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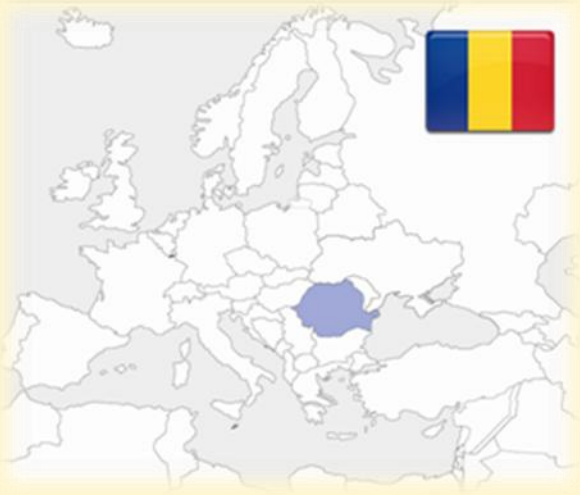
2012 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE OF THE EUROPEAN UNION COMMITTEE OF EXPERTS ON RARE DISEASES



STATE OF THE ART OF RARE DISEASE ACTIVITIES IN ROMANIA

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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 Porphyria 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 Romania. 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 report[1].

[1] http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivities.pdf

RARE DISEASE ACTIVITIES IN ROMANIA

Definition of a rare disease

Stakeholders in Romania 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

On 29 February 2008, the Romanian Ministry of Health and the country's National Alliance for Rare Diseases (RONARD) signed an accord to form a partnership ("Rare Diseases, a priority for health care in Romania) in order to instate a national plan for rare diseases, following work which started in August 2007 to develop a National Plan, and a National Conference on Rare Diseases in November 2007 on the theme of "Rare diseases: From evaluation of needs to establishing priorities".

A member from the ministry and from the National Alliance for Rare Diseases (RONARD) were appointed to work together to review the national plan which was developed by rare disease stakeholders and presented to the government at the end of 2007, with the aim of creating an estimate of funding and resources required for each element of the plan. An expert team, including geneticists, paediatricians, endocrinologists, pneumologists, cardiologists, haematologists, informatics specialists, public policy experts and other specialists will be gathered to help evaluate the plan and develop a cost analysis for each item. The country's 2008 health budget was then to be readjusted to include funding for various elements of the rare disease plan.

An official decision of the Romanian Government[2] (26 March 2008) stipulated the necessity of various national health programmes in Romania, including a two-year health programme for rare diseases to be funded by the state, covering the diagnosis of rare diseases, the medical treatment of rare diseases and the establishment of several registries linked to specific rare diseases, and rare diseases in general. This "national programme for haemophilia, thalassaemia and other rare diseases" came into force in June 2008 and in reality covers some aspects of health care for rare diseases, but the coverage is limited and does not include all rare diseases and all aspects of health care provision for rare diseases. A budget is currently dedicated to this Programme (Order 1591 /1110/ 30 December 2010 - MH / National Health Security). A working document has been developed with a timeline for implementing specific elements of the programme, which seeks to improve access to information; establish an adequate strategy for ensuring prevention, diagnosis, treatment and rehabilitation services; create a national registry; stimulate research; create rare disease training initiatives for professionals from various fields; and collaborate with various EU and international organisations.

In August 2009, a National Committee for Rare Diseases (composed of professionals and representatives of patient associations), involving the Ministries of Health, Education, and Labour, as well as the National Medicine Agency, the Authority of People with Disabilities and the Child Welfare Authority. The main aim of this Committee in 2009-2010 was to elaborate the Romanian National Plan for Rare Diseases. The activities of this committee include government decisions for coordination, guidance and control of services for rare disease patients, including social integration.

The National Programme for diagnosis and treatment for rare diseases is currently coordinated in its methodology by the Commission of Genetics of Ministry of Health, under supervision of Commission of Rare Diseases of Ministry of Health.

Interventions are already put in place for the following purposes:

1. Specific medication assurance:
    a. Prophylaxis and treatment of hemorrhagic events for hemophilic patients and iron chelators for thalassemic patients
    b. Treatment of patients with:
        i. Multiple sclerosis
        ii. Pulmonary Hypertension (PHT)
        iii. Mucoviscidosis
        iv. Degenerative neurological disorders
        v. Miastenia gravis
        vi. Osteogenesis imperfecta
        vii. Fabry disease
        viii. Pompe disease

[2] http://www.ms.ro/?pag=133

ix. Tirozinemia
x. Bulous epidermolysis
xi. Prader Willi syndrome

2. Interventions for early diagnosis and management of spinal amyotrophy and muscular dystrophy (Duchenne and Becker) – coordinating Clinical Pediatric Hospital "Prof. Dr. Al. Obreja" Bucharest, and in second step several hospitals in different towns from Romania;
3. Interventions for assurance of dietetic food for patients with phenylketonuria;
4. Intervention for establishing of National Registry for Rare Diseases.

Four meetings of the National Committee for Rare Diseases were organised in 2011. In July 2011 the Romanian Association for Rare Cancers was established and at the National Committee for Rare Diseases meeting in November 2011 rare cancers were included in the proposal for the National Plan for Rare Diseases. The EUCERD Recommendations on Quality Criteria for Centres of Expertise for Rare Diseases were also discussed and most have been included in the content of the Romanian National Plan for Rare Diseases.

During 2011, the Ministry of Health Rare Diseases Operative Commission was founded (ASC nr. 1132/11.04.2011), coordinated by the National Committee for Rare Diseases. It is involved directly in elaborating and executing of the decisions of the National Committee for Rare Diseases. A Rare Disease Commission has also been created at the University of Medicine and Pharmacy in collaboration with the Member States Rare Diseases Commission. The objectives were to:

- Develop formal address via which committees of the Social Fund can supply data for national programs developed by National House of Health Insurance to Establish a National Registry for Rare Diseases;
- Establish in 2012 an official website within the working groups to disseminate information and requirements formulated at the EU Commission for National Rare Diseases committee;
- Develop treatment programs according to Directive no. 2011/24/UE European Parliament and the Council of 9 March 2011 on the application of patients' rights in cross border healthcare.

In terms of funding and governmental support, in July 2011 the budget allocation for National Program for Rare Diseases was increased by €2,000,000: 43 more patients affected by rare diseases were included in the program (7 patients with Hunter Syndrome, 3 patients with Harley Syndrome, 1 patient with Congenital Afibrinogenemia and 33 patients with congenital primary immunodeficiency).

On 28 June 2011 the official opening of the Pilot Reference Centre for Rare Diseases took place in Zalau (see section entitled "Centres of expertise"). Romania marked an important advance in services provided to Romanian rare disease patients. The Minister of Health allocated a financial support for the new Pilot Centre, amounting to €80,000.

Centres of expertise

There are no official centres of expertise in Rare Diseases in Romania at the moment, and currently the genetic diagnosis of rare diseases is carried out in Medical Genetics Centres based in university hospitals. Expert care is currently provided by many different centres, including: National Institutes of Oncology (Trestioreanu – Bucharest and Chiricuta - Cluj Napoca), Institute of Cerebrovascular diseases (Bucharest), Heart Institute (Cluj), National Institute of Endocrinology (Parhon - Bucharest), National Institute for Mother and Child (Alfred Rusescu - Bucharest), National Institute for Research and Development "Victor Babes (Bucharest), Fundeni Clinical Institute (Bucharest), etc. In addition, in major Romanian medical centres (Bucharest, Iasi, Constanta, Cluj, Timisoara, Targu Mures) there is a programme in place for the diagnosis of foetal anomalies which also aims to improve care during pregnancy and diagnosis of possible genetic disorders.

A network for Pulmonary Hypertension (PHT) has been composed, including the following following institutes: Institute of Cardiovascular Diseases "CC Iliescu" (Bucharest), Pneumology Hospital (Iasi), Hospital "Victor Babes" (Timisoara), Heart Institute (Cluj) Institute of Cardiovascular Diseases and Transplantation - Pediatric Cardiology Clinic (Targu Mures), Children's Emergency Hospital "Louis Turcanu" (Timisoara), Heart Centre - Cardiovascular Surgery Clinic (Cluj), Department of Paediatric Cardiology (Bucharest).

In addition, many university hospitals are centres of expertise for several specialities, including care for patients with rare diseases. Many national institutes/regional university hospitals serve as tertiary care centres for patients with rare diseases. An extension of expertise to improve its geographical distribution is a provision of the working document of the National Plan currently under consideration. An outline for a system of centres of expertise has been proposed in the National Plan for Rare Diseases based on a network of centres at national, regional and county level by category of disease.

In the view of Romanian Ministry of Health, expertise has developed around the medical Universities and currently many rare diseases are diagnosed and treated. The Operative Commission of Rare Disease recently founded by the Ministry of Health Rare Disease Commission, will establish a network of Expertise Centres, with specialised laboratories for diagnosing and follow-up rare diseases in University Centres. These centres will include not only genetic laboratories, but all laboratories and facilities needed for the diagnosis and follow-up of the patients with rare diseases, gathered around specialised medical teams involved in this domain. In 29 November 2011 the Ministry of Health Operative Commission of Rare Diseases held a meeting in order to establish the criteria for centres of expertise and networks of these centres in Romania. The university centres were identified by the Commission and documentation was elaborated to be sent to these centres in order to begin the implementation of criteria for centres of expertise for Rare Diseases. In this perspective, the main university centres identified were: Bucharest, Iasi, Cluj, Timisoara, Craiova, Targu Mures. The methodology for the identification of centres of expertise affiliated to "Carol Davila" University of Medicine and Pharmacy Bucharest was discussed, as was the accreditation of these centres in field of rare diseases proposed. A common registry of Rare Diseases was also proposed to be implemented in every Centre of Expertise based on the existing database for different rare diseases, with a deadline in 2013.

The official opening of the Pilot Reference Center for Rare Diseases "NoRo" took place on 28 June 2011 in Zalau. The establishment of the NoRo Center was made possible through the project "Norwegian - Romanian (NoRo) Partnership for Progress in Rare Diseases" (2009-2011) with financial support from the Norwegian Cooperation Programme for sustainable economic development in Romania. The project involved 11 partners: Romanian Prader Willi Association (main applicant), Norwegian Prader Willi Association, Frambu - Norwegian Center for Rare Diseases, Ministry Health Romania, City Hall Zalau, County Council Salaj, Acasa Foundation, "St. Family" Greek Catholic Church Zalau, Romanian National Alliance for Rare Diseases, Romanian Medical Genetics Society and Medical University "Victor Babes" Timisoara. The opening event was attended by Mrs. Minister of Health and Care Services Norway Anne-Grete Strom-Erichsen, Mr. Minister of Health Romania Cseke Attila, Mr. Ambassador of Norway in Romania Oystein Hovdkinn, Director of the Norwegian Cooperation Programme in Romania and Bulgaria Tore Lasse By, representatives of EURORDIS, Orphanet Romania and patients´ associations from Hungary, Italy, France, Denmark, Spain, Norway, Bulgaria, Russia, Sweden, the Secretary General of the Second National Plan for Rare Diseases France, local officials and members of EUCERD. Also was present Mr. Bercea Virgil, Greek Catholic Bishopric of Oradea, who officiated the holy ceremony of the opening.

In addition an International Conference entitled "The European approach for rare diseases" was held on 29 June 2011, in Zalau to mark the official opening of the first Pilot Reference Centre for Rare Diseases in Romania. The Romanian Prader Willi Association and Romanian National Alliance for Rare Diseases organised the event. This event was based around the theme of quality care, the empowerment of patients and families and the examples of the Frambu model and the French National Plan for Rare Diseases. The program included two roundtables around the themes "Addressing the needs of patients" and "Innovation in the field of rare diseases." The 92 participants included representatives of the rare diseases centres around Europe were present (i.e. Norway's Frambu, Sweden's Agrenska, Spain's CREER, Hungary's Centre for Rare Diseases).

Pilot European Reference Networks

Romanian teams participate, or have participated, in the following European Reference Networks for rare diseases: Dyscerne, ECORN CF, ENERCA, TAG and Care-NMD.

Registries

A national rare disease registry is one of initiatives proposed for inclusion in a national plan for rare diseases. An official decision of the Romanian Government[3] of 26 March 2008 stipulates that National Registries should be established and maintained for cardio-vascular diseases (including congenital anomalies), cancers, diabetes mellitus, haemophilia, thalassaemia, psychiatric diseases as well as a National Registry for rare diseases.

There are currently a number of patients' registries in Romania in the field of rare diseases including: the National Registry of Haemophilia, the National Registry of Primary Immunodeficiency, the National Registry of Infant Diabetes Mellitus, the National Registry of Thalassemia, the National Registry of Cystic Fibrosis, the National Registry for Pulmonary Hypertension, the National Registry for Hyperparathyroidism, the National Registry for Acromegaly, and the National Registry of Neuromuscular Diseases. The National Registry of congenital Hypothyroidism and National Registry of Neuroendocrine tumours are under development.

[3] http://www.ms.ro/?pag=133

The Ministry of Health Rare Diseases Operative Commission has established a plan for a National Registry of Rare Diseases based on databases of centres of expertise from each University Centre, able to cover the entire country. The classification of rare diseases is scheduled to be improved in Romania: currently rare diseases are listed in a range of National Programmes apart from that for rare diseases, such as the Oncology Programme, Metabolic Diseases Programme, and Neurological Programme. The centres of expertise will be involved in this activity.

The Meeting of Ministry of Health Operative Commission of Rare Diseases held on 29 November 2011 in Bucharest proposed a common registry of Rare Diseases to be implemented in every Centre of Expertise based on the existing database for different rare diseases. The deadline for establishing a National Registry of Rare Diseases is for 2013. This registry will include common data file identification, a type of program that is included each type of disease tracking centre for each patient (data developed on existing programs out National Health Insurance Agency). The inclusion of new specialities with activity in the field of rare diseases was also discussed, also, in order to extend the present nomenclature of rare diseases.

Romania contributes to the following European registries: EUROCARE CF and the European Registry for CML (EUTOS).

Neonatal screening policy

Some 200,000 babies are born every year in Romania. According to national health policy a newborn screening program for phenylketonuria (PKU) and congenital hypothyroidism (CHT) is mandatory. The screening is performed in 4 public medical centers throughout the country (Bucharest, Iasi, Cluj-Napoca and Timisoara).

The current policy for prenatal screening and diagnosis in Romania includes a national programme for all pregnant women over age 35 at conception offering tests free of charge. Biochemical screening, ultrasound and CVS/amniocentesis are performed in 6 public medical centres throughout the country. Prenatal screening/diagnosis is also offered to all pregnant women independently of maternal age with costs eligible to be covered by national health insurance. At this time, prenatal testing procedures are invasive and performed for the most common clinically significant foetal aneuploidies. Prenatal diagnosis is also used to determine whether a foetus has a rare monogenic disorder. Usually, for a foetus at increased risk for rare monogenic diseases, CVS/amniocentesis and DNA isolation are performed in many public or private clinics. Then, the DNA samples are sent abroad for molecular diagnosis of rare monogenic diseases (sequencing for entire gene or selected exons).

In 2011 Romania joined contributed to the efforts aimed at the preparation of European guidelines on diagnostic tests or population screening (in the scope of the Tender on New Born Screening European Network of Experts) respecting national decisions and competences.

Genetic testing

Genetic testing is available in Romania but is not covered in the National Programme for Rare Diseases. Physicians specialising in genetics only are allowed to provide genetic counselling, and testing is usually performed in the scope of specific projects.

Genetic testing can be carried out before birth (via amniocentesis or chorionic villus samples) and after birth and includes molecular or cytogenetic tests. DNA tests, sexual chromatin, conventional karyotype and FISH analysis are offered by public or private laboratories. Such genetic testing laboratories are placed in university centres (Bucharest, Cluj, Craiova, Iasi, Oradea, Targu-Mures and Timisoara). Some of them are officially recognised at national level as having specific expertise in the field. Private laboratories offer a variety of modern molecular tests for purchase.

Genetic testing is recommended by a physician (i.e. obstetrician, paediatrician, medical geneticist, haematologist and oncologist). Usually the results of genetic tests are interpreted by a medical geneticist who can also offer the genetic counselling. In Romania the health insurance does not cover the costs of genetic tests. But some genetic tests are free of charge for children who are enrolled in national health programme for birth defects. Other times, the patients could be enrolled in research programmes so that genetic tests are available for free.

Romania, as is the case of other European countries, cannot provide genetic tests for all disorders: other specific tests unavailable nationally are available abroad. Form S2 for Health Care Abroad/E112 offers is used in these cases.

Diagnostic tests are registered as available in Romania for 29 genes and an estimated 26 diseases in the Orphanet database[4].

[4] Information extracted from the Orphanet database (May 2011).

There are no national practice guidelines for genetic testing yet, but guidelines are being developed. Professional organisations (Romanian Society of Medical Genetics) and other NGOs are working on these guidelines.

National alliances of patient organisations and patient representation

RONARD (The Romanian National Alliance for Rare Diseases) is the national alliance for rare diseases founded and initiated by the Romanian Prader Willi Association (RPWA) which organises meetings and information services.

The NoRo project (2009-2011) has been developed in partnership with the Ministry of Health and funded by the Norwegian Programme of Cooperation with Romania and its goals are derived from the National Plan for Rare Diseases. Rare disease patient representatives from Romanian National Alliance for Rare Diseases and the professionals involved in NoRo project continue to organise the meetings of the National Committee for Rare Diseases in order to update and advocate for the implementation of the National Plan for Rare Diseases in Romania.

In addition, many other former or recently patients associations, as Muscular Dystrophy Association, Congenital Heart Disease Foundation, PKU Life Romania Association, and Romanian Association for Haemophilia, National Association Myasthenia Gravis, Romanian Network of Hereditary Angioedema, Romanian Society for Multiple Sclerosis, Mini Debra Association for Patients with Epidermolysis Bullosa, Romanian Association for Patients with. Neuroendocrine Tumours, Pulmonary Hypertension Patients Association, have intense activities in the field of implementation of National Plan.

Official information centre for rare diseases

The Romanian Prader Willi Association established an Information Centre for Rare Genetic Diseases in 2005[5], providing information for patients and medical experts, encouraging the exchange of information and experiences between people affected by the same rare disease, and providing counselling and support groups as well as training. Through the NoRo project a virtual platform for rare diseases has been developed (www.edubolirare.ro), both for information and authorised trainings of different professionals, including personal assistants.

Sources of information on rare diseases and national help lines

Orphanet activity in Romania

Since 2004 there is a dedicated Orphanet team in Romania, currently hosted by Universitatea de Medicina si Farmacie "Gr T Popa", Iasi. This team was designated as the official Orphanet team for Romania by the Ministry of Health in 2010. This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. An Orphanet country site is in development. At the end of 2011 the scientific advisory board was renewed and forms have been sent to specialists to update information available/ introduce new information.

Official information centre for rare diseases

The Romanian Prader Willi Association established an Information Centre for Rare Genetic Diseases in 2005, providing information[6] for patients and medical experts, encouraging the exchange of information and experiences between people affected by the same rare disease, and providing counselling and support groups as well as training. The activities are financed by different projects and the service is accredited by the Ministry of Labour.

Help line

The NoRo helpline (080 080 1111), was initiated by the Romanian Prader Willi Association/ RONARD, which continues to provide and fund this Ministry of Labour accredited service. The helpline is also subsidised by the Ministry of Labour. In 2011 the helpline was improved by introducing Orphacodes in the call information management software. In addition, a caller profile analysis was carried out, together with the other members of the European Network of Help Lines for Rare Diseases. Legal attestation has been granted assuring that the service operates according to the Romanian legislation of data protection and privacy.

[5] http://www.apwromania.ro/oamenirari/ghid_servicii_en/index.html

[6] http://www.apwromania.ro/oamenirari/ghid_servicii_en/index.html.

Other patient organisations in Romania also run specific helplines, including the Romanian Society of Rare Diseases provides an official contact via the e-mail address rarediseasesromania@yahoo.com and work on a website was underway in the second half of year. This site provides official news.

Other sources of information on rare diseases

The site http://bolirare.ro/ provides some information on rare and genetic diseases, in Romanian. A monthly magazine for patients (Rare people and rare diseases) is available. A trimestrial scientific journal in cooperation with RSHG and Medical University of Timisoara entitled the "Romanian Journal of Rare Diseases[7]" was also launched in 2010. This publication is the international official journal of the National Committee for Rare Diseases, founded and initiated as part of the NoRo project ("The Norwegian-Romanian Partnership (NoRo) for progress in Rare Diseases") of the Romanian Prader Willi Association funded by the Norwegian Government through a grant of the Norwegian Cooperation Programme for growth and sustainable development in Romania.

Good practice guidelines

The Operative Commission of Rare Diseases will work to create guidelines for rare diseases in Romania. Every speciality establishes clinical practice guidelines, which published in the Official Romanian Monitor, the official legislative journal under the authority of the Ministry of Health.

The Romanian Society of Medical Genetics is working to elaborate best practice guidelines for rare diseases in Romania according to European regulations.

Training and education initiatives

The Ministry of Health Commission for Rare Diseases foresees a workplan for training sessions and conferences involving all expertise centres, starting in 2012, and lectures on rare diseases will be centralised on a specific website.

One of the most important missions of the National Commission of Rare Diseases is to determine a relevant analysis of rare diseases in Romania, as part of university education, because the introduction of this subject in university curriculum is a necessity determined by continuous adaptation to socio-economic environment. In other words, the quality and specificity of academic and university environment is influenced by continuous society dynamics. Considering the scientific and medical aspects of rare diseases, it is necessary to include such topics in the university curricula for students of Universities of Medicine and Pharmacy all over the country; the graduate courses and doctoral theses focused on this topic should include the latest information based on field research at the highest level on rare diseases. Due to a high level of academic training information adaptive to continuous medical changes, Faculty of Medicine graduates would acquire not only the necessary information in order to perform their medical activities at the highest level, but also the professional skills that will allow their rapid integration under conditions of competition.

Currently, rare diseases are included in optional/ facultative lectures covering rare diseases for medical students, as well as post graduate lectures on Medical/ Clinical Genetics are organised in major university centres. An increase in the trend of rare diseases being discussed in such contexts has been recently observed.

Leaflets with information concerning major genetic disorders are available for parents in some Medical Genetics Centres.

In some Medical Genetics Centres, after receiving genetic counselling, the parents receive a Medical Genetics Certificate that contains detailed information about the affected child, diagnosis, Orphanet information and patients' associations (with contact details).

In 2010 Romanian Prader Willi Association/ RONARD was accredited for organising training/ educative courses in the field of rare diseases and these courses started in 2011. This initiative includes new services for patients with rare diseases in the context of the NoRo project, such as a virtual platform for rare diseases in Romania (eUniversity)[8] which contains information for the general public and training modules. The training modules are authorised by the Ministry of Work and Education and targeted at different professionals involved in rare diseases (personal assistants, social workers, psychologists, special education teachers) and a training course for medical doctors: "Management of the rare diseases" accredited by the Doctors Collegium for CME. A training calendar for patients have been elaborated and the training courses were due to start once the Pilot Reference Centre for Rare Diseases "NoRo" opened in 2011.

[7] www.rjrd.ro

[8] www.edubolirare.ro

National rare disease events in 2011

The Romanian National Alliance for Rare Diseases marked Rare Disease Day with events organised by member organisations in Bucharest, Timisoara, Cluj-Napoca, Iasi, Zalau, Targu Mures and Oradea[9]. Celebrated under the slogan "Rare, but Equal", the aim of the day was to raise awareness amongst the general public and decision-makers about rare diseases and their impact on patients' lives.

The Rare Diseases Day campaign in Romania was a success and captured the attention of all institutions. Around 1000 participants took part in the events in the 3 main towns, six conferences, and a press and TV campaign. The theme of 2011 Rare Disease Day was a good way to support efforts to advocate at the Ministry of Health for the Romanian National Plan for Rare Diseases to be included in the National Strategy for Public Health.

The media coverage of Rare Disease Day in Romania was greater than usual. Coverage included a serial about patients' lives in the national newspaper, several documentaries presenting the everyday life of patients, and various other TV programs and reports in national newspapers. On 24 February 2011, "Carol Davila" University of Medicine and Pharmacy hosted a conference for both professionals and patients which revealed the gaps in health that exist for rare disease patients between and within countries and gaps in health that exist for rare disease patients compared to others in society. This national event in Bucharest included the participation of representatives from Ministry of Health, National Drug Agency, Romanian Genetics Society, National Doctors Collegiums' was accompanied by a press conference and was well covered in the press and on TV. A booklet entitled "Rare Inequal" was published with patients' stories, which had a great impact.

On 5 March 2011, the University of Medicine and Pharmacy Iasi and Orphanet Romania organised events in connection with Rare Disease Day in Iasi.

At the National Conference of Thrombosis and Haemostasis in November 2011, a special workshop about rare diseases in field of thrombosis and hemostasis was held.

Hosted rare disease events in 2011

No rare diseases events hosted by Romania were announced in 2011 by *OrphaNews Europe.*

Research activities and E-Rare partnership

National research activities

Funding is currently available from some sources in Romania, although there are no specific programmes for rare diseases research in Romania. Research projects dedicated to rare diseases are included in the same category with other research projects. In 2011 there was a general call for projects (non-rare disease specific), which is still under evaluation. There are currently no other fund-raising initiatives for rare disease research in Romania.

Participation in European research projects

Romania contributes/contributed to the EUROPEAN LEUKEMIA NET European research project and the European Network for Study of Adrenal Tumours - ENS@T.

E-Rare

Romania is not currently a partner of the E-Rare consortium.

IRDiRC

Romanian funding agencies are not currently committed members of the IRDiRC.

Orphan medicinal products

Orphan medicinal product committee

No specific activity reported.

Orphan medicinal product incentives

No specific activity reported.

Orphan medicinal product availability

From 1 January 2007, date at which Romania became an EU Member State, all medicinal products were required to obtain new authorisations according to EU standards: this created significant delay in the

[9] http://ziuabolilorrare.wordpress.com

importation of certain orphan medicinal products. As a consequence of the creation of the National Plan for Rare Diseases, the Ministry of Public Health enlarged coverage of orphan medicinal products from July 2008 onwards in their health programme.

The list of orphan medicinal products available/commercialised in Romania is available on the website of the Romanian National Medicines' Agency[10] and includes: Aldurazyme, Atriance, Busilvex, Carbaglu, Cystadane, Diacomit, Elaprase, Evoltra, Exjade, Fabrazyme, Firazyr, Gliolan, Glivec, Increlex, Inovelon, Litak, Lysodren, Myozyme, Naglazyme, Nexavar, Onsenal, Orfadin, Pedea, PhotoBarr, Prialt, Replagal, Revatio, Revlimid, Savene, Siklos, Soliris, Somavert, Sprycel, Sutent, Tasigna, Thalidomide Pharmion, Thelin, Thromboreductin, Torisel, Tracleer, Trisenox, Ventavis, Volibris, Wilzin, Xagrid, Xyrem, Yondelis, Zavesca.

Orphan medicinal product pricing policy

No specific information reported.

Orphan medicinal product reimbursement policy

The National Programme for Rare Diseases provides for the reimbursement of 17 orphan medicinal products in Romania.

Other initiatives to improve access to orphan medicinal products

In Romania there are several ways of accessing orphan medicinal products via Order N° 962/2006 for approval of the application of art. 699, paragraph (1) of Law N° 95/2006 including: compassionate use of drugs for a certain patient (in the case where the drug already has marketing authorisation); compassionate use of drugs for a group of patients with an invalidating disease, either chronic or serious, or a disease considered to be life-threatening (the provision of a centrally authorised product); the off-label use of drugs. However, the public payer will not always reimburse the orphan medicinal product provided.

Many companies (i.e. Genzyme, Novartis) use humanitarian programs, sponsorship or partnership with medical societies in order to provide the orphan medicinal products, like Tasigna, Evoltra, Fabryzyme, Myozyme, and others. This way was a successful manner to give access of the patients to some orphan medicinal products. Other ways include the enrolment of patients in clinical trials for orphan medicinal products.

Orphan devices

No information reported yet.

Specialised social services

There are currently no respite care services available in Romania. Therapeutic and rehabilitation programmes (not specifically targeted at rare disease patients) are available and patients generally do not have to pay: these programmes are provided by patient organisations and governmental institutions, and some by private companies. RPWA in partnership with ACASA Foundation has initiated a programme for "patient groups rehabilitation and training programmes" as part of the NoRo project. Patient organisations also provide social services such as centres for integration through occupational therapy: these activities are funded through projects, and if the patient organisation provides an accredited service, subventions are available from the Ministry of Labour. Patients with chronic disabilities can apply for special aid compensation and funding for a personal assistant and/or reduced taxes when necessary.

[10] http://www.anm.ro/_/Lista%20medicamentelor%20orfane%20valide%20in%20Romania.xls

DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2011 IN ROMANIA

National plan/strategy for rare diseases and related actions

The National Programme for diagnosis and treatment for rare diseases is currently coordinated in its methodology by the Commission of Genetics of Ministry of Health, under supervision of Commission of Rare Diseases of Ministry of Health.

Four meetings of the National Committee for Rare Diseases (composed of professionals and representatives of patient associations) were organised in 2011. In July 2011 the Romanian Association for Rare Cancers was established and at the National Committee for Rare Diseases meeting in November 2011 rare cancers were included in the proposal for the National Plan for Rare Diseases. The EUCERD Recommendations on Quality Criteria for Centres of Expertise for Rare Diseases were also discussed and most have been included in the content of the Romanian National Plan for Rare Diseases.

During 2011, the Ministry of Health Rare Diseases Operative Commission was founded (ASC nr. 1132/11.04.2011), coordinated by the National Committee for Rare Diseases. It is involved directly in elaborating and executing of the decisions of the National Committee for Rare Diseases. A Rare Disease Commission has also been created at the University of Medicine and Pharmacy in collaboration with the Member States Rare Diseases Commission. The objectives were to:

- Develop formal address via which committees of the Social Fund can supply data for national programs developed by National House of Health Insurance to Establish a National Registry for Rare Diseases;
- Establish in 2012 an official website within the working groups to disseminate information and requirements formulated at the EU Commission for National Rare Diseases committee;
- Develop treatment programs according to Directive no. 2011/24/UE European Parliament and the Council of 9 March 2011 on the application of patients' rights in cross border healthcare.

In terms of funding and governmental support, in July 2011 the budget allocation for National Program for Rare Diseases was increased by €2,000,000: 43 more patients affected by rare diseases were included in the program (7 patients with Hunter Syndrome, 3 patients with Harley Syndrome, 1 patient with Congenital Afibrinogenemia and 33 patients with congenital primary immunodeficiency).

On 28 June 2011 the official opening of the Pilot Reference Centre for Rare Diseases took place in Zalau (see section entitled “Centres of expertise”). Romania marked an important advance in services provided to Romanian rare disease patients. The Minister of Health allocated a financial support for the new Pilot Centre, amounting to €80,000.

Centres of expertise

In 29 November 2011 the Ministry of Health Operative Commission of Rare Diseases held a meeting in order to establish the criteria for centres of expertise and networks of these centres in Romania. The university centres were identified by the Commission and documentation was elaborated to be sent to these centres in order to begin the implementation of criteria for centres of expertise for Rare Diseases. In this perspective, the main university centres identified were: Bucharest, Iasi, Cluj, Timisoara, Craiova, Targu Mures. The methodology for the identification of centres of expertise affiliated to “Carol Davila” University of Medicine and Pharmacy Bucharest, was discussed, as was the accreditation of these centres in field of rare diseases proposed. A common registry of Rare Diseases was also proposed to be implemented in every Centre of Expertise based on the existing database for different rare diseases, with a deadline in 2013.

The official opening of the Pilot Reference Center for Rare Diseases “NoRo” took place on 28 June 2011 in Zalau. The establishment of the NoRo Center was made possible through the project "Norwegian - Romanian (NoRo) Partnership for Progress in Rare Diseases" (2009-2011) with financial support from the Norwegian Cooperation Programme for sustainable economic development in Romania. The project involved 11 partners: Romanian Prader Willi Association (main applicant), Norwegian Prader Willi Association, Frambu - Norwegian Center for Rare Diseases, Ministry Health Romania, City Hall Zalau, County Council Salaj, Acasa Foundation, “St. Family” Greek Catholic Church Zalau, Romanian National Alliance for Rare Diseases, Romanian Medical Genetics Society and Medical University "Victor Babes" Timisoara. The opening event was attended by Mrs. Minister of Health and Care Services Norway Anne-Grete Strom-Erichsen, Mr. Minister of Health Romania Cseke Attila, Mr. Ambassador of Norway in Romania Oystein Hovdkinn, Director of the Norwegian Cooperation

Programme in Romania and Bulgaria Tore Lasse By, representatives of EURORDIS, Orphanet Romania and patients´ associations from Hungary, Italy, France, Denmark, Spain, Norway, Bulgaria, Russia, Sweden, the Secretary General of the Second National Plan for Rare Diseases France, local officials and members of EUCERD. Also was present Mr. Bercea Virgil, Greek Catholic Bishopric of Oradea, who officiated the holy ceremony of the opening.

In addition an International Conference entitled "The European approach for rare diseases" was held on 29 June 2011, in Zalau to mark the official opening of the first Pilot Reference Centre for Rare Diseases in Romania. The Romanian Prader Willi Association and Romanian National Alliance for Rare Diseases organised the event. The event was based around the theme of quality care, the empowerment of patients and families and the examples of the Frambu model and the French National Plan for Rare Diseases. The program included two roundtables around the themes “Addressing the needs of patients" and "Innovation in the field of rare diseases." The 92 participants included representatives of the rare diseases centres around Europe were present (i.e. Norway’s Frambu, Sweden’s Agrenska, Spain’s CREER, Hungary’s Centre for Rare Diseases).

Registries

The Meeting of Ministry of Health Operative Commission of Rare Diseases held on 29 November 2011 in Bucharest proposed a common registry of Rare Diseases to be implemented in every Centre of Expertise based on the existing database for different rare diseases. The deadline for establishing a National Registry of Rare Diseases is for 2013. This registry will include common data file identification, a type of program that is included each type of disease tracking centre for each patient (data developed on existing programs out National Health Insurance Agency). The inclusion of new specialities with activity in the field of rare diseases was also discussed, also, in order to extend the present nomenclature of rare diseases.

Romania contributes to the following European registries: EUROCARE CF and the European Registry for CML (EUTOS).

National alliances of patient organisations and patient representation

RONARD (The Romanian National Alliance for Rare Diseases), the national alliance for rare diseases founded and initiated by the Romanian Prader Willi Association (RPWA), has been active in 2011 in the activities of the NoRo project (2009-2011), developed in partnership with the Ministry of Health and funded by the Norwegian Programme of Cooperation with Romania. Its goals are derived from the National Plan for Rare Diseases, and outputs included the official opening of the Pilot Reference Center for Rare Diseases “NoRo” on 28 June 2011 in Zalau.

Sources of information on rare diseases and national help lines

Help line

In 2011 the NoRo/RONARD rare diseases helpline was improved by introducing Orphacodes in the call information management software. In addition, a caller profile analysis was carried out, together with the other members of the European Network of Help Lines for Rare Diseases. Legal attestation has been granted assuring that the service operates according to the Romanian legislation of data protection and privacy.

Training and education initiatives

The Ministry of Health Commission for Rare Diseases foresees a workplan for training sessions and conferences involving all expertise centres, starting in 2012, and lectures on rare diseases will be centralised on a specific website.

In 2010 Romanian Prader Willi Association/ RONARD was accredited for organising training/ educative courses in the field of rare diseases and these courses started in 2011. This initiative includes new services for patients with rare diseases in the context of the NoRo project, such as a virtual platform for rare diseases in Romania (eUniversity)[11] which contains information for the general public and training modules. The training modules are authorised by the Ministry of Work and Education and targeted at different professionals involved in rare diseases (personal assistants, social workers, psychologists, special education teachers) and a training course for medical doctors: “Management of the rare diseases” accredited by the Doctors Collegium for CME. A training calendar for patients have been elaborated and the training courses were due to start once the Pilot Reference Centre for Rare Diseases “NoRo” opened in 2011.

[11] www.edubolirare.ro

National rare disease events in 2011

The Romanian National Alliance for Rare Diseases marked Rare Disease Day with events organised by member organisations in Bucharest, Timisoara, Cluj-Napoca, Iasi, Zalau, Targu Mures and Oradea[12]. Celebrated under the slogan "Rare, but Equal", the aim of the day was to raise awareness amongst the general public and decision-makers about rare diseases and their impact on patients' lives.

The Rare Diseases Day campaign in Romania was a success and captured the attention of all institutions. Around 1000 participants took part in the events in the 3 main towns, including three"Play and Decide" sessions, six conferences, and a press and TV campaign. The theme of 2011 Rare Disease Day was a good way to support efforts to advocate at the Ministry of Health for the Romanian National Plan for Rare Diseases to be included in the National Strategy for Public Health.

The media coverage of Rare Disease Day in Romania was greater than usual. Coverage included a serial about patients' lives in the national newspaper, several documentaries presenting the everyday life of patients, and various other TV programs and reports in national newspapers. On 24 February 2011, "Carol Davila" University of Medicine and Pharmacy hosted a conference for both professionals and patients which revealed the gaps in health that exist for rare disease patients between and within countries and gaps in health that exist for rare disease patients compared to others in society. This national event in Bucharest included the participation of representatives from Ministry of Health, National Drug Agency, Romanian Genetics Society, National Doctors Collegiums' was accompanied by a press conference and was well covered in the press and on TV. A booklet entitled "Rare Inequal" was published with patients' stories, which had a great impact.

On 5 March 2011, the University of Medicine and Pharmacy Iasi and Orphanet Romania organised events in connection with Rare Disease Day in Iasi.

At the National Conference of Thrombosis and Haemostasis in November 2011, a special workshop about rare diseases in field of thrombosis and hemostasis was held.

Research activities and E-Rare partnership

IRDiRC

Romanian funding agencies are not currently committed members of the IRDiRC.

Specialised social services

RPWA in partnership with ACASA Foundation has initiated a programme for "patient groups rehabilitation and training programmes" as part of the NoRo project.

[12] http://ziuabolilorrare.wordpress.com

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- Genetic and Rare Disease Information in Romanian
  http://bolirare.ro

[13] 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.
[14] All websites and documents were last accessed in May 2012. A more detailed list of sources is available in the full report: http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivities.pdf