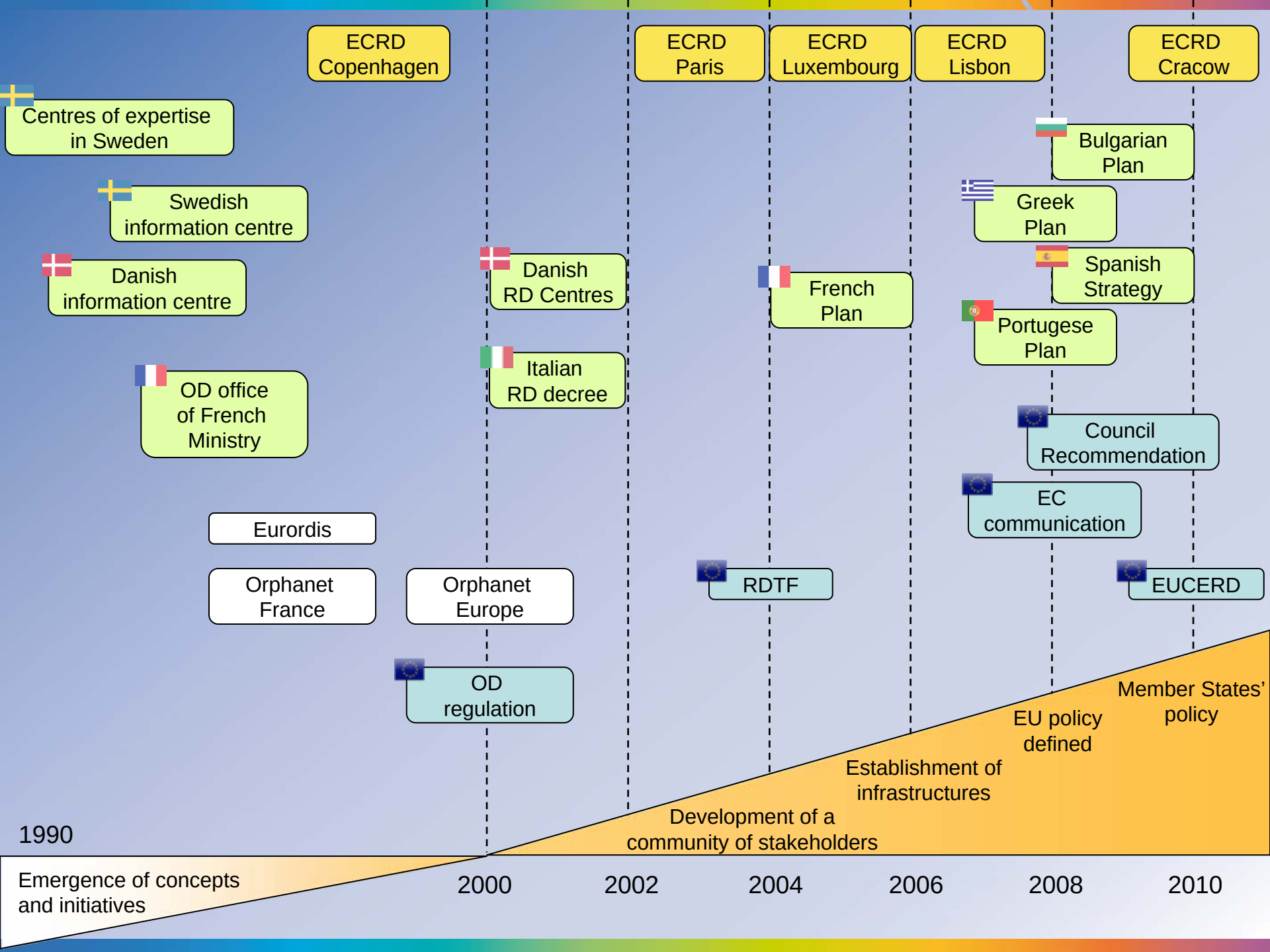
- **EC Communication** « Rare Diseases: Europe's challenge »

9 June 2009

- « **Council Recommendation** on an action in the field of rare diseases »

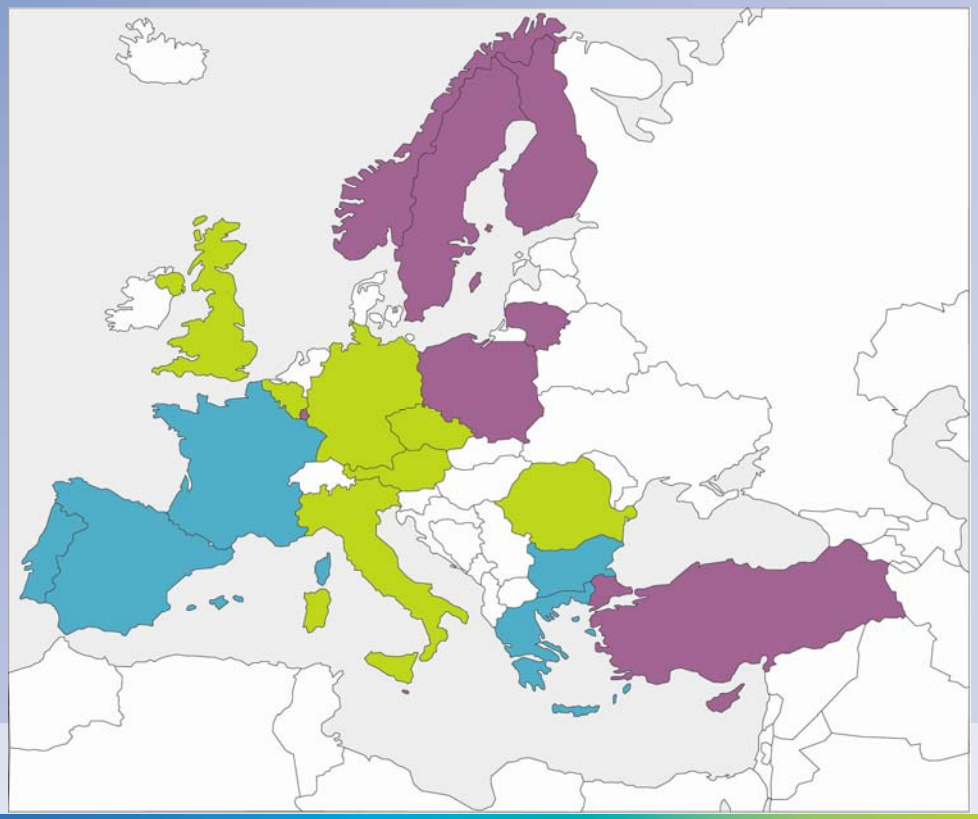
30 November 2009

- **European Union Committee of Experts in Rare Diseases:**
  - 51 representatives of MS, of EC DGs, of patients, of experts, of the Industry


ECRD Copenhagen
ECRD Paris
ECRD Luxembourg
ECRD Lisbon
ECRD Cracow
Centres of expertise in Sweden
Swedish information centre
Danish information centre
Danish RD Centres
French Plan
Bulgarian Plan
Greek Plan
Spanish Strategy
Portugese Plan
Italian RD decree
OD office of French Ministry
Council Recommendation
EC communication
Eurordis
Orphanet France
Orphanet Europe
RDTF
EUCERD
OD regulation
1990
Emergence of concepts and initiatives
Development of a community of stakeholders
Establishment of infrastructures
EU policy defined
Member States' policy
2000
2002
2004
2006
2008
2010

Policy development in Member States

- Adopted
  - 2004: French Plan / 2010: 2nd French Plan
  - 2008: Portuguese Plan
  - 2008: Greek Plan
  - 2009: Bulgarian Plan
  - 2009: Spanish Strategy



- In preparation
  - Austria
  - Belgium
  - Czech Republic
  - Germany
  - Italy
  - Romania
  - UK

- First steps taken
  (RD Committees established/ investigations into situations planned):
  - Cyprus
  - Finland
  - Luxembourg
  - Lithuania
  - Malta
  - Norway
  - Poland
  - Sweden
  - Turkey

Specific services to be provided

- **Services expected from the health care system**
  - Proper health care system
  - Affordability of clinical services
  - Medical Genetics services
  - Services for disabled people
  - Availability and affordability of Orphan Drugs

- **Additional expert services for RD**
  - Research funding
  - Expert centres / Expert laboratories
  - Information/training
  - Patient organisations

Trends in Rare Disease Inventory and Classification

Orphanet directory of diseases

- **Comprehensive list of rare diseases: over 6,000**
  - Identity card + genes
  - Unique Orpha number
    - ✓ Stable despite the evolution of knowledge
    - ✓ Linked to parent and child diseases in every classification
  - **Files available on request**
  - Suitable to code clinical activity / lab activity in information systems

- **Classifications of rare diseases**
  - List of all published classifications
  - Visualisation of each classification
  - Possibility to click at any level to obtain detailed information

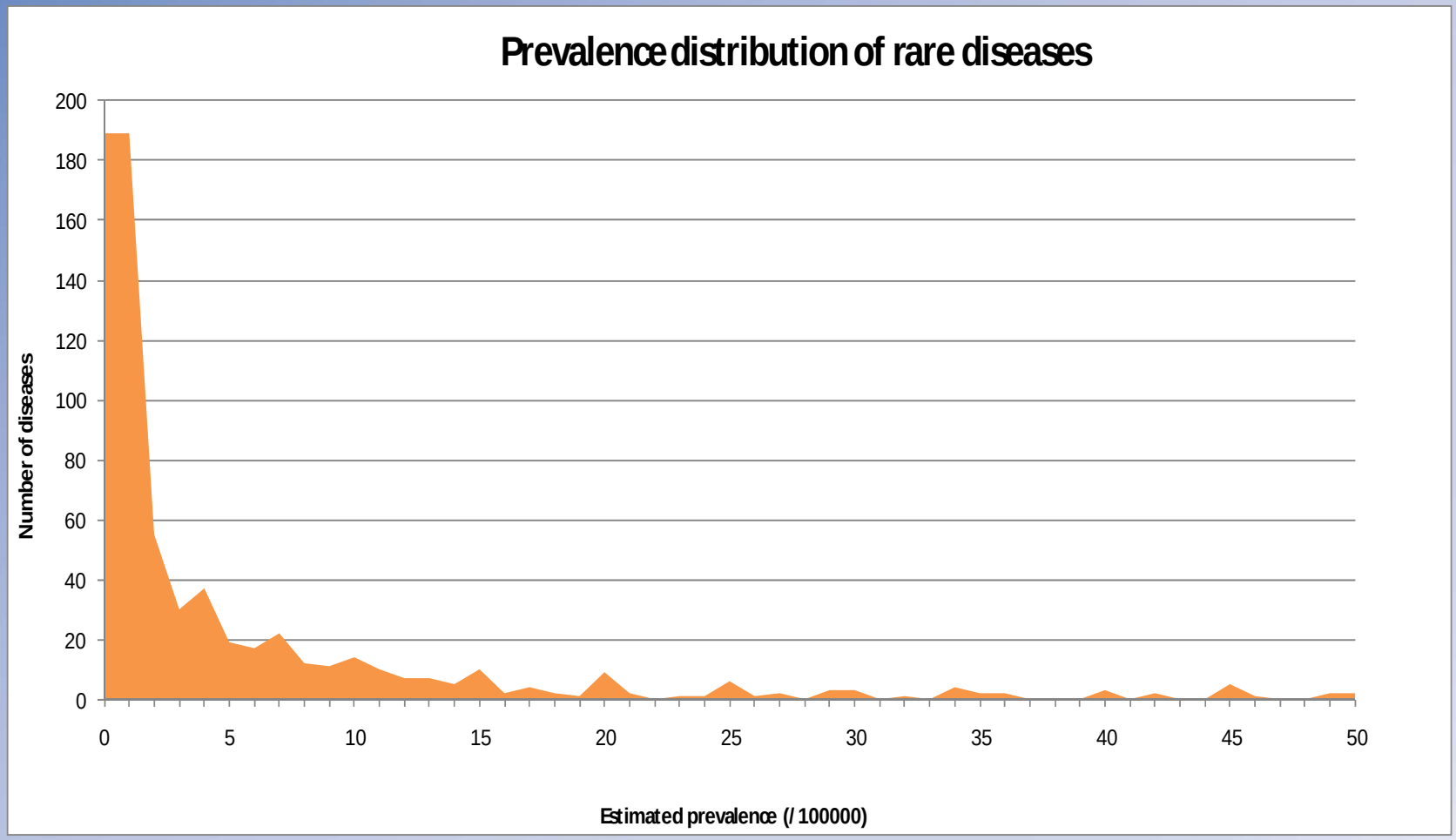
RD will be in the next edition of ICD

- All rare diseases should be finally listed in the Index of ICD11: the International Classification of Diseases to be published in 2014
- Rare Diseases serve as a model to shape the future structure of ICD11 as they are lower nodes in any hierarchy and in all fields of medicine
- Multi-terminology server aims to allow interoperability between Orphanet classifications and multiple terminologies (SnoMed-CT, MedDRA, MeSH….)

Contribution of RD categories in % of total prevalence

Dysmorphology	16.40	Ophthalmology	3.72
Oncology	10.87	Pneumology	3.45
Neurology	10.78	Infectiology	2.59
Metabolism	7.39	Neuromuscular	2.42
Haematology	6.82	Vascular disease	2.21
Cardiology	6.69	Ear-Nose-Throat	1.79
Bone	5.55	Nephrology	1.65
Dermatology	5.36	Gastroenterology	1.65
Internal Medicine	4.53	Hepatology	1.34
Endocrinology	4.46	Immunology	0.32

Distribution of prevalence rates



European Networks

Call for proposals from DG Public Health
since 2007

Calls for proposals from DG Research

since 2000

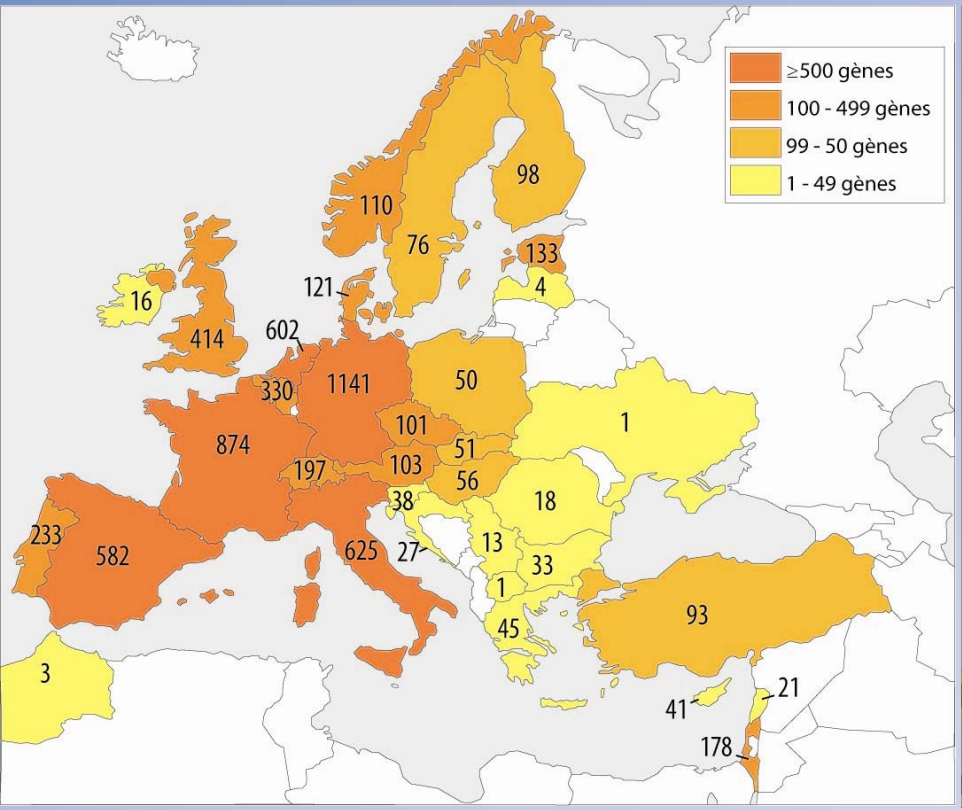
Current Pilot Networks ….

- European network of **paediatric Hodgkin's lymphoma**
  Project Leader: University of Leipzig (D)
- European Network of Reference for **Rare Paediatric Neurological Diseases (NEUROPED)**
  Project Leader: European Network for Research on Alternating Hemiplegia (AT)
- A reference network for **Langerhans cell histiocytosis** and associated syndromes
  Project Leader: Assistance Publique Hôpitaux de Paris (FR)
- European Centres of Reference Network for **Cystic Fibrosis (ECORN-CF)**
  Project leader - Klinikum der Johann Wolfgang Goethe-Universität, Germany
- European Network of Centres of Reference for **Dysmorphology**
  Project leader - University of Manchester, UK.
- Patient Associations and **Alpha1 antitrypsin** International Registry (PAAIR)
  Project leader - Stichting Alpha1 International Registry, the Netherlands
- European **Porphyria** Network - providing better healthcare for patients and their families (EPNET)
  Project leader - Assistance Publique - Hôpitaux de Paris, France
- European Network of **Rare Bleeding Disorders**
  Project leader - Università degli Studi di Milano, Italy

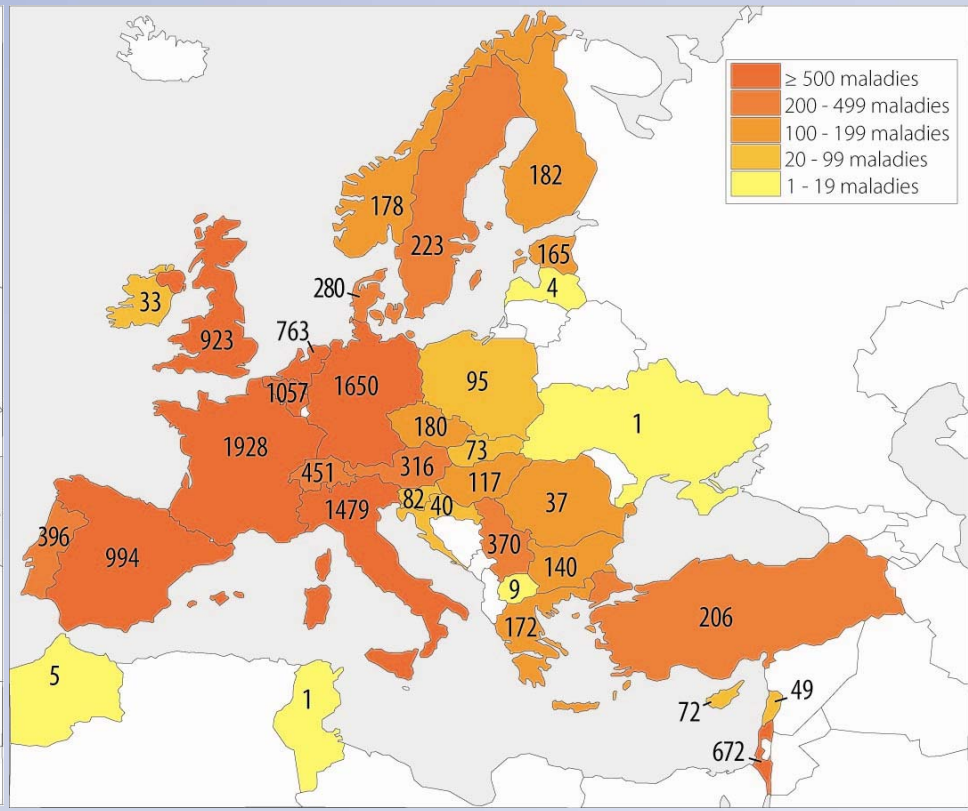
Trends in Diagnostic Test Development

Major progresses in gene identification translated into diagnostic tests

Number of genes tested by country

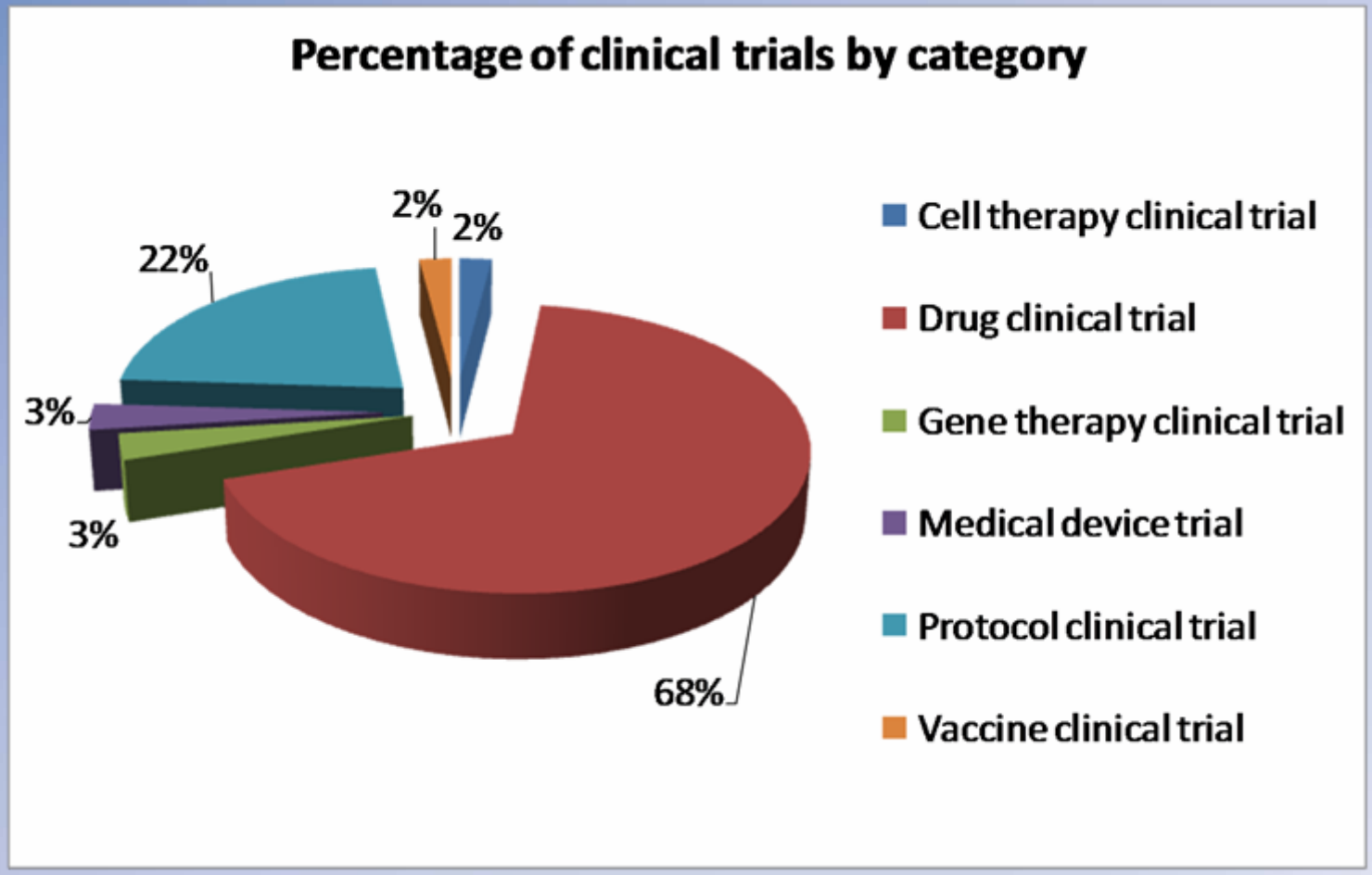


Number of diseases tested by country



Trends in Clinical Trials

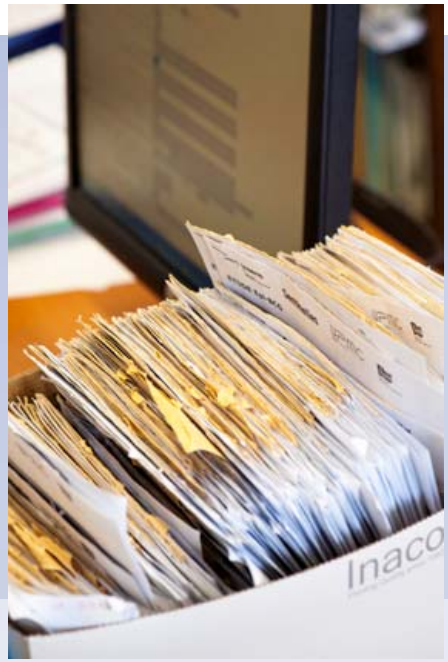
666 ongoing national or international unique clinical trials for 312 diseases



Rare Diseases with the highest number of clinical trials in Europe

Leukemia, myeloid, acute	45
Leukemia, lymphoblastic, acute	34
Glioblastoma	32
Myelodysplastic syndromes	28
Cystic fibrosis	27
Atypical hemolytic uremic syndrome	26
Diffuse large B-cell lymphoma	20
Chronic myeloid leukemia	19
Astrocytoma	17
Graft versus host disease	17
Hodgkin lymphoma, classical	17
Myeloma, multiple	17
Friedreich ataxia	16
Mantle cell lymphoma	16
Ependymoma	14
Leukemia, B-cell lymphocytic, chronic	14
Pulmonary fibrosis, idiopathic	14
Follicular lymphoma	13
Leukemia, promyelocytic, acute	13
Amyotrophic lateral sclerosis	12

Trends in Patient Registries



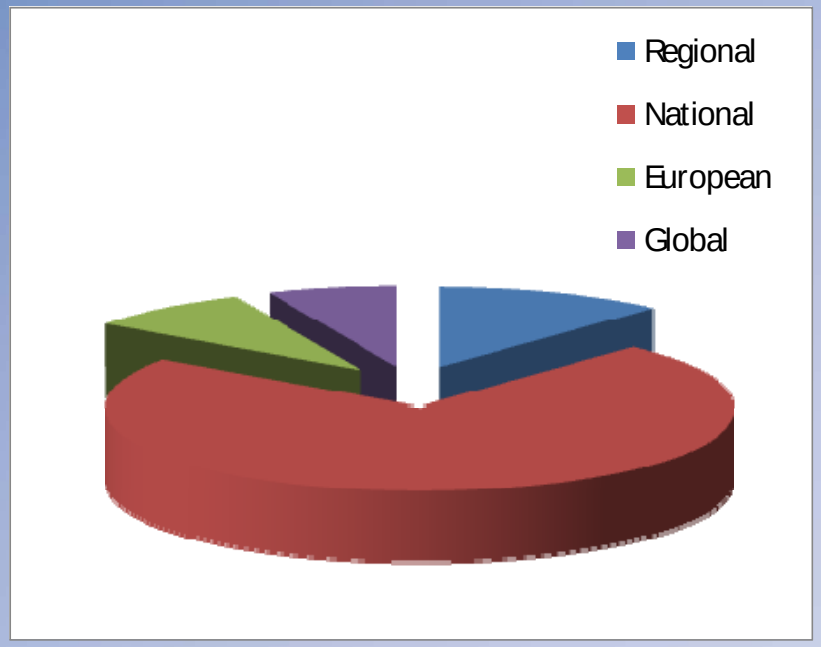
395 Registries as strategic tools

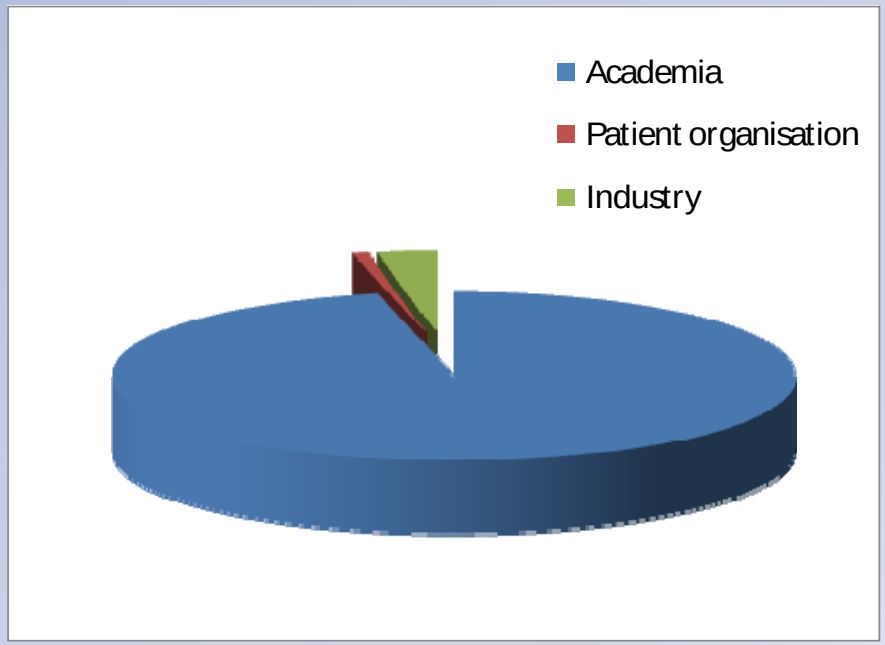
Number of patient registries per country

- France 103
- Germany 51
- Great Britain 50
- Italy 47
- Spain 28
- Belgium 19
- Netherlands 10
- Austria 13
- Ireland 9
- Portugal 7
- Switzerland 6
- Greece 2
- Bulgaria 4
- Denmark 3
- Romania 2

- Orphanet Report Series on Orphanet front page

Characteristics of Patient Registries

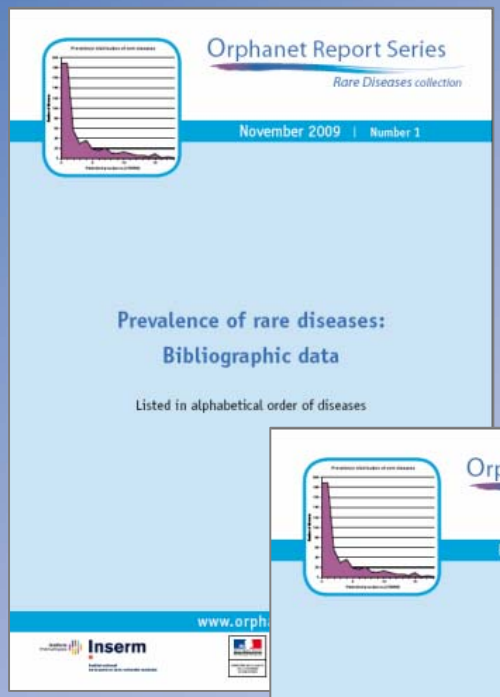


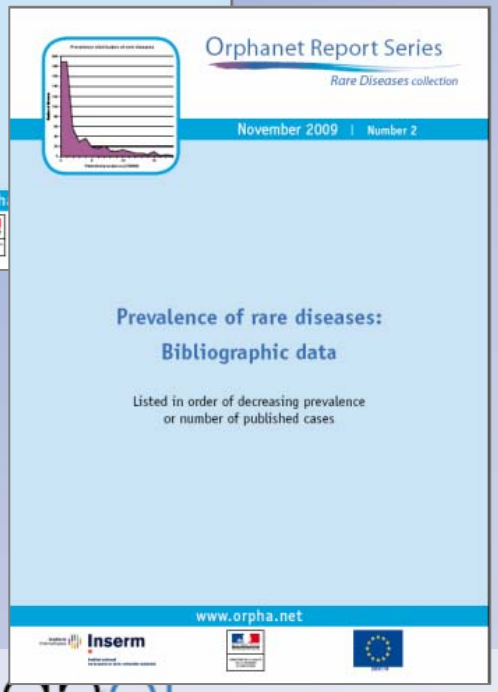


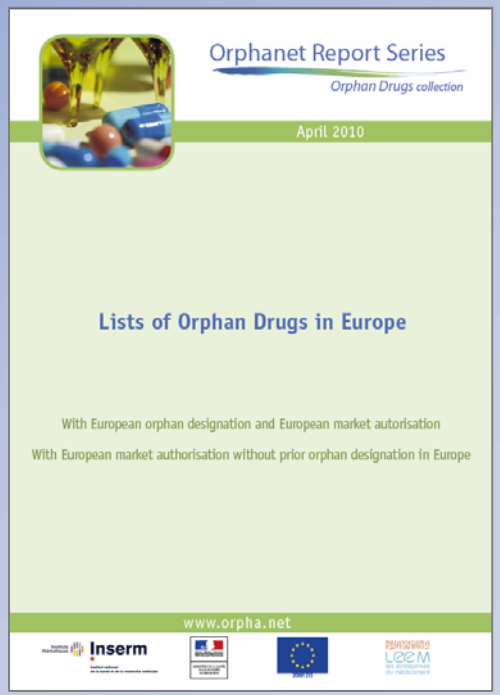
60 International Patient Registries around a medicinal product

- Cystic fibrosis
- Alpha 1 anti-trypsin
- Bleeding disorders
- Langerhans cell histiocytosis
- Severe chronic neutropenia
- Biliary atresia
- Neuromuscular diseases
- Wilson disease
- Fanconi anemia
- Pulmonary hypertension
- Metabolic diseases: Gaucher, Fabry, Pompe, MPS1…
- Ondine syndrome
- Primary immunodeficiencies
- Retinal dystrophies
- Huntington disease

Documents available on orpha.net







The way forward…

- Close surveillance of policy developments
  - EUCERD annual report at www.eucerd.eu
  - OrphaNews Europe at www.orpha.net
- Dialogue and cooperation between stakeholders
  - EUCERD as the tool
  - Orphanet as a Joint Action by 2011
- A common view shared by member states on key issues
  - Assessment of the clinical added-value
  - Public/private partnership for patient registries when there are products in development or marketed

Thank you for your attention