

**2012 REPORT ON THE STATE OF THE ART
OF RARE DISEASE ACTIVITIES IN EUROPE
OF THE
EUROPEAN UNION COMMITTEE OF EXPERTS
ON RARE DISEASES**



**STATE OF THE ART OF RARE DISEASE ACTIVITIES IN
ITALY**

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More information on the European Union Committee of Experts on Rare Diseases can be found at www.eucerd.eu.

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ACRONYMS

General

CAT - Committee for Advanced Therapies at EMA
CHMP - Committee for Medicinal Products for Human Use at EMA
COMP - Committee on Orphan Medicinal Products at EMA
DG - Directorate General
DG Enterprise - European Commission Directorate General Enterprise and Industry
DG Research - European Commission Directorate General Research
DG Sanco - European Commission Directorate General Health and Consumers
EC - European Commission
ECRD - European Conference on Rare Diseases
EEA - European Economic Area (Iceland, Switzerland, Norway)
EMA - European Medicines Agency
ERN - European reference network
EU - European Union
EUCERD - European Union Committee of Experts on Rare Diseases
EUROCAT - European surveillance of congenital anomalies
EUROPLAN - European Project for Rare Diseases National Plans Development
EURORDIS - European Organisation for Rare Diseases
FDA - US Food and Drug Administration
HLG - High Level Group for Health Services and Medical Care
HTA - Health Technology Assessment
IRDiRC – International Rare Diseases Research Consortium
JA - Joint Action
MA - Market Authorisation
MoH - Ministry of Health
MS - Member State
NBS - New born screening
NCA - National Competent Authorities
NHS - National Health System
PDCO - Paediatric Committee at EMA
RDTF - EC Rare Disease Task Force
WG - Working Group
WHO - World Health Organization

Pilot European Reference Networks

Dyscerne - European network of centres of expertise for dysmorphology
ECORN-CF - European centres of reference network for cystic fibrosis
Paediatric Hodgkin Lymphoma Network - Europe-wide organisation of quality controlled treatment
NEUROPED - European network of reference for rare paediatric neurological diseases
EUROHISTIONET - A reference network for Langerhans cell histiocytosis and associated syndrome in EU)
TAG - Together Against Genodermatoses – improving healthcare and social support for patients and families affected by severe genodermatoses
PAAIR - Patients' Association and Alpha-1 International Registry Network
EPNET - European Porphyrin Network - providing better healthcare for patients and their families
EN-RBD -European Network of Rare Bleeding Disorders
CARE-NMD -Dissemination and Implementation of the Standards of Care for Duchenne Muscular Dystrophy in Europe project
ENERCA - European network for rare and congenital anaemia – Stage 3

GENERAL INTRODUCTION TO THE REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE OF THE EUROPEAN UNION COMMITTEE OF EXPERTS ON RARE DISEASES

The 2012 Report on the State of the Art of Rare Disease Activities in Europe was produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD), through the EUCERD Joint Action: Working for Rare Diseases (N° 2011 22 01), which covers a three year period (March 2012 – February 2015).

The report aims to provide an informative and descriptive overview of rare disease activities at European Union (EU) and Member State (MS) level in the field of rare diseases and orphan medicinal products up to the end of 2011. A range of stakeholders in each Member State/country have been consulted during the elaboration of the report, which has been validated as an accurate representation of activities at national level, to the best of their knowledge, by the Member State/country representatives of the European Union Committee of Experts on Rare Diseases. The reader, however, should bear in mind that the information provided is not exhaustive and is not an official position of either the European Commission, its Agencies or national health authorities.

The report is split into five parts:

Part I: Overview of rare disease activities in Europe

Part II: Key developments in the field of rare diseases in 2011

Part III: European Commission activities in the field of rare diseases

Part IV: European Medicines Agency activities and other European activities in the field of rare diseases

Part V: Activities in EU Member States and other European countries in the field of rare diseases

Each part contains a description of the methodology, sources and validation process of the entire report, and concludes with a selected bibliography and list of persons having contributed to the report.

The present document contains the information from Parts II and V of the report concerning Italy. A list of contributors to the report and selected sources are in annex of this document. For more information about the elaboration and validation procedure for the report, please refer to the general introduction of the main report¹.

¹ <http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArRDActivities.pdf>

RARE DISEASE ACTIVITIES IN ITALY

Definition of a rare disease

Stakeholders in Italy accept the European Regulation on Orphan Medicinal Products definition of a prevalence of no more than 5 in 10,000 individuals.

National plan/strategy for rare diseases and related actions

Although there is no specific national plan/strategy for rare diseases in Italy, they have been designated since 1998 as a health care priority in the context of the 3-year national health plans, which are intended by the national government as directions for actions at a national level, whilst the responsibility for actual implementation of measures is attributed to the regional governments. A coordinated and comprehensive framework of actions has been set up by the Ministry of Health Decree 279/2001, which established a national network for prevention, surveillance, diagnosis and treatment of rare diseases, a National Registry of Rare Diseases, and a waiver for medical care cost, diagnostic work up and therapy for patients with a suspicion, or diagnosis, of one the rare diseases included in an identified list. The Ministerial Decree 279/2001 established an inventory (*Livelli Essenziali di Assistenza - LEA*) of rare conditions (284 single rare diseases and 47 groups of diseases), which receive specific cost exemption. These diseases are assessed as being chronic, debilitating and requiring a high cost treatment. The LEA lists services provided by the National Health System (NHS) to citizens representing the “essential” services, granted to all Italian citizens or foreigners legally resident in Italy, and they are currently provided after paying a prescription charge as “co-payment”. In accordance with Decree 279/2001, all LEA services are totally free for citizens affected by a rare disease in the list. A major problem is that only a few hundred of rare diseases and some groups of diseases are included in this inventory, which is not regularly updated, denying cost exemption and official identification of Reference Centres for diseases not included in the list. The act that updates the LEAs, recently drawn up by the Ministry of Health, has not yet come into force, because the Ministry of Finance is still assessing its feasibility and LEAs remain as first defined in 2001. When effective, the act will allow progress in quality, appropriateness and efficiency, because it includes not only a new list of 109 additional diseases, but also a new list of procedures (for example, laboratory assays for the diagnosis of metabolic diseases).

A Committee ensures the interregional coordination for rare diseases between the Ministry of Health, *Istituto Superiore di Sanità* (ISS – the Italian National Institute for Health - NIH), and all Italian Regions. This Committee has several aims, which include harmonisation of the regional service networks for rare diseases, implementation of the National Registry for rare diseases and management of the list of rare diseases for which patients can obtain free diagnosis and treatment. Rare diseases’ costs are included in the national health care budget and dedicated funds are available for the implementation of regional projects aimed at strengthening the regional service networks (€30 million for 2008 with €5 million for the following years).

In 2008 the National Centre for Rare Diseases (NCRD) was established at ISS, with the mission of promoting and developing scientific research and public health actions, as well as providing technical expertise and information on rare diseases and orphan medicinal products, aimed at the prevention, treatment and surveillance of these diseases. The NCRD took over the activities carried out for many years by a specific unit within the ISS to tackle rare diseases².

In 2009, following an agreement between the Ministry of Health, the NIH and the Italian Regions, €8 million have been allocated to research projects on rare diseases: €5 million from Ministry of Health and Welfare and €3 million from AIFA (the Italian Drug Medicines Agency).

An agreement has been signed between the Government, the Regions and the special statute Provinces of Trento and Bolzano based on the proposal of the Ministry of Labour, Health and Social Policy, concerning guidelines for the correct use of bound resources by the special statute Regions and Provinces, as provided in art. 1, par. 34 and 34bis, Law dated 23 December 1996, n. 662, in order to implement the primary and nationally important objectives for year 2010, including the allotment of €20 million for rare diseases.

On 11-13 November 2010 the Italian Federation for Rare Diseases (UNIAMO F.I.M.R ONLUS), in collaboration with EURORDIS, organised a national conference on rare diseases³ in Florence in the context of the EUROPLAN project. All stakeholders showed great interest in the sessions and worked together to draw up

² www.iss.it/cnmr

³ http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_italy_europlan.pdf

a final report, whose results were presented during a final plenary session open to the public. The aim was to develop an integrated, global and long term strategy for rare diseases in Italy, with the active involvement of all stakeholders to share common European guidelines.

Several drafts of laws focusing on the incentives for research and access to therapies for rare diseases and the production of orphan medicinal products have been presented to the Italian Parliament over the last few years and their approval lies outside the direct domain of the Ministry of Health.

In 2011 a Working Group was established at the Ministry of Health in Rome to thoroughly analyse the issues related to the National Plan for Rare Diseases and to draft the preliminary document. By spring 2012 a draft proposal should be ready for stakeholders' consultation, based on the previous work from 2010 onwards and various stakeholders' meetings at the Ministry of Health.

As concerns related initiatives, during the 25 May 2011 session of the Permanent Conference for relations between State, Regions and Autonomous Provinces of Trento and Bolzano, an agreement was ratified, formalising the engagement of health authorities in guaranteeing, through concrete actions, the global management and appropriate pathways of health care continuity, which must be homogenous throughout Italy, for patients affected by neuromuscular diseases. This goal was achieved via the intensive work carried out by the Ministerial Conference for Neuromuscular Diseases.

Centres of expertise

In 2001 the Ministerial Decree 279/2001 foresaw the establishment of a national network for rare diseases (*Rete Nazionale delle Malattie Rare*), made up of hospitals and referral centres, for around 500 rare diseases, those included in the aforementioned list (LEA). Since 2001, 215 Regional Centres have been designated by official regional decisions. Soon after the delivery of the Ministerial Decree, the Italian Constitution was changed, and health programmes and their organisation were delegated to the Regions. Because of their autonomy, the 20 Regions used different criteria to identify centres for rare diseases and adopted different models to organise their networks.

According to the n. 279/2001 decree, each patient suspected to have a rare disease is addressed to designated hospitals where a free of charge diagnosis can be achieved and, if the disease is confirmed, free treatment is offered by any hospital or outpatient facility within the National Health System (NHS). Coordination centres have been created at regional level in order to manage the activities of referral centres, to exchange information between them, and to provide expertise and data to the regional rare disease registries.

In 2011 UNIAMO (*Federazione Italiana Malattie Rare - FIMR*)⁴ developed the project "A Community for Rare Diseases", aimed at defining a model to assess the quality of expertise centres for rare diseases in Italy. The project gathered all relevant stakeholders who reached a common definition of a Centre of Expertise.

Pilot European Reference Networks

Italy participates, or has participated, in the following European Reference Networks for rare diseases: Dyscerne, ENERCA, EPNET, EPI, EUROHISTIONET, NEUROPED, PAAIR, EN-RBD (main partner) and TAG.

Registries

The Italian National Registry for Rare Diseases, was established at ISS in 2001 in accordance with article 3 of Ministerial Decree 279/2001. It is located at Italian NCRD – ISS and it is supported by public funds. The general objectives include epidemiological surveillance of rare diseases, and planning and evaluating health care national programs. Specific objectives are: i) estimation of incidence and prevalence; ii) temporal and geographical distribution of cases and diseases at national level; iii) diagnostic delay. This registry is also a tool to support clinical research and to promote discussion among health professionals regarding the definition of diagnostic criteria. The National Registry collects the data coming from Regional registries. From 2002 onwards each Italian Region established its Regional Registry for rare diseases. These registries collect epidemiological information provided by accredited Centres for rare diseases (*Presidi* and *Centri*) and every 6 months they send the agreed common data set to the National Registry. The Regional Registries differ in their internal organisation, aims and collected information. In fact, some of them have mainly epidemiological and public health purposes in support of regional planning, while others are aimed at evaluating health services and diagnostic procedures. Agreements have been established between regional administrations in order to create interregional registries. These registries have been established between Piedmont and Valle d'Aosta, and between Veneto and Autonomous Provinces of Trento and Bolzano, Emilia-Romagna, Liguria, Campania and

⁴ <http://www.uniamo.org/>

Puglia. Each interregional system has its informatics infrastructure, acting as a network connecting different Centres involved in the management of patients with rare diseases. All steps concerning diagnosis, clinical follow-up and treatment are linked by a unique information system shared by all professionals involved in patients' management.

On November 2011 the Italian NCRD-ISS published the ISTISAN Report "National Registry and Regional / Interregional Registries for rare diseases"⁵, describing the surveillance system for rare diseases in Italy. Besides a background on the European initiatives on rare diseases, this Report provides detailed information of the evolution of Italian regulatory and institutional context; the steps towards planning and implanting the National Registry; the description of regional/interregional registries; the data quality assessment; the methodological models for estimating epidemiological indicators. Finally, the report describes the epidemiological results collected in years 2007-2010. The report highlights the strengths of this system for public health initiatives and its potentialities to stimulate research on specific rare diseases or groups of them. Up to 31 March 2011, 132,430 diagnostic schedules had been recorded, corresponding to 123,099 primary cases and 9,330 duplicate cases (7%). About 500 rare diseases were under surveillance in the National Registry. The more frequent notified group of diseases included hereditary coagulation disorders (7.5%; n = 9,825 cases), while the most frequent diseases were keratoconus (3.9% n = 5,148 cases) and amyotrophic lateral sclerosis (3.5%; n = 4,628). The National Registry is an important tool for epidemiological surveillance of rare diseases and for evaluating health care programs. The Registry has a strong legal support and it is in compliance with the legal and ethical requirements; it is a population-based registry but with different geographical coverage; it provides important public health indicators (patient mobility, delay in diagnosis), and it is a web-based registry. The National registry is linked to other interregional, regional and international registries.

Italy also participates in European registries such as EUROCAT, EIMD, EURO-WABB, TREAT-NMD, HAE-registry, RBDD, AIR and EUROCARE CF.

Neonatal screening policy

In Italy, neonatal screening is mandatory for cystic fibrosis, congenital hypothyroidism and phenylketonuria (Law 104, 5 February 1992). Some Regions perform screening of additional diseases including adrenal hyperplasia, biotinidase deficiency, maple-syrup urine disease, and galactosaemia. Other Regions, including Tuscany, Sicily and Emilia Romagna, adopted wider neonatal screening programs to include a number of metabolic disorders, based on the guidelines developed by scientific societies. According to SIMMESN (the Italian Society of Metabolic Medicine and Newborn Screening), about one fifth of the Italian newborn population underwent an expanded screening in 2009.

At European level, the "Tender on EU newborn screening practices" had the aims of identifying and evaluating all aspects deemed relevant to the implementation of a public health action in newborn screening (NBS), taking into consideration the views of professionals, patients and health authorities. This project, funded by European Commission DG SANCO, was coordinated by Italian NCRD – ISS, with the intent to support actions at the Community level to identify the strategies which the European Commission could adopt to promote the establishment and improvement of NBS programmes in the EU. All relevant documents elaborated in the Tender and the final reports are available at the website www.iss.it/cnmr. In line with the results obtained during this Tender, in 2011 the Italian Ministry of Health funded a specific project on neonatal screening aimed at harmonising access to health services in the Italian Regions. The project, coordinated by the NCRD – ISS, is carried out in collaboration with the Ministry of Health, Italian Agency for Regional Health Services (AGE.NA.S), *Tavolo Interregionale Malattie Rare*, and two Italian Scientific Societies (SISMMESN and SIGU).

Genetic testing

In an international context, Italy is one of the few countries to monitor genetic test use (this survey was implemented in the 1980s), and recently this monitoring has expanded to include clinical and laboratory activities carried out by Medical Genetic Institutes and also private laboratories since 2009. This census promoted by the *Società Italiana di Genetica Umana* (SIGU; Italian Society of Human Genetics) surveys the services provided by Italian Medical Genetic Centres and involves the NHS bodies, the IRCCSs (Excellence Centres for Healthcare and Research), the University Institutes, the CNR (Research National Council) laboratories, and private laboratories. Data collection takes into account the typology of the Institutes, number and functions of the laboratory staff, cytogenetic analyses, genetic-molecular and immunogenetic analyses, and clinical activity, including genetic counselling. Certified quality systems adopted by the Institutes and the

⁵ <http://www.iss.it/binary/publ/cont/undici20WEB.pdf>

adequacy of some genetic tests have been also checked. The next survey concerning the 2011 data will be carried out in 2012.

In 2010, in collaboration with SIGU, a group of experts determined that changes were needed to improve the organisation of genetic services⁶. The study revealed that only 28% of the 278 Centres surveyed were certified according to quality standards. Moreover, the foetal karyotype was examined on either trophoblast or amniocytes in about one every 4.4 pregnancies and only 11.5% of cytogenetic analyses and 13.5% of molecular tests were accompanied by genetic counselling. This study gathered data from laboratories and services over a one-year period, including 217 molecular genetics and 171 cytogenetic laboratories, and 102 clinical genetic services. The authors of the study published in *Genetic Testing and Molecular Biomarkers* recommend reorganising the structure of genetic testing in Italy, which they qualify as oversized, and to improve quality management, as well as to access to pre- and post-test counselling. This study also underlines the necessity of transborder testing services because of a lack of availability to testing for many rare diseases in Italy.

Diagnostic tests are registered as available in Italy for 793 genes and an estimated 794 diseases in the Orphanet database⁷. Within the national framework there are consolidated procedures to send biological and genetic samples abroad when necessary.

ISS is in charge of carrying out the National External Quality Control Scheme for genetic tests. This scheme includes molecular and cytogenetic tests and has been addressed to public laboratories which use genetic tests. This activity is dependent on a Steering Committee, composed of experts who evaluate the results of cytogenetic and molecular genetic tests. All the strategies used for the project have been discussed and determined through a consensus by the Steering Committee. In 2009 this scheme was extended also to private genetic laboratories. A Steering Committee, composed of experts, evaluates the results of cytogenetic and molecular genetic tests. All strategies used for the project have been discussed and determined through a consensus by the Steering Committee. In 2009 a fee for participation was introduced by National Decree for all participant laboratories (public and private). At the end of each trial of external quality control each laboratory receives its own results. In addition, the NCRD – ISS organises a national Conference to illustrate the main results.

The NCRD-ISS is a member of the management board of the European Molecular Genetics Quality Network (EMQN⁸) a not-for-profit organisation promoting quality in molecular genetic testing by establishing, harmonising and disseminating best practice. EMQN provides external quality assessment to labs worldwide in collaboration with other organisations, including EuroGenTest, CF Network, ESP, UKNEQAS for Molecular Genetics, RCPA QAP, and the EAA.

National alliances of patient organizations and patient representation

In Italy, UNIAMO is the National Alliance of Rare Disease Patient Organisations. Member of EURORDIS and established in 1999, UNIAMO gathers over 100 patient organisations representing over 600 rare diseases. UNIAMO publishes a newsletter and organises regular meetings and conferences. The goal of this Federation is to serve as a reference and representative voice for rare diseases, bringing opinions of patients and their families in the public health decision-making processes at regional and national level. It is committed in the protection of patients' rights and improvement of the quality of life of rare disease patients and their families. UNIAMO is currently organising Regional Delegations: a coordination of territorial groups in order to develop or strengthen the relationship of solidarity and cooperation between member organisations and to foster, at local level, initiatives and policies promoted by the Federation.

There is no public funding scheme for activities of the patients' organisations, but national governmental institutions (e.g. the Welfare Ministry) and local institutions support specific actions. Grants for activities of patients' organisations are coming mainly from private sponsorship, charities and income tax donations. UNIAMO's goals for 2010-2012 were reached taking advantage from these funds, which have granted continuity to the Federation's activities, and sustained the following projects:

- "Knowing to assist", carried out in collaboration with Farindustria and scientific societies, is aimed at training general practitioners and paediatricians regarding rare diseases. The project is based on a covenant of understanding signed by several Institutions. The project, which covers the whole Italian territory, started in 2009, and will conclude in 2012.

⁶ <http://www.liebertonline.com/doi/abs/10.1089/gtmb.2009.0097>

⁷ Information extracted from the Orphanet database (September 2011).

⁸ <http://www.emqn.org/emqn/Home>

- “Galeno Help” results from a memorandum of understanding between UNIAMO and the Professional Pharmacists Union (UPFARM), with the intention of giving practical support to patients who need drugs which are difficult to find. Many of these drugs can be prepared in the galenic laboratories of the pharmacies in a personalised manner. “Galeno Help - Pharmacist helps for rare disease patients” is a national service offering the possibility to quickly and easily find the nearest participating pharmacy.
- “Mercury”, funded by the Ministry of Labour and Social Affairs in cooperation with the signatories of the aforementioned covenant of understanding, has been designed to train the general practitioners and paediatricians in rare diseases. The major goal of the project is to implement and enhance the web site *Malatirari.it* and turn it into a platform to meet the rare disease community’s needs along the complex path from suspected case to diagnosis of a rare disease. The site will become a virtual place where information based on direct experience can be shared by patients, relatives and health professionals involved in the diagnosis and treatment of these diseases.
- “The Atlantis Code” is aimed at fostering the culture of research in rare diseases. Developed in partnership with the Telethon Foundation, it involves rare disease patient organisations in the attempt to identify research priorities and provide answers to the patients’ needs. Three seminars were organised. The outcomes of this survey were matched up with the results of a similar investigation carried out by EURORDIS at European level.
- “Momo” intends to bring together, with a unique voice, the demands of different groups of rare disease patients at Regional level. For this purpose, regional UNIAMO Delegations were created in the context of a progressive regionalisation of the Federation.
- “A Community for Rare Diseases”, is aimed at developing a model to assess the quality of expertise centres for rare diseases in Italy. Since many Regions are reorganising their network of expertise centres, it was felt important to share similar inclusion criteria. Participants included the Ministry of Health, Ministry of Labour and Social Affairs, ISS, Regions, local health authorities, Orphanet Italy, expert centres, municipal districts, general practitioners, primary care paediatricians, biobanks and patients organisations.
- “The Diaspro Rosso” is aimed at identifying the social cost of rare diseases incurred by families.

The ISS hosted the activities of the National Council for Rare Diseases (the “*Consulta*”), established in September 2006 by a Directorial Decree of the Ministry of Health and Welfare: the Council was a national independent representative body, collaborating with the NCRD. It was originally composed of 34 members (one for each participating rare disease patient organisation), which was then lowered to 28; these members were elected by 264 rare disease patient organisations’ representatives. The *Consulta* aimed at identifying the priorities in the field of rare diseases, to define the problems, to recognise solutions for the patients and their families, to involve rare disease patients in the legislative bodies’ decisions, and to strengthen the links between RD organisations and the society. By the end of 2010, the *Consulta*⁹ constituted itself as a private legal organisation which keeps on executing the tasks entrusted by the Minister of Health and affords some of the daily problems of rare disease patients.

The Council for Neurodegenerative Diseases was established by the Ministry of Labour, Health and Social Affairs, through a Ministerial Decree (27 February 2009). The Council brings together patients organisations for neurodegenerative diseases, such as Amyotrophic Lateral Sclerosis, Muscular Dystrophy, Spinal Atrophy, Advanced Stage Muscular Dystrophy and Locked-in syndrome, experts on these disorders, and representatives from Regions and the Ministry of Health. Based on the final document produced by the Council, a proposal for an agreement among State and Regions on health care pathways has been drawn up and is currently assessed by the Regions.

The Veneto Region issued a call in March 2010 for the provision of contributions to Social Promotion Associations, for projects and initiatives identified in several areas of interest, including initiatives aimed at increasing the awareness and knowledge of rare diseases. Several of these projects have been funded in 2011.

Sources of information on rare diseases and national help lines

Orphanet activity in Italy

Since 2001, a dedicated Orphanet team was established in Italy, which is currently hosted by the Bambino Gesù Children Hospital in Rome. This team is in charge of collecting data on rare diseases-related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations, networks) for entry into the Orphanet database. This group was designated in 2010 by the Ministry of Health as

⁹ www.cndmr.it

the official Orphanet team for Italy. The Orphanet portal is available in Italian and the team also maintains the Orphanet Italy national website¹⁰.

On the occasion of the tenth anniversary of Orphanet Italy, an updated Italian Directory of Services, *Annuario Orphanet delle Malattie Rare 2011*, was presented at the Ministry of Health. In attendance was Italian Health Minister, as well as the Director of the Paediatric Hospital Bambino Gesù, which hosts the Italian Orphanet headquarters; Orphanet country coordinator and Scientific Director at Paediatric Hospital Bambino Gesù; President of Farmindustria, which financed this second book; and President of Uniamo FIMR – the Italian Federation for Rare Diseases.

In May 2011 Orphanet Italy signed a collaboration agreement with *Fondazione Cesare Serono* linking the two web sites in order to spread information on rare diseases to a broader public.

From September 2011 onwards the Italian Society of Anesthesia, Analgesia and Intensive Paediatric Care (SIAATIP) collaborates with Orphanet Italy to develop the "Orphanet Emergency" guidelines, designed to improve the hospital emergency management of rare diseases, through recommendations about the care of patients who need medical treatment under emergency.

At the end of 2011 OrphaNews Italia was launched with a first issue in December 2011: OrphaNews Italia¹¹ offers a complete translation into Italian of the contents of OrphaNews Europe, and is available from the homepage of Orphanet Italy and also from the Orphanet Italian country site.

Official information centre for rare diseases

The NCRD-ISS performs scientific research and public health activities, both at national and international level and since many years plays a key role in disseminating information on rare diseases through the official website¹² and the Italian national helpline for rare diseases "*Telefono Verde Malattie Rare*". The website (in Italian and English), updated weekly, is addressed to health operators and institutions, social workers, associations, patients and their families and in general to wide public. The site has been structured on two levels: the central site containing general information, and satellite websites containing specific projects and different topics, including Registries (Italian National Registry for Rare Diseases, Italian National Registry for Orphan Drugs, Italian National Registry for Congenital Anomalies), Orphan drugs, Guidelines, Narrative medicine, Folic Acid Italian Network, European projects, Genetic Tests, Patient Organisations. The section "Centres for rare diseases in Italy" lists all Centres accredited by Regions for diagnosis and treatment, which can be searched by disease, code number, Region, etc. Moreover, all contact details of the Regional Coordination Centres are available.

Help line

The Italian national helpline for rare diseases "*Telefono Verde Malattie Rare*" (no. 800.89.69.49) was set up at the NCRD-ISS on February 2008 and is funded by Ministry of Health. This helpline collaborates with all stakeholders, including the Ministry of Health for legislative and regulatory issues, and it is advertised on the NCRD-ISS web page¹³. The line is free and available five days per week (from 9 am to 1 pm). From abroad it is possible to access the line information by using the e-mail address tvmr@iss.it. A group of psychologists, sociologists and medical doctors trained and experienced on telephone counselling, public health policies and management of rare diseases are involved in this activity. The aim of the service is to inform health operators, social workers, patients and their families, and the public at large, on rare diseases (including exemptions from the costs of medical care in Italy), and to address them to the national/Regional network of specialised centres. *Ad hoc* literature researches are performed for specific questions. Information about patient organisations, orphan medicinal products and clinical trials running in Italy and abroad are also provided. A web based system is used for data collection and to provide data, also using national and international databases (e.g. Orphanet, PubMed, ClinicalTrials.gov, etc.).

Other sources of information on rare diseases

Information for patients and health professionals is also provided by websites run by Centres for rare diseases present in some Regions. A specific mail address (esenzioni@sanita.it) at the Ministry of Health provides information on issues concerning LEA services and co-payment exemption for rare disease patients. Online

¹⁰ <http://www.orphanet-italia.it/national/IT-IT/index/homepage/>

¹¹ <http://www.orpha.net/actor/cgi-bin/OAhome.php?Ltr=ItaliaNews>

¹² www.iss.it/cnmr

¹³ www.iss.it/cnmr

Regional information is also available. Other services are run by patient organisations and are largely heterogeneous in their coverage.

The website www.malattirari.it set up by UNIAMO, besides providing general information on legislative and administrative issues and orphan medicinal products, provides information at regional level thanks to the contributions of patient organisations and health professionals.

Best practice guidelines

The Ministry of Health and ISS are involved in the National Guidelines System (NGS), which is officially entitled to issue guidelines and to make available any other document drawn up by Consensus Conferences carried out by the NGS. Guidelines published by NCRD, as part of the NGS, include those for Down's syndrome, alternating hemiplegia, hereditary epidermolysis bullosa.

With the aim to promote the development of high quality best practice guidelines and their use in Italy and across Europe, NCRD organises national and international training courses providing participants (health care professionals, policy makers, patients) with the opportunity to learn about the core methodology used to develop best practice guidelines. On November 2011, the NCRD organized the Course "Guidelines on rare diseases: basic principles for the development". In addition NCRD encourages the international debate on role and quality of best practice guidelines in the field of rare diseases.

About 72 *Percorsi Diagnostico-Terapeutico-Assistenziali-PDTA* (Diagnostic Therapeutic Care guidelines) dedicated to diagnosis, treatment and clinical management of rare diseases have been developed since 2010 by the Lombardy Region¹⁴.

The working group of the National Committee for Bioethics (CNB) and the National Committee for Biosecurity, Biotechnology and Life Sciences (CNBBSV) published two reports in 2010 dealing respectively with the issues related to the long storage of biological samples obtained by neonatal screenings, and susceptibility testing and personalised medicine. In 2011, the CNB drafted a document relating to orphan medicinal products for people with rare diseases¹⁵.

Training and education initiatives

In Italy, a second level Master degree in rare diseases is organised by the University of Turin. Rare diseases are present in the undergraduate training and post-graduate courses of the Optional Integrated Degree Course of Medicine and School of Specialisation at the Universities of Padua, Siena and Pisa.

The NCRD organises residential courses and learning activities dedicated to the empowerment of patients, health professionals and policy makers¹⁶. This program is included within the project "Rare diseases: from monitoring to training" funded by the Ministry of Health.

The NCRD and the ISS External Relations Office have developed in several Regions a project for training general practitioners (GP) and paediatricians to look for rare diseases, in order to reduce delay to diagnosis, to manage patients' care appropriately in the framework of the Italian rare diseases network, and to improve communication skills. To reach this goal, the courses employ an interactive method, Problem-Based Learning (PBL). PBL is an instructional approach that uses a problem as a didactic initial stimulus; learning is achieved by working in small groups assisted by a trained PBL facilitator at the explanation or solution of the problem. The GPs' and paediatricians' participation to the courses has been active and all professionals got positive results in learning assessment questionnaires; ratings reported in satisfaction questionnaires were mostly positive. The training showed that PBL enhances participant activity and provides the opportunity to practice skills, so that they can produce changes in professional practice, and, ultimately, in health care outcomes. The next step for improving the training model will be to share it with patient organisations and to work with them.

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A relevant role in education of medical doctors is carried out by patient organisations (for example, UNIAMO's projects "Knowing to assist" and "Mercury", see the "National alliances of patient organisations and patient representation" section).

¹⁴ <http://malattierare.marionegri.it/content/view/111>

¹⁵ http://www.governo.it/bioetica/pdf/Malattie_rare_25112011

¹⁶ <http://www.iss.it/cnmr/appu/index.php?lang=1&tipo=56&anno=2011>

National rare disease events in 2011

Since February 2008, UNIAMO coordinates the Rare Disease Day events organised by its members throughout the national territory. It provides them with information leaflets, posters, gadgets, T-shirts and banners, created in collaboration with Farindustria, the Serono Foundation and Novartis. Awareness has been achieved through dozens of local events, in squares, sports halls and schools and through many articles and interviews on rare diseases in newspapers and on TV.

UNIAMO FIMR, in collaboration with its member associations, promoted and coordinated various events to celebrate the Rare Disease Day throughout Italy under the patronage of the President of the Republic of Italy. Events in 2011 to mark the day included the national event "*Rari ma uguali*" (Rare but equal). Orphanet Italy organised a communication campaign on rare diseases with the distribution of information material (a CD-Rom version of the book "*Annuario Orphanet delle Malattie Rare 2011*", Orphanet Italy leaflets, Rare Disease Day pins, balloons, bandanas, etc.) at the Bambino Gesù Children Hospital in Rome. On 26 February 2011, in collaboration with the Barbareschi Foundation, UNIAMO organised an event at the Argentina Theatre in Rome to raise awareness on rare diseases.

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On 28 February 2011, the NCRD-ISS organised the ceremony "*Il Volo di Pegaso*" and the theatre show "*Controvento*", based on rare disease stories.

On 12 April 2011, the Besta Neurological Institute organised in Milan a workshop to show the results of a pilot study on social costs and welfare needs for rare diseases: the study was carried out by the Institute in collaboration with ISFOL (Institute for the Development of Workers' Professional Education), UNIAMO, Orphanet Italy, and Farindustria.

On 4 June 2011, the Bambino Gesù Children Hospital organised in Gaeta a workshop on "Mass Media and Rare Diseases", to stress the role of media in disseminating knowledge on rare diseases, and the responsibility of the reporters in spreading sound information.

The NCRD-ISS organised in 2011 the following events: the 3th meeting on "Narrative medicine and rare diseases (Rome, 13 June 2011); "The communication challenge on rare diseases: words and images on display" (Rome, 14 June 2011); "Primary prevention of congenital anomalies" within the SANIT - International Health Forum (Rome, 14-17 June 2011); "Guidelines on rare diseases: basic principles for the development" (Rome, 21 November 2011).

On 1 July 2011, UNIAMO presented in Rome the project "A Community for rare diseases", aimed at developing a model to assess the quality of expert centres for rare diseases in Italy.

In December Telethon-Italy organised a fundraising event to promote research on genetic diseases.

Other events addressed to rare diseases included: 67th National Conference of the Italian Society of Paediatrics (Milan, 9 June 2011), Rotary Workshop on Rare Diseases – State of the Art and Operative Proposals (Rome, 17 June 2011), National Conference on Williams Syndrome (Rome, 24 September 2011), 16th Meeting of the Italian Society of Human Genetics (Milan, 14-15 November 2011), 11th National Meeting of Genetics, Immunology and Translational Paediatrics (Messina, 26 November 2011).

Hosted rare disease events in 2011

Amongst the hosted rare disease events in Italy this year and announced in OrphaNews Europe were: the Europlan Final Conference (Rome, 25 February 2011), 4th International Symposium on Pulmonary Rare diseases and Orphan Drugs (25-26 February 2011, Milan), Fifth Meeting on the Molecular Mechanisms of Neurodegeneration (13-15 May 2011, Milan), 8th International Health Forum, SANIT (Rome, 14-17 June 2011), EPIRARE kick-off meeting (Rome, 11 July 2011).

In addition to this, an international Medical Genetic Course was held under the sponsorship of Orphanet Italy at the Bambino Gesù Children Hospital in Rome on 23-24 June 2011. This event was addressed to doctors, biologists, researchers, medical students, with the aim of analyzing thoroughly clinical, biological and therapeutic aspects of some inherited rare diseases. A course was also organised by the European School of Oncology in collaboration with the Rare Care project in Stresa from 31 March – 1 April 2011, focusing on all

the main rare solid cancers of the adult. The 3rd Goldrain Course in Prenatal Genetic Diagnosis took place from 15 to 21 October 2011 at the Goldrain Castle in South Tyrol. The 2nd Course in Eye Genetics-EuroMediterranean University Center of Bologna Eye Genetics was held in Bologna on 28 September – 1 October 2011: this 4-day long postgraduate level course is addressed to both researchers and clinicians seeking an up-to-date introduction to the field of ophthalmogenetics today.

Research activities and E-Rare partnership

National research activities

In Italy, there are efforts to coordinate research between Regions, Italian Drug Agency (AIFA)¹⁷, Ministry of Health and ISS. Funds for rare diseases research are provided by Ministry of Health, ISS, AIFA and Ministry of Education, University and Research, Telethon, patient organisations and a few charities. The last Health Ministry call for projects for rare diseases¹⁸ had a total budget of €8 million. The call for projects was published in 2008 and 13 projects were granted in 2010.

A bilateral agreement between Italy (ISS) and USA (NIH) was established with the purpose of developing and increasing research in different fields, including rare diseases since 2002. This agreement is still active.

AIFA issued calls to fund independent researches on the development of orphan medicinal products. In particular, AIFA financed a three-year initiative, launched in 2005, to support clinical research on drugs of interest to the NHS where commercial support is inadequate: one of the concerned areas was the field of rare diseases and orphan medicinal products. Three topics were included in the clinical research area concerning rare diseases: the benefit-risk profile of orphan medicinal products designated by EMA; the benefit-risk profile of off-label drug use (and in particular generics); the benefit-risk profile of drugs for non-responders to standard treatments. Projects in these topic areas were funded for up to a maximum of €300,000, with the therapy costs funded separately. From 2008 onwards rare diseases and orphan medicinal product research is being funded by the Ministry of Health, within the general health research call, with a specific budget reserved for rare diseases research. A specific call to fund research projects on rare diseases was issued by the Ministry of Welfare in 2009.

In 2011 Telethon was able to fund 230 research projects on genetic diseases thanks to fundraising activities in 2010.

Foundations and associations promote campaigns funding genetic research or research on specific diseases. Voluntary funds can be collected through general taxation.

Participation in European research projects

Italy participates, or has participated, in European rare disease research projects including: AAVEYE, ADIT, ANTIMAL, BIG HEART, BIOMALPAR, BIO-NMD, CARDIOGENET, CUREHLH, CUREFXS, CLINIGENE, CONTICANET, CSI-LTB, ENRAH, EURADRENAL, EUCILIA, EUCLYD, EMSA-SG, EUROBONET, EUROGROW, EURO-LAMINOPATHIES, EUROPAPNET, EUROBNFS, EURO-CGD, EURO-SCAR, EUROTRAPS, EURPIFNET, EUROSD, EPINOSTICS, ERMION, EUROGEBETA, EURORETT, EUROPSPA, EUMITOCOMBAT, EURAMY, EURAPS, EUREGENE, EUROCARE-CF, EUROPEAN LEUKEMIA NET, EUROSCA, EUROWILSON, GENESKIN, GENOMIT, INHERITANCE, IPF-AE, HAE III, HMA-IRON, HSCR, KINDLERNET, MTMPATHIES, LEISHMED, LIGHTS, MALARIA AGE EXPOSURE, MANASP, MITOCIRCLE, MOLDIAG-PACA, MCSCS, MILD-TB, MM-TB, MYELINET, MYORES, MTMPATHIES2, NANOMYC, NEUROKCNQPATHIES, NEUROPRION, NEUROPROMISE, NEUROSIS, NMD-CHIP, NSEURONET, OSTEOPETR, PEROXISOMES, PNSEURONET, PROTHETS, PODONET, PEMPHIGUS, RD PLATFORM, RISCA, READ-UP, SIOPEN-R-NET, SKIN-DEV, SPASTICMODELS, SME MALARIA, STEM-HD, TAMAHUD, TUB-GENCODEV, TARGETHERPES, VITAL, WHIPPLE'S DISEASE, WHIM-Thernet and WHIMPATH.

E-Rare

Italy, represented by ISS, is a partner of the E-Rare project and took part in all three Joint Transnational Calls. Italy participated in 12 of the 13 consortia selected for funding by the first call. In the second E-Rare transnational call, Italy participated in 8 of the 16 consortia/projects selected for funding with a budget of about €1 million. Italy participated in the 3rd Joint Transnational Call in 2011 and Italian teams have been funded to participate in 7 of the selected consortia.

¹⁷ <http://www.agenziafarmaco.gov.it/>

¹⁸ http://www.quotidianosanita.it/cronache/articolo.php?&&articolo_id=1144&&cat_1=1&&cat_2=0

IRDIRC

The ISS and Italian Telethon Foundation are committed members of IRDiRC.

Orphan medicinal products^{19,20}

AIFA is the main body in charge of the introduction of orphan medicinal products into the Italian market. The National Registry of Orphan Drugs includes data on diagnosis and follow-up of patients treated with orphan medicinal products. These drugs are authorised at central level by EMA (European Medicines Agency) and reimbursed by NHS. The National Registry of Orphan Drugs, established by AIFA and managed in collaboration with NCRD, surveys forms for each rare disease and its related drugs, and collects, checks and analyses data sent by Regional Centres authorised to distribute these drugs. The goal of the registry is to have a nationwide coverage, to address all Italian Centres qualified to distribute and prescribe orphan medicinal products.

Orphan medicinal product committee

There is no specific orphan medicinal product committee at national level in Italy.

Orphan medicinal product incentives

AIFA has established an innovative funding scheme (*Fondo AIFA 5%*). Established under Article 48 of Law 326/2003 and operative since 2005, Italian pharmaceutical companies are required to donate 5% of their promotional expenditure to an independent research fund. The fund collects €45 million each year: half of this allowance is used for the reimbursement of orphan and life saving drugs awaiting market entry, while the other half is aimed at supporting independent research, drug information programs and pharmaceutical vigilance. This funding program for independent clinical research on drugs is open to researchers working in public and non profit institutions. One of the research areas of the program is dedicated to orphan medicinal products for rare diseases. At the beginning of 2009, three calls for proposals (2005-2007) had been finalised and 69 studies received funding in the area of rare diseases. Since 2008, however, rare diseases and orphan medicinal product research were not listed among the priority areas.

Orphan medicinal product market availability situation

In Italy, 47 out of the 66 orphan medicinal products approved by EMA are launched on the market. The cost of 44 of them is fully paid by the National Health System (NHS), based on a therapeutic indication, while 3 of them are reimbursed under special circumstances (Law 648/96). The other EMA approved drugs have a pending request at AIFA by the companies in charge of pricing and reimbursement²¹. A list of orphan medicinal products with European marketing authorisation and the date of their publication in the Official Gazette concerning their marketing in Italy is available²².

Orphan medicinal product pricing policy

Prices of all medicines for reimbursement by the National Health Service, including hospital-only drugs, are set by AIFA. Two interministerial committees are involved in this process, the Pricing and Reimbursement Committee and the Technical-Scientific Commission¹⁵.

Orphan medicinal product reimbursement policy

In Italy drugs are catalogued in A and C classes, depending on their reimbursement. Costs of class A drugs are totally paid by NHS and free of charge for citizens, while class C drugs are paid entirely by patients. Reimbursement is granted for all orphan medicinal products which follow the centralised marketing authorisation procedure. Moreover, for all drugs which are not currently classified in class A, reimbursement is regionally based within "extra LEA services", which means further services decided by the individual Regions and covered by their own economic resources. Many Regions in the last years have supplied class C drugs to their population. According to AIFA, the orphan medicinal product availability in 2010 included 6,839,423 daily

¹⁹ This section has been written using information from the KCE reports 112B: *Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* pp.49-53.

²⁰ This section has been written using the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*. 2005 Revision pp.15-16.

²¹ According to the Final Report of the Europlan National Conference, 11-13 November 2010.

http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_italy_europlan.pdf p16.

²² http://www.iss.it/binary/orfa/cont/Farmaci_orfani_in_Italia_Feb_2009.pdf (document accessed May 2011 and last updated in February 2009).

doses (DDs), with a total cost of €661,709,750, while the corresponding total cost of non-orphan medicinal products was €12,981,636,953 for 21,971,349,308 DDs. Thus, the DDs cost for orphan medicinal products was about €100, compared to €1.60 for non-orphan medicinal products.

Some orphan medicinal products can only be dispensed if the details of the patient are entered into the National Registry of Orphan Drugs, containing information on diagnosis and follow-up of the patient²³.

Other initiatives to improve access to orphan medicinal products

Italy also has an off-label, compassionate use procedure, regulated by Law 648/96²⁴ (a list of eligible drugs is annexed to this law). The Technical Committee of AIFA can include a given medication in the official list allowing it to be prescribed at the NHS charge, if for a specific disease there is no therapeutic choice. Three types of medical products can be included: innovative drugs for which the sale is authorised abroad, but not in Italy; drugs which have not yet received an authorisation, but have undergone clinical trials; and drugs to be used for a therapeutic indication different from the one which had been authorised²⁵. A Ministerial Decree of 8 May 2003²⁶ allows for the prescription (paid by the producer) of drugs not yet authorised, but subjected to phase II or III clinical trials for the same therapeutic indication, for which a favourable evaluation in terms of efficacy and safety is expected.

The off-label use of a drug at the expense of the NHS can also be decided by a doctor, as envisaged by article 3, paragraph 2 of Law Decree²⁷ 23/1998, provided that this decision is made on a named patient basis, documented evidence is provided, and no other treatment is possible. "Fondo AIFA 5%" also finances the use of medicines with non-approved indications.

The Ministerial Decree 11/2/1997 allows the import of unauthorised orphan medicinal products on a patient basis: in this instance, the payer is the Region or the NHS in the case of hospital or reference centre use²⁸.

At the end of 2010, a new deal between central Government and the Regions will mean that 'potential/important therapeutic innovations' will be automatically included on regional formularies, so they should be available simultaneously and quickly across Italy¹⁵.

Orphan devices

No specific information reported.

Specialised social services

Respite care services are unevenly distributed within Italy and are mainly provided by governmental or accredited institutions and sometimes by the private sector: full or partial reimbursement is offered and some patient organisations provide services free of charge. A new act has been proposed defining the services that the entire population is entitled to; this includes "respite intervention" for families affected by severe disabilities, either in residential structures or semi-residential ones. Lodging, meals and other housing services are to be paid for by patients, or by municipalities, in the case of low-income situations.

Therapeutic recreational programmes are provided, although unevenly, by local authorities' social services under the administration of the municipalities. The institutional framework is complex: at governmental level, this competence belongs to the Ministry of Social Affairs, but the legislative power in terms of social policies is under the exclusive responsibility of Regions (Constitutional Law no. 3 October 18, 2001). It is the competence of the State to determine the essential level of benefits relating to civil and social rights that must be guaranteed throughout the national territory; the municipalities are the holders of administrative functions relating to social interventions undertaken at local level (Law n.328 November 8, 2000). Some municipalities assure public services, but more often services are run by private bodies (companies or patient

²³ *Orphan Drugs in Europe : Pricing, Reimbursement, Funding & Market Access Issues*, Donald Macarthur (2011) p.83

²⁴ Law 23-12-1996 n. 648. *Conversione in legge del D.L. 21 October 1996, n. 536, recante misure per il contenimento della spesa farmaceutica e la rideterminazione del tetto di spesa per l'anno 1996* (published in GU 23 December 1996, n. 300).

²⁵ KCE reports 112B: *Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* p.50.

²⁶ Ministerial Decree 8 May 2003 *Uso terapeutico di medicinale sottoposto a sperimentazione clinica* (published in GU 28 July 2003, n. 173).

²⁷ Law Decree 17-2-1998 n. 23 *Disposizioni urgenti in materia di sperimentazioni cliniche in campo oncologico e altre misure in materia sanitaria*. (published in GU 17 February 1998, n. 39).

²⁸ *EMINET Initial investigation to assess the feasibility of a coordinated system to access orphan medicines*, C. Hahl, F. Bachner (2011) p54.

²¹ *Istat 2008: Gli interventi e i servizi sociali dei comuni singoli e associati*.

http://www3.istat.it/salastampa/comunicati/non_calendario/20110419_00/testointegrale20110419.pdf

organisations) commissioned by social authorities. Some summer camps are informally or formally organised by patient organisations (for example, Dynamo Camp in Tuscany). These services are sometimes fully reimbursed, or there is a partial contribution according to the family income.

Additional social and/or financial support is available for families and patients with disabilities (Law Decree n. 509, 23 November 1988). Services promoting social integration of patients with disabilities in schools and the workplace are provided by the Government. The provision of specialised social services is thus unevenly distributed at national level. The average per-capita social spending of municipalities varies from €30 to €250²¹, and it is not considered satisfactory because the rules of access to services and the sharing costs are different in Regions. Furthermore there is a reduction in available resources: in year 2008-2011 there was a 89% cut of the National Welfare Fund, down from €1 billion 200 million to €69 million, only covered in part by Regions and municipalities.

DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2011 IN ITALY

National plan/strategy for rare diseases and related actions

In 2011 a Working Group was established at the Ministry of Health in Rome to thoroughly analyse the issues related to the National Plan for Rare Diseases and to draft the preliminary document. By Spring 2012 a draft proposal should be ready for stakeholders' consultation, based on the previous work from 2010 onwards and various stakeholders' meetings at the Ministry of Health.

As concerns related initiatives, during the 25 May 2011 session of the Permanent Conference for relations between State, Regions and Autonomous Provinces of Trento and Bolzano, an agreement was ratified, formalising the engagement of health authorities in guaranteeing, through concrete actions, the global management and appropriate pathways of health care continuity, which must be homogenous throughout Italy, for patients affected by neuromuscular diseases. This goal was achieved via the intensive work carried out by the Ministerial Conference for Neuromuscular Diseases.

Centres of expertise

In 2011 UNIAMO (*Federazione Italiana Malattie Rare - FIMR*)²⁹ developed the project "A Community for Rare Diseases", aimed at defining a model to assess the quality of expertise centres for rare diseases in Italy. The project will gather all relevant stakeholders who helped reached a common definition of a Centre of Expertise.

Registries

On November 2011 the Italian National Centre of Rare Diseases at the ISS (NCRD-ISS) published the ISTISAN Report "National Registry and Regional / Interregional Registries for rare diseases"³⁰, describing the surveillance system for rare diseases in Italy. Besides a background on the European initiatives on rare diseases, this Report provides detailed information of the evolution of Italian regulatory and institutional context; the steps towards planning and implanting the National Registry; the description of regional/interregional registries; the data quality assessment; the methodological models for estimating epidemiological indicators. Finally, the report describes the epidemiological results collected in years 2007-2010. The report highlights the strengths of this system for public health initiatives and its potentialities to stimulate research on specific rare diseases or groups of them. Up to 31 March 2011, 132,430 diagnostic schedules had been recorded, corresponding to 123,099 primary cases and 9,330 duplicate cases (7%). About 500 rare diseases were under surveillance in the National Registry. The more frequent notified group of diseases included hereditary coagulation disorders (7.5%; n = 9,825 cases), while the most frequent diseases were keratoconus (3.9% n = 5,148 cases) and amyotrophic lateral sclerosis (3.5%; n = 4,628).

²⁹ <http://www.uniarno.org/>

³⁰ <http://www.iss.it/binary/publ/cont/undici20WEB.pdf>

Neonatal screening policy

In line with the results of the European Commission funded Tender on EU newborn screening practices, in 2011 the Italian Ministry of Health funded a specific project on neonatal screening aimed at harmonising access to health services in the Italian Regions. The project, coordinated by the NCRD – ISS, is carried out in collaboration with the Ministry of Health, Italian Agency for Regional Health Services (AGE.NA.S), *Tavolo Interregionale Malattie Rare*, and two Italian Scientific Societies (SISMMESN and SIGU).

Sources of information on rare diseases and national help lines

Orphanet activity in Italy

On the occasion of the tenth anniversary of Orphanet Italy in 2011, an updated Italian Directory of Services, *Annuario Orphanet delle Malattie Rare 2011*, was presented at the Ministry of Health. In attendance was Italian Health Minister, as well as the Director of the Paediatric Hospital Bambino Gesù, which hosts the Italian Orphanet headquarters; Orphanet country coordinator and Scientific Director at Paediatric Hospital Bambino Gesù; President of Farindustria, which financed this second book; and President of Uniamo FIMR – the Italian Federation for Rare Diseases.

In May 2011 Orphanet Italy signed a collaboration with *Fondazione Cesare Serono* linking the two web sites in order to spread information on rare diseases to a broader public.

From September 2011 onwards the Italian Society of Anesthesia, Analgesia and Intensive Paediatric Care (SIAATIP) collaborates with Orphanet Italy to develop the "Orphanet Emergency" guidelines, designed to improve the hospital emergency management of rare diseases, through recommendations about the care of patients who need medical treatment under emergency.

At the end of 2011 OrphaNews Italia was launched with a first issue in December 2011: OrphaNews Italia offers a complete translation into Italian of the contents of OrphaNews Europe, and is available from the homepage of Orphanet Italy and also from the Orphanet Italian country site.

Good practice guidelines

On November 2011, the NCRD organised the Course "Guidelines on rare diseases: basic principles for the development". In addition NCRD encourages the international debate on role and quality of best practice guidelines in the field of rare diseases.

In 2011, the National Committee for Bioethics (CNB) drafted a document relating to orphan medicinal products for people with rare diseases.

Training and education initiatives

The NCRD and the ISS External Relations Office have developed in several Regions a project for training general practitioners (GP) and paediatricians to look for rare diseases, in order to reduce delay to diagnosis, to manage patients' care appropriately in the framework of the Italian rare diseases network, and to improve communication skills. To reach this goal, the courses employ an interactive method, Problem-Based Learning (PBL). PBL is an instructional approach that uses a problem as a didactic initial stimulus; learning is achieved by working in small groups assisted by a trained PBL facilitator at the explanation or solution of the problem. The GPs' and paediatricians' participation to the courses has been active and all professionals got positive results in learning assessment questionnaires; ratings reported in satisfaction questionnaires were mostly positive. The training showed that PBL enhances participant activity and provides the opportunity to practice skills, so that they can produce changes in professional practice, and, ultimately, in health care outcomes. The next step for improving the training model will be to share it with patient organisations and to work with them.

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Hosted rare disease events in 2011

Amongst the hosted rare disease events in Italy this year and announced in OrphaNews Europe were: the Europlan Final Conference (Rome, 25 February 2011), 4th International Symposium on Pulmonary Rare diseases and Orphan Drugs (25-26 February 2011, Milan), Fifth Meeting on the Molecular Mechanisms of Neurodegeneration (13-15 May 2011, Milan) 8th International Health Forum, SANIT (Rome, 14-17 June 2011), EPIRARE kick-off meeting (Rome, 11 July 2011).

Research activities and E-Rare partnership

National research activities

In 2011 Telethon was able to fund 230 research projects on genetic diseases thanks to fundraising activities in 2010.

E-Rare

In the second E-Rare transnational call, Italy participated in 8 of the 16 consortia/projects selected for funding with a budget of about €1 million. Italy participated in the 3rd Joint Transnational Call in 2011 and Italian teams have been funded to participate in 7 of the selected consortia.

IRDiRC

The ISS and Italian Telethon Foundation are committed members of IRDiRC.

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³¹ The contributors and validators of the report have contributed information which is accurate to the best of their knowledge. However, readers should take note that the contents of this report are illustrative and not exhaustive.

³² All websites and documents were last accessed in May 2012. A more detailed list of sources is available in the full report:
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