

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



PART II: KEY DEVELOPMENTS IN THE FIELD OF RARE DISEASES IN EUROPE IN 2011

This work was financed by the EUCERD Joint Action: Working for Rare Diseases N° 2011 22 01

This document has been produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD, formerly the European Commission's Rare Diseases Task Force) through the EUCERD Joint Action: Working for Rare Diseases (N° 2011 22 01, Coordinator: Kate Bushby, University of Newcastle, United Kingdom), within the European Union's Second Programme of Community Action in the Field of Health.

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

Disclaimer:

The findings and conclusions in this report are those of the contributors and validating authorities, who are responsible for the contents; the findings and conclusions do not necessarily represent the views of the European Commission or national health authorities in Europe. Therefore, no statement in this report should be construed as an official position of the European Commission or a national health authority.

Copyright information:

The "2012 Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases" is copyrighted by the European Union Committee of Experts on Rare Diseases (EUCERD). This product and its contents may be used and incorporated into other* materials on the condition that the contents are not changed in any way (including covers and front matter) and that no fee is charged by the reproducer of the product or its contents for their use. The product may not be sold for profit or incorporated into any profit-making venture without the expressed written permission of EUCERD. Specifically:

- 1) When the document is reprinted, it must be reprinted in its entirety without any changes.
- 2) When parts of the documents are used or quoted, the following citation should be used.

*Note: The "2012 Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases" contains material copyrighted by others. For material noted as copyrighted by others, the user must obtain permission from the copyright holders identified in the document.

To quote this document:

Aymé S., Rodwell C., eds., "2012 Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases", July 2012.

ISBN : 978-92-79-25357-7

DOI : 10.2772/52507

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

©European Union, 2012

CONTENTS

ACRONYMS.....	5
GENERAL INTRODUCTION	5
A. EUROPEAN COMMISSION ACTIVITIES IN 2011	12
A.1. EUROPEAN COMMISSION ACTIVITIES RELATED TO RARE DISEASES IN THE FIELD OF PUBLIC HEALTH IN 2011.....	12
A.1.1. <i>European Commission Directorate General for Health and Consumers’ activities in the field of rare diseases in 2011</i>	12
A.1.2. <i>Newly funded activities and outcomes of tenders in the field of rare diseases funded by DG Health and Consumers in 2011</i>	15
A.1.3. <i>Activities of the European Commission DG Health and Consumers indirectly related to rare diseases</i>	19
A.2. EUROPEAN COMMISSION ACTIVITIES RELATED TO RESEARCH IN THE FIELD OF RARE DISEASES IN 2011 ..	21
A.2.1. <i>7th Framework Programme for research, technological development and demonstration activities (2007-2013)</i>	21
A.2.2. <i>The International Rare Diseases Research Consortium (IRDiRC)</i>	22
A.3. EUROPEAN COMMISSION ACTIVITIES RELATED TO RARE DISEASES IN THE FIELD OF ORPHAN MEDICINAL PRODUCTS AND THERAPIES FOR RARE DISEASES IN 2011	24
A.3.1. <i>European legislation and activities in the field of clinical trials in 2011</i>	24
A.3.2. <i>European legislation and activities in the field of medicinal products for paediatric use in 2011</i>	24
A.3.3. <i>Other EC activities and initiatives relative to the field of orphan medicinal products in 2011</i>	25
B. EUROPEAN MEDICINES AGENCY ACTIVITIES IN 2011	26
B.1. <i>The European Medicines Agency’s (EMA) activities in the field of orphan medicinal products and therapies for rare diseases in 2011</i>	26
B.2. <i>EMA Committee for Orphan Medicinal Products’ (COMP) activities in 2011</i>	28
B.3. <i>EMA Committee on Human Medicinal Products (CHMP) activities in 2011</i> CHMP opinions concerning orphan medicinal products	29
B.4. <i>EMA activities in the field of clinical trials in 2011</i>	30
B.5. <i>EMA activities in the field of medicinal products for paediatric use in 2011</i>	31
B.6. <i>Other EMA activities and initiatives relevant to rare diseases and orphan medicinal products in 2011</i> ..	31
B.7. <i>International cooperation between regulators in the field of orphan medicinal products</i>	32
C. OTHER EUROPEAN RARE DISEASE ACTIVITIES.....	34
C.1. ACTIONS UNDERTAKEN BY RECENT EUROPEAN UNION PRESIDENCIES.....	34
C.2. E-RARE	34
C.3. CLINICAL GENETICS AS A MEDICAL SPECIALITY.....	34
C.4. RESOLUTION ON PHARMACY PREPARED MEDICINAL PRODUCTS ADOPTED BY THE COUNCIL OF EUROPE	35
C.5. INTERNATIONAL RARE DISEASE EVENTS IN 2011	35
D. EUROPEAN MEMBER STATES’ ACTIVITIES IN 2011	39
D.1. AUSTRIA.....	39
D.2. BELGIUM	42
D.3. BULGARIA	43
D.4. CYPRUS	46
D.5. CZECH REPUBLIC.....	47
D.6. DENMARK.....	48
D.7. ESTONIA.....	49
D.8. FINLAND	50
D.9. FRANCE.....	51
D.10. GERMANY	56
D.11. GREECE	58
D.12. HUNGARY	60
D.13. IRELAND.....	61

D.14. ITALY	62
D.15. LATVIA	65
D.16. LITHUANIA	65
D.17. LUXEMBOURG	66
D.18. MALTA	67
D.19. THE NETHERLANDS	68
D.20. POLAND	70
D.21. PORTUGAL	72
D.22 ROMANIA	74
D.23. SLOVAK REPUBLIC.....	76
D.24. SLOVENIA	77
D.25. SPAIN	78
D.26. SWEDEN	80
D.27. UNITED KINGDOM	81
E. OTHER EUROPEAN COUNTRIES' ACTIVITIES IN 2011	85
E.1. CROATIA	85
E.2. ISRAEL	86
E.3. NORWAY	86
E.4. SWITZERLAND	87
E.5. TURKEY.....	90

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
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

This document 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 present 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 the following 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.

1. METHODOLOGY AND SOURCES

The main sources of data for the update of the present report were those collected through the systematic surveillance of international literature and the systematic query of key stakeholders carried out in order to produce the OrphaNews Europe newsletter, various reports published by the European Commission (including past reports of the workshops of the Rare Diseases Task Force and EUCERD) and other specialised reports on topics concerning the field of rare diseases and orphan medicinal products, including the reports of the national conferences organised in the context of the EUROPLAN project. The principal information sources and the collection of data are described in detail here below.

- **European Commission websites and documents**

Information and documentation from the European Commission was used in order to establish this report, principally accessed through the rare disease information web pages of the Directorate General Public Health¹ and Directorate General Research CORDIS website² as well as the site of the European Medicines Agency³, in particular the pages of the COMP⁴ (Committee of Orphan Medicinal Products).

- **OrphaNews Europe**

Data from the OrphaNews Europe⁵ newsletter for the period 2007-2011 was reviewed and analysed in order to identify initiatives, incentives and developments in the field of rare diseases. The data chosen for analysis and inclusion in the report is mainly information concerning actions of the Commission in the field of rare diseases, the development of rare disease focused projects funded by the Commission

¹ http://ec.europa.eu/health/rare_diseases/policy/index_en.htm

² http://cordis.europa.eu/home_fr.html

³ www.ema.europa.eu

⁴ http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000263.jsp&murl=menus/about_us/about_us.jsp&mid=WC0b01ac0580028e30

⁵ <http://www.orpha.net/actor/cgi-bin/OAhome.php?Ltr=EuropaNews>

and other bodies, and developments in the field of rare diseases at MS level (in particular data concerning the development of national plans and strategies for rare diseases). A similar analysis of the French language newsletter OrphaNews France⁶ (which focuses particularly on developments in the field of rare diseases in France) was carried out in order to collect information for the section concerning France.

- **EUCERD Publications**

Parts III, IV and V of this report present an update of the information previously published in the *2009 Report on initiatives and incentives in the field of rare diseases of the EUCERD*⁷ (July 2010) and the *2011 EUCERD Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases*⁸. The methodology for the production of these previous reports is outlined in their respective introductions.

- **Reports of the EUCERD meetings**

The reports of 2011 meetings of the EUCERD (22-23 March 2011 and 24-25 October 2011) were used in order to identify upcoming initiatives and incentives in the field of rare diseases, and to report on the events held to mark Rare Disease Day 2011.

- **Rare Diseases Task Force publications**

Various reports of the RDTF have been used as sources of data to collect information on the state of affairs at both EU and Member State levels pre-2010, notably the reports of the RDTF WG on Standards of Care (concerning European Centres of Reference) produced between 2005-2008, including the *RDTF Final Report – Overview of Current Centres of Reference on rare diseases in the EU – September 2005*⁹ and the *RDTF Meeting Report: Centres of Reference for Rare Diseases in Europe – State-of-the-art in 2006 and Recommendations of the Rare Diseases Task Force – September 2006*¹⁰, as well as the *RDTF Final Report – State of the Art and Future Directions – March 2008*¹¹.

- **Reports on orphan medicinal products**

The information provided for each Member State concerning the state of affairs in the field of orphan medicinal products has been elaborated, when referenced, from the basis of the 2005 revision of the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products*¹² published in 2006 by the European Commission and produced using data collected by the EMA and Orphanet. This information has been updated when information is available and quoted when still applicable. Another valuable source of information on Orphan Drug policy, at EU and Member State levels was the 2009 KCE 112B report published by the KCE-Belgian Federal Centre of Healthcare Expertise (*Federaal Kenniscentrum voor de Gezondheidszorg/Centre federal d'expertise des soins de santé*) entitled "*Orphan Disease and Orphan Drug Policies*" (*Politiques relatives aux maladies orphelines et aux médicaments orphelins*)¹³. This report notably provided information for the Member State sections on Belgium, France, Italy, the Netherlands, Sweden and the United Kingdom. The Office of Health Economics Briefing Document "*Access Mechanisms for Orphan Drugs: A Comparative Study of Selected European Countries (No. 52 October 2009)*" also provided information on orphan medicinal product availability and reimbursement for the Member State sections on France, Germany, Italy, Spain, Sweden, the Netherlands and the United Kingdom. Further detail for Part V has been provided for this year's edition thanks to the JustPharma report *Orphan Drugs in Europe: Pricing, Reimbursement, Funding &*

⁶ <http://www.orpha.net/actor/cgi-bin/OAhome.php>

⁷ <http://www.eucerd.eu/upload/file/Reports/2009ReportInitiativesIncentives.pdf>

⁸ <http://www.eucerd.eu/upload/file/Reports/2011ReportStateofArtRDActivities.pdf> ; <http://www.eucerd.eu/upload/file/Reports/2011ReportStateofArtRDActivitiesII.pdf> ; and <http://www.eucerd.eu/upload/file/Reports/2011ReportStateofArtRDActivitiesIII.pdf>

⁹ <http://www.eucerd.eu/upload/file/Publication/RDTFECR2005.pdf>

¹⁰ <http://www.eucerd.eu/upload/file/Publication/RDTFECR2006.pdf>

¹¹ <http://www.eucerd.eu/upload/file/Publication/RDTFERN2008.pdf>

¹² http://ec.europa.eu/health/files/orphanmp/doc/inventory_2006_08_en.pdf

¹³ *Politiques relatives aux maladies orphelines et aux médicaments orphelins*
http://www.kce.fgov.be/index_fr.aspx?SGREF=3460&CREF=13646

*Market Access Issues, 2011 Edition*¹⁴ by Donald Macarthur: this report is referenced in footnotes when used. Information for the overview was also taken from the *Nature Reviews: Drug Discovery* article produced by the COMP/EMA Scientific Secretariat, *European regulation on orphan medicinal products: 10 years of experience and future perspectives*¹⁵.

- **EURORDIS website and websites of national alliances of patient organisation**

The site of EURORDIS the European Organisation for Rare Diseases¹⁶, and the book *The Voice of 12,000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe* (produced using the results of the EURORDISCare¹⁷ surveys), were used to provide information on EURORDIS activities and projects and to collect data concerning umbrella patient organisations in each of the European Member States and country-level rare disease events. The websites of national patient alliances were also consulted for information. In addition to this the Rare Disease Day 2011 site¹⁸, maintained by EURORDIS, also provided information on events at Member State level¹⁹ concerning Rare Disease Day.

- **EUROPLAN national conferences final reports**

In the context of the EUROPLAN project (2008-2011), 15 national conferences were organised in collaboration with EURORDIS and national rare disease patient alliances in 2010-2011 in order to present the Council Recommendation on an action in the field of rare diseases, as well as discuss the Europlan recommendations/guidance document for the development of national plans and strategies in the field of rare diseases²⁰ and its application at national level. These conferences were attended by a range of stakeholder groups at national level and the final reports²¹ of these conferences were presented in a common format for ease of comparison. Information provided in these reports has helped update the information provided in this document. Readers of this report are encouraged to refer to these reports in addition to the present report as they provide further detail of the discussions of national approaches to rare disease policy.

- **Orphanet**

The Orphanet database was consulted to retrieve data on centres of expertise and the number of genes and diseases tested at Member State level, as well as specific information concerning rare disease research projects, registries, clinical trials and rare disease/orphan medicinal product policies outside of Europe for Part I. Orphanet also provides links²² to other web-based information services and help-lines which were used to collect information at country-level. The Orphanet Country Coordinators also provided valuable input into the elaboration of information at country level, notably via contributions to OrphaNetWork News. The report produced by the RDPlatform project²³, in particular the report *Rare diseases research, its determinants in Europe and the way forward*²⁴ was also used as a source for Part I.

- **OrphaNetWork News**

OrphaNetWork News is the internal newsletter of Orphanet, which communicates information to partners on Orphanet activities in each partner country. The data for this newsletter is collected through a systematic query of Orphanet Country Coordinators and Information Scientists in order to collect information concerning Orphanet country teams' involvement in rare disease meetings and

¹⁴ <http://www.justpharmareports.com/images/Orphan%20Drugs%20in%20Europe-%20Pricing,%20Reimbursement,%20Funding%20&%20Market%20Access%20Issues,%202011%20Edition.pdf>

¹⁵ <http://www.ncbi.nlm.nih.gov/pubmed/21532564>

¹⁶ <http://www.EURORDIS.org/secteur.php3>

¹⁷ http://www.EURORDIS.org/article.php3?id_article=1960

¹⁸ <http://www.rarediseaseday.org/>

¹⁹ <http://www.rarediseaseday.org/country/finder>

²⁰ http://www.europlanproject.eu/public/contenuti/files/Guidance_Doc_EUROPLAN_20100601_final.pdf

²¹ <http://www.EURORDIS.org/content/europlan-guidance-national-plans-and-conferences#EUROPLAN%20%20National%20Conference%20Final%20Reports>

²² http://www.orpha.net/consor/cgi-bin/Directory_Contact.php?lng=EN

²³ <http://www.rdplatform.org/>

²⁴ http://asso.orpha.net/RDPlatform/upload/file/RDPlatform_final_report.pdf

conferences, as well as participation in Rare Disease Day events and partnerships. The review at national level yielded information for the events section for each Member State report.

A selected bibliography and contributions are provided at the end of each volume of the report.

2. REPORT PREPARATION, REVISION AND VALIDATION

The present report provides an updated compilation of information from the previous reports of the EUCERD on the state of the art of rare diseases activities in Europe (*2009 Report on initiatives and incentives in the field of rare diseases of the EUCERD* and *2011 EUCERD Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases*) which have covered activities up to the end of 2010. The present edition takes into account advances and activities in the field of rare diseases and orphan medicinal products at EU and MS level in 2011.

Once this information from the previous report was updated using the sources cited above, a draft of each country section (Part V) was sent in February 2012 to EUCERD Member States representatives with a guidance document providing an explanation of the type of information to include if available for each category. The Member State representatives were asked to contact a range of identified key stakeholders in their country for input. The stakeholders identified for each country included: representatives at the EUCERD in the respective countries, and their alternates, the Orphanet Country Coordinators, National Alliances of rare disease patient alliances, partners of the E-Rare consortium, Member State representatives on the COMP, representatives of national competent authorities, coordinators of national plans for rare diseases and other rare diseases experts identified at national level. The Member State representatives integrated the stakeholder feedback into their report before returning it to the Scientific Secretariat for homogenisation and extraction of developments in 2011 to be included in Part II. Final validation of Parts II and V were sent to the EUCERD Member State representatives for final validation, to the best of their knowledge, in May 2012.

Part III and IV of the report on activities at European Union level was sent for validation, to the best of their ability, by the representatives at the EUCERD of the European Commission Directorate Generals for Health, Research and Innovation, Enterprise and Industry, and the EMA respectively: this process was carried out in March/April 2012 by the Scientific Secretariat of the EUCERD. The European Commission and its agencies are not responsible, however, for the completeness and the accuracy of the information presented in this report. The new activities in 2011 were extracted and added to Part II.

Part I was the final volume of the report to be elaborated: the overview of the state of the art of rare disease activities in Europe is the result of an analysis of the information collected for Parts III, IV and V. Part I was drafted by the Scientific Secretariat of the EUCERD and then sent to all EUCERD members and their alternates for their input before publication.

3. REPORT STRUCTURE

The report is structured into three main parts: Part I consists of an overview of the activities in the field of rare diseases in Europe at EU and MS level; Part II is an extraction of the developments at EU and MS level in 2011 based on Parts III, IV and V; Part III concerns activities of the European Commission; Part IV concerns European Medicines Agency activities and other European activities/events at European level apart from the activities of the European Commission; Part V concerns activities at EU MS level, as well as five other non-EU European countries where information was available.

Each part is followed by a selected bibliography outlining the sources used to produce that part of the report, which includes a list of the European Commission documents referred to in the report and a list of web addresses by country listing national sources of information on rare diseases and links to documents

concerning national plans or strategies for rare diseases when in place. Each part is also followed by a list of contributors to the report, organised by country with mention of the validating authority in each country, and stating their contribution to the current and/or previous report. A list of frequently used acronyms has also been included in each part to ease reading.

Part I provides an overview of the state of the art of rare disease activities in the field of rare diseases in Europe at EU and MS level. This part thus serves as a summary to highlight key areas of the Parts III, IV and V, which serve to provide more detailed background information at EU and MS level. The overview is structured into a number of topics: political framework, expert services in Europe research and development, orphan medicinal products and therapies for rare diseases, patient organisations and information services.

Part II is a new section of the report, providing information extracted from Parts III, IV and V, relative only to the new activities and initiatives reported for the year 2011.

Part III of the report focuses on activities in the field of rare diseases at EC level is split into four sub-sections:

1. EC activities related to rare diseases in the field of public health
2. EC activities related to rare diseases in the field of research
3. EC activities in the field of orphan medicinal products and therapies for rare diseases

The sub-section concerning the EC activities actions in the area of Public Health is divided into three parts: an overview of EC DG Health and Consumers' activities in the field of public health, activities in the field of rare diseases funded by DG Health and Consumers, and activities of DG Health and Consumers indirectly related to rare diseases. The sub-section concerning the EC activities in the field related to research in the field of rare diseases presents information concerning DG Research and Innovation's 5th, 6th and 7th framework programmes for research, technological development and demonstration activities related to rare diseases, as well as information concerning the International Rare Disease Research Consortium (IRDiRC) and Open Access Infrastructure for Research in Europe (OpenAire) initiatives.

Part IV of the report contains information on the activities in the field of rare diseases of the EMA and other rare disease activities at the European level, including selected transversal EU activities and conferences at European level:

- European Medicine Agency's (EMA) activities in the field of orphan medicinal products and therapies for rare diseases, EMA Committee for Orphan Medicinal Products' activities, EMA Committee on Human Medicinal Products' activities, European legislation and activities in the field of clinical trials, European legislation and activities in the field of advanced therapies, European legislation and activities in the field of medicinal products for paediatric use, other EMA activities and initiatives relevant to rare diseases and orphan medicinal products, EU-USA collaboration in the field of orphan medicinal products and other EC activities and initiatives in the field of orphan medicinal products.
- The sub-section concerning other European rare disease activities provides information on transversal rare disease activities and initiatives at EU level and includes information on the High Level Pharmaceutical Forum, actions undertaken in the scope of recent European Union presidencies, the E-Rare ERA-Net for rare diseases and outcomes of European and International rare disease congresses and conferences in 2011.

Part V concerns the rare disease activities in the field of rare diseases in each of the 27 Member States plus Norway and Switzerland as EFTA countries, Croatia and Turkey as candidates for EU membership, and Israel: Iceland has chosen to not contribute a country report this year. These sections are organised in alphabetical order by country.

The information on each country is clearly divided into a number of categories:

- Definition of a rare disease
- National plan/strategy for rare diseases and related actions
- Centres of expertise²⁵

²⁵ The term "official centre of expertise" used in this report means officially designated via a (ministerial) procedure.

- Pilot European Reference Networks
- Registries
- Neonatal screening policy
- Genetic testing²⁶
- National alliances of patient organisations and patient representation;
- Sources of information on rare diseases and national help lines
- Good practice guidelines
- Training and education initiatives
- National rare disease events in 2011²⁷
- Hosted rare disease events in 2011²⁸
- Research activities (National research activities, Participation in European research projects²⁹, Participation in E-Rare, Participation in IRDiRC)
- Orphan medicinal products (Orphan medicinal product committee, Orphan medicinal product incentives, Orphan medicinal product availability³⁰, Orphan medicinal product pricing policy, Orphan medicinal product reimbursement policy, Other initiatives to improve access to orphan medicinal products)
- Orphan devices
- Specialised social services

The categories for which information is provided depend wholly on the information available following data collection from the described sources and contact with stakeholders. If no detail has been given for a topic, the mention “no specific activity/information reported” has been added.

²⁶ This section contains data extracted in September 2011 from the Orphanet database of the number of genes for which there is a diagnostic test registered in Orphanet and the estimated number of diseases for which diagnostic tests are registered in Orphanet (the term ‘estimated’ is used as the concept of a single disease is a variable one).

²⁷ As announced in OrphaNews Europe.

²⁸ As announced in OrphaNews Europe.

²⁹ Past and ongoing participation in DG Research and Innovation financed projects. Some countries have added information on additional European projects.

³⁰ Contacts were asked to provide information on availability of orphan medicinal products (i.e. which drugs are launched on the market/sold at national level). As this information is often hard to identify, some countries instead provided information on which drugs are accessible (i.e. reimbursed, on a positive drug list etc.). It is explicitly explained in each case which of these concepts is being referred to.

A. EUROPEAN COMMISSION ACTIVITIES IN 2011

A.1. EUROPEAN COMMISSION ACTIVITIES RELATED TO RARE DISEASES IN THE FIELD OF PUBLIC HEALTH IN 2011

A.1.1. European Commission Directorate General for Health and Consumers' activities in the field of rare diseases in 2011

A.1.1.1. European Union Committee of Experts on Rare Diseases (EUCERD)

Meetings and workshops of the EUCERD in 2011

In 2011 the EUCERD met twice (22-23 March 2011³¹ and 24-25 October 2011³²) and held a number of workshops: Workshop on National Centres of Expertise for Rare Diseases and Networking Between Centres of Expertise (21-22 March 2011³³), Workshop on Recommendations on Quality Criteria for Centres of Expertise for Rare Diseases in Member States (8 September 2011), EUCERD/EMA Workshop "Towards a Public-Private Partnership for Registries in the Field of Rare Diseases" (4 October 2011³⁴) and the EUCERD/EuroBioMed event "Sharing Data to Improve Health Care Management for Rare Diseases" (4 November 2011³⁵).

Reports and Recommendations of the EUCERD in 2011

In 2011 the EUCERD issued a number of reports including the *Preliminary Analysis of the Outcomes and Experiences of Pilot European Reference Networks for Rare Diseases (May 2011)*³⁶, the *EUCERD report on the State of the Art of Rare Disease Activities in Europe (July 2011)*³⁷ and the *EUCERD Recommendations on Quality Criteria for Centres of Expertise for Rare Diseases in Member States (24 October 2011)*³⁸.

The *Preliminary Analysis of the Outcomes and Experiences of Pilot European Reference Networks for Rare Diseases*³⁹ considers the experience of EC-funded pilot European Reference Networks (ERNs) and other EC-funded networks for rare diseases. The report offers conclusions and recommendations which will help better define the objectives and goals of future ERNs, taking into account the specifics of the Council Recommendation and of the Cross-Border Healthcare Directive. The EUCERD report highlights that for the ERNs, specific concepts need to be defined and stabilised. National-level expertise needs to be identified and designated, and, in terms of organisation, the ERNs need to be genuine infrastructures, ideally "coordinated by an expert in networking whose position is financed at European level". A mechanism for evaluating the ERNs also needs to be developed. How best to support existing ERNs and also identify new ones must be worked out, and the ever-present issues of financing and sustainability need to be addressed.

The 2011 "Report on the State of the Art of Rare Disease Activities in Europe" of the European Union Committee of Experts on Rare Diseases, provides a comprehensive overview of rare disease and orphan medicinal product activities at both the European Union (EU) and Member State (MS) levels up to the end of 2010. The lengthy report is a hybrid of updated data from the previous report and brand-new information that

³¹ <http://www.orpha.net/nestasso/EUCERD/upload/file/Meeting/EUCERD/EUCERDPublicSummaryReport230311.pdf>

³² <http://www.orpha.net/nestasso/EUCERD/upload/file/EUCERD3Abstract.pdf>

³³ <http://www.orpha.net/nestasso/EUCERD/upload/file/EUCERDReport220311.pdf>

³⁴ <http://www.orpha.net/nestasso/EUCERD/upload/file/EUCERDWorkshopRegistries2011.pdf>

³⁵ <http://www.orpha.net/nestasso/EUCERD/upload/file/Rare2011.pdf>

³⁶ <http://www.eucerd.eu/upload/file/Reports/ERN2011Analysis.pdf>

³⁷ <http://www.eucerd.eu/upload/file/Reports/2011ReportStateofArtRDAActivities.pdf>

³⁸ <http://www.orpha.net/nestasso/EUCERD/upload/file/EUCERDRecommendationCE.pdf>

³⁹ <http://www.eucerd.eu/upload/file/Reports/ERN2011Analysis.pdf>

was carefully selected to enhance understanding of the rare disease activities across Europe. As such, it presents an informed overview of rare disease and orphan medicinal product activities, elaborated in concertation with a wide range of stakeholders from each of the MS and at the EU level. The information has been divided into three principal sections:

- Part I, available for the first time, presents the Overview of Rare Disease Activities in Europe and Key Developments in 2010⁴⁰
- Part II delineates the European Commission and Other European Activities⁴¹
- Part III outlines Activities in EU Member States and Other European Countries⁴²

The report outlines the political context that has spawned the growth of rare disease activities across Europe and also summarises the political frameworks of other regions across the world. Amongst the topics examined at both the MS and EU levels are the national strategies for rare diseases either implemented or under elaboration; centres of expertise; registries; newborn screening policies; genetic testing resources and activities; patient organisation activities; information resources; guidelines for best practice; educational initiatives; research and funding mechanisms and participation in EU-level projects; rare disease conferences and events; orphan medicinal product and device incentives, availability, reimbursement and pricing policies; and specialised social services. New to this year's edition are the topics of genetic testing, European national conferences, orphan devices, other initiatives to improve access to orphan medicinal products, and orphan medicinal product pricing policy. Each section of the report finishes with a bibliography of sources used, including a list of any European Commission documents referred to and a list of web addresses organised by country listing national sources of information on rare diseases and links to documents concerning national plans or strategies for rare diseases when appropriate. The report also furnishes a list of contributors, organised by country and with mention of the validating authority for each country. The report has met with praise at both the EU and MS levels for providing valuable insight into understanding the current resources and activities in the field of rare diseases across Europe that will help determine future strategies to meet the needs of rare disease patients and their families in Europe and further afield.

The *EUCERD Recommendations on Quality Criteria for Centres of Expertise for Rare Diseases in Member States*⁴³ were the first set of recommendations to be elaborated and adopted by the EUCERD. Developing Centres of Expertise and European Reference Networks in the field of rare diseases has been proposed in the Council Recommendation on an Action in the Field of Rare Diseases, and more recently in the Cross-Border Healthcare Directive, as a means of organising care for the thousands of heterogeneous rare conditions affecting scattered patient populations across Europe. In order to share knowledge and expertise more efficiently, the EUCERD recommendations seek to introduce harmonious standards of quality practices by elaborating criteria for the Member States to incorporate into their process to designate Centres of Expertise. The 45 recommendations build upon this work already achieved by the EUCERD and RDTF and assist the Member States to develop their healthcare pathways at both the national and EU levels in the field of rare diseases. The recommendations cover the Mission and Scope of the Centres of Expertise; the Criteria for Designating Centres of Expertise; the Process of Designating and Evaluating National Centres of Expertise; and the European Dimension of Centres of Expertise.

A report documenting the outcomes of the EUCERD workshop (4 October 2011) organised with the European Medicines Agency (EMA) on public-private partnership for registries in the field of rare diseases was published in Autumn 2011⁴⁴. Experts from academia, the biopharmaceutical industry, patient organisations, and regulatory agencies, all lent their expertise to the event, which culminated in a consensus towards disease-based registries that could ultimately be shared amongst all relevant public and private partners. This consensus, shifting from the medicinal product- or patient-based designs to a larger-encompassing disease-based model, moves forward the challenge of how to coordinate, manage and share the goldmine of data that the disease registries potentially yield.

OrphaNews Europe developments in 2011

A new search engine feature for *OrphaNews Europe*⁴⁵, powered by Google Custom Search, was added to the archives in 2011, and a tool for the translation of the newsletter into other languages was developed. Italy

⁴⁰ <http://www.eucerd.eu/upload/file/Reports/2011ReportStateofArtRDActivities.pdf>

⁴¹ <http://www.eucerd.eu/upload/file/Reports/2011ReportStateofArtRDActivitiesII.pdf>

⁴² <http://www.eucerd.eu/upload/file/Reports/2011ReportStateofArtRDActivitiesIII.pdf>

⁴³ <http://www.orpha.net/nestasso/EUCERD/upload/file/EUCERDRecommendationCE.pdf>

⁴⁴ <http://www.orpha.net/nestasso/EUCERD/upload/file/EUCERDWorkshopRegistries2011.pdf>

⁴⁵ <http://www.orpha.net/actor/cgi-bin/OAhome.php?Ltr=EuropaNews>

identified national funding for these translations and the first edition of *OrphaNews* in Italian⁴⁶ was launched in December 2011.

A.1.1.2. European Commission work plans implementing the second programme of Community action in the field of health (2008-2013): developments in 2011

Following its adoption on 22 February, the Work Plan for 2011⁴⁷ implementing the second programme of Community action in the field of health (2008-2013) was published in the Official Journal of the European Union. The 2011 Work Plan placed more emphasis and resources on "... a focused cooperation with the Member States". The Plan's Smart Growth priority, part of the European Commission strategy for reinvigorating Europe in the next 10 years, specifically included rare diseases within its scope. Meanwhile, cancer and rare diseases were priorities under the "Diseases" theme – one of five main areas of focus of the 2011 Work Plan. A Call for Proposals for projects, operating grants, conferences and joint actions have been issued by the Executive Agency for Health and Consumers following the publication of the Work Plan⁴⁸. According to the announcement, "...This call for proposals is seeking for very specific projects in seven different areas, where only one project per call will be funded; exception will be made for the rare disease networks". Grants included in the call included a Joint Action to *Support to the implementation of national plans/strategies on rare diseases and related measures to implement Council Recommendation and Commission Communication on rare diseases* (i.e. a Joint Action to support the work of the EUCERD) and project grants to support European rare diseases information networks.

The 2012 Work Plan⁴⁹ of the Health Programme adopted on 1 December 2011 was published in the Official Journal of the European Union on 8 December 2011. It set the annual priorities for implementation of the EU Health Programme. Based on this decision, the Executive Agency for Health and Consumers (EAHC) launched the calls for proposals for joint actions, operating grants, projects and conference grants. Of note to the rare disease community was the Support for European rare diseases information networks project call.

Under the provisions of the Commission Implementing Decisions on the awarding of grants for proposals corresponding to the years 2008, 2009, 2010 and 2011 under the Second Health Programme (2008-2013), the Commission has funded activities to a total of €21'434'895 in the area of rare diseases during this period. An additional funding of €4.5 million is planned for 2012.

Mid-Term Evaluation of the EU Health Strategy 2008-2013 final report encompasses rare diseases in its scope

The final report of the *Mid-Term Evaluation of the EU Health Strategy 2008-2013* was made available online in 2011⁵⁰. Prepared by the Public Health Evaluation and Impact Assessment Consortium, the evaluation was commissioned by DG Sanco in order to guide the implementation of the Strategy going forward, and to take stock of the actions implemented to date. Rare diseases fall within the scope of the EU Health Strategy and the number of Member States (MS) that have adopted an action plan on rare diseases, on the basis of the Council Recommendation of 8 June 2009 on an Action in the Field of Rare Diseases, is listed as a proposed implementation indicator that can serve to measure future progress of MS against the EU Health Strategy. The report cites the issue of the *Communication on a European Action in the Field of Rare Diseases* as an action that demonstrates progress made in relation to stated EU Health Strategy actions. A table in the report that lists the numbers of EC action areas in relation to the EU Health Strategy does not distinguish rare diseases from chronic, common or communicable disorders and thus is of limited interest to the rare disease community. Globally, the report finds that "*In most MS, the influence of the EU Health Strategy on national health strategies is limited*"... and that... "*The EU Health Strategy's main value is that it acts as a guiding framework and, to some extent, as a catalyst for actions at the EU level*".

A.1.1.3. Eurobarometer European Awareness of Rare Diseases Report

Published on 28 February 2011, in honour of the fourth International Rare Disease Day, the *European Awareness of Rare Diseases Report* presents the results of a Eurobarometer survey conducted by TNS Opinion & Social at the request of the Directorate General for Health and Consumers (DG Sanco) and coordinated by Directorate General Communication.

⁴⁶ <http://www.orpha.net/actor/cgi-bin/OAhome.php?Ltr=ItaliaNews>

⁴⁷ http://ec.europa.eu/health/programme/docs/wp2011_en

⁴⁸ http://ec.europa.eu/health/programme/how_does_it_work/call_for_proposals/index_en.htm

⁴⁹ http://ec.europa.eu/health/programme/docs/wp2012_en.pdf

⁵⁰ http://ec.europa.eu/health/strategy/docs/midtermevaluation_euhealthstrategy_2011_report_en.pdf

Seeking to gauge the awareness for rare conditions as well as the level of public support for European-level measures, the survey found that “...approximately 2 out of every 3 respondents know that rare diseases affect a limited number of people and require very specific care. Almost 1 in every 5 personally knows of someone suffering from a rare disease”. While there were “significant differences” in awareness between the Member States, some “...95% of respondents believe there should be more European cooperation in this area and that rare disease patients should have the right to access appropriate care in another Member State”. The survey, in the form of questionnaire, was undertaken in each of the 27 European Union Member States, with approximately 1000 citizens from each country participating, for a total of 26,574 interviews. The release of the report coincides with the formal adoption of the Cross Border Healthcare Directive – legislation of particular relevance to rare disease patients and their families. In a press release, John Dalli, European Commissioner for Health and Consumer Policy, stated: “I am encouraged to see that EU citizens want more European cooperation on rare diseases. This is important, because the required medical expertise may not be available within national borders. ...I want to stress that the European Commission is engaged in added value action to help citizens access the care they need across the EU”.

While the results of the Eurobarometer survey are clearly encouraging, rare disease stakeholders cannot rest on their laurels. The assessment found that detailed knowledge of rare diseases and available resources was scant, despite support for national and European-level action as well as improved research, access to care and awareness-raising. Nevertheless, the key finding of the survey is that “...the European public almost unanimously supports a coordinated EU strategy for improving the treatment of people suffering from rare diseases. It is only within the context of other major national health issues that respondents are slightly less supportive although even here the majority of Europeans are still willing to make rare diseases a priority”. The full Eurobarometer report⁵¹ is available in English, French and German. Fact-sheets for each of the Member States are available in the country's EU language and also in English.

A.1.2. Newly funded activities and outcomes of tenders in the field of rare diseases funded by DG Health and Consumers in 2011

A.1.2.1. Joint Actions

Joint Action to support the Orphanet database (2011-2013⁴)

Orphanet⁵² is the reference portal for information on rare diseases and orphan medicinal products in Europe. Orphanet, and was established in 1997 by the French Ministry of Health (*Direction Générale de la Santé*) and the INSERM (*Institut National de la Santé et de la Recherche Médicale*). Both agencies are still funding the core project. The European Commission funds the encyclopaedia and the collection of data in European countries (since 2000 with DG Public Health grants and since 2004 with DG Research funding). Orphanet is accessed by 20,000 users each day from over 200 countries. Orphanet provides direct online access to all stakeholders to: an inventory of rare diseases and an encyclopaedia in 6 languages (English, French, Spanish, German, Italian and Portuguese); a search by sign and symptom function to facilitate diagnosis; expert clinics in Europe including national centres of expertise and European networks; medical laboratories and available tests; patient organisations; ongoing research including clinical trials and registries; an inventory of orphan medicinal products; OrphaNews France and Europe (newsletters about scientific and political progress in the field of rare diseases); and the thematic studies and reports offered by the *Orphanet Report Series*⁵³. Reports in the series include lists of rare diseases with their prevalence⁵⁴, lists of orphan medicinal products in Europe⁵⁵, lists of rare disease registries in Europe⁵⁶ and lists of collaborative research projects and clinical networks in the field of

⁵¹ http://ec.europa.eu/health/rare_diseases/eurobarometers/index_en.htm

⁵² www.orpha.net

⁵³ http://www.orpha.net/consor/cgi-bin/Education_Home.php?lng=EN

⁵⁴ http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf

⁵⁵ http://www.orpha.net/orphacom/cahiers/docs/GB/list_of_orphan_medicinal_products_in_europe.pdf

⁵⁶ <http://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf>

rare diseases funded by the European Commission⁵⁷. Orphanet data is collected in each European Member State and is expert validated.

The site gives access to:

- An inventory of diseases including 5,954 diseases and classifications of these diseases developed using existing published expert classifications. Each disease has a unique Orphan number and is indexed with ICD10 and OMIM, and its 'identity card' includes the relevant prevalence class, age of onset class, mode of inheritance and associated genes. At the moment, not every disease has a completed 'identity card'.
- An encyclopaedia covering 3,077 rare diseases, written by world-renowned experts and peer-reviewed. Systematically produced in both English and French, this encyclopaedia is partly translated into German, Italian and Spanish. 1148 new or updated abstracts or definitions were produced in 2011.
- An inventory of orphan medicinal products at all stages of development, from orphan designation to European market authorisation.
- A directory of specialised services in the 36 European partner countries, providing information on:
 - Specialised clinics and centres of expertise
 - Medical laboratories
 - Ongoing research projects
 - Clinical trials
 - Registries
 - Networks
 - Technological platforms
 - Patient organisations
 - Orphan medicinal products
- A range of other services for specific stakeholders:
 - For health care professionals: an assistance-to-diagnosis tool (search by signs and symptoms);
 - For professionals in the field of emergency health care: an encyclopaedia of emergency guidelines;
 - For researchers and the pharmaceutical industry: availability of data from the database for research purpose;
 - For all: newsletters with both scientific and political content;
 - For all: regularly published thematic studies and reports on overarching subjects, downloadable from the site: "the Orphanet Report Series".

This central role of Orphanet is fully recognised by the European Commission and the Council as a key element for improving the diagnosis and care in the field of rare diseases in order to provide and disseminate accurate information in a format adapted to the needs of professionals and of affected persons:

- Point 4.3 of the Commission Communication states that the Commission should contribute establishment of an EU dynamic inventory of rare diseases will contribute to tackle some of the main causes of neglecting the issue of rare diseases including the ignorance of which diseases are rare. The Commission will ensure that this information continues to be available at European level, building in particular on the Orphanet database, supported through Community programmes.
- Point II.4 of the Council Recommendation states that Member States should contribute actively to the development of the EU easily accessible and dynamic inventory of rare diseases based on the Orphanet network and other existing networks as referred to in the Commission Communication on rare diseases.
- Article 13.a of the Directive on Cross Border Health Care states that it should be possible to make health professionals aware of the tools available to them at Union level and to assist them in the correct diagnosis of rare diseases, in particular using the Orphanet database and European reference networks.

In this context, the Commission proposed in 2010 that Orphanet would be funded as a Joint Action between the European Commission and the Member States from April 2011. The expected outcomes of this Joint Action

⁵⁷ <http://www.orpha.net/orphacom/cahiers/docs/GB/Networks.pdf>

are a comprehensive and complete information will be made available, including: an inventory of rare diseases; an expanded encyclopaedia of rare diseases (translated into French, German, Spanish, Italian and possibly more) a directory of expert clinics, medical laboratories, networks, registries and patient organisations; information on orphan medicinal products. The Orphanet dataset will be available for re-use in different formats to ensure dissemination of the Orphanet nomenclature of rare diseases and maximise the use of collected information on expert services. Customised websites at national level in national language(s) will be available in order to disseminate national data at MS level. Orphanet will have the governance needed to ensure its mission at international level.

The Kick-Off Meeting of the Orphanet Joint Action, gathering all national country coordinators and Member State health representatives took place on 7 and 8 June 2011 in Paris. The meeting had a rich agenda, which included reviewing the contents and operating procedures of Orphanet, brain-storming to identify priority actions on the national and European levels, and establishing governance. The overriding aim of the Joint Action is to improve and adapt the presence of Orphanet in each participating country. Objectives thus include improving the existing services –including the inventory of rare diseases and the classification being elaborated via a collaboration with World Health Organization expert groups; concentrating on expanding and updating the core encyclopaedia of rare diseases; and annotation with signs and symptoms. Developing new tools and services are also objectives of the Joint Action, including building an Orphanet ontology and developing several new services. Priority initiatives that are natural to the Joint Action include expanding the language availability of the Orphanet database and related documents. Polish and Flemish are amongst languages that could be added soon to the six official existing European languages of the site (English, French, German, Italian Portuguese, and Spanish). The Orphanet Clinical Guidelines were also amongst the documents considered a priority for translation into national languages. Capitalising on the newly developed Orphadata tools the Joint Action country partners will be able to customise the popular Orphanet Report Series to feature national data. Orphanet country sites will also be developed under the Joint Action, allowing each country to feature its own special mix of news, publications and events related to rare diseases and orphan medicinal products in its own language. Orphanet will also become a more interactive site via the activities of the Joint Action. Indeed, the “IT side” of Orphanet was presented and discussed, including the new challenges expanded services and languages engender.

Putting in place appropriate governance is one the biggest changes the Joint Action ushers in, one which will encompass all the partner countries in the Steering Committee, in charge of supervising national activities and formulating future strategies. The Orphanet Joint Action now also has an external International Advisory Board which will report to the Steering Committee and review all the Joint Action activities.

Within the framework of the Joint Action, Orphanet seeks to become more cost-effective, more user-friendly and to achieve sustainability.

Other developments in 2011 included the launch of Orphadata⁵⁸. Inspired by the growing number of requests for data from its database, Orphanet decided to create a comprehensive, high-quality and freely-accessible dataset related to rare diseases and orphan medicinal products that would be available in a reusable format. Launched in May 2011, was developed within the context of the RD Portal and the new Orphanet Europe joint action contracts funded by DG Sanco. Additional support is also provided by GSK. The dataset is a partial extraction of the data stored in Orphanet and will be updated monthly. For user convenience, the date of the last data release will be provided. Freely accessible in six languages (English, French, German, Italian, Portuguese and Spanish) the Orphadata dataset encompasses:

- An inventory of rare diseases, cross-referenced with OMIM, ICD-10 and with genes in HGNC, OMIM, UniProtKB and Genatlas
- A classification of rare diseases established by Orphanet, based on published expert classifications
- Epidemiology data related to rare diseases in Europe (class of prevalence, average age of onset, average age at death) extracted from the literature
- A list of signs and symptoms associated with each disease, with their frequency class within the disease

It is also possible, on request, to access other types of Orphanet data, including:

- An inventory of Orphan Medicinal products at all stages of development, from EMA (European Medicines Agency) orphan designation to European market authorisation, cross-linked with diseases
- Summary information on each rare disease in six languages (English, French, German, Italian, Spanish, Portuguese)
- URLs of other websites providing information on specific rare diseases

⁵⁸ www.orphadata.org

- A directory of specialised services, providing information on centres of expertise, medical laboratories, diagnostic tests, research projects, clinical trials, patient registries, mutation registries, and patient organisations in the field of rare diseases, in each of the countries in Orphanet's network.

Orphadata provides a guide for users that defines and describes the elements of the dataset. Orphanet hopes that this latest offer will contribute to furthering research toward better understanding and treating rare diseases.

Another development Orphanet in 2011 was a partnership developed with Canada, extending Orphanet across the Atlantic for the first time. Negotiations are also ongoing with Japanese and Chinese stakeholders to explore the possibility of launching Orphanet into Asia, as well as with Brazil and Australia.

The 2010 Impact Factor for the *Orphanet Journal of Rare Diseases*⁵⁹ (OJRD) was announced in 2011: the Journal continues its steady ascent, increasing to 5.93 from 5.83 in 2009. The OJRD more than doubled its impact factor from 2007 to 2008 (from 1.30 to 3.14) and gained another impressive hike from 2008 to 2009. This year's increase moves the journal into tenth place out of the 106 journals in the 'Medicine, Research and experimental' category of the Journal Citation Reports.

EUCERD Joint Action: Working for rare diseases (2012-2015)

A new joint action between the European Commission and the EU Member States to support the EUCERD was approved in 2011 and will start in March 2012. The Joint Action will kick-off in mid-March and run through February 2015. Coordinated by Pr. Kate Bushby (Vice-Chair of the EUCERD, Joint Coordinator of TREAT-NMD, Newcastle University, UK) several work packages for the EUCERD Joint Action have already been planned in order to address the identified priority areas: national plans and strategies for rare diseases, rare diseases in international nomenclatures, specialised social services for rare diseases, quality of care for rare diseases and integration of European rare diseases initiatives. The Joint Action will also support the production of *OrphaNews Europe* and the annual EUCERD Report on the State of the Art of Rare Disease Activities in Europe. Over the next three years of the EUCERD Joint Action, committee members, along with invited experts, will convene regularly to move forward these initiatives.

A.1.2.2. Project grants

Building consensus and synergies for the EU Registration of Rare Diseases Patients (EPIRARE) Project

The general objective of this initiative is to build consensus and synergies to address regulatory, ethical and technical issues associated with the registration of rare diseases patients and to elaborate possible policy scenarios. Specific attention will be given to the scenario of the creation of an EU platform for the collection of data on rare disease patients and the communication of this data among qualified users, based on a feasibility study. To this aim, the project will define the options for the preparation of a legal basis, the possible scope to achieve the most effective synergies, the corresponding governance framework and the possible options for sustainability. The feasibility of registration of a minimum data set common to all rare diseases designed to inform policy-making, the conditions to admit research-driven disease or treatment-specific modules and the ways to ensure a long-lasting data flow will be assessed. The development of guiding reports, including the legal and organisational framework for the registration of rare disease patients is strategic for building up an evidence base for Community, public health policies, health service management, clinical research and the assessment of orphan medicinal products effectiveness and appropriateness of use. The successful establishment of a, EU registration of health data, for rare diseases, may represent an important example paving the way to the EU-wide registration of data regarding other health conditions.

EPIRARE launched in 2011 a survey of registry leaders to explore the functioning, resources, problems, needs and expectations of existing registries in European Member States and in other Countries. The final aim is to develop tools and services in support of existing registries and to favour the creation of new ones where needed. The survey is directed to both active and past rare disease registries. The preliminary results are available online⁶⁰.

⁵⁹ www.ojrd.com

⁶⁰ <http://www.epirare.eu/quest4.html>

A.1.2.3. Call for Tenders

Outcomes of the Call for Tender: Evaluation of population newborn screening practices for rare disorders in Member States of the European Union (2009-2011)

In July 2009 a call for tender was launched for an evaluation of the current situation of newborn screening (NBS) practices for rare disorders in the MS of the EU and was awarded to the Istituto Superiore di Sanità in Italy. The tender started on 30 December 2009 and ended in July 2011. A consensus conference was organised in June 2011 to finalise the report on NBS practices⁶¹ and the expert opinion⁶² containing recommendations on best practices which were published in 2012. An executive report⁶³ to the EC was also issued.

Outcomes of the Call for Tender: Creation of a mechanism for the exchange of knowledge between Member States and European authorities on the scientific assessment of the clinical added value for orphan medicines (2010-2011)

A call for tender⁶⁴ was launched in 2010 for the creation of a mechanism for the exchange of knowledge between Member States and European authorities on the scientific assessment of the clinical added value for orphan medicines (CAVOD). This call was awarded to Ernst and Young for a duration of 9 months. The study was published in late 2011⁶⁵: it aims to identify and assess possible options for creating a mechanism for the exchange of knowledge between Member States (MS) and European authorities on the scientific assessment of the relative effectiveness of orphan medicines. The European Union Committee of Experts on Rare Diseases (EUCERD) is considering carefully the data provided by the CAVOD report and will issue a recommendation to the EC and MS on improving informed decisions based on the clinical added value of orphan medicinal products information flow in 2012 suggesting how to best coordinate and exchange information health technology assessment for orphan medicinal products, capitalising on mechanisms already in place at the MS level and at EU-level structures, such as the European Medicines Agency and the EUnetHTA network.

A.1.3. Activities of the European Commission DG Health and Consumers indirectly related to rare diseases

Directive 2011/24/EU OF on the application of patients' rights in cross-border healthcare

Directive 2011/24/EU, adopted in March 2011, clarifies patients' rights to access safe and good quality treatment across EU borders, and be reimbursed for it. The Directive will provide a firm basis for increased cooperation between national health authorities through several actions. Some provisions are addressing the issue of rare diseases.

In particular Article 12 foresees enhanced cooperation of Member States in the area of European reference networks (ERN). It foresees that Commission is going to adopt through legal means (delegated and implementing acts) the criteria and conditions which the ERN and the healthcare providers must fulfil.

To prepare these acts, the Commission will carry out appropriate consultations and has set up the Cross-Border Directive expert group which will assist the Commission on this task. In the case of the implementing acts the Commission will be assisted by the Committee on Cross-Border Healthcare composed of Member States representatives created on the 21 June 2011.

The main added value of the ERN and therefore of the Centres of Excellence/Reference is to facilitate improvements in access to diagnosis and delivery of high-quality, accessible and cost-effective healthcare in the case of patients who have a medical condition requiring a particular concentration of expertise or resources, particularly in medical domains where expertise is rare.

It further clarifies that ERN could also be focal points for medical training and research, information dissemination and evaluation, especially for rare diseases. The Directive is not aiming to "create" new centres,

⁶¹ http://ec.europa.eu/eahc/documents/news/Report_NBS_Current_Practices_20120108_FINAL.pdf

⁶² http://ec.europa.eu/eahc/documents/news/Expert_opinion_document_on_NBS_20120108_FINAL.pdf

⁶³ http://ec.europa.eu/eahc/documents/news/Executive_Report_to_EC_20120108_FINAL.pdf

⁶⁴ http://ec.europa.eu/eahc/documents/health/tenders/2010/EN/EAHC_2010_05_tenderSpecifications_EN.pdf

⁶⁵ http://ec.europa.eu/eahc/documents/news/CAVOD_Final%20Report_vf_corrected_281011.pdf

but to identify already established centres of expertise and to encourage voluntary participation of healthcare providers in the future ERN.

Further more, Article 13 requires the Commission to support Member States in making health professionals more aware of diagnostic tools which may help rare disease patients, and in making patients more aware of the possibility of requesting a treatment abroad according and up to the entitlements they have in their Member State of affiliation. Article 8 also encourages Member States to seek the advice of experts when dealing with patients with rare diseases.

Revision of the Directive of the European Parliament and Council of 27 October 1998 on *in vitro* diagnostic medical devices

The European Commission launched in June 2010 a public consultation on the revision of Directive 98/79 EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices (the IVD Directive). Council Directive 90/385/EEC relating to active implantable medical devices, Directive 93/42/EEC concerning medical devices and Directive 98/79/EC on *in vitro* diagnostic medical devices harmonise safety and performance rules for medical devices in the EU. The IVD Directive, in particular, sets out the regulations governing the safety and efficacy of diagnostic tests marketed in Europe and creates a single market for *in vitro* diagnostic devices across the EU. The existing IVD Directive has been criticised for being inflexible and arbitrary in the way it classifies tests. The blanket exemption for tests produced in health institution laboratories is also criticised for being too broad and poorly defined. Due to both technological advances and identified emerging weaknesses identified in the regulatory framework, a public consultation was launched in 2008⁶⁶ on the Recast of the Medical Devices Directives. Responses to this underlined a necessity for the revision of the IVD Directive, which has remained largely unchanged since its adoption in 1998, despite significant technological advancement in the sector.

In the context of the recast of the regulatory framework for medical devices and following the consultation mentioned above, the European Commission launched in 2010 a public consultation on technical aspects related to the revision of Directive 98/79/EC on *in vitro* diagnostic (IVD) medical devices. The summary of the responses to the public consultation launched in June 2010 on issues related to *in vitro* diagnostic medical devices were published online in February 2011⁶⁷. Responses to this underlined a necessity for the revision of the IVD Directive, which has remained largely unchanged since its adoption in 1998, despite significant technological advancement in the sector.

The EU-funded Network of Excellence EuroGentest⁶⁸ has also produced a position paper on the revision of the IVD Directive, which has been adopted as EuroGentest policy. One central proposal of the EuroGentest document is that the exemption from CE-marking for in-house tests manufactured in public health service laboratories should be retained, but that it should be restricted to laboratories accredited to ISO 15189⁶⁹ or equivalent. This would provide a balance between test availability and patient safety. There have been calls for the abolition of the in-house exemption. If this were to occur, however, it would severely limit the scope of testing available - especially for rare diseases. The EuroGentest response⁷⁰ to the 2010 consultation robustly supports the retention of the exemption, while emphasising that patient safety should be ensured by restricting it to accredited laboratories.

Establishment of an eHealth network

In December 2011, the European Commission adopted a Decision⁷¹ establishing an eHealth Network, as foreseen by the Directive on Patients' Rights in Cross-border Healthcare⁷². For the first time, EU legislation includes provisions on eHealth with clear objectives to find modern, innovative solutions for providing better and safer healthcare for all Europeans. The Network will bring together the national authorities responsible for eHealth on a voluntary basis to work on common orientations for eHealth. The aim is to ensure EU wide interoperability of electronic health systems and wider use of eHealth. The eHealth Network is expected to translate the results of numerous research projects and pilot projects into real-life accessible services for European citizens. The utility of eHealth may be especially significant in the field of rare diseases, which is marked by scattered expertise and resources. eHealth will allow for remote diagnosis, remote monitoring of patients' conditions and secure sharing of patient records between healthcare professionals.

⁶⁶ http://ec.europa.eu/consumers/sectors/medical-devices/files/recast_docs_2008/public_consultation_ivd_final_en.pdf

⁶⁷ http://ec.europa.eu/consumers/sectors/medical-devices/files/recast_docs_2008/ivd_pc_outcome_en.pdf

⁶⁸ <http://www.eurogentest.org/web/index.xhtml>

⁶⁹ <http://www.eurogentest.org/laboratories/qau/info/public/unit1/qmanagement/accreditation.xhtml>

⁷⁰ http://ec.europa.eu/health/medical-devices/files/ivd/50_ivd_en.pdf

⁷¹ http://ec.europa.eu/health/ehealth/docs/decision_ehealth_network_en.pdf

⁷² http://ec.europa.eu/health/ehealth/policy/index_en.htm

A.2. EUROPEAN COMMISSION ACTIVITIES RELATED TO RESEARCH IN THE FIELD OF RARE DISEASES IN 2011

A.2.1. 7th Framework Programme for research, technological development and demonstration activities (2007-2013)

The Seventh Framework Programme of the European Union for research, technological development and demonstration activities (FP7, 2007-2013⁷³) is composed of four main specific programmes – “Cooperation”, “Ideas”, “People” and “Capacities” – including cross-cutting issues such as support for SMEs, international cooperation, the contribution of research to EU policy, and societal considerations. Rare disease research specifically features under the heading of the Health theme, one of ten themes proposed under the specific programme on “Cooperation”. This specific programme is designed to gain or strengthen leadership in key scientific and technological areas by supporting trans-national cooperation between universities, industry, research centres, public authorities and stakeholders across the European Union and the rest of the world.

The European Commission has already published several calls for proposals covering research on rare diseases in various thematic areas of FP7. For the period 2007–2011, 66 research projects with an EU contribution of over €325 million are being supported. They will ultimately lead to better diagnostic methods, new treatments, better care and prevention strategies for rare diseases.

The European Commission released on 20 July 2011 the content of a new call for proposals⁷⁴ which opened several opportunities for rare diseases in the HEALTH theme of the work programme for 2012. The indicative budget for the rare disease activities is €108 million.

Report on Rare Disease Research, its Determinants in Europe and the Way Forward (2011)

One project delivered a “*Report on Rare Disease Research, Its Determinants in Europe and the Way Forward*”⁷⁵. This report prepared in the context of the RareDiseasePlatform project (RDPlatform), a three-year support action project of the European Union's Seventh Framework Programme (HEALTH-F2-2008-201230) that ran from May 2008 through April 2011 was published in 2011. This report sheds light on where research and development (R&D) in the field of rare diseases has been - and where it needs to go next. The report presents a compilation of data gathered within the RDPlatform project. As such it offers readers an inventory of publicly-funded research initiatives on the national and international levels in the field of rare diseases and orphan medicinal products. The data, accessible on pan-European rare disease and orphan medicinal products informational portal Orphanet, encompasses ongoing research projects, clinical trials, and registries. Other areas covered in the report include testing, therapeutic development, and R&D determinants (such as prevalence and medical area). The rare disease ontologies, data repositories and bioinformatic tools are given special emphasis in the report.

Breaking activities down by country, the RDPlatform report provides a snapshot of national, multi-national and EU project involvement for over 30 countries. The policy decisions that supported the research actions are outlined, including European-level policies. This information can be instructive to countries developing their own measures in the field of rare diseases and orphan medicinal products. The report also considers possible future actions to more efficiently build upon what has already been accomplished.

The *Report on Rare Disease Research, Its Determinants in Europe and the Way Forward* adds to a growing toolbox of resources designed to help move rare disease and orphan medicinal product research forward as productively as possible. Drafted by experts from the RDPlatform project, the report was reviewed by a large number of stakeholders and discussed at a workshop earlier this year. Together with the *Rare Diseases and Orphan Products* report produced late 2010 by the Institute of Medicine in the USA, the RDPlatform report will serve as a key document for the recently-formed International Rare Diseases Research Consortium (IRDIRC).

⁷³ http://cordis.europa.eu/fp7/home_en.html

⁷⁴ http://ec.europa.eu/research/participants/portal/page/cooperation;efp7_SESSION_ID=QJMWPGCQHMZgQwqLihGhQY2XH6RRrITxDH4hWgkvQBlz3NBsJYrW!1086760178?callIdentifier=FP7-HEALTH-2012-INNOVATION-1

⁷⁵ http://asso.orpha.net/RDPlatform/upload/file/RDPlatform_final_report.pdf

A.2.2. The International Rare Diseases Research Consortium (IRDiRC⁷⁶)

In early April 2011, some 80 participants from research funding agencies, research organisations, industry, patient representatives and regulatory agencies gathered for the second meeting in Bethesda⁷⁷ and the official launch of the International Rare Diseases Research Consortium (IRDiRC).

Research funding agencies represented at this second workshop were:

- European Commission (DG Research and Innovation; DG Health and Consumers)
- National Institutes of Health - NIH (USA)
- Canadian Institutes of Health Research - CIHR (Canada)
- Instituto de Salud Carlos III (Spain)
- Istituto Superiore di Sanita (Italy)

To develop a policy document framing the international effort, different breakout sessions were organised to trigger the discussion on the different policy items:

- Understanding Pathophysiology of Rare Diseases (Genomics analyses and In vitro and animal models),
- Ontologies/Disease Classification/Natural History,
- Biomarkers,
- Patient Registries and Biospecimen Repositories,
- Preclinical Research and Clinical Trials,
- Communication/Publication/Information/Intellectual Property Rights/Data Policy.

The second reunion picked up the pace with the endorsement by members to fulfil certain goals, including, notably, a commitment to the development of 200 new rare disease treatments by the year 2020 and the development of diagnostics for most rare disorders. Related challenges identified include the need to establish and provide access to harmonised data and samples, perform the molecular and clinical characterisation of rare diseases, boost translational, preclinical and clinical research, and streamline ethical and regulatory procedures.

The third workshop of the IRDiRC⁷⁸ was held in Montreal, Canada on 8-9 October 2011 and was hosted by the Canadian Institutes for Health Research and Genome Canada and co-organised with the European Commission and the US National Institutes of Health, just before the 12th International Congress of Human Genetics. Some 100 international participants representing public and private funding organisations, scientists, regulators, industry, and patient groups were onboard, working together to develop common scientific and policy frameworks that will guide the activities of the participating IRDiRC members. Identifying priority research areas was a principal topic, as well as addressing the regulatory challenges in an international context. Initial goals put forward by the IRDiRC founders include 200 new treatments for rare diseases by the year 2020 and have a diagnosis available for most rare diseases. A series of Round Table presentations provided an update of the current and planned actions by the funding agencies committed to IRDiRC.

Governance

IRDiRC will be governed by an Executive Committee, three Scientific Committees and a number of working groups⁷⁹. Until the end of 2012, IRDiRC will be run by an Interim Executive Committee with representatives of all participating funding agencies. It will be chaired by Dr Ruxandra Draghia-Akli, from the European Commission. To be considered as an IRDiRC funding member, the funding organisation should invest a minimum of \$10 million USD over 5 years in research projects/programmes contributing towards IRDiRC objectives. Letters of intent concerning IRDiRC membership must be signed by the authorising official committing the research funds.

IRDiRC will have three Scientific Committees, one each for Diagnostics (including sequencing and characterisation), Therapies (including pre-clinical and clinical development) and Interdisciplinary aspects of rare diseases research (including ontologies, natural history, biobanking, registries etc). The Scientific Committees will advise the Executive Committee on research priorities and progress made from a scientific

⁷⁶ http://ec.europa.eu/research/health/medical-research/rare-diseases/irdirc_en.html

⁷⁷ http://ec.europa.eu/research/health/medical-research/rare-diseases/events-04_en.html

⁷⁸ http://ec.europa.eu/research/health/medical-research/rare-diseases/events-05_en.html

⁷⁹ http://ec.europa.eu/research/health/medical-research/rare-diseases/governance_en.html

viewpoint. Nominations for the three IRDiRC Scientific Committees were opened at the end of 2011 and the first members were appointed on 29 February 2012.

The IRDiRC Working Groups will be composed of representatives of all projects funded within the scope of IRDiRC. They will cooperate to ensure synergies between all research projects within the scientific area of the working group, by exchanging results, expertise, experiences and information.

Organisational support for IRDiRC activities

The EC announced its commitment to supporting the logistical organisation of IRDiRC activities through a dedicated support action topic in the FP7-HEALTH-INNOVATION⁸⁰ call for proposals (Work Programme 2012).

Committed Members of the IRDiRC

The funding agencies now committed to the IRDiRC are from the following countries: Australia, Canada, Italy, France, Germany, the Netherlands, Spain, the United Kingdom, and the United States, in addition to the European Commission⁸¹.

⁸⁰ <http://ec.europa.eu/research/participants/portal/page/cooperation?callIdentifier=FP7-HEALTH-2012-INNOVATION-1> and <http://ec.europa.eu/research/participants/portal/page/cooperation?callIdentifier=FP7-HEALTH-2012-INNOVATION-2>

⁸¹ http://ec.europa.eu/research/health/medical-research/rare-diseases/committed-members_en.html

A.3. EUROPEAN COMMISSION ACTIVITIES RELATED TO RARE DISEASES IN THE FIELD OF ORPHAN MEDICINAL PRODUCTS AND THERAPIES FOR RARE DISEASES IN 2011

A.3.1. European legislation and activities in the field of clinical trials in 2011

Revision of the EC Clinical Trials Directive

The Clinical Trials Directive, implemented in 2004, was developed in order to harmonise European regulatory systems pertaining to the clinical research environment, improve the protection of study participants, optimise safety information, and ensure quality and data credibility across Europe.

A European Commission public consultation was held in from 9 October 2009 to 8 January 2010⁸² to assess the impact of the Directive and the replies were published soon after⁸³. The Commission has scheduled adoption of the legislative proposal⁸⁴ for 2012. In February 2011, a concept paper was submitted by the Directorate General for Health and Consumers for public consultation: this consultation did not repeat a previous consultation of 2009/2010, but aimed to investigate the more technical aspects. This concept paper presented: a 'preliminary appraisal' of which option appears to be the most suitable one to address some of the key concerns of the Clinical Trials Directive, on the basis of the current state of the impact assessment; and the main figures that are being used to evaluate the impacts of the different policy options. The summary of responses to the Public consultation on the concept paper on the Revision of the 'Clinical Trials Directive' 2001/20/EC were published online in July 2011⁸⁵.

A.3.2. European legislation and activities in the field of medicinal products for paediatric use in 2011

ERA-NET PrioMedChild projects related to orphan medicinal products and paediatric populations

Many of the medicines currently prescribed to children may never have been studied in paediatric populations, meaning that medicinal products are administered without precise information on dosage, potential toxicity and evidence of clinical safety and efficacy at the recommended dosages. The ERA-NET PrioMedChild⁸⁶ (Priority Medicines for Children) is a network of eleven research funding organisations from different EU Member States working on the development of research around medicines for children. Under the umbrella of ERA-NET PrioMedChild, the national funding organisations of the Netherlands, Estonia, Finland, France, Great Britain, Italy, Latvia and Poland jointly provided funds in the order of €8 million to support the European call. The research projects were funded for three years in consortia with a minimum of three participants from at least three countries and a maximum number of 8 research groups. Regardless of its size, each collaborative consortium should have the optimal critical mass to achieve ambitious scientific goals and should clearly show the added value from working together. The ERA-NET PrioMedChild received €1.7 million from the European Commission's DG Research to set up the network and collaboration, but no funds for research. The Joint Call

⁸² http://ec.europa.eu/health/files/clinicaltrials/docs/2009_10_09_public-consultation-paper.pdf

⁸³ http://ec.europa.eu/health/files/clinicaltrials/2010_03_30_summary_responses.pdf

⁸⁴ http://ec.europa.eu/governance/impact/planned_ia/docs/47_sanco_clinical_trials_directive_en.pdf

⁸⁵ http://ec.europa.eu/health/files/clinicaltrials/ctresp_2011-06/ct_summary.pdf

⁸⁶ <http://www.priomedchild.eu/home/>

was funded out of national research budgets. Partnerships between research funding organisations seek to bring coherence and cooperation to national research programmes and policies on research for Priority Medicines for Children. PrioMedChild aims to contribute to ensuring more effective and safer medicines for children. At the end of 2010 seven projects were granted, the majority of which are directly related to the field of rare diseases and orphan medicinal products: New drugs for rare diseases: cost-effectiveness modelling in cryopyrin associated periodic syndromes; Rare diseases: use of clinical trial simulation for the choice and optimisation of study design; A faster and better tool for clinical decisions in children with leukaemia ; and Developing an effective treatment for childhood cancer with fewer side effects. The other projects of the PrioMedChild network will look at Validating non invasive imaging of the serotonergic- and dopaminergic system and adult neurogenesis with MRI; towards a better insight in the neurobiological mechanisms underlying psychiatric disorders in the paediatric population; Paediatric Accelerator Mass Spectrometry Evaluation Research Study; and Neonatal Exposure to Excipients. These seven projects contribute to making medication use safer for paediatric populations, including children with rare conditions.

A.3.3. Other EC activities and initiatives relative to the field of orphan medicinal products in 2011

EMINET Report (2011)

As part of the European Medicine Information Network (EMINet) project, a report was published in 2011 on an *Initial Investigation to Assess the Feasibility of a Coordinated System to Access Orphan Medicines*⁸⁷. This new report, commissioned by the European Commission DG Enterprise and Industry, presents a country-by-country survey of accessibility to orphan medicines, with an emphasis on product distribution through Centres of Expertise and derogatory procedures for accessing products in situations of restricted availability (typically Compassionate Use-type programmes). Taking Pompe disease and pulmonary arterial hypertension as examples, the EMINet report surveys both the availability of treatments across Europe and the distribution of centres of expertise for the diseases. The EMINet findings, combined with the results of the Ernst & Young CAVOD report, which focuses on developing a coordinated approach to providing orphan medicinal product information to all Member States prior to price negotiation in order to streamline health technology assessment and facilitate pricing decisions, contribute to the debate on efficient and equitable distribution of orphan medicinal products. Both reports seek to further the understanding of product access and availability for rare disease treatments across Europe. This feeds in to the reflection on a coordinated system for accessing orphan medicinal products.

⁸⁷ http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/access_orphans_initialinvest_052011_en.pdf

B. EUROPEAN MEDICINES AGENCY ACTIVITIES IN 2011

B.1. The European Medicines Agency's (EMA) activities in the field of orphan medicinal products and therapies for rare diseases in 2011

2011 Work programme

The European Medicines Agency (EMA) adopted its Work Programme for 2011⁸⁸ in December 2010. The 2011 Work Programme outlined its strategic and budgetary agenda for the year. Section 2.1 is dedicated to Orphan Medicinal Products. Amongst new issues figuring in 2011's work programme was the anticipated increase in the volume of applications stemming from the consequence of the Agency's rare diseases policy (including due to collaboration with the FDA and continuous support to rare diseases provided by DG Research and DG Health and Consumers).

The work programme also highlighted the development of activities following the Pharmaceutical Forum conclusions on health technology assessment bodies for orphan medicines, in particular through the Clinical Added Value of Orphan Drugs (CAVOD) initiative. The Work Programme estimated that some 180 applications for orphan designation will be received in 2011, revealing a sustained, slightly increasing volume (173 were received in 2010). Amongst the objectives and initiatives for the year were the maintenance of core activities and reaching an agreement on the framework for collaboration as part of the developing collaboration with the Commission and Member States HTA bodies on added value of orphan medicinal products. In terms of Scientific Advice and Protocol Assistance, the EMA anticipated growth in the number of applications with 73 in 2011 compared to 68 in 2010. The work programme highlighted adaptive and other innovative designs of clinical trials and use of biomarkers as endpoints in clinical trials as topics to be particularly relevant for 2011. Also it was expected an increase uptake of biomarker qualification and the novel-methodologies procedures. Interactions with health technology assessment bodies and with national authorities providing scientific advice were expected to become more important.

The European Medicines Agency's Management Board, at its meeting on 15 December 2011, adopted the Agency's work programme⁸⁹ and budget for 2012 which are driven by the implementation of the pharmacovigilance legislation. The work programme forecasts a stable number of applications for marketing authorisation for human and veterinary medicines in 2012. The Agency expects some 112 applications in total (2011: 111), with 52 applications for new medicines for human use, in addition to 13 new orphan medicines and 39 generic applications (2011: 47, 13 and 45 respectively). The Board noted the 10% increase in expected requests for scientific advice for human medicines, which includes an increasing number of joint scientific advice with health technology assessment bodies (HTAs). New pharmacovigilance legislation, implementing revised policies on handling of conflicts of interests and ethical and good clinical practice (GCP) aspects of clinical trials, progress of Agency interaction with healthcare professionals, supply shortages of medicines caused by insufficient good manufacturing practice (GMP) compliance, are all listed as priority areas in the work plan.

In the document it is noted that orphan medicinal product designations are expected to increase steadily in number and complexity as a consequence of the incentives for development and marketing of advanced therapies and innovative products for disease subsets. Continued collaboration with the FDA on joint designation assessment is also expected. Objectives for 2012 include the development of a pilot project on orphan medicines to explore how to better communicate and justify significant-benefit decisions reached by the Committee for Orphan Medicinal Products (road map initiative), a review of orphan medicines development to identify bottlenecks in development and provide feedback for the EU research policy on rare diseases, and the identification of advanced therapy medicinal products (ATMPs) designated as orphan medicinal products and their specific regulatory needs.

⁸⁸ http://www.ema.europa.eu/docs/en_GB/document_library/Work_programme/2011/02/WC500102044.pdf

⁸⁹ http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500122955&mid=WCOB01ac058009a3dc

EMA Road Map to 2015

In late 2010, the EMA's Management Board adopted the new Road Map to 2015 that takes into account the public consultation⁹⁰ held in the first half of 2010 that brought responses from "EU institutions, Member States, and organisations representing patients and consumers, healthcare professionals, pharmaceutical industry, academia and health technology assessment bodies". The new plan builds upon the accomplishments made from the objectives of the 2005-2010 strategy and continues to focus on the "high-quality delivery of the Agency's core business in an increasingly complex regulatory and scientific environment". In the new plan, three priority areas have been identified: Addressing public health, Facilitating access to medicines, and Optimising the safe use of medicines. The proposed vision also specifies that "another aspect which will remain high on the public health agenda relates to the availability of medicines for rare diseases and other current unmet medical needs such as medicines for the paediatric population". Particularly relevant to rare diseases, Strategic Area 1 includes amongst its objectives the stimulation of medicine development in the areas of unmet medical needs, including rare disorders. To address the challenge of existing gaps in medicine development, the EMA proposes undertaking an analysis of "the reasons for discontinuation of the development of medicines for human use starting with selected designated orphan medicines and propose remedial action. Any solution should favour a holistic approach, including the use of novel endpoints, different study designs and a more appropriate use of the accelerated assessment scheme for medicines intended for unmet medical needs, rare diseases and neglected diseases in the EU and beyond".

The final Road Map was published in January 2011⁹¹ and detailed information on the implementation of the road map was provided in the document 'From vision to reality'⁹².

EMA annual report for 2010

The European Medicines Agency Annual Report for 2010 recognises the increasing volume of core business activities and the achievement of a number of "important milestones" such as the launching of the new website, the publication of new rules on conflicts of interests and the new policy on access to documents. Another important development in 2010 was the publication of a report on the evaluation of the Agency and the European medicines network carried out by Ernst & Young on behalf of the European Commission. The report shows that the European medicines network, i.e. the Agency, the European Commission and the national competent authorities in the Member States, has been successful in delivering high-quality scientific opinions on medicines for human and veterinary use in an efficient and effective manner.

In 2010 the EMA received 174 orphan designation applications, of which 123 positive opinions were issued by the Committee for Orphan Medicine Products (COMP). Of these, oncology products once again were in the majority. In 2010, almost half of orphan designations concerned products for paediatric populations. In terms of marketing authorisation, there were 12 orphan medicinal product applications amongst the total 91 requests, quite similar to 2009 (11 applications). Of the 53 new products receiving marketing authorisation in 2010, six were new orphan medicines. Amongst the medicines of notable public-health interest that received a positive opinion from the CHMP in 2010 the report highlights a designated orphan medicine intended for the treatment of Gaucher disease (major public-health interest in the light of the shortage of the authorised medicine for the treatment of this disease), designated orphan medicines intended for the treatment of pulmonary conditions (one for suppressive therapy of chronic pulmonary infection due to *Pseudomonas aeruginosa* in cystic fibrosis, and another for idiopathic pulmonary fibrosis), a designated orphan medicine intended for the treatment of inborn errors in primary bile acid synthesis due to enzyme deficiencies and an orphan medicine intended for the treatment of patients with chronic lymphocytic leukaemia.

Six positive opinions were adopted by the Committee for Medicinal Products for Human Use (CHMP) recommending marketing authorisation for orphan-designated products in 2010. Indications include angioedema attacks, Gaucher disease, chronic pulmonary infection due to *pseudomonas aeruginosa* in cystic fibrosis, idiopathic pulmonary fibrosis, the treatment of inborn errors in primary bile acid synthesis due to enzyme deficiency and chronic lymphocytic leukaemia.

The report also documents the ongoing protocol assistance for orphan medicinal product development, continued support for small and medium-sized enterprises (SMEs development). Scientific Advice requests continued to increase in 2010, with the largest number (over half) relating to Clinical topics, and the remaining requests divided between Quality and Pre-Clinical issues. Protocol Assistance requests for orphan-designated products dipped to 68 for the year, after peaking at 77 requests in 2009.

⁹⁰ http://www.ema.europa.eu/docs/en_GB/document_library/Report/2010/01/WC500067952.pdf

⁹¹ http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/01/WC500101373.pdf

⁹² http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/10/WC500115960.pdf

Other highlights of the report include the adoption of two positive opinions for Compassionate Use; the activities of the Paediatric Committee and the Committee for Advanced Therapies, post-marketing activities, and the EU telematics strategy for pharmaceuticals.

Finally, the report outlines the considerable activities undertaken to strengthen and expand European and international cooperation and to further engage consumers, patients, and health professionals. The actions to improve communication and transparency are also detailed. A full report is available online⁹³.

Revision of the fee reduction policy for designated orphan medicinal products

As of 1 February 2009, designated orphan medicinal products are eligible for reductions for all fees payable under Community rules pursuant to amended Regulation (EEC) 2309/93. Covered in the reductions, applicable to orphan products designated in accordance with Regulation (EC) 141/2000, are the fees for pre-authorisation activities (protocol assistance such as scientific advice), as well as for products using the centralised procedure: the application for marketing authorisation, inspections, and post-authorisation activities. The EMA revised the fee reduction policy in April 2011 to ensure adequate incentives are still offered with the EU contribution received for 2011. The revised policy was adopted with an aim to ensuring that incentives for Small and Medium-sized Enterprises (SMEs) developing orphan medicinal products are maintained at the same level as previous years. In order to keep this objective the fee reductions for bigger pharmaceutical companies have been decreased.

The main changes introduced for 2011 are the following: 75% fee reduction for protocol assistance and follow-up procedures for non-SMEs. SMEs continue to benefit from a 100% reduction, as required by Article 7(3) of Regulation (EC) No 2049/2005. 10% fee reduction for initial marketing authorisation applications for non-SMEs. SMEs continue to benefit from a 100% reduction.

B.2. EMA Committee for Orphan Medicinal Products' (COMP) activities in 2011

Positive opinions on orphan designations

The Committee for Orphan Medicinal Products⁹⁴ (COMP) adopted 111 positive opinions on orphan designations in 2011. Over eighty diseases are covered by these designations. The European Commission then granted 107 of these orphan designations. Five orphan medicinal products received marketing authorisation in 2011.

COMP publication in Nature Reviews

The Committee for Orphan Medicinal Products (COMP) and the European Medicines Agency Scientific Secretariat have produced an article for *Nature Reviews: Drug Discovery* that details the progress made since the adoption of European Commission (EC) Regulation Number 141/2000, commonly referred to as the Orphan Drug Regulation in 2000. The first decade of the Orphan Drug Regulation yielded more than 850 positive opinions for orphan product designation, adopted from 1235 applications reviewed since 2000. The authors note that “*distribution of the prevalence of conditions for which the designations have been adopted to date shows that the most frequently designated conditions have been those that affect fewer than 1 in 10,000 patients (that is, ~50,000 patients in the EU)*”. The number of applications has increased steadily each year during the first decade of the Orphan Drug Regulation. The authors cite the economic climate and the growing collaborations between the EMA and the Food and Drug Administration (FDA) in the USA as possible contributing factors to the increase in applications. This perspective article reviews the designation criteria and the incentives available under the ODR. Other interesting statistics concern the number of designated products that have received authorisation. Sixty-three designated products had received marketing authorisation by the end of 2010, of which oncology is by far the most common therapeutic area (41%). Interestingly, the average time span between designation and authorisation is only 2.8 years, indicating that designated products were at an advanced developmental stage. Some of the incentives of the Orphan Drug Regulation, however, are geared to support the developmental process.

⁹³ http://www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2011/06/WC500108073.pdf

⁹⁴ This section reproduces information from <http://www.ema.europa.eu/htms/general/contacts/COMP/COMP.html>

The article discusses other areas in which the COMP is active, including an advisory role to the EC “established in the EC Regulation Number 141/2000, Article 4(1) (b) — the COMP strongly supported the proposal from the EC Directorate-General for Research (DG Research) to fund the preclinical and clinical development of medicines for the treatment of rare diseases in the Seventh Framework Programme. Before this, the COMP had been regularly liaising with the DG Research and identifying areas in which research into rare diseases is particularly needed, taking into account the number of designations and the lack of development, or failures seen by regulators”. The COMP also is involved with the World Health Organization revision of the ICD 11 for rare diseases. The COMP also liaises internationally – particularly with the FDA in the USA. The two regulatory bodies are streamlining many procedures in a bid to accelerate the availability of rare disease products on both sides of the Atlantic.

Finally, the paper considers future challenges and opportunities, speculating on the possible role the COMP and the EMA might play to help get authorised products distributed to patients across Europe – a procedure that presently is the responsibility of the Member States. The paper looks at some ways to address the existing unmet medical needs of patients with rare diseases and gives a “resounding yes” to the question of whether the orphan medicinal product incentives will be needed ten years from now. The paper concludes that “the needs of many patients with rare diseases are far from fulfilled, and so continued committed efforts are required from the EU, its institutions and member states”.

EMA’s Committee for Orphan Medicinal Products initiative to publish prevalence information

The July 2011 Committee Report of the European Medicine Agency’s Committee for Orphan Medicinal Products includes the news that the COMP agrees to support an initiative to publish the prevalence data and data sources for the conditions for which products receive orphan designation. The measure is another action in an overall campaign designed to heighten transparency. Ascertaining prevalence can be extremely difficult, particularly for rare disorders. It is hoped that the initiative will aid future applications.

B.3. EMA Committee on Human Medicinal Products (CHMP) activities in 2011

CHMP opinions concerning orphan medicinal products

In 2011, the EMA’s Committee on Human Medicinal Products CHMP issued positive opinions for marketing authorisation applications for Vyndaquel (tafamidis) for amyloidosis, Plenadren (hydrocortisone) for adrenal insufficiency, Votubia (everolimus) for astrocytoma, Tobi podhaler (tobramycin) for cystic fibrosis, and Esbriet (pirfenidone) for pulmonary fibrosis.

In 2011, the CHMP kept the recommendation that physicians switch back to prescribing the full dose of Fabrazyme according to the authorised product information, depending on the availability of enzyme replacement therapy and the severity of the disease. Temporary treatment recommendations to manage patients relying on this medicine have been in place since 2010 due to a supply shortage and have been regularly updated.

EMA’s first positive opinion for paediatric marketing authorisation

In June 2011, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued its first positive opinion for a paediatric-use marketing authorisation (PUMA) for Buccolam (midazolam) from ViroPharma SPRL, intended to treat prolonged, acute, convulsive seizures in paediatric patients between 3 months and 18 years of age. According to Article 30 of Regulation (EC) No. 1901/2006, paediatric-use marketing authorisations can be granted for medicines which are already authorised, but no longer patented, and which will be exclusively developed for use in children. Such products benefit from 10 years of market protection as an incentive. A paediatric investigation plan (PIP) which sets out the development of the medicine in children and is subject to approval from EMA’s Paediatric Committee (PDCO) is a prerequisite to obtaining a PUMA. The PIP for Buccolam was approved in August 2009. Many authorised medicines have not been studied adequately in children. The dedicated development of established medicines for children ensures that adequate information on the efficacy and the safety of a medicine is established and the correct dose and appropriate pharmaceutical form can be prescribed. To date, 26 applications for PIPs for

PUMAs have been received and seven opinions have been issued by the PDCO. A large majority of rare diseases affect paediatric populations.

B.4. EMA activities in the field of clinical trials in 2011

EudraCT Database

A European database – EudraCT⁹⁵ – contains all ongoing or completed interventional clinical trials of medicinal products falling within the scope of “Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use” (known more commonly as the “Clinical Trials Directive”⁹⁶, i.e. with at least one investigator site in the EU (including the European Economic Area) and commencing after implementation of the Directive 2001/20/EC by the Member States. This database gives the competent authorities of the Member States, EMA and the Commission the necessary information to communicate on clinical trials and to maintain oversight of clinical trials and IMP development. This provides for enhanced protection of clinical trial subjects and patients receiving IMPs. Paediatric clinical trials with investigator sites inside the EEA or which form part of a Paediatric Investigation Plan (PIP)⁹⁷, but that are conducted in third countries, are included (paediatric clinical trials with sites in the EU/EEA are already available). Following the guidelines published by the European Commission, all trials in the register have been authorised by the national medicine regulatory authority and have obtained a positive opinion from the ethics committee for clinical trials in the Member State concerned. Furthermore, clinical trials that include the paediatric population and have received a negative ethics committee opinion are being made public. Phase I clinical trials in adults will not be publicly available unless they form part of a PIP. The Clinical Trials Register contains historical data (all eligible trials contained in the EudraCT since its establishment in May 2004) and will contain all future trials recorded in the EudraCT.

Public access does not currently extend to data concerning trial results. However, there are plans to eventually include summaries of results, based on a guideline to be published by the European Commission, in late 2012 following the launch of an updated version of the EudraCT. The Clinical Trials Register does not provide data for non-interventional studies (observational, et al) for authorised products. Such data can be found via the website of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP⁹⁸).

EMA-NIH collaboration to harmonise clinical trial register data sets

The EMA is working with the National Institutes of Health in the USA, which manages the ClinicalTrials.gov⁹⁹ registry of federally and privately supported clinical trials conducted in the United States and around the world as well as the Health Level 7 - Clinical Trial Registration and Results project¹⁰⁰ on the harmonisation of data sets submitted by the sponsor to clinical trial registers, as well as the World Health Organization. Such harmonisation is particularly welcomed by the rare disease community, which already faces the challenges of scattered patient populations and expertise.

⁹⁵ <https://eudract.ema.europa.eu/>

⁹⁶ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:121:0034:0044:en:PDF>

⁹⁷ http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000302.jsp&murl=menus/special_topics/special_topics.jsp&mid=WC0b01ac058002d4ea&jsenabled=true

⁹⁸ <http://www.encepp.eu/>

⁹⁹ <http://clinicaltrials.gov/>

¹⁰⁰ <http://www.hl7.org/index.cfm?ref=nav>

B.5. EMA activities in the field of medicinal products for paediatric use in 2011

European Network of Paediatric Research – Enpr-EMA

The European Medicines Agency (EMA) announced in 2011 the publication of the first membership list of the European Network of Paediatric Research at the European Medicines Agency (Enpr-EMA)¹⁰¹. Established to build a high-level network of existing research networks, investigators and centres with recognised expertise in performing clinical studies in children, the Enpr-EMA seeks to facilitate high-quality ethical research on medicines for use in children through networking and stakeholder collaboration with members from both within and outside the European Union as part of the EMA's accordance with European Paediatric Regulation (EC) No 1901/2006. Enpr-EMA's also aims to: coordinate studies relating to paediatric medicines and avoid unnecessary testing in children; build up scientific and administrative competence at a European level; help with the recruitment of patients for clinical trials; and promote European Commission framework programme applications. Enpr-EMA does not perform clinical trials or fund studies or research or decide on areas for paediatric research, as this is the responsibility of Member States, the European Commission or each individual network. The European Medicines Agency is responsible for ensuring collaboration within the network. The Enpr-EMA membership list¹⁰² was compiled following a call for expressions of interest in 2010. Some 32 networks and centres have thus far applied for membership. Of these, 16 networks and centres have become members of Enpr-EMA. A second category of networks has been established for those "... *undergoing clarification before membership of Enpr-EMA*". Networks grouped into a third category do not currently qualify for membership.

Database of clinical studies involving children available via the EMA

In 2011 the European Medicines Agency made available a database¹⁰³ housing information on clinical studies of medicines authorised in the European Union that involved paediatric populations and were completed prior to the 2007 Paediatric Regulation came into effect. Via the Article 45 Paediatric Studies Database, it is possible to access information including the name and goal of the study, the medicinal product involved, and data on the patients, including age. Some trial outcomes are also available. The database is part of a global aim of the Agency to enhance transparency. The Agency is also specifically focused on improving information on medicinal products for paediatric populations.

B.6. Other EMA activities and initiatives relevant to rare diseases and orphan medicinal products in 2011

EMA guidance for stem cell-based medicines

The European Medicines Agency (EMA) has issued a reflection paper¹⁰⁴ on stem cell-based medicines that encompasses the different types of stem cells used in medicines, and addresses considerations for the development of stem cell-based medicines. In particular, the document "*stresses the fact that companies developing medicines including stem cells need to pay close attention to the way the medicines are manufactured, to make sure that the final medicine is as consistent and reproducible as possible*". The reflection paper also offers consideration for pre-clinical and clinical testing. Adopted by the EMA's Committee for Advanced Therapies in January 2011, the reflection paper was open for public consultation in 2010 and was discussed at a public workshop last May 2010. Stem cell-based medicines could potentially be used in the treatment of many rare diseases.

¹⁰¹ http://www.ema.europa.eu/ema/index.jsp?curl=pages/partners_and_networks/general/general_content_000303.jsp&mid=WC0b01ac05801df74a

¹⁰² http://www.ema.europa.eu/ema/index.jsp?curl=pages/partners_and_networks/q_and_a/q_and_a_detail_000108.jsp&mid=WC0b01ac05802b9f0f

¹⁰³ <http://art45-paediatric-studies.ema.europa.eu/clinicaltrials/>

¹⁰⁴ http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/02/WC500101692.pdf

Good manufacturing practice database expands access to all Member States

EudraGMP¹⁰⁵ is the Community database on manufacturing and import authorisations and Good Manufacturing Practice (GMP) certificates launched by the European Medicines Agency in April 2007. In July 2009 GMP non-compliance of manufacturers was added. Now a new version of the database has been developed that offers public access to information on manufacturing inspection by regulatory authorities from all the European Economic Area countries, including all the EU Member States, Iceland, Liechtenstein and Norway. The move represents a global effort of the EMA to increase transparency. According to a press release, the wider access will, “...improve the sharing of information between regulators and industry; aid the coordination of activities related to manufacturing authorisations and GMP certificates between regulatory agencies in different European countries; eliminate the need for industry to submit applications in paper form; and facilitate the sharing of information on the outcome of inspections in the EU with regulatory authorities elsewhere in the world”. The increased access is particularly welcome to the fields of rare diseases and orphan medicinal products, which depend upon the coordination and sharing of information and activities.

EMA website update

The European Medicines Agency has updated its website in order to allow users of the site to search and share contents more readily. According to a press release, new features include: a 'share' button that allows users to bookmark pages and share them via tools such as email, Facebook or Twitter; a 'search by type' feature: lets users browse the human European public assessment reports for generic, biosimilar or orphan medicines, medicines authorised under exceptional circumstances or medicines granted conditional approval; an improved document searching: allows document library searches by reference number, year of publication or consultation status; an enhanced event searching: permits keyword and year-by-year searches within the calendar of events and meetings; and searching PIPs by condition (allows a search of all opinions and decisions on paediatric investigation plans (PIPs) by a given condition or disease). These updates build upon the EMA's drive towards more openness and transparency.

EMA Database of European Experts

The European Medicines Agency (EMA) has created a database of European experts¹⁰⁶ that furnishes information on declarations of interest. The database, publicly available, coincides with the entry into force of new rules around conflicts of interests of scientific experts nominated by competent authorities for medicines regulation across the European Union and involved in the Agency's activities. In a press release, the database is described as “...a major building block of the Agency's new rules on the handling of conflicts of interests of its scientific experts, which aim at protecting the Agency's scientific opinion-making processes from the influence of any improper interests”. Conflicts of interests are classified into three categories: “direct”, “indirect” and “no interests” and experts provide a signed declaration of interests form detailing any direct or indirect financial or other interests that could affect their impartiality.

B.7. International cooperation between regulators in the field of orphan medicinal products

In 2011 the US Food and Drug Administration and the EMA hosted the first joint workshop on applications for orphan designation, marking the first occasion in which sponsors have been able to discuss in real time applications for designation with both Regulatory Authorities.

The FDA published a report¹⁰⁷ of their activity in the realm of innovative medicines in 2011. Orphan medicinal products come out well making up almost a third of the 35 innovative medicinal products that were approved by the FDA in fiscal year 2011. Moreover, the FDA approved nearly half (16) of the innovative drugs under the agency's “priority review” programme. This scheme accelerates the approval process for drugs that may offer major advances in treatment. The FDA defines innovative medicines as “new molecular entities”, novel chemical structures, including biological products, which have never been approved before to treat any

¹⁰⁵ <http://eudragmp.ema.europa.eu/inspections/displayWelcome.do>

¹⁰⁶ http://www.ema.europa.eu/ema/index.jsp?curl=pages%2Fabout_us%2Flanding%2Fexperts.jsp&url=menus%2Fabout_us%2Fabout_us.jsp&mid=WC0b01ac058043244a&searchTab=&authorityId=&alreadyLoaded=true&isNewQuery=true&startLetter=View+all&selectedCountry=&jsenabled=true

¹⁰⁷ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM278358.pdf>

disease, and often represent the most innovative drugs entering the market. Ten of the innovative products approved in fiscal year 2011 have orphan indications.

C. OTHER EUROPEAN RARE DISEASE ACTIVITIES

C.1. Actions undertaken by recent European Union presidencies

Hungarian presidency of the European Union (January – June 2011)

On 26 February 2011 experts came together in Budapest to commemorate Rare Disease Day 2011 at an informal event of the EU supported by the Hungarian presidency¹⁰⁸, organised by HUFERDIS president Gabor Pogany. The event was attended by a range of stakeholders from Hungary and Europe and gave insights into actions at Hungarian and European level in the field of rare diseases. During the day Dr. Ildikó Horváth, Head of Department for Health Politics, State Secretariat for Healthcare, Ministry of National Resources, and her colleague Ildiko Szy presented more than 20 professional clinical guidelines for rare diseases.

C.2. E-Rare

E-Rare-2 launched at the end of 2010 its third Joint Transnational Call for proposals which closed in early 2011. Research groups from nine countries (Austria, Belgium, France, Germany, Greece, Israel, Italy, Spain and Turkey) were eligible to participate in this call that seeks to promote transnational research collaboration on rare diseases. The selected¹⁰⁹ projects cover at least one of the following areas: definition of new nosological entities, epidemiological studies, genotype/phenotype correlations, natural history of diseases; characterisation of the genetic/molecular basis of specific diseases; pathophysiological and genetic studies of rare diseases; and diagnostic and therapeutic research (interventional clinical trials are excluded). Thirteen consortia were funded with a budget of around €9 million foreseen. The rare disease areas of the chosen projects include haematology, metabolic diseases, neurology, dermatology, and congenital malformations. Therapeutic approaches include pluripotent stem cells, gene therapy vectors and customised animal models.

In late 2011 E-Rare ERA-NET on rare diseases launched its 4th Joint Transnational Call issued a call entitled “European Research Projects on Rare Diseases driven by Young Investigators”¹¹⁰. The aim is to provide to young, independent investigators the opportunity of building transnational collaborations in the field of rare disease research. The transnational project should be based on complementarities and sharing of expertise, demonstrating a clear added value of the cooperation and impact of the expected results on patients affected by rare diseases. Eligible under this call will be young investigators who have been awarded their first PhD/MD or equivalent of doctoral degree since at least 2 and up to 10 years.

E-Rare issued its very first newsletter¹¹¹ and made over its website in 2011.

C.3. Clinical genetics as a medical speciality

The European Union of Medical Specialists (UEMS), a non-profit organisation founded in 1958 to determine high quality standards harmonising specialist training for European physicians, represents some 1.5 million European medical specialists in 38 specialist sections throughout 35 national member associations. In April 2009, the UEMS Council adopted the text entitled *Description of Clinical Genetics as a Medical Specialty in EU: Aims and objectives for specialist training*¹¹². The document, which defines educational goals for a specialisation in genetic medicine, has already been endorsed by the European Society of Human Genetics, the UEMS Multidisciplinary Joint Committee for Clinical Genetics, and the UEMS Specialist Sections & European

¹⁰⁸ <http://sites.rirosz.hu/rby/ritka-nap-2011/programme-in-english>

¹⁰⁹ <http://ns356946.ovh.net/~erare2/content/funded-projects-joint-transnational-call-2011>

¹¹⁰ <http://www.e-rare.eu/content/joint-call-european-research-projects-rare-diseases-driven-young-investigators-itc-2012>

¹¹¹ <http://www.e-rare.eu/newsletter/subscriptions>

¹¹² <http://admin.uems.net/uploadedfiles/1305.pdf>

Boards. This is good news for rare disease patients in countries where clinical genetics is not yet recognised: Belgium, Greece and Spain.

The EC Regulation No 213/2011¹¹³ amending Annexes II and V to Directive 2005/36/EC of the European Parliament and of the Council on the recognition of professional qualifications entered into force on 4 March 2011. Published in the *Official Journal of the European Union*, the amendment states that:

(7) Medical genetics is a specialty that responds to the rapid development of knowledge in the field of genetics and its implication in numerous specialised fields, such as oncology, foetal medicine, paediatrics, chronic diseases. Medical genetics plays a growing role in screening and in the prevention of numerous pathologies. Specialist medical training in medical genetics is not listed in point 5.1.3 of Annex V to Directive 2005/36/EC. However, it has developed into a separate and distinct specialist medical training in more than two fifths of the Member States, which justifies its inclusion into point 5.1.3 of Annex V to Directive 2005/36/EC.

(8) In order to ensure a sufficiently high level of specialist medical training, the minimum period of training required for the medical specialty of medical genetics to be automatically recognised should be four years.

Recognition of the speciality is critical both for the training of professionals and the organisation of related services.

C.4. Resolution on pharmacy prepared medicinal products adopted by the Council of Europe

Resolution CM/ResAP(2011)1¹¹⁴ on quality and safety assurance requirements for medicinal products prepared in pharmacies for the special needs of patients was adopted by the Committee of Ministers of the Council of Europe on 19 January 2011. Special needs can arise from factors such as patient age, medical condition (such as rare diseases), individual disposition or environmental factors. The resolutions help to harmonise the preparation of medicinal products in community and hospital pharmacies throughout Europe and address the added value of pharmacy preparations; the responsibilities of health-care professionals; the preparation process; the product dossier; labelling; the reconstitution of medicinal products in health-care establishments; and authorisation for pharmacies or licences for companies making preparations for pharmacies.

C.5. International Rare Disease Events in 2011

Rare Disease Day 2011 (28 February 2011)

The Fourth edition of the annual Rare Disease Day 2011, organised by EURORDIS, was held on 28 February 2011. Rare Disease Day 2011 included 55 countries (up from 46 in 2010, 30 in 2009 and 18 the first year) with newcomers including Armenia, Iran, Mexico, Morocco, Nepal, Panama, Peru, Thailand, the United Arab Emirates, and Uruguay. EURORDIS has partnerships with 22 national alliances and added Cyprus and Switzerland as new alliances joining the celebrations.

The official Rare Disease Day (RDD) website¹¹⁵, maintained by EURORDIS, received almost 50,000 visits from some 150 countries between 1 January and 3 March 2011. On 28 February the site logged some 10,000 visits. The number of RDD friends leapt to 292 from 187 last year, including patients, patient organisations, caregivers, healthcare professionals, researchers, members of the biopharmaceutical industry and public authorities. Scores of testimonials addressing the subject of this year's theme "Rare but Equal" were posted on the RDD website. RDD was also active on the major social networking sites with over 14,000 fans on Facebook, 1,446 followers on Twitter, 432 photos posted on Flickr, and a hundred videos on YouTube.

One of the most significant benefits of the awareness-raising day is the momentum the event provides for advancing the national plans that countries are urged to create following the *Council Recommendation on*

¹¹³ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:059:0004:0007:EN:PDF>

¹¹⁴ <https://wcd.coe.int/wcd/ViewDoc.jsp?Ref=CM/ResAP%282011%291&Language=lanEnglish&Ver=original&BackColorInternet=DBDCF2&BackColorIntranet=FDC864&BackColorLogged=FDC864>

¹¹⁵ <http://www.rarediseaseday.org/>

an Action in the Field of Rare Diseases. Indeed, France took the occasion of RDD to unveil its second plan, and frameworks for strategies were evoked in Croatia, Hungary, and Ireland. Belgium chose the occasion to hold a symposium for the drafting of a national plan, and in Switzerland, a member of the Health Commission proposed a vote for a strategy. Across the Atlantic, meanwhile, the U.S. Senate unanimously adopted a resolution officially designating 28 February, 2011 as Rare Disease Day in all states. The icing on the cake of recognition came from the Vatican when Pope Benedict XVI included a personal message to rare disease patients and families including a wish that advances in research will help patients.

Significant publications released in honour of RDD included the release of the Eurobarometer survey *European Awareness of Rare Diseases Report*. At the national level, the Rare Disease UK group released a major report outlining recommendations for a strategy for rare diseases. Luxembourg released a study undertaken by the Rare Disease Working Group entitled *Rare diseases: A National Survey on the Situation of Persons with Rare Diseases in Luxembourg*. RDD 2011 also marked the relaunch of the Orphanet site in Portuguese.

This year's RDD also caused a stir in the press – including a 20 page supplement in the UK newspaper *The Independent*. Other leading country dailies and press agencies lending awareness for the rare disease cause on RDD include *Les Echos* (France), *El Pais* (Spain), *Romania Libera* (Romania), the *Emirates News Agency*, and the *Cyprus Mail*, for example. There were also publications and websites launched presenting the patient experience and perspective in Canada, Denmark, Georgia, Panama, and Russia.

At the EU level, the *European Symposium- Rare but Equal- Addressing Health Inequalities for Rare Disease Patients in Europe* was organised by EURORDIS with the support of DG SANCO. Amongst the 86 participants were four representatives from the European Commission along with Member of Parliament Antonia Parvanova, shadow rapporteur on the recently adopted EU Directive on Cross-Border Healthcare and Patient Mobility. The symposium provided a venue for discussing the issue of health inequalities as well as strategies to remedy the inequalities rare disease patients endure. The Cross-Border Healthcare Directive was cited as a mechanism for levelling the field. The European Commission confirmed that diminishing rare disease health inequalities is a priority. Stefan Schreck, DG SANCO, Head of Unit for Health Information, evoked the EUCERD as an engine to facilitating better rare disease healthcare based upon the principles of equity and solidarity.

The EUCERD fully endorses the International Rare Disease Day campaign to raise awareness for the health inequities in the field – and particularly supports the promotion of rare diseases in the Third EU Public Health Programme (2014 to 2020) - and will continue working hard to level the playing field for all the rare disease stakeholders out there.

Final Europlan conference (Rome, 25 February 2011)

On 25 February 2011 the final conference of the Europlan project was held¹¹⁶. Europlan, a three-year DG Sanco-funded project coordinated by the Italian National Centre for Rare Diseases (Istituto Superiore di Sanita) launched in April 2008, as an instrument to help the European Union Member States (MS) define a strategic plan for rare diseases following the adoption of a Council Recommendation on an Action in the Field of Rare Diseases that calls on the MS to elaborate and adopt a rare disease plan or strategy by the end of 2013.

At the final Europlan meeting, it was observed that one of the strongest elements of the Europlan project was its role in adding the European dimension to individual national strategies. This point is critical to the field of rare diseases, which relies on coordination and collaboration at the European and international levels. The 2011 Eurobarometer survey results demonstrate that there is support for European cooperation. Commission representatives cited the E-Rare project as an effective strategy for the funding of collaborative research.

A Round Table meeting reviewed some of the overall results of the Europlan project such as its role in harmonising concepts and terminology between the MS and in helping to raise awareness at the MS level for key EU documents in the field of rare diseases and orphan medicinal products. During this session, the need for integrating the elements of the national rare disease plans into the national health care systems was discussed. The importance of mapping existing resources - which Orphanet, the pan-European information portal for rare diseases and orphan medicinal products, is doing – was also evoked. Other elements identified include the need for inclusivity – i.e., involving all the various stakeholders in the development of a national plan; the need for the national protocols for diagnostics and care of a disease to include the provisions for patient coverage for testing and care; and the healthcare pathways – the multidisciplinary algorithms of care structured to support the implementation of clinical guidelines and protocols.

¹¹⁶ <http://www.europlanproject.eu/ContenutoPage/127/en-GB/final-meeting/proceedings.aspx>

Discussion of the status of particular countries was also raised. While Bulgaria has a concrete plan, accessing funding remains problematic, especially in the area of diagnostics. Croatia hopes to put forward a plan in 2012. Denmark is in a period of regression, illustrated by the country's information centre exclusively for rare diseases that has been extended to encompass all diseases. Greece has a plan on paper, but it is not yet legally recognised and the country has no national committee to implement it. There are also significant problems with access to orphan medicinal products in Greece. Starting a process to develop a plan in a country with 21 autonomous regions is a priority Italy – but the country's organisation presents a daunting challenge. Italy also reports a long time for orphan medicinal product approvals to be processed. The Netherlands is a country with a solid general health plan, which could explain why the Minister of Health is not in favour of developing a plan specifically for rare diseases. Furthermore, the country's Steering Committee for Orphan Drugs is to be shelved at the end of 2011. In Poland, the process of elaborating a plan has not yet begun, but awareness is increasing. Poland needs to focus on all elements of rare disease strategising – not just the orphan medicinal products. Spain does have a plan, but it has neither a budget nor a time-table. The UK seems to be moving forward, thanks in large part to the steam of the Rare Disease UK and similar patient-driven efforts.

With several plans existing only on paper, other countries reporting a regression, and other MS lacking resources, the dream that each MS will have a specific strategy to care for its rare disease patients, and which includes cooperation between the EU countries to share resources, is a fragile one. This is a critical time for each stakeholder to continue acting as a catalyst to push change forward. The recent adoption of the Cross Border Health Care Directive increases the need for concerted effort, with each EU country identifying its pockets of expertise and making them known, within the context of acknowledging and respecting the individual dynamic of each country, particularly its size and resources. Analysis of the results of this first Europlan project can help refine the second leg of the plan, which is being funded via the upcoming DG Sanco three-year EUCERD Joint Action (*Support to the implementation of national plans/strategies on rare diseases and related measures to implement Council Recommendation and Commission Communication on rare diseases*). The second phase of Europlan will continue to offer support and guidance to countries that have delineated a strategy and will aid countries that have not developed a plan to move forward, taking into account the specifics of each country in terms of size, prioritisation of measures and health care systems. There will also be an emphasis on the exchange of expertise between countries, as well as identifying outcome indicators that can be monitored. Around twenty national conferences are being planned for the second phase of Europlan within the EUCERD Joint Action.

EUCERD/EMA workshop on a public-private partnership model for rare disease registries (London, 4 October 2011)

On 4 October, stakeholders gathered at the Canary Wharf, London-based European Medicines Agency for a brainstorming session on how to best design, manage and share rare disease registries in a way that will be purposeful and satisfying for all players¹¹⁷. Experts from academia, the biopharmaceutical industry, patient organisations, and regulatory agencies all lent their expertise to the event, which culminated in a consensus towards disease-based registries that could ultimately be shared amongst all relevant public and private partners. This consensus, shifting from the drug- or patient-based designs to a larger-encompassing disease-based model, moves forward the challenge of how to coordinate, manage and share the goldmine of data that the disease registries potentially yield.

Well constructed and managed rare disease registries can significantly speed up clinical research in the fields of rare diseases and orphan medicinal products, further the understanding of many elements including prevalence, natural history, and treatment outcome for rare diseases, provide regulatory bodies – including pricing and reimbursement agencies - with crucial data, serve as a resource for trial recruitment, and help patient organisations to coordinate efforts and share information.

The EUCERD/EMA workshop, organised in the context of the ongoing scientific activities of the EU Committee of Experts on Rare Diseases (EUCERD) dedicated to registries in the field of rare diseases, builds upon the Rare Diseases Task Force (RDTF) report, Patient registries in the field of rare diseases¹¹⁸, based on outcomes of the 2008 RDTF workshop on this field, updated in 2011, as well as the tender report on the *Creation of a mechanism for the exchange of knowledge between Member States and European authorities on the clinical added-value of orphan drugs (CAVOD)* and the Orphanet Report Series Disease registries in Europe¹¹⁹.

¹¹⁷ <http://www.orpha.net/nestasso/EUCERD/upload/file/EUCERDWorkshopRegistries2011.pdf>

¹¹⁸ <http://www.eucerd.eu/upload/file/RDTFRegistriesrev2011.pdf>

¹¹⁹ <http://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf>

Future meetings already being planned will tackle the complex questions of how to protect important privacy rights for industry, academic and patient registry partners, how to manage post-marketing authorisation data for orphan drugs, how to coordinate at an international level, and harmonisation between registries. The EpiRare project (European Platform for Rare Disease Registries) launched in April 2011, seeks to gather more information on the needs of stakeholders, while the International Rare Diseases Research Consortium brings to the table the international perspective, expectations and experience.

European Agency for Health and Consumers Rare Disease media event (Luxembourg, 25-26 October 2011)

The European Agency for Health and Consumers (EAHC) organised a media initiative¹²⁰ focused on exploring what is being done at the European level to improve the situation for rare disease patients and their families. The two-day event featured a busy agenda of presentations from some of the main rare disease players in Europe, including pan-European information portal Orphanet and rare disease patient umbrella group EURORDIS, as well as a number of projects focusing on individual groups of diseases, and powerful testimonies from patients and their families. The event brought a fresh reminder of the situation millions of rare disease patients grapple with as the momentum for each of the European Union Member States to develop a specific strategy for meeting the needs of its rare disease patients, as put forward in the European Council Recommendation on an action in the field of rare diseases continues. The conference included presentations of some of the activities and initiatives that are funded at the European-level and described how they are contributing to improving the lives of rare disease patients and moving forward the search to better understand and treat this large group of heterogeneous diseases. A ten-minute video, narrated by Commissioner for Health and Consumers Mr John Dalli served to illustrate on a concrete level some of the complex issues rare disease patients and their families face.

Rare 2011 (Montpellier, 4 November 2011)

On 4 November 2011, the European Committee of Experts on Rare Diseases (EUCERD) organised, in collaboration with EuroBioMed, the first European day of the French 'Rare2011' conference in Montpellier, France¹²¹. The day consisted of three sessions highlighting priority topics in the field of rare diseases which call for collaboration at European level: Ensuring Visibility of Rare Diseases in Health Information Systems, Partnering to Optimise the Use of Patient Data to Improve Clinical Research and Healthcare, and Improving Access to Expertise and Quality Care. A wide range of stakeholders including researchers, policy makers, members of the industry and patient representatives were present at this event, of which the proceedings are detailed in this present document.

¹²⁰ http://ec.europa.eu/eahc/health/Rare_Diseases_conference_2011.html

¹²¹ <http://www.orpha.net/nestasso/EUCERD/upload/file/Rare2011.pdf>

D. EUROPEAN MEMBER STATES' ACTIVITIES IN 2011

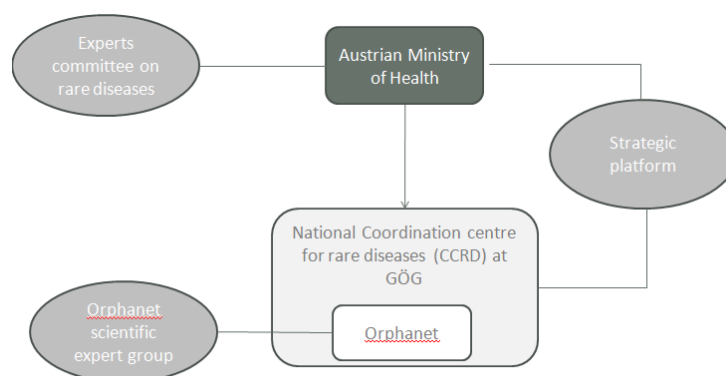
D.1. AUSTRIA

National plan/strategy for rare diseases and related actions

As response to a petition by health professionals and patient organisation for a national action plan on rare diseases in Feb 2008 and considering the recommendations of the European Council of 8 June 2009 to implement a national action plan on rare diseases until 2013 the highest Austrian Health Advisory board (“Oberster Sanitätsrat”) of the Austrian Ministry of Health (BMG) established a subcommittee for rare diseases in May 2009, consisting of 17 members from 13 different organisations or institutions (covering the main stakeholders in the field). This working group was managed by the Austrian Orphanet team and laid the foundation for a national plan of action for rare diseases. It was the first time in Austria that an expert committee of this size, covering a broad spectrum of viewpoints, was working on rare diseases in a comprehensive manner, with topics ranging from the description of the situation of rare diseases in general to legal and ethical aspects, equality in legal and practical terms, the identification of concrete problems, bottlenecks and restrictions that patients, relatives, physicians and scientists are confronted with, and, finally, the identification of possible measures and strategies aiming to improve the situation, to combat (structural) deficits, to optimise health care pathways, and to minimise disease burden wherever possible.

However, due to the many topics on the agenda and the lack of resources of the Board Members the Austrian Ministry of Health decided to establish a National Coordination Centre for Rare Diseases (CCRD, Nationale Kontaktstelle für Seltene Erkrankungen, NKSE). The CCRD was established by 1 January 2011 at the Austrian Health Institute (Gesundheit Österreich GmbH, GÖG) and has a team of 1.4 full time equivalents and integrates part of the Austrian Orphanet team. Most members of the subcommittee for rare diseases are still involved in the topic as they kindly accepted their appointment to the Expert committee on rare diseases that was established in mid 2011 by the Ministry of Health (see Figure 1 below). In addition to the previous structure a strategic platform was set up, the is composed of Ministry of Health delegates, academic experts and payers (Austrian provinces and the Main association of the Austrian social security institutions),

Figure 1: Organisational Chart of the Austrian CCRD in 2011



The establishment of the CCRD was one of the first steps of the development of a national plan for rare diseases as proposed by the subcommittee for rare diseases in November 2010. The founding of CCRD included a sustained funding of Orphanet as the national information system for rare diseases and the involvement of both, the Medical University of Vienna and the GÖG as partners in the Joint Action Orphanet Europe.

The main activities of the CCRD in 2011, besides setting up its organisational structures and processes were as follows:

- Acting as the the main driving force in drawing the national plan of action until end of 2013;

- Awareness raising among professionals / experts / doctors / patients on the topic of rare diseases;
- Active participation in the EU-funded project Orphanet as well as other European initiatives in this area (e.g. the EU Working Group on Mechanisms for a coordinated access to orphan medicinal products as part of the platform for Access to Medicines in Europe which is part of the Corporate Social Responsibility Process launched by Commissioner Tajani);
- Information provision:
 - Establishment of Orphanet national scientific advisory board;
 - Establishment of national Orphanet website;
 - Updating of information on rare diseases in Austria;
- Perform a large scale needs assessment survey regarding rare disease involving academics, stakeholders and – for the first time in Austria – patients and draft a report that is planned to be published in summer 2012;
- Drafting eligibility criteria for the establishment of Centres of Expertise based on EUCERD recommendations and discuss them with the Austrian stakeholders;
- Acting as the communication hub between actors in the field, focussing in the first years on health care professionals and other stakeholders and will contribute to ensuring that the unique challenges faced by people with rare diseases to meet are targeted;
- Acting as the focal point for European activities in the field of rare diseases, i.e. to keep track of developments and trying to draft a landscape of activities involving Austrian institutions.

Neonatal screening policy

Detailed information regarding the Austrian NBS is provided by a completely revised homepage¹²² that was made available online at the end of 2011 and that is available in three languages (German, English, and Turkish). As additional service, nearly all diseases listed and explained on the NBS homepage are directly linked to the relevant disease entity in the Orphanet database.

National alliances of patient organisations and patient representation

3 December 2011 was a milestone for patients suffering from rare diseases in Austria as on this date the umbrella organisation for patient organisations dealing with rare diseases was founded. This national “Allianz für seltene Erkrankungen” is called “Pro Rare Austria” and was founded by Dr. Riedl who is also spokesperson of DEBRA Austria, the Epidermolysis bullosa patient support group. As first broadly recognised activity the new Pro Rare team organised the Rare Disease Day 2012 in Vienna but also participated in a number of rare disease events (e.g. at the Mariazell follow-up Congress on Rare Diseases on 3-4. December 2011 hosted by the Medical University of Vienna).

Pro Rare Austria demands:

- Official recognition of defined rare diseases
- Public acknowledgment of the special status of patients suffering from rare diseases, namely
 - Exemption from any co-payments or cost-sharing for any treatment related to their rare disease
 - Unrestricted access to medicinal investigations, tests and diagnosis in Austria, and if not available nationally, within the EEA
 - Unrestricted access to all available therapies and medicines especially orphan drugs in Austria, and if not available nationally, within the EEA
 - Austrian-wide uniform regulations with regards to long term care, care-support and childcare
- Improvement of medical care by establishment or designation of regional and/or national reference clinics/reference centres
- Promotion of scientific research aimed at developing therapies

Delegates of Pro Rare and a few other patient organisations were also invited to become member of the newly established Expert Committee for rare diseases (see Graph 1).

Apart from Pro Rare general alliances of patient organisations (both for rare and non-rare diseases) do exist on the province level (ARGE Selbsthilfe Carinthia, Upper Austria, Lower Austria, Salzburg, Styria, Tyrol, Vorarlberg, and Vienna). They are united under the supra-umbrella *Arbeitsgemeinschaft (ARGE) Selbsthilfe*, which is located in Vienna. The *ARGE Selbsthilfe* can provide limited funding (up to € 900 for a period of 6 months with repeat applications possible) for all patient organisations (including those in the rare diseases field), however, funding is confined to support the formation of a new patient organisation or to provide

¹²² <http://www.meduniwien.ac.at/hp/neugeborenen-screening/>

interim aid for an existing one bridging a limited time gap. The Austrian Health Institute supports Pro Rare by providing meeting rooms and optional funding for further education in the field.

Thematically restricted support for patient organisations will possibly be part of the future National Plan for Rare Diseases, integrated into the priority “Improving awareness and knowledge about rare diseases”.

Sources of information on rare diseases and national help lines

Orphanet activities in Austria

In 2011, the Orphanet-Austria¹²³ national website providing a national entry point to the Orphanet database was launched based on the self-developed country website which was launched back in 2008. The objectives are to provide basic information on the Orphanet database and the local Orphanet team, as well as to raise public awareness on rare diseases in general. The team reports about major events and activities organised either by Orphanet Austria itself or by other stakeholders.

Official information centre for rare diseases

Until 2010, Orphanet was the only official source of information specific to rare diseases in Austria. In January 2011, the national Coordination Centre for Rare Diseases (Nationale Koordinationsstelle für Seltene Erkrankungen, NKSE) was established at the Austrian Health Institute Gesundheit Österreich¹²⁴ (as part – and first structural measure – of the national plan of action under development). NKSE is funded by the Austrian Ministry of Health (Bundesministerium für Gesundheit) and shall act in the mid-term as information provider next to its other functions. Orphanet Austria was integrated into this coordination centre to enable maximum synergy between the two structures. In the first phase the CCRD launched the Austrian Orphanet Website¹²⁵ and provided information to health professionals, e.g. by presenting on rare disease specific congresses and events.

Other sources of information

In 2011 rare disease specific information was also provided on the official governmental health platform for Austria. Examples of information provided are excerpts regarding the patient, payer and stakeholder survey performed by the Austrian National Coordination Body for Rare Diseases (NKSE)¹²⁶ as well as information regarding the establishment of the NKSE¹²⁷.

National rare disease events in 2011

A day dedicated to rare diseases was held on 26 February 2011 at the Paracelsus Medical University Salzburg to celebrate the 4th Rare Disease Day. Also on 26 February 2011, the “walk for rare diseases” took place in Vienna, again featuring more participants than in previous years.

On 2 and 3 December 2011, the Medical University of Vienna and the National Action Platform for Rare Diseases (NASE) held the Austrian Congress on Rare Diseases 2011 in Vienna. The conference was planned as a follow-up event from the 2010 congress in Mariazell and once again was attended by a large range of stakeholders to encourage discussion, to raise awareness and to look for solutions.

In addition to these events, the Second Regional Forum for Rare Diseases was held on 20-21 May 2011 in Innsbruck.

Research activities and E-Rare partnership

E-Rare

Austria participated in the 3rd Joint Transnational Call in 2010/11 and Austrian teams will participate in all together seven of the funded projects-

IRDiRC

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

¹²³ <http://www.orpha.net/national/AT-DE/index/startseite/>

¹²⁴ <http://www.goeg.at/de/Bereich/Koordinationsstelle-NKSE.html>

¹²⁵ www.orpha.net/national/AT-DE/index/startseite

¹²⁶ www.gesundheit.gv.at/Portal.Node/ghp/public/content/aktuelles/seltene-erkrankungen-befragung.html

¹²⁷ www.gesundheit.gv.at/Portal.Node/ghp/public/content/aktuelles/koordinationsstelle-seltene-erkrankungen.html

D.2. BELGIUM

National plan/strategy for rare diseases and related actions

Work advanced in 2011 on a proposal for a Belgian Plan for Rare Diseases. The final set of proposals consisting of the updated recommendations of phase 1¹²⁸ (recommendations elaborated in 2010 for diagnostics and treatment, codification and inventory, information, awareness and patient empowerment, and access and cost) integrated with the recommendations of phase 2 (recommendations elaborated in 2011 for non-medical costs of rare diseases, international networking, research and adherence, advanced therapy medicinal products, ethical issues, teaching and education, including therapeutic education, and clinical trials) was sent to the minister of Social Affairs and Public Health at the end of the first semester of 2011. This report is available online on the website of the King Baudouin Foundation in English, French, German and Dutch languages¹²⁹. The proposed plan consists of 42 recommendations and measures that can be grouped into five central themes: Expertise and multidisciplinary; Collaboration and networking; Knowledge, information and awareness; Equity in access; and Governance and sustainability.”

A new government is now in place which will analyse the propositions in terms of financing and the existing plans for cancer and chronic diseases.

Recently, the Centres for Human Genetics (represented by the High Council for Anthropogenetics) have formulated suggestions for the development of a national health care structure for the management of patients with rare diseases.

Centres of expertise

An additional budget of €2 million is foreseen for the development and the strengthening of multidisciplinary centres of expertise recognised by the National Institute for Health and Disability (NIHDI) and work under a convention. A group of experts is currently working to set up the criteria for prioritisation and the working modalities of the centres of expertise in order to implement this action.

On the other hand, genetic counselling, carried out by a multidisciplinary team, will be financed through a new convention with the 8 Belgian genetics centres. The convention also includes guarantees for the adequate quality control and registration of clinical activities. The Belgian Centres for Human Genetics have a full service offering, i.e. they offer different types of tests and technologies, and patient and family counseling.

Registries

As epidemiological data on Belgian rare disease patients is very scarce and fragmented and as this information is essential for health care planning and monitoring a specific budget was foreseen in 2011 for the preparation of a conceptual note concerning the creation of a Central Registry of Rare Diseases. The conceptual note, approved by a group of stakeholders was accepted in December 2011 and a new budget was allocated for 2012-2013 to the Scientific Institute of Public Health.

Genetic testing

All genetic centres have or are in the process of obtaining an accreditation of their diagnostic activities. An accreditation of the laboratories will be obligatory by January 2014.

The reimbursement conditions of genetic tests are currently being revised. The new nomenclature offers a stratified reimbursement system and includes a comprehensive list of diagnoses and genes for which testing is available in Belgium.

Genetic testing abroad is possible, when referred by the Belgian genetic centres: the genetic centres send the samples to a foreign reference laboratory. The genetic tests carried out abroad will be reimbursed by convention with the 8 Belgian genetic centres. A list of authorised tests and the foreign reference laboratories is in preparation: this initiative part of a proposal for the creation of a convention between the NIHDI and the genetic centres that will be launched in 2012.

National rare disease events in 2011

On 22 February 2011 a symposium was organised by the Consultative Committee on Bioethics and the Fund for Rare Diseases and Orphan Drugs in collaboration with RaDiOrg.be on the theme of health care for rare diseases and its societal and ethical dimensions.

¹²⁸ <http://www.kbs-frb.be/publication.aspx?id=271066&LangType=2060>

¹²⁹ <http://www.kbs-frb.be/publication.aspx?id=288128&LangType=1033>

On 26 March 2011, RaDiOrg.be held their members meeting, which concentrated on the proposals made by the Fund for Rare Diseases and Orphan Drugs for a Belgian Plan for Rare Diseases. Particular focus was given to the discussion on the role of patient organisations in the plan, especially the role patients can play in giving feedback on their experiences of centres of expertise in Belgium.

Research activities and E-Rare partnership

E-Rare

The Research Foundation Flanders (FWO)¹³⁰ and Fund for Scientific Research (FRS-FNRS) participated in the 3rd Joint Transnational Call in 2011. Belgian teams will participate in four of the 13 funded projects.

IRDIRC

Belgian funding agencies have not yet committed national funding to the IRDiRC.

Specialised social services

A budget is foreseen in the framework of the Chronic Disease Programme for the financing of respite care structures for children with chronic diseases, including rare diseases patients. Three projects are currently being developed and have started in 2011.

D.3. BULGARIA

National plan/strategy for rare diseases and related actions

A National Consulting Council on Rare Diseases has been established by the Ministry of Health, and meets once a month to supervise the progress and implementation of the national plan for rare diseases. Since 2011 there has been a tendency to gradually transfer all rare diseases treatment coverage from the Ministry of Health to National Health Insurance Fund. However, the Ministry of Health stays a major actor in rare diseases treatment provision through the Ministry of Health-operated Fund for Children's Treatment and Commission for Treatment Abroad.

Registries

Following the very successful model of "The National registry of thalassaemia major patients in Bulgaria", BAPES (Bulgarian Association for the Promotion of Education and Science) has initiated recently 5 new rare diseases registries. In May 2011 the first results from a joint study of BAPES and Wilson disease patient association were published¹³¹. The Crohn Disease National Registry is already working and its first statistics¹³² were officially adopted in June 2011 at a Crohn Disease national workshop. The Bulgarian Scientific Society of Gastroenterology, Gastrointestinal Endoscopy and Abdominal Echography and the university gastroenterology clinics throughout the country have greatly supported and contributed to both Crohn and Wilson patient registries. Just before the Second National Conference for Rare Diseases in September 2011 the provisional results of two new rare diseases patient registries were announced for Gaucher disease and Mucopolysaccharidosis type 2. The corresponding patient associations have provided data, which were analysed by BAPES. In December 2011 BAPES has reached agreements with the Bulgarian Scientific Society for Clinical and Transfusion Haematology and the Bulgarian Scientific Chirurgic Society for launching two new rare diseases registries for primary myelofibrosis and neuroendocrine tumors respectively. A unique character of all BAPES-managed epidemiological registries for rare diseases is that they involve joint activities by all relevant stakeholders.

Sources of information on rare diseases and national help lines

Official information centre for rare diseases

The Information Centre for Rare Diseases and Orphan Drugs (ICRDOD)¹³³ site was substantially renewed and upgraded at the end of 2011. Besides a new look and new layout of content, the site offers several new

¹³⁰ www.fwo.be

¹³¹ http://www.raredis.org/?page_id=2447&mel=4&smel=44&lang=en

¹³² http://www.raredis.org/?page_id=2454&mel=4&smel=43&lang=en

¹³³ <http://www.raredis.org/>

features for its users, such a subscription for its newsletter “Rare Diseases & Orphan Drugs”, an online registry of rare diseases patients, an updated Rare Diseases Library in Bulgarian, as well as better interaction between the different users and ICRDOD team.

ICRDOD published in March 2011 an updated review of the access to orphan medicinal products for rare diseases in Bulgaria¹³⁴: the report contains 4 sections: orphan medicinal product designation and marketing authorisation; pricing, inclusion in the Positive drug list and reimbursement; mechanisms for accelerated access to innovative medicines; conclusions. There are 2 annexes, attached to the review: list of orphan medicinal products in EU and Bulgaria, which contains information about the trade name, ATC code, active substance, indication(s), marketing authorisation holder and date of marketing authorisation for each item (additionally, it is indicated whether the drug is present in the Positive drug list of Bulgaria and if it is reimbursed by public funds); and a list of references.

Training and education initiatives

The first Eastern Europe Rare Diseases Summer School¹³⁵ designed for Russian health authorities and legislative institutions was held on 11-18 September 2011. It was a joint initiative of BAPES, the National Association of Rare Diseases Patient Organisations “Genetics” (Russia) and the Italian National Centre for Rare Diseases (CNMR). The event gave the Russian policy and decision makers an opportunity to learn more about rare disease topics and to understand the significant added-value that rare diseases actions and measures bring to the table. The participants came from a wide range of public fields – federal and regional legislative bodies and health authorities, leading medical institutions, academia, patient organisations and the pharmaceutical industry. The week-long event, which covered a variety of topics including centres of expertise, orphan medicinal products, registries, and national plans, was considered a success by attendees, who reported feeling much better informed on the needs of rare disease patients by the end of the training. Several rare diseases school initiatives are being planned for 2012.

Furthermore, BAPES organised for a second consecutive year in a row a two-day rare disease training seminar for medical students. 30 medical students had the chance to get acknowledged with the main rare diseases concepts, such definition, major problems, important initiatives, etc. The information and education services, offered by ICRDOD and Orphanet were also presented as high quality and reliable source of information, that medical students could use anytime now during their training or further in their future professional practice. Patient representatives took part in the event too, giving personal testimonials and their own point of view on rare diseases issues.

A training workshop for people with rare diseases was held on 1-7 May 2011 in Veliko Tarnovo.

National rare disease events in 2011

Every January, there is an annual meeting of the Consultants of the Information Centre for Rare Diseases and Orphan Drugs (ICRDOD).

For the fourth consecutive year Rare Disease Day was marked in Bulgaria by various events organised by the National Alliance of People with Rare Diseases with the support of BAPES.

This year's event started on 12-13 February 2011 in Plovdiv with a training workshop “Psychological methods – way of self-help to improve quality of life of people with rare diseases and their families”. On 28 February 2011 a formal press-conference was held in Sofia. Rare disease stakeholders presented the newest achievements in this field across Europe and current problems in Bulgaria. The main focus of the Rare Disease Day in Bulgaria was the relation between patients and GPs. A series of training workshops on rare diseases for general practitioners was organised in Sofia, Plovdiv, Varna, Stara Zagora and Pleven. Leading medical experts presented the specifics of selected rare diseases as cystic fibrosis, pulmonary hypertension, epidermolysis bullosa, primary immunodeficiencies, thalassemia major, hereditary angioedema, Wilson disease, porphyrias, acromegaly. This initiative was a response to the requests of Bulgarian rare diseases patients at last year's Bulgarian EUROPLAN national conference. Parents of children with rare diseases particularly stressed the importance of GPs' awareness of rare diseases and the need for more efficient communication with them. The importance of Orphanet as an important source of quality information on rare diseases' field was outlined during this training workshops. GPs and even profile specialists were reminded that whenever they have a possible rare disease case they should feel free to seek some expert help and refer to validated information such as that of Orphanet. Medical students and patient associations organised a “teddy bear hospital” in Varna to help children overcome their fear of hospitals and doctors by playing games. The finale of the event was a

¹³⁴ http://raredis.org/pub/OD_Report_04042011_EN.pdf

¹³⁵ http://raredis.org/pub/Newsletter/Rare_Diseases_Summer_School_2011.pdf

charity rock concert on the main city square in Pleven (27 February 2011). Information was distributed in Bulgaria's major cities on 28 February.

The Second National Conference for Rare Diseases and Orphan Drugs was held on 9-11 September 2011¹³⁶ in Plovdiv. Topics¹³⁷ included epidemiological registries for rare diseases, best practice guidelines for rare diseases management, health policy and legislation, access to orphan medicinal products in Bulgaria, the Bulgarian National Plan for Rare Diseases, European projects and programmes. The forum succeeded in creating a stage for a useful discussion of the current problems of rare diseases patients and medical professionals. A particular focus was the underperforming of the current National programme, which has not come yet to establish a national registry or reference centres. Just two years before the planned end of this plan, Bulgarian rare diseases stakeholders agreed that it is crucial to have a clear declaration of political willingness from the Ministry of Health for the implementation of the National plan, as well as an adequate funding for the foreseen activities, so the plan could reach its initial objectives. All the plan-identified measures should be supported in balanced way.

Research activities and E-Rare partnership

IRDIRC

Bulgarian funding agencies are not yet committed members of the IRDiRC.

Orphan medicinal products

ICRDOD issued an updated report in March 2011 reviewing access to medicines for rare diseases in Bulgaria¹³⁸. The report contains information on important orphan medicinal products' activities and explained how they are set up in Bulgaria in 4 sections: orphan medicinal product designation and marketing authorisation; pricing, inclusion in the Positive Drug List (PDL) and reimbursement; mechanisms for accelerated access to innovative medicines; and conclusions.

Orphan medicinal product committee

Orphan medicinal products are subject as are all other medicinal products to the Commissions on the pricing of medicines and on the Positive drug list. In order to optimise these procedures, in 2011 the two commissions were merged into a single one under the Ministry of Health. From 2011, orphan medicinal products reimbursed by the Ministry of Health, the second one by the National Health Insurance Fund (NHIF).

Orphan medicinal product market availability situation

All orphan medicinal products, authorised under centralised procedure in EU could be available in Bulgaria, after adoption of the new Regulation N° 10/17 November 2011 for the conditions and the order of treatment with medicinal products without marketing authorisation in Bulgaria, as well for the conditions and the order for including, changes, excluding and distribution of medicinal products from the list in article 266A, paragraph 2 from the Law of medicinal products for human medicine, which replaced Regulation N° 2/10 January 2001. The important change, regarding availability of orphan medicinal products in the Regulation N° 10/17 November 2011 is that it arranged the distribution of the drugs, including orphan medicinal products, that have been priced but are not available on the Bulgarian market or such that have not been priced and included in reimbursement list. Article 266A is new and was enforced from 5 August 2011, arranging the use of the medicinal products authorised in the EU countries that are not distributed on the Bulgarian market.

Despite the recent increase of these figures, institutions dealing with planning and funding for treatment and rehabilitation of patients with rare diseases still do not have actual and reliable data on the number and distribution of patients in the country and information on the compliance and effectiveness of this expensive treatment.

¹³⁶ www.conf2011.raredis.org

¹³⁷ http://raredis.org/pub/Newsletter/Conference_Book_2011.pdf

¹³⁸ *Orphan drugs in Bulgaria: Periodic review of the access to orphan drugs in Bulgaria:*
http://raredis.org/pub/OD_Report_04042011_EN.pdf

D.4. CYPRUS

National plan/strategy for rare diseases and related actions

The first draft of the National Strategic plan for rare diseases was prepared by the National Steering Committee for rare diseases following numerous meetings and hard work by all involved parties. The National Steering Committee for rare diseases consists of Ministry of Health officials, experts in different fields related to rare diseases and patient representatives.

Initially, in early 2011 a document was prepared by the National Steering committee which consisted of the following three parts: a) a detailed description of the current situation and practices in the field of rare diseases in Cyprus, b) an extensive analysis of the five chapters to be addressed in the strategic plan, namely prevention, diagnosis, treatment and management, palliative care - social inclusion – supportive measures, registries and research and c) a proposed action plan.

In June 2011 a two-day workshop was organised by this committee with the support and under the auspices of the Ministry of Health. During this workshop, local stakeholders from all areas and fields relevant to rare diseases participated in brainstorming sessions, commented and shared their experiences on the current situation in Cyprus and forwarded their suggestions regarding the development of a National Strategic plan to the members of the National Steering committee. The leader of the Europlan project was invited to address this meeting with a lecture and to share experiences: different working groups reviewed the current situation and the proposed actions for designing a national plan of action for rare diseases. The workshop was a success in the sense that it achieved extensive discussions and active involvement of all participants and ended with a strong conclusive report of strong interest and commitment for active involvement of many, in the future steps for achieving progress and agreement on a National plan of action for rare diseases in Cyprus. The National Steering Committee undertook the responsibility of reviewing the conclusions, comments and suggestions of the workshop in order to enable those that hold the general consensus in the strategic plan. The final draft of the strategic plan will be reviewed once again by the local stakeholders in a second workshop which will take place on the 28 of February 2012 before being finalised and submitted to the Ministerial Council for its final approval. The overall goal is to proceed to the finalising of the proposed strategic plan and its approval by the Council of Ministers within 2012.

Centres of expertise

The procedure for officially designating centres of expertise for rare diseases in Cyprus is included as part of the National Strategic plan for Rare Diseases. Hence it is expected that once the strategic plan is approved centres of expertise for rare diseases in Cyprus will be officially designated.

Neonatal screening policy

In 2011, an advisory committee has been established by the Minister of Health with the task of addressing the current situation of newborn screening in Cyprus and to evaluate the new emerging needs and possible expansion of the offered screening program.

National alliances of patient organisations and patient representation

In 2011, the Cyprus Alliance for Rare Disorders (CARD) expanded its rare disease awareness programme through the organisation of several educational and informative events. These events had as a focus increasing knowledge about the challenges that rare disease patients face and stress the need for a national plan for rare disorders.

National rare disease events in 2011

The Cyprus Society of Human Genetics organised a seminar on 24 February 2011 to mark Rare Disease Day. The seminar was addressed by representatives of the Ministry of Health and CARD and was attended by many health professionals, scientists and stakeholders in the field of rare diseases as well as patients and their representatives. In addition, CARD organised a Press Conference on 28 February 2011, in honour of Rare Disease Day, to highlight issues concerning rare diseases in Cyprus.

Research activities and E-Rare partnership

IRDIRC

Funding agencies in Cyprus are not yet committed members of the IRDiRC.

D.5. CZECH REPUBLIC

National plan/strategy for rare diseases and related actions

A taskforce (“*Meziresortní a mezioborová komise pro vzácná onemocnění* – Interministerial and interdisciplinary commission for rare diseases”, henceforward “Taskforce”) convenes every other month and has created dedicated working parties with the aim to establish the basis for the National Action Plan by 2013. A group of stakeholders was gathered in 2011 (including the Ministry of Labour and Social Affairs, experts and payers) and a deadline for elaborating the plan has been established for June 2012. The Czech ten-year strategy¹³⁹ reveals the budgetary sources for the plan, which will include “existing budgetary chapters and domestic and foreign subsidies” such as the Ministry of Health and the country’s public health insurance. A budget for the strategy has not yet been announced and is in the process of substantiation by the Taskforce. The Ministry of Health has been trying to assure funding within the frame of the EEA Norway Grants scheme (2008-2014) for the National Coordination Centre at University Hospital Motol¹⁴⁰ and via annual Ministry of Health targeted appropriation schemes, both which have deadlines in June 2012.

Centres of expertise

The Czech National Strategy for Rare Diseases foresees the concentration of care for rare diseases in 10 to 20 different centres, with a National Coordination Centre at the Motol Teaching Hospital in Prague, which will coordinate at the regional level with University Hospital Brno. This centre will assure its funding through the Norway Grants scheme by June 2012. Its major aim, beyond structuring the rare diseases field in the country, would be to identify additional *de facto* centres of expertise and propose their transformation into *de iure* centres by the Taskforce. First steps were taken and at their last meeting (November 2011) the Taskforce decided to officially establish three pilot *de iure* rare diseases centres for a) cystic fibrosis¹⁴¹, b) metabolic diseases¹⁴² and c) epidermolysis bullosa¹⁴³, based on a compiled criteria drawn from the published EUCERD and EURORDIS centres of expertise recommendations.

Establishment of centres gives them government recognition, but still does not imply a dedicated budget line. Treatment and diagnostics will thus continue to be provided within standard health insurance procedures administered by a group of health insurance companies. However, in the future and following gradual reform of health care funding (after 2012) it is planned that respective rare diseases or related rare disease diagnostic groups will be concentrated into dedicated centres. In this regard it is expected that the major condition for health care reimbursement would be centre-based care. In addition, it is expected that in duly justified instances (e.g. very rare diseases) care will be assured within European Reference Networks (i.e. in line with the EC Directive on cross-border healthcare sections 54 and 55). Currently, cross-border healthcare falls into the domain of the Centre for International Reimbursements¹⁴⁴.

Neonatal screening policy

In early 2011 the National coordination centre for neonatal screening was officially established by the Czech Ministry of Health¹⁴⁵ and its operation is funded by targeted annual appropriation schemes.

Genetic testing

In November 2011 a new law On Specific Health Care Services 373/2011 Sb was passed. It stipulates (Part 6; section 28) that germinal genome is allowed to be tested within the context of rare diseases in genetic laboratories that are accredited according to the ISO 15189 norm, in accordance with “OECD guidelines for quality assurance in molecular genetic testing”¹⁴⁶. Moreover, new law 372/2011 Sb stipulates provisions regarding informed consent procedures in the domain of health care services.

¹³⁹ http://ec.europa.eu/health/rare_diseases/docs/national_czech_en.pdf

¹⁴⁰ http://www.mfcr.cz/cps/rde/xchg/mfcr/xsl/Financial_Mechanism_EEA.html

¹⁴¹ www.cfklub.cz, www.cfregistr.cz, ublg.if2.cuni.cz

¹⁴² www.udmp.cz

¹⁴³ www.debra.cz

¹⁴⁴ <http://www.cmu.cz/en?Itemid=224>

¹⁴⁵ www.novorozensky-screening.cz

¹⁴⁶ <http://www.oecd.org/dataoecd/43/6/38839788.pdf>

National alliances of patient organisations and patient representation

In December 2011 foundations were established for the creation of an overarching Czech National Alliance for Rare Diseases¹⁴⁷. This alliance will link together other patient support groups via a democratic, bottom-up, activity spearheaded by several larger patient support groups. Its registration with the Ministry of Interior is expected to be completed by May 2012, including establishment of its bylaws and governance structure. This association plans to join EURORDIS and participate in its activities. Creating an alliance for rare disease patient groups is a provision of the national strategy being developed, together with the Coalition for Health Association¹⁴⁸. The Coalition for Health Association includes all diseases, while the Czech National Alliance for rare diseases will collaborate on topics of common interest. However, there are 43 patient organisations in the Czech Republic. Some groups benefit from aid from the Ministries of Health and of Labour and Social Affairs; the system will be streamlined under the National Action Plan, since representatives of the Coalition for Health are members of its Taskforce. Following official registration of the Czech National Alliance for Rare Diseases its representatives will be included in the Taskforce.

Sources of information on rare diseases and national help lines

Help line

A help line for rare diseases is under preparation and is planned to be funded within the Norway Grants mechanism with the National Coordination Centre for Rare Diseases in University Hospital Motol.

National rare disease events in 2011

Amongst the rare disease events hosted by the Czech Republic in 2011 were the Metabolic Days¹⁴⁹ (Mikulov, 11-13 May 2011), Czech National Genetics Meeting¹⁵⁰ (Třeboň, 7-9 September 2011) and the Czech National DNA diagnostics conference¹⁵¹ (Prague, 24-25 December 2011).

Research activities and E-Rare partnership

IRDiRC

Czech funding agencies are not yet committed members of the IRDiRC.

D.6. DENMARK

National plan/strategy for rare diseases and related actions

During 2011 it was decided to let the National Board of Health establish a working group to elaborate a national strategy for Rare Diseases. The working group has a broad representation of stakeholders, to elaborate a national plan for RD, was founded at the end of 2011 and met at the start of February 2012 for the first time. The recommendations in previous report on rare diseases from 2001 will be assessed to see what is still needed, what has changed and what new recommendations can be added considering the European perspective and the recommendations for a national strategy.

National alliances of patient organisations and patient representation

In 2011, Rare Disorders Denmark had the following main activities:

1. Lobbying for a national plan for rare diseases and handicaps. In May 2011, RDD published and disseminated a booklet about the importance of a national plan and throughout the year met with politicians and civil servants to promote the forming of a working group.
2. Developing a special training programme for rare disease families with children under the age of 18 – “Rare Family Days”. In the framework of a randomised study, two family courses were conducted for 16 families. The results will be published in 2012, along with a new concept for “Rare Family Days”.
3. Cooperating with the Centre of Disability and Social Psychiatry (ViHS) to transfer a Focus Point of Contact for very rare disease patients and relatives with no possibility to join or form a patient

¹⁴⁷ www.vzacna-onemocneni.cz/

¹⁴⁸ www.koaliceprozdravi.cz

¹⁴⁹ www.dedicnemetabolickeporuchy.cz/

¹⁵⁰ www.trebon2011.slg.cz/

¹⁵¹ www.dnakonference.cz

organisation/society. RDD built and ran a temporary website for dialogue between the members of the Focus Point and prepared to fully take over the Focus Point in 2012.

4. In June 2011, RDD participated in the EURORDIS POLKA project as a work package leader: among other activities, RDD performed a survey in cooperation with the Centre of Expertise in Aarhus, University Hospital of Skejby. The aim of the survey was to discover the perception of the quality and more of the Centre from health care professionals and rare disease patients.

Sources of information on rare diseases and national help lines

Official information centre for rare diseases

At the end of 2010, the Ministry for Social Affairs closed the Centre for Rare Diseases and Disabilities (*Center for Små Handicapgrupper* – CSH) as an independent institution. This decision was a consequence of the merger of 3 information and knowledge networks and 13 research centres in areas overseen by the Ministry of Social Affairs to form a new Centre for Disability and Social Psychiatry (*Videnscenter for Handicap og Socialpsykiatri - ViHS*¹⁵²) as of 1 January 2011. The experience of the first year of the new structure is, that the Help Line is functioning well, but that the knowledge-based work with short diagnosis descriptions has become more difficult and is not at the same level as before. The future general information about rare diseases is expected to be discussed in the working group of the National Strategy.

Help line

Up until 2010 CSH ran a rare disease help line which provided information and support. As a result of the reorganisation of the CSH, there is established a dedicated “Rare Disability Team” within the ViHS’s counselling service which mans the help line from January 2011 onwards.

National rare disease events in 2011

To mark Rare Disease Day 2011, Rare Disorders Denmark encouraged policy makers and others stakeholders to become friends of the Day. In addition, the alliance launched a new feature on its website, “Rare stories”. This section gives patients, caregivers and others interested in rare diseases the opportunity to tell their own story and share it with others¹⁵³.

Hosted rare disease events in 2011

In 2010 the following rare disease events were announced in *OrphaNews Europe*: VI Cornelia de Lange Syndrome World Conference (27-31 July 2011, Copenhagen), European Conference on Post Polio Syndrome (31 August – 02 September 2011, Copenhagen). In addition, in November 2011, a nordic conference about Huntingtons Disease was held in Copenhagen.

Research activities and E-Rare partnership

IRDIRC

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

D.7. ESTONIA

National plan/strategy for rare diseases and related actions

There is currently no plan for rare diseases in Estonia. In 2008, Estonian Government adopted Eesti Rahvastiku Arengukava 2009-2020 (*Estonian National Health Plan 2009-2020*, hereafter referred to its Estonian acronym, ERTA). ERTA 2009-2020 provides recommendations and indicates the directions to be taken to improve healthcare and brings together the tasks necessary to achieve this. The plan also assembles a large number of strategic documents which have already been implemented or which are soon to be implemented in other fields that have a role to play in achieving ERTA’s objective. In 2012 a working group will be set up to discuss the activities on the field of rare diseases which will be added to the implementation plan of ERTA.

¹⁵² More information on the organisation of the ViHS can be accessed here

http://www.csh.dk/fileadmin/pdf/Rapporter_og_andet/Organisering_af_ViHS-1.doc (accessed 27/01/2011)

¹⁵³ www.sjaeldnediagnoser.dk/historier

Centres of expertise

In summer 2011 Tallinn Children's Hospital genetics services joined with Tartu University Hospital, the United Laboratory and the Department of Genetics and thus one common Department of Genetics was formally established at Tartu University Hospital. Tallinn Children's Hospital genetics service became the branch office of Department of Genetics, Tartu University Hospital. All of the genetic specialty services are represented with the diagnosis and treatment of rare diseases provided all over Estonia.

Sources of information on rare diseases and national help lines

Orphanet activities in Estonia

In 2011 the Orphanet Estonia national website¹⁵⁴, in Estonian, was launched by the Orphanet Estonia team.

Training and education initiatives

In 2009-2011 the number of advanced courses on rare disorders organised by the Department of Continuing Education at the Tartu Medical University increased, due to rising interest in the subject. This activity is also planned for the future (i.e. a new course is planned for 2012).

Research activities and E-Rare partnership

IRDiRC

Estonian funding agencies have not yet committed national funding to the IRDiRC.

Specialised social services

In 2011, several respite camps were organised by the Estonian Agrenska Foundation¹⁵⁵.

D.8. FINLAND

National plan/strategy for rare diseases and related actions

Funding specifically focused on national plan related activities was applied for in late 2011 from the Ministry of Social Affairs and Health (this was accepted in 2012). During 2011 a nationwide survey was performed to identify centres who consider themselves as experts related to a rare disease or disease group. The Ministry of Social Affairs and Health decided to invite stakeholders in the field, including hospital districts, governmental institutes like the National Institute for Health and Welfare, the Orphanet National Advisory Board, the umbrella organisation for rare diseases HARSO and the Harvinaiset Network for Rare Diseases to name representatives for a steering committee for elaborating the national plan. There will be a focus on establishing centres of expertise, with a step which will include patients before they reach the centres (i.e. early health care pathways to diagnostic processes).

National alliances of patient organisations and patient representation

Representatives of patient associations decided to set up a national alliance at their meeting at the Family Federation Finland, in Helsinki on 6 June 2011. During this meeting it was decided to set up a work group, led by Elina Nykyri, head of the Finnish Turner Association, to prepare a constitutive meeting held on 8 October 2011. A first statutory meeting was planned for 21 January 2012.

Good practice guidelines

Information on 35 monogenic diseases belonging to the Finnish Disease Heritage¹⁵⁶ can be found at a database findis.org. For each disease, the prevalence or incidence and a short description of clinical symptoms are provided, as well as genetic locus and a molecular description for identified mutations. As the character and consequences of all known mutations, Finnish and foreign, are described at the DNA and polypeptide level and disease allele frequencies reported for Finnish mutations, the database can be used as a best practice guideline

¹⁵⁴ <http://www.orpha.net/national/EE-ET/index/avaleht/>

¹⁵⁵ <http://www.agrenska.ee/>

¹⁵⁶ <http://www.findis.org/main.php?action=disease>

for molecular diagnostics of these diseases. However, this database does not provide guidelines or information related to treatment or follow up of these diseases.

The database follows the Quality Criteria for Health Related Websites recommended by the European Commission. Funding for the database has been provided by the Academy of Finland, Centre of Excellence in Disease Genetics.

National rare disease events in 2011

Rare Disease Day 2011 was coordinated by the Finnish Network for Rare Diseases, Harvinaiset. Awareness raising campaigns were launched on the website harvinaiset.fi and in social media between 25 and 28 February 2011 in cooperation with local associations and groups. Stories, photos, videos and messages around the theme "rare but equal" were shared. The members of the Finnish Network for Rare Diseases visited schools, institutions and other focus groups to inform about the Rare Disease Day and issues concerning rare diseases. Members of the Network also launched their own press releases concerning the day.

On 21 October 2011, a rare disease event was organised in Helsinki by medical specialist societies and Swedish Orphan Biovitrum. 150 health professionals, researchers and policy makers attended. The main theme of the meeting was rare disease research and treatment, the current situation and future possibilities. Special national funding into research was requested because funding possibilities have diminished in recent years. Much of the general discussion focused on the assessment of marketed drugs for reimbursement but also on the need for centres of expertise, and involvement and empowerment of patients and their families to the RD field. A 700 name petition was handed over to the minister of Social Affairs and Health. The petition drew attention to the unequal situation of rare disease patients compared to common disease patients.

On 20 October 2011 the Orphanet Finland team organised a one-day meeting for the Orphanet National Advisory Board members which focused on the national plan for rare diseases and allowed members to express their expectations for the plan. Discussion also focused on how to structure centres of expertise in Finland, including their criteria, funding, role of the university hospitals and importance of the research in the context of centres etc. Importance of networks and cooperation between specialists in various fields were highlighted in many speeches.

Research activities and E-Rare partnership

IRDIRC

Finnish funding agencies are not yet committed members of the IRDiRC.

D.9. FRANCE

National plan/strategy for rare diseases and related actions

The second French National Plan for Rare Diseases¹⁵⁷ was elaborated by the Ministry of Health during 2009-2010 from the results of the evaluation of the first plan and from the conclusions of seven working groups, which had gathered during 34 meetings 184 representatives of health professionals, rare disease experts, researchers, patient organisations and administration. The second plan was launched on 28 February 2011 on the occasion of Rare Disease Day with a budget of €180 million. The ten objectives of the first plan have been consolidated into three main objectives:

- Improve the quality of care for rare disease patients;
- Develop research on rare diseases;
- Amplify European and international cooperation in the field of rare diseases.

These three objectives encompass actions such as:

- Quality assessment and networking of the French Reference Centres;
- Improvement of access to biological and genetic diagnosis;
- Development of neonatal screening of rare diseases;
- Proper use and facilitated access to drugs, orphan medicinal products and any other medical product necessary to patients;

¹⁵⁷ http://www.sante.gouv.fr/IMG/pdf/Plan_national_maladies_rares.pdf

- Information and training of health professionals;
- Information of patients;
- Strengthening of research.

The second plan includes 15 measures and 47 specific actions. The key measures of the plan are:

- Creation of a Foundation for Scientific Cooperation on Rare Diseases (called the “*Fondation Maladies Rares*”¹⁵⁸);
- Creation of a National Rare Disease Database (called the “*Banque Nationale de Données Maladies Rares*” or BNDMR) to allow mapping of patients’ needs and healthcare delivered, and facilitate their recruitment for clinical trials;
- Improvement of the monitoring of various activities relating to rare disease patients, which includes the adoption of the Orphanet nomenclature;
- Organisation of access to next-generation sequencing (NGS) technology for genetic diagnosis. Most of the French academic laboratories will be equipped at the end of the second year of the plan with NGS facilities to optimize molecular diagnosis for a large set of rare diseases. Various levels of NGS will be developed during the plan for maximal diagnosis coverage;
- Restructuring of rare disease Reference and Competence Centres into a limited number (around twenty) of coherent “clinical networks” (called “*filières maladies rares*”), gathering all rare disease relevant stakeholders and centered on a homogeneous group of diseases. These networks aim to allow a better and easier orientation of patients towards appropriate diagnosis, treatment, social care and follow-up. These future French networks should be connected to the future European networks for rare diseases.

The additional actions foreseen in the plan to improve the quality of care are:

- Setting up of a permanent working group for the monitoring of rare disease Reference Centres and future reference networks;
- Measures to ensure access and reimbursement of new drugs or drugs necessary to patients but prescribed out of their marketing authorization;
- Enhancement of clinical practice guideline development;
- Training of medical doctors and paramedical professionals;
- Coordination of health care and social care.

The implementation of the second plan is the mission of a dedicated Steering Committee (called the “*Comité de suivi et de prospective*”) which held its first meeting on 19 May 2011. Five thematic working groups reporting to the Steering Committee were established to help implementing the plan. These include a permanent group dedicated to the monitoring of Reference Centres and their future networks. The Steering Committee is in charge of the follow up of the plan and making sure that the implementation of the plan is on schedule, of the effective involvement of relevant bodies and institutes in the implementation, and of surveying new methods of diagnosis, prevention, treatment and care for patients with rare diseases.

In addition to this, the evaluation of this second plan will soon be considered, and before the end of 2013 a third plan will be discussed to extend this work.

Second French National Plan for Cancers (including rare cancers) 2009-2013

A second national plan for cancers¹⁵⁹ was announced on 2 November 2009 for the period 2009-2013. The National Cancer Institute (*Institut National du Cancer – INCa*) has published a report entitled “The Situation of Cancer in France in 2011”. This report gives an overview of the measures in place for cancers, including rare cancers, and gives key facts and figures concerning the situation of patients in France. The report was published at the same time as a new web portal on cancer data on the INCa site¹⁶⁰. The INCa also released at the end of 2011 its first report on the activity of expertise for rare cancers of adult patients, including updates on their organisation, collaborations, translational research and clinical trials, survey of cases in national databases, and elaboration of recommendations for rare cancers amongst other actions¹⁶¹.

¹⁵⁸ The “Fondation Maladies Rares” was created in February 2012: <http://fondation-maladiesrares.org>

¹⁵⁹ http://www.plan-cancer.gouv.fr/images/stories/fichiers/plancancer20092013_english.pdf

¹⁶⁰ <http://lesdonnees.e-cancer.fr/>

¹⁶¹ <http://www.e-cancer.fr/toutes-les-actualites/360/6714-synthese-de-lactivite-2010-des-centres-experts-cliniques-pour-cancers-rares-de-ladulte>

Other French national initiatives related to rare diseases

A plan aimed at rare disabilities (of which rare diseases can be a cause) was adopted on 27 October 2009 for the period 2009-2013¹⁶². The National Solidarity Fund for Autonomy (*Caisse Nationale de Solidarité pour l'Autonomie* – CNSA) is in charge of implementing this plan. Measures of the plan include the creation of 300 additional places in care centres, regional relays, and national “resource centres”. Three national “resource centres” were created in 2011 for patients with a visual or hearing deficiency associated with other deficiencies or diseases. Cooperation between “resource centres” for rare disabilities and “reference centres” for rare diseases is planned.

On 16 May 2008, the French Ministry of Health announced the second national plan for autism for the period 2008-2010. In 2011, the evaluation of this plan began in the perspective of a next third plan.

On 25 January 2011 the Minister of Research funded the RADICO (“Rare Diseases Cohorts”) project for a duration of 10 years and a total of €10 million. The RADICO project finality is to create and follow selected cohorts of rare disease patients in the perspective for instance of therapeutic research or better understanding of the condition.

In 2011, the web portal “Epidemiology – France”¹⁶³ was launched, aiming to provide a directory of databases to advance research and expertise in the field of health in France. The initiative is supported by the INSERM (French National Institute for Healthcare and Medical Research), the National Competitiveness, Industry and Services Directorate of the French Ministry of the Economy and the LEEM (French Pharmaceutical Companies Union). It brings together information on around 300 databases and includes a search by the theme “Rare Diseases” which includes mostly nationally designated registries.

Centres of expertise

The reflection on restructuring of the existing rare disease Reference Centres into a limited number of “clinical networks” began in 2011 within the framework of the second National Plan. It will continue in 2012.

In 2011 the Hospitals of Angers and Nantes in association with the French Alliance for Rare Diseases created a platform to support patients with rare disease in the *Pays de la Loire* region. This unique platform will help patients to find their way in the health and social care system.

An experimental programme is underway in Montpellier to provide support to patients with rare disease and training sessions to professionals of health and social sector. This action is set up with the partnership of the French Alliance for Rare Diseases and centres of expertise settled in the area.

Registries

The second National Plan foresees the creation of a National Rare Disease Database (BNDMR) containing a minimal data set to be filled in concerning rare disease patients in order to collect a minimum amount of common information. The reflection on the minimum data set began in 2011.

A new call for proposals for national rare diseases registries was launched in 2011 as each year. A new set of seven national registries were qualified for the period 2012-2015 for the following rare diseases: thalassemia, Gaucher disease, congenital neutropenia, Pompe disease, cystic fibrosis, histiocytosis, and biliary atresia.

Neonatal screening policy

In 2010, an assessment of the opportunity to extend neonatal screening to one or more inborn metabolic errors of metabolism by tandem mass spectrometry in the general French population began. The first results were published in 2011 by the HAS. The HAS recommends the extension of the screening programme to medium chain acyl-CoA dehydrogenase deficiency. The decision to put this recommendation into practice has not yet been taken. That requires reorganising first the whole neonatal screening programme because tandem mass spectrometry cannot replace all the existing screening techniques and cannot be used in all the laboratories which currently participate in the programme. Furthermore the HAS is still working on the possibility of extending the programme to other inborn metabolic errors and on the generalisation of sickle cell anaemia screening to all newborns in France.

Neonatal screening for deafness (of which rare diseases can be a cause), on which the HAS had given recommendations in 2007, will be launched in a near future.

¹⁶² http://www.cnsa.fr/IMG/pdf/CNSA_Schema-national-Handicap-rare-2.pdf; http://www.cnsa.fr/article.php3?id_article=726

¹⁶³ <http://epidemiologie-france.fr/>

Genetic testing

The French Biomedicine Agency published its 2010 annual report¹⁶⁴ in 2011. For the second consecutive year, the Agency includes data on postnatal genetic testing carried out in France culled via a partnership with Orphanet. The 2010 report of the Biomedicine Agency demonstrates that France continues to be a model for other countries in terms of the range of its genetic test offered, its healthcare coverage in this area, and its remarkable transparency of data.

The final text of the Bioethics Law¹⁶⁵ was adopted on 23 June 2011 and published in July 2011. The text includes indications on how to inform family members in the case of genetic disease, as well as the delivery of tests proposed to pregnant women. The legislation on research using embryos will remain unchanged.

National alliances of patient organisations and patient representation

In 2011 the *Alliance Maladies Rares* (French Alliance for Rare Diseases) launched a practical guide to rare diseases to make it available in centres of expertise for rare diseases and for members of the Alliance. The guide is destined to patients and their families, and provides information on the organisation of expert care and the services in place for patients and their families. The guide also gives information on the organisations of patients with rare diseases in France. The Alliance also launched an awareness raising campaign aimed at children via the newspaper for children called *Le Petit Quotidien*. Information packs for teachers were also made available to help classes understand what is a rare disease and life for children with such a condition.

Sources of information on rare diseases and national help lines

Help line

The help line *Maladies Rares Info Services* launched in 2011 a series of internet chat sessions on the first Monday of each month: each session has a theme and internet users can ask the team questions the hour-long sessions. *Maladies Rares Info Services* also implemented a “rare diseases barometer”. The purpose of this barometer is to collect objective data on the issues to which patients are confronted. Data are collected by means of qualitative and quantitative surveys targeting users of the information and support service.

National rare disease events 2011

Each year in December, an annual *Téléthon* is organised by the AFM (*Association française contre les myopathies*) over 30 hours: around €100 million are raised annually during this campaign. The funds raised go towards rare disease research, information services (including the French Rare Disease Platform), awareness campaigns, patient care and patient organisations. Each year, to coincide with the *Téléthon* organised by the AFM, the *Alliance Maladies Rares*, in association with the *Groupama Fondation pour la santé* and the AFM, organises a Rare Disease March (*Marches des Maladies Rares*) involving patients and patient organisations. The *Téléthon*¹⁶⁶ and Rare Disease March¹⁶⁷ aim to raise awareness about rare diseases in addition to the Rare Disease Day which is celebrated each February.

A number of events were organised to mark 2011’s Rare Disease Day. Firstly, the 28 February 2011 marked the official publication of the second French National Plan for Rare Diseases which will cover the period 2011-2014. The plan was launched by the Secretary of State for Health, Nora Berra, and the Minister of Higher Education and Research, Valérie Pécresse.

The French Alliance for Rare Diseases and Orphanet joined forces with the high speed train (TGV) network from 26-27 February 2011 to raise awareness of rare diseases: TGV passengers were encouraged to participate in a quiz about rare diseases and to learn more of the issues surrounding these conditions in the buffet coaches of trains between Paris and six major French towns.

On 28 April 2011, *France Television* confirmed their support of the *Téléthon* for another 3 years. The 2011 edition, the 25th anniversary, was aired, for the first time, on all five national channels of the French network to assure 30 uninterrupted hours of coverage.

Every year in June, Orphanet and the *Alliance Maladies Rares* organise jointly a one day meeting for all patient organisations to discuss themes of interest in the field of information and dissemination of good practices. On 30 June 2011 the 12th Forum¹⁶⁸ was held at the *Groupama Fondation* around the theme “Sharing

¹⁶⁴ http://www.agence-biomedecine.fr/uploads/document/RA_BIOMED_2010_Internet.pdf

¹⁶⁵ <http://www.service-public.fr/actualites/001820.html>;

<http://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000024323102&dateTexte=&oldAction=rechJO&categorieLien=id>

¹⁶⁶ <http://www.afm-telethon.fr/le-telethon/le-telethon-2011>

¹⁶⁷ <http://www.alliance-maladies-rares.org/article/marche-des-maladies-rares-2011-98>

¹⁶⁸ <http://www.orpha.net/orphacom/cahiers/docs/FR/XIIforum.pdf>

of health data for better healthcare". Topics discussed include the personal medical record (DMP), and the centralisation of data collected by reference centres.

Eurobiomed organised the conference Rare2011 on 2-4 November 2011 in Montpellier in collaboration with local and national partners both from the public and the private sector. This second conference (the first one was organised in 2009) started with two days dedicated to rare diseases at national level, and finished with one day focused on the European context, organised by the EUCERD. Over 300 participants were present from 19 countries. In particular the measures foreseen by the Second National Plan for Rare Diseases were presented in addition to a number of topics concerning research and development, and access to orphan medicinal products, as well as a discussion on how stakeholders should best work together in the field of rare diseases.

Research activities and E-Rare partnership

National research activities

Apart from national funding programmes covering rare diseases, funding opportunities for rare disease research in 2011 included grants and calls launched by the following organisations/institutes: Fédération Nationale d'Aide aux Insuffisants Rénaux, Fondation Groupama, la Fondation de France, Association pour la Recherche sur la Sclérose latérale, Fondation de recherche ELA, National Niemann-Pick Disease Foundation (NNPDF), Universal Biotech, ARTHRITIS Fondation Courtin, Connaître les Syndromes Cérébelleux (CSC), Association Strümpell-Lorrain (ASL-HSP) et Association Française Ataxie de Friedreich (AFAF), Institut de Recherche en Santé Publique (IReSP), Fondation Line Pomaret Delalande, Association Neurofibromatoses et Recklinghausen, Fondation Jérôme Lejeune, ECD Global Alliance, Vaincre la Mucoviscidose, Agence de la biomédecine, NA Advocacy, Genespoir, Association pour l'étude de la pathologie pédiatrique, Retina France etc.

E-Rare

France took part in the 3rd transnational call launched at the start of 2011 in the context of E-Rare2: French teams have been funded to participate in 13 of the selected projects.

IRDiRC

The AFM (*Association Française contre les myopathies*) and French National Research Agency (*Agence Nationale de Recherche*), are committed members of the IRDiRC.

Orphan medicinal products

Orphan medicinal product incentives

A law adopted by Parliament on 22 March 2011 will allow non-profit organisations to become pharmaceutical establishments and will give the status of medicine to gene-therapy products. As a direct result, the Généthon Bioprod non-profit laboratory, inaugurated in November 2010, will be able to produce products for gene-therapy for clinical trials.

Orphan medicinal product reimbursement policy

This process for off-label use and reimbursement of medicinal products will be modified in 2012 further the law reinforcing the monitoring of safety of drugs and other healthcare products, published on 29 December 2011.

Other initiatives to improve access to orphan medicinal products

The new law reinforcing the monitoring of safety of drugs and other healthcare products, published on 29 December 2011, maintains the possibility of an ATU (temporary use authorisation), in particular in the case of rare diseases. The drug must fulfill the following criteria: the treatment cannot be postponed; there is no alternative therapeutic to the drug; the efficacy and security of the treatment are strongly presumed by the results of clinical trials (cohort ATU) or from scientific published data and knowledge (nominative ATU); the patient cannot be treated within a clinical trial. The ATU is given for a limited period, but renewable. A therapeutic protocol and data collection concerning safety and efficacy are mandatory for both cohort and nominative ATU.

D.10. GERMANY¹⁶⁹

National plan for rare diseases and related actions

The national action league for people with rare diseases - *Nationales Aktionsbündnis für Menschen mit Seltenen Erkrankungen* (NAMSE)¹⁷⁰, a co-ordination and communication platform comprising all key bodies and organisations, continues work on the implementation of a National Action Plan on Rare Diseases. The process is organised in a steering committee and four working groups. At the end of this process the national action league for people with rare diseases will recommend different actions for the German National Action Plan for Rare Diseases.

Sources of information on rare diseases and national help lines

Other sources of information on rare diseases

On 1 January 2011 Section 42b AMG (Arzneimittelgesetz, Medicinal Products Law) came into force stipulating pharmaceutical companies and sponsors of clinical trials to report results of clinical trials to the federal higher authorities for purposes of publication in a public database run by the German Institute of Medical Documentation and Information (DIMDI)¹⁷¹.

Good practice guidelines

In 2011 the Institute for Quality and Efficiency in Health Care (IQWiG) published a rapid report (V 10-01) concerning the question "What type of evidence is currently being considered in the development of clinical practice guidelines for rare diseases?"¹⁷².

Training and education initiatives

Germany is elaborating a national catalogue of learning objectives for medicine for medical students. In this process criteria are being developed to integrate rare diseases in this catalogue to better incorporate them in basic medical training.

National rare disease events in 2011

The German Society of Human Genetics (GfH) holds an annual conference (Regensburg, 16-18 March 2011) in association with the Swiss and Austrian Societies of Human Genetics, where topics concerning rare diseases are given a spotlight. Several paediatric subspecialties have a tradition of focussing on rare diseases, especially the Arbeitsgemeinschaft Pädiatrische Stoffwechselerkrankungen (Paediatric Metabolic Medicine), Paediatric nephrology, Deutsche Gesellschaft für Kinderendokrinologie und –diabetologie (DGKED) e.V. (Paediatric endocrinology) and Paediatric rheumatology, all holding yearly meetings often including patient organisations. ACHSE organises meetings for patient organisations twice a year.

A number of actions and events were organised to mark Rare Disease Day 2011 in Germany. Events were organised by ACHSE members with support and coordination of ACHSE in 11 German cities: Bad Oeynhausen, Berlin, Dessau, Essen, Hamburg, Hannover, Cologne, Magdeburg, Stuttgart, Würzburg. People from different rare disease patient organisations teamed up to organise different events. In Dessau, Magdeburg and Cologne there were events in the hospitals organised by the hospitals' staff. This day provided the opportunity to raise awareness, and to inform public about the problems and needs of people living with rare diseases. As in the previous year, at all the events hundreds of red ACHSE-balloons were released to rise into to sky. Apart from these awareness events the Eva Luise and Horst Köhler foundation for people with rare diseases in cooperation with ACHSE awarded another Eva-Luise-Köhler- Award for a research project that has not been realised yet, thus strengthening research for rare diseases.

A short film was produced for the ACHSE-project "Wissenskarawane für die Seltenen" (caravan of knowledge for people with rare diseases) by SympathieFilm which was financed by the statutory health insurance funds Barmer GEK, TK, DAK, KKH, HEK.

¹⁶⁹ The German Federal Ministry of Health can only verify the information and data which concern federal responsibilities. The information provided here is illustrative and not exhaustive, and that it is validated by the EUCERD Member State representative to the best of their knowledge.

¹⁷⁰ <http://namse.de/>

¹⁷¹ <http://www.dimdi.de/static/de/amg/pharmnet/index.htm>

¹⁷² https://www.iqwig.de/download/V10-01_Executive_Summary_Evidence_for_guidelines_on_rare_diseases.pdf

On 26 February the 2nd Rare Disease Day Symposium was organised by Orphanet at the Medical School of Hanover. This event was well attended by 36 different support groups taking part by presenting information booths to the public. The motto of Rare Disease Day “rare but equal” was reflected by 8 interesting talks from experts presenting different aspects of the actual health care situation for patients with rare diseases in Germany. Different structures were highlighted, including a report of experiences of the first official centre for rare diseases in Germany during its first year of existence. The audience also learned about the structure of different networks and their impact on patient care, the latest developments in the field of orphan medicinal products and how to improve quality of specialised centres by certifying them. About 250 people visited this event. The press also attended the meeting, with the local print media publishing a report on this day, along with reports on television of the Symposium.

A symposium on rare diseases was held at the Heidelberg University Hospital on 15 April 2011. The event was well attended and several support groups took part in the meeting by presenting information booths to the public. Talks covered different topics in the field of rare diseases were given by representatives of associations and of the German Parliament, clinicians and researchers as well as a round table discussion with people living with a rare disease and clinicians was presented. The topics included: health policy, the latest scientific developments on rare diseases and the role of networks to improve the care of rare disease patients. The event was reported on in the local print media and on television.

Rare diseases were also one of the topics of the Year of Science 2011 – Research for Our Health – which was organised by the Federal Ministry of Education and Research (BMBF) in collaboration with Wissenschaft im Dialog (WiD) - an initiative by the German Science - and numerous partners from different fields such as science, industry, politics and culture. One of the events was a photo exhibition titled “Orphans of Medicine – Living with a rare disease” which was hosted in Munich 29 June to 22 July 2011. The exhibition was organised by ACHSE and funded by the BMBF. In addition, rare diseases were one of the topics presented in the exhibition titled “Discoveries” on the island of Mainau from 20 May to 4 September 2011.

A meeting of the networks for rare diseases funded by the German Federal Ministry for Education and Research (BMBF) was held on 20 September 2011 in Munich. The participants included representatives of the funded networks, PT-DLR (Project Management Organization at the DLR, acting on behalf of the BMBF) and ACHSE.

Research activities and E-Rare partnership

National research activities

In September 2010, the BMBF launched a new call for proposals for the possible extension of the 10 rare disease research networks which started in 2008 and the creation of new networks was published. After the evaluation of 39 proposals by a review board of international rare disease experts, the BMBF has selected 12 networks for funding starting in 2012 with more than €21 million for three years.

Additional funding of rare disease research is ongoing in other funding initiatives of the BMBF such as the National Genome Research Network (NGFN), Innovative Therapies, Regenerative Medicine, Molecular Diagnostics, Clinical Trials and others with about €20 million in 2011. All these activities are funded within the framework programme “Health research”. In co-operation with the Federal Ministry of Health, the BMBF assumes responsibility for the programme which is financed with funds from the BMBF.

The *Eva Luise und Horst Köhler Stiftung für Menschen mit Seltenen Erkrankungen*, a foundation of the First Lady and the president of the Federal Republic of Germany, is dedicated to patients with rare diseases and supports research projects into rare diseases annually since 2006, including in 2011.

E-Rare

Germany participated in the E-Rare joint transnational calls in 2007, 2009 and 2011 and funds the participating German research groups of 35 transnational research projects with a total of about €10 million.

IRDiRC

The Federal Ministry of Education and Research (BMBF) is a committed member of IRDiRC.

Orphan medicinal products

Orphan medicinal product pricing policy

All orphan medicinal products are reimbursed directly after market authorisation. As the German maximum reimbursement prices scheme (Festbeträge) normally does not cover orphan medicinal products, they were excluded from any on reimbursed prices. Only generic products and those considered to belong to the same pharmacological or therapeutic group can be subject to maximum reimbursement prices that eventually set

the retail-price of the manufacturer. Effective 1 January 2011, for every new drug with patented or non-generic substances a binding ex-factory price based on the value of the drug have to be negotiated on Federal Level. This is carried out by the Federal Association of Sickness Funds and the manufacturer. If no agreement can be achieved, the price is set by arbitrage committee, in which both contract parties are represented. For the first 12 months following marketing authorisation each new drug is still reimbursed at the full price set by the manufacturer. Mandatory Price Negotiations have been introduced by the Act for the New Order for the Drug Market in Social Health Insurance (AMNOG). According to this law, previous to price negotiations the value of the drug is evaluated. The manufacturer issues a Dossier when they enter the market. It is assessed by the German Institute for Quality and Efficiency in Health Care (IQWiG). The Federal Joint Committee (G-BA) appraises and decides on the added value of the drug compared to standard therapy.

Orphan medicinal product reimbursement policy

Once authorised at European level, all orphan medicinal products are fully reimbursed by the statutory health insurance (GKV). Until 31 December 2010, all newly authorised drugs could be put on the marketplace without any restrictions on reimbursed prices. Only generic products and those considered to belong to the same pharmacological or therapeutical group could be subject to maximum reimbursement prices that eventually set the retail-price of the manufacturer. Effective 1 January 2011, the act on new regulations for the drug-market (AMNOG) is mandating that all drugs with patented substances are subject to a cost/benefit analysis followed by a price negotiation. However, while this procedure that is limited to 12 months following marketing authorisation, is running, the product is still reimbursed at the price set by the manufacturer. Orphan medicinal products authorised by EMA under EU-regulation 141/2000 with an annual turnover below 50 million Euros are exempted from the benefit assessment, because the benefit is taken as granted. Still, price negotiations are mandatory also for these drugs.

D.11. GREECE

National plan/strategy for rare diseases and related actions

The Greek National Plan of Action for Rare Disorders (to run over the period 2008-2012¹⁷³) was adopted in 2008. No funding has been officially allocated to the National Plan of Action for Rare Disorders, and none of the eight strategic priority actions have yet started. As of yet, there is no legal framework for the Plan so no progress has been made.

In fact, most of the objectives of the proposed nation plan of action for RD are or could be incorporated in the existing structure and function of Greek national health system (GNHS). Implementation of strategic priorities for RD is coordinated by the Ministry of Health and mainly by the Hellenic Centre of Disease Control and Prevention (KEELPNO) jointly to those of common diseases.

In 2010 the new Scientific Committee for RD appointed by KEELPNO organised (with minimum funding) a program to evaluate the implementation and efficacy of the main strategic priorities defined in the scope of the Europlan project that are incorporated in the Greek NHS. The program started in 2011 with the following main objectives: i) to identify the expertise centres (CEs) involved in the care of patients with rare diseases, describe their structures and activities, evaluate the quality of health services they provide; ii) to investigate measures to upgrade the quality of the provided care; and iii) to introduce applicable strategies defined by Europlan, which are not included in the activities of expertise centres. Preliminary data from the survey are reported.

Centres of expertise

By the end of the 2011 the multidisciplinary centres of expertise (basically day care clinics) for the management of thalassemia, cystic fibrosis, neuromuscular disorders, hereditary bleeding diseases and primary immunodeficiencies were identified and evaluated. Identified centres of expertise include:

- Thalassaemia: 15 centres (Two follow more than 400 patients, four 150-200 patients and nine 70-150 patients)
- Cystic Fibrosis: 3 centres (2 for children and adolescents and 1 for adults)

¹⁷³ http://www.ygeianet.gov.gr/HealthMapUploads/Files/SPANIES_PATHISEIS_TELIKO_LOW.pdf

- Neuromuscular Diseases: 6 centres (2 for children and adolescents , 2 for adults and 2 for all ages)
- Hereditary Bleeding disorders: 4 centres (3 for adults and 1 for children and adolescent) and
- Primary immunodeficiency: 2 centres for children and adolescents

These centres of expertise collaborate with the follow expert laboratories.

- The Laboratory of Medical Genetics of the University of Athens, “Agia Sophia” Children Hospital, for the molecular pre and post natal diagnosis of thalassemia, cystic fibrosis, and neuromuscular diseases; it also serves as national reference laboratory for a number of genetic diseases.
- The national Thalassemia Prenatal Diagnosis Centre covering 60-70% of prenatal diagnosis of thalassemia.
- The laboratories of a) Genetic Neurological Diseases and b) Muscle pathology of the Department of Neurology, Athens University serving also as the National Reference Laboratory.

According to the evaluation of new Scientific Committee for Rare Diseases, certain centres of expertise involved in the management of these five diseases/groups of rare diseases, fulfil the EUCERD Recommendations on Quality Criteria for National Centres of Expertise for Rare Disease in Member States.

Sources of information on rare diseases and national help lines

Orphanet activities in Greece

The Orphanet Greece national website in Greek was launched in 2011¹⁷⁴.

National rare disease events in 2011

National rare disease events are either events for the patients and the public to disseminate basic information on clinical signs and treatment of rare diseases or scientific events addressed to expert physicians and scientists.

The National Association of Rare Diseases (PESPA) announced Rare Disease Day 2011, which was held under the auspices of President of the Republic Karolos Papoulias. A speech was given by Professor of Cancer Prevention and Professor of Epidemiology at the University of Harvard, Mr. Dimitrios Trichopoulos, Member of the Greek Academy of Sciences, and a retrospective exhibition of paintings by Katerina Lambrou, at the Cultural Center of Athens with donations going to the National Association of Rare Disorders and the Greek Society of Tuberous Sclerosis. PESPA organised a national conference on “Autoimmune Diseases: Today and Tomorrow” on 25-26 November 2011.

Events related to rare diseases are organised by most of the national patients organisations on the day devoted to the particular disease. National patient organisations organised during 2011 their annual meetings, conferences or congresses and discussed with specialists the recent advances in management and other topics related to the interest of the societies.

A considerable number of educational events on rare diseases aimed at physicians and the scientific community are organised each year by university departments, research institutes, expertise centres and scientific speciality societies in the form of meetings, workshops, lectures, training courses etc. Scientific events are usually focused on a single rare diseases or a number of homogeneous rare diseases.

Sponsorship for these events comes mainly by pharmaceutical companies and occasionally from patients organisations.

Research activities and E-Rare partnership

E-Rare

Greece currently participates in E-Rare-2, and is represented by two institutions: GSRT and the Hellenic Center for Disease Control and Prevention (KEELPNO). GSRT participated in the 3rd Joint Transnational Call launched in 2011 with the amount of €200 000. Two Greek teams were approved for funding after the evaluation of the call.

IRDiRC

Greek funding agencies are not currently committed members of the IRDiRC. Nevertheless the possibility to join IRDiRC through E-Rare-2 is under consideration.

¹⁷⁴ <http://www.orpha.net/national/GR-EL/index/%CE%B1%CF%81%CF%87%CE%B9%CE%BA%CE%AE-%CF%83%CE%B5%CE%BB%CE%AF%CE%B4%CE%B1/>

D.12. HUNGARY

National plan/strategy for rare diseases and related actions

In 2011, the Ministry of Health appointed a National Coordinator and the National Plan Organising Committee (including the advisory board of the National Rare Diseases Centre and the patient groups) started to develop the National Plan with his leadership to develop a rare disease plan and to elaborate the plan.. At the end of 2011, the main content of the plan was finalised and an expert meeting was held to finalise the chapters. Expert opinion will be sought by the end of March 2012, and it is hoped by end of June 2012 the plan will be ready to be included in the negotiations of the national budget at the start of August 2012.

The National Institute for Health Development (OEFI) became the new host organisation of the National Rare Disease Centre (NRDC) in May 2011. The OEFI is subordinated to the Chief Medical Officer and is a part of the central public health institutions. The continuation of the NRDC operation has been ensured by the modification of the foundation deed of OEFI.

Neonatal screening policy

A HURO-euro programme started in May 2011 on the “Newborn screening and molecular genetic diagnosis of rare diseases: developing a Euro-regional infrastructure and cooperation”. The University of Szeged is the project leader, and the Clinic de Urgență pentru Copii "Luis Țurcanu", (Timișoara) and Universitatea de Vest "Vasile Goldis" (Arad) are the Romanian partner institutions.

Training and education initiatives

The Epidemiology of Rare Diseases has been accepted as research area by the Health Sciences Doctoral School of University of Debrecen. The students are involved in the folic acid supplementation, prenatal screening, patient pathway and diagnostic delay investigations.

National rare disease events in 2011

HUFERDIS, the Hungarian rare disease alliance, organised the Hungarian Rare Disease Day as an informal central event of the EU supported by the Hungarian presidency¹⁷⁵ on 26 of February 2011 in Budapest. The event was attended by a range of stakeholders from Hungary and Europe and gave insights into actions at Hungarian and European level in the field of rare diseases. Many parallel programmes were organised: an expert conference, poster section, games and handcrafting for children, entertainment programmes, “Rare Beauties” Art Exhibition, concerts, press conference, all-day exhibition of the HUFERDIS member associations. During the day Dr. Ildikó Horváth, Head of Department for Health Politics, State Secretariat for Healthcare, Ministry of National Resources, and her colleague Ildiko Szy presented the enacted clinical guidelines for rare diseases. More than 800 people, several journalists and TV teams participated at the event. Many interviews were given. These all guarantee that awareness about rare diseases is developing continuously.

The second Hungarian Europlan Conference on Rare Diseases¹⁷⁶ (16-17 November 2011) was organised by HUFERDIS, together with the Ministry of National Resources, in Budapest, without European grant support. All stakeholders were present during the two day conference aimed at defining further concrete steps to develop a national action plan for rare diseases. 125 participants took part in the two day event including experts, patients and representatives of government and the Industry. Participants at the conference monitored a number of main priorities: the creation of a Committee to lead the development of a national plan, the accreditation of centres of expertise for rare diseases, the inclusion of rare diseases in health care and social care systems (currently under reorganisation), the organisation of external quality control of accredited institutions, the provision of information on rare diseases in Hungarian, the participation of Hungary in EU projects, the organisation of awareness campaigns, and the organisation of a body to maintain a rare disease information helpline.

Other events included a symposium on “Prenatal Diagnosis of Down Syndrome: How Best to Deliver the News” was organised in Debrecen by the local patient organisations, the Debrecen University’s departments and the NRDC. A working group meeting was held in Budapest for the partners involved in the audit for the prenatal screening and diagnosis of Down syndrome organised by NRDC and VRONY. A symposium on “Multidisciplinary care for Rare Disease” was organised in Pecs by the National Rare Disease Research Coordinating Centre and NRDC.

¹⁷⁵ <http://sites.rirosz.hu/rbv/ritka-nap-2011/programme-in-english>

¹⁷⁶ <http://europlan.rirosz.hu/euroterv-ii-konferencia-1/az-elhangzott-eloadasok>

Research activities and E-Rare partnership

IRDIRC

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

D.13. IRELAND

National plan/strategy for rare diseases and related actions

On 20 January 2011 the Genetic and Rare Disorders Organisation, Irish Platform for Patients' Organisations, Science and Industry IPPOSI and Medical Research Charities Group, MRCG in collaboration with EURORDIS organised a National Conference on Rare Diseases¹⁷⁷ in the scope of the Europlan project (see section "National rare disease events"). The conference welcomed over 160 participants from all stakeholder groups. The Conference was "an important milestone" in the development of a national health strategy for rare disease patients.

There is currently no national plan/strategy for rare diseases in Ireland, but the first steps have been taken to elaborate a plan. A National Steering Group of stakeholders has been established (Spring 2011) under the aegis of the Department of Health and Children to work on the development of a five-year national plan, starting with a mapping exercise and focusing on the structure, governance and monitoring of a national strategy. The Minister for Health appointed four patient representatives from GRDO, IPPOSI and MRCG to the Steering Group: the Steering Group held their first meeting in April 2011 and meets every 1-2 months with the aim of completing the first plan in the second half of 2012. A national consultation on the national plan and second national conference on rare diseases are planned for 2012.

Neonatal screening policy

Neonatal screening for cystic fibrosis started as of 1 July 2011¹⁷⁸. New governance arrangements are being developed for screening.

Registries

The Medical Research Charities Group (MRCG) created a Steering Group in 2008 involving the MRCG, Health Services Executive (HSE), Health Research Board (HRB) and the Health, Information and Quality Authority (HIQA) to oversee research into the area of patient registries in Ireland. The aim was to identify existing patient registries in Ireland, to describe these in detail (functions, methodologies, standards, funding mechanisms) and also to identify best practice and guidelines for quality standards in this area. The research was presented at an IPPOSI/MRCG run event in October 2011. The outcome report from that event entitled "Towards a National Strategy for Patient Registries in Ireland, considerations for Government¹⁷⁹" was launched in 2011. Part of a national strategy on Patient Registries in Ireland is the mainstreaming of the role and work of registries into existing and forthcoming policy. The immediate priority is the inclusion of a stronger focus on Patient Registries in: the programme of work of the Quality and Clinical Care Directorate of the HSE, including the development of clinical standards in specific areas of policy and the appointment of clinical leads in particular areas of policy; the work of the Health Information Quality Authority; and the Health Information Bill. The Health Information Bill is expected to be published in 2012 and will address ethical and legal issues concerning data collection and sharing patient data.

National alliances of patient organisations and patient representation

In 2011, GRDO, together with the Medical Research Charities Group (MRCG) and the Irish Platform for Patients' Organisations, Science and Industry (IPPOSI) and other patient organisations grouped together to form the Rare Diseases Towards 2013 Task Force which will support this National Steering Group charged with the development of a national plan for rare diseases and provide input from the appropriate stakeholders. At the end of 2011 GRDO launched a survey to gather information relating to patient support and advocacy

¹⁷⁷ <http://www.europlan.ie/> and

http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_ireland.pdf

¹⁷⁸ <http://www.hse.ie/eng/services/healthpromotion/newbornscreening/>

¹⁷⁹ <http://ipposi.ie/index.php/information-centre/patient-registries/179-towards-a-national-strategy-for-patients-registries-report>

organisations operating in Ireland for people with rare conditions. This information will be used to assist the Taskforce to engage with the Rare Diseases Steering Committee of the Department of Health.

Training and education initiatives

In 2011 IPPOSI and the School of Medicine at University College Dublin launched a Rare Disease Module for 3rd year medical students. IPPOSI/UCD planned the first module of its kind in Ireland to focus exclusively on rare diseases and the impact on patients. The lecturers on this module are scientists, clinicians and patients describing their own condition to students. The plan is to role this out to other medical schools in Ireland and Europe to bring patients and their patient organisations into the classroom.

National rare disease events in 2011

IPPOSI, the Irish Platform for Patients' Organisations, Science and Industry holds 2-3 conferences annually to tackle various questions in the field of rare diseases and orphan medicinal products.

On 20 January 2011, the Irish Europlan conference in Dublin took place. The organising committee included members of GRDO (The Genetic and Rare Disease Organisation), IPPOSI, the Irish Platform for Patient Organisations, Science and Industry and the MRCG, the Medical Research Charities Group, Fighting Blindness, Muscular Dystrophy Ireland, EURORDIS, Genzyme Ireland, the National Centre for Inherited Metabolic Disorders, the National Centre for Medical Genetics and the University College of Dublin. The Europlan conference provided a wide range of views from the academic, clinical, private and patient organisation sectors under the topics "Centres of Expertise", "Orphan Drugs and Access to Treatment", "Research" and "Patient Empowerment and Support".

GRDO hosted an information/patient-focused discussion event on Monday 28 February to mark International Rare Disease Day 2011. Those present included people with rare conditions, patient advocates, scientists and clinicians. Topics address included Genetic Testing and Genetic Counselling, Orphan Drugs, Pre-implantation and Genetic Diagnosis.

Research activities and E-Rare partnership

IRDiRC

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

D.14. 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*)¹⁸⁰ 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.

¹⁸⁰ <http://www.uniarno.org/>

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 diseases¹⁸¹”, 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).

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 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 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

¹⁸¹ <http://www.iss.it/binary/publ/cont/undici20WEB.pdf>

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.

The NCRD-ISS published the manual "Common stories of rare diseases: How to navigate the world of strange names", in collaboration with the Psychoanalytic Institute for Social Research and Italian National Council of Social Work. This tool is addressed to train in rare diseases social workers and health and social professionals.

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.

On 20-26 February 2011 Mediaset and National TV channels aired a spot entitled "Mum, what are rare diseases?" promoted by UNIAMO FIMR. The alliance also announced the partnership of the Volley League A1 A2 with Rare Disease Day. During the weekend of 26-27 February 2011 all players of the 40 male and female teams wore rare disease T-shirts during their presentation while the speakers read a short message of information on rare diseases.

On 25 February 2011, the NCRD – ISS organised in Rome the final EUROPLAN conference and the first meeting of EPIRARE (European Platform for Rare Disease Registries). EUROPLAN and EPIRARE are coordinated by NCRD-ISS and are three-year projects co-founded by the European Commission within the EU Program of Community Action in the field of Public Health.

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.

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.

D.15. LATVIA

National plan/strategy for rare diseases and related actions

Work has recently been finished on a national plan by the working group, which included health care specialists and representatives from the Ministry of Health. In December 2011, the plan was written and submitted to the Ministry of Health for evaluation. The costs related to rare diseases are currently included in the national health care budget.

Centres of expertise

A rare cardiovascular diseases network (Poland, Lithuania and Latvia through the P. Stradins Clinical University Hospital, Centre of Cardiology) started in May 2011. This project will last until January 2013.

National alliances of patient organisations and patient representation

In 2011 Caladrius (in collaboration with Latvian State University Children's Hospital) organised two visits of the high-qualified cardio surgeons: as a result, high-complicated operations were carried out for 11 children with inborn heart pathology. In 2011 Caladrius organised 4 seminars about methods of alternative therapy.

National rare disease events in 2011

To mark Rare Disease Day 2011, the Latvian Rare Disease Organisation, Caladrius, organised informative seminar for public and media representatives about Genetic and rare diseases.

The Latvian Haemophilia Society organized meeting for people with rare bleeding disorders on 16-17 April 2011 to celebrate World Haemophilia day: this was most attended meeting in many years, people wore red as recommended by the global dress code. Many professionals participated and event was mentioned in media.

Research activities and E-Rare partnership

IRDIRC

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

D.16. LITHUANIA

National plan/strategy for rare diseases and related actions

A working group was established by Order No. V-564 of 1 Jun 2011 of the Ministry of Health of the Republic of Lithuania to frame the National Plan on activities related to rare diseases which will be finalised for the second half of 2012. Representatives from the universities, university hospitals, non-governmental organisations of patients and medical professionals as well as state institutions (Ministry of Health, the National Health Insurance Fund, the State Medicines Control Agency) are involved in the working group.

Centres of expertise

An outpatient clinic for cystic fibrosis patients was established in 2011.

Neonatal screening policy

The basic prices paid from Compulsory Health Insurance Fund budget for the newborn screening programmes for phenylketonuria and hypothyroidism were re-counted and approved by the Order No. V-962 of the Minister of Health of Republic of Lithuania in 10 November 2011.

Sources of information on rare diseases and national help lines

Orphanet activities in Lithuania

In 2011, the Orphanet Lithuania national website was launched by the Orphanet Lithuania team, in Lithuanian¹⁸².

Good practice guidelines

A national agreement for cystic fibrosis diagnostic, treatment and management for adults was reached and published in journal *Pulmonology, immunology and allergology* (1(8), 2011)

National rare disease events in 2011

Various rare disease patient organisations invited the public to participate in various events, and also organised online publications and articles in the newspapers to mark Rare Disease Day.

The Centre for Medical Genetics in Vilnius University Hospital Santariškių clinics issued an online invitation via their internet portal to commemorate the Rare Disease Day 2011. The Orphanet-Lithuania coordinator attended the Morning News talk show on national TV, where he spoke about the problems that patients and their families face when dealing with rare diseases in Lithuania in particular.

The Lithuanian Association for the Genetic Neuromuscular Disorders “Sraunija” produced a play entitled “Little Prince” where the main character was a boy with a rare disease. An interview of the Lithuanian Cystic Fibrosis Association chairman and a pediatric neurologist was released in the press on that day. A representative of the Rare Disease Initiative spoke on national radio to raise awareness of the lack of information about rare diseases and the problems of families affected by these disorders. A clinical geneticist was also interviewed on national radio about rare diseases in Lithuania and other countries, and the diagnostic and treatment possibilities.

A section on rare diseases took place in the 2011 Paediatric Congress in Vilnius.

Research activities and E-Rare partnership

IRDIRC

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

D.17. LUXEMBOURG

National plan/strategy for rare diseases and related actions

The Task Force on Rare Diseases Luxembourg (“*Groupe de travail maladies rares*”) was created in 2005 to analyse the needs of rare disease patients in the country and to develop a national strategy for improvement. This Task Force will work out a national plan for rare diseases based on the results of a survey carried out between May 2006 and February 2007 aimed at analysing the strengths and weaknesses of the healthcare system and the experiences of rare disease patients. The results of this survey were published on 28 February 2011¹⁸³.

The results of the survey show that, as in many other European countries, obtaining a diagnosis is often difficult for rare diseases patients in Luxembourg; that medical and scientific knowledge is often insufficient, as Luxembourg does not have university hospitals or specialised investigation centres; that often there is a lack of information on diseases or specialised treatment centres abroad. Whereas the orientation of patients to a specialist or a specialised centre abroad (when these are identified) is a procedure foreseen in the national sickness fund, patients regret a lack of coordination between the health professionals; there is a lack of quality care for quite a number of rare pathologies; As parts of the care and treatment might not be covered by the sickness fund there are inequalities in the access to a diagnosis, treatments and care; and that rare diseases have serious social consequences. A list of recommendations have been made on the basis of these results including: the elaboration of a national plan for rare diseases; the improvement of information and

¹⁸² <http://www.orpha.net/national/LT-LT/index/prad%C5%BEia/>

¹⁸³ *Les maladies rares: Enquête sur la situation des personnes atteintes de maladies rares au Grand-Duché de Luxembourg*
<http://www.sante.public.lu/fr/catalogue-publications/maladies-traitements/maladies-rares/index.html>

awareness of rare diseases; the guarantee of equal access to diagnosis, care and treatment; the provision of specific help services for patients with rare diseases and their families; to the support of rare disease patient organisations and their involvement in national rare disease actions; to intensification of international collaboration; the promotion of advanced research; and the support for the sustainability of rare disease initiatives at national level.

According to the results of the survey, 95% of patients with rare diseases residing in Luxembourg have sought or have been oriented by their treating doctor for medical care in neighbouring countries (such as Germany, Belgium and France), with 50% of patients travelling 1 to 5 times a year abroad for medical care.

National rare disease events in 2011

To mark Rare Disease Day 2011, the Ministry of Health of Luxembourg together with the National Interdisciplinary Rare Disease Working Group has organised a press conference on 28 February 2011 to launch the national report : "Rare diseases: a national survey on the situation of persons with rare diseases in Luxembourg."¹⁸⁴ In 2005, following the European Conference on Rare Diseases held under Luxembourg's Presidency of the EU, an interdisciplinary working group was constituted, gathering medical experts, neurologists, paediatricians, biological specialists, experts in metabolic diseases, the patient's association ALAN and the Ministry of health. The objective was the constitution of a platform for the interdisciplinary exchange, the study of the situation in Luxembourg and the elaboration of initiatives for improvement

The analysis of the situation of rare diseases in Luxembourg was a priority. The objectives of the study were to evaluate the burden of disease of rare diseases in Luxembourg, to analyse the medical and psychosocial care the patients receive, to collect feedback on problems and needs (in the medical, social, education, professional and leisure area), to evaluate the strengths and weaknesses of the health and social security system as concerns rare disease patients. Based on the results of the inquiry recommendations were formulated for the elaboration of a National Plan for Rare Diseases.

Research activities and E-Rare partnership

IRDiRC

Funding agencies in Luxembourg are not currently partners of the IRDiRC.

D.18. MALTA

National plan/strategy for rare diseases and related actions

A detailed framework that will form the basis for a national strategy for rare diseases is being created. The plan is to propose a request for a first budget for the strategy of rare diseases from the National Budget for 2013. The national strategy will have a time span of a number of years with plans to incrementally implement a number of measures that will aim towards increasing the profile and care services tailored for rare diseases in Malta.

Research activities and E-Rare partnership

IRDiRC

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

¹⁸⁴ *Les maladies rares: Enquête sur la situation des personnes atteintes de maladies rares au Grand-Duché de Luxembourg*
<http://www.sante.public.lu/fr/catalogue-publications/maladies-traitements/maladies-rares/index.html>

D.19. THE NETHERLANDS

National plan/strategy for rare diseases and related actions

The Minister of Health, Welfare and Sport, Mrs. E. Schippers, sent a letter (with annex) to Parliament on 29 February 2012, in which she expounded the strategy of the Netherlands regarding rare diseases for the years 2012-2015¹⁸⁵. Some important points in this report are the following:

- Strengthening the role of university hospitals with regard to patient care and research in rare diseases;
- Funding is designated for care and research;
- Improving reimbursement of orphan medicinal products applied in university hospitals starting 1 January 2012 and in the out-patient setting (starting some time in 2013, neither of the changes will jeopardise the accessibility of orphan medicinal products);
- A separate scientific programme is indicated (already started in 2011);
- The Steering Committee on Orphan Drugs was dissolved (as of 31 December 2011), but stakeholders in the former Steering Committee on Orphan Drugs will assume more tasks and responsibility in their own area of expertise;
- ZonMw (The Netherlands Organisation for Health Research and Development) assume tasks not taken up by the stakeholders that remain from the tasks of the former Steering Committee. The ministry of Health, Welfare and Sport provides additional funding for the years 2012-2015;
- The Forum Biotechnology and Genetics (also fully subsidised by the ministry of Health, Welfare and Sport) will assume more responsibility on rare diseases and orphan medicinal products;
- A statement on screening.

In addition to the national strategy initiated by the government for 2012-2015, preparations for a national plan on rare diseases for all stakeholders have started. The input of all stakeholders was collected via information from different meetings organised by several stakeholders in the last years and via newly installed working groups in 2011 and a new website and is coordinated by the Dutch Steering Committee on Orphan drugs. This process will be continued in 2012 under the auspices of a sounding board especially formed for this task. On 1 October 2011 the site <http://www.nationaalplan.nl/> was launched in order to collect input for the national plan for rare diseases in a systematic way. The National Plan for Rare Diseases with input from all stakeholders is in an advanced stage of preparation, anticipated to be ready before summer 2012^{186,187}. The national plan will consist of four chapters comprising the issues of information, care, research and availability of knowledge (education) and availability of therapy. However, within the purview of the Recommendation of the Council, the national plan will be incorporated into the national strategy. Stakeholders are, on the other hand, free to develop and implement initiatives on their own.

Sources of information on rare diseases and national help lines

Orphanet activities in the Netherlands

In 2011, the Orphanet Netherlands national website was launched in Dutch by the Orphanet Netherlands team¹⁸⁸.

Official information centre for rare diseases

Until the end of 2011, the Steering Committee on Orphan Drugs functioned as an information centre for rare diseases and orphan medicinal products in the Netherlands. The secretariat of the Steering Committee answered various questions from pharmacists, medical specialists, patients and their families and

¹⁸⁵ An English language translation of the annex is under preparation.

¹⁸⁶ Following the adoption of the European Union Council Recommendation in June 2009, the Dutch government took no immediate initiatives to support a national plan/strategy for rare diseases. The reason being that there was already a 'strategy' in place since 2001 aimed at patients with rare disorders and at providing information about and accessibility of orphan drugs, embedded in wider governmental policies. This 'strategy' had a ten year time line. Nevertheless, the Steering Committee on Orphan Drugs along with the Dutch Genetic Alliance VSOP and the Forum Biotechnology and Genetics (FBG), lobbied for a national plan to be put on the political agenda, and both stated their intention at the 2010 Europlan National Conference on Rare Diseases to cooperate with stakeholders to prepare a national plan. Moreover, the Steering Committee on Orphan Drugs expressed their concerns about the preparation of a Dutch plan to the Minister of Health in December 2010.

¹⁸⁷ In a letter to the Minister of Health with a copy to Parliament, VSOP reacted rather critically on the ministers' strategy report, stating that she depicted the situation and governmental efforts too positively, leaving several real problems unaddressed, for example related to the lack of reference centres, the lack of a national registration, and the lack of standards of care.

¹⁸⁸ <http://www.orpha.net/national/NL-NL/index/homepage/?lng=FR>

pharmaceutical companies about rare diseases and orphan medicinal products. Furthermore, the Steering Committee had a signaling function in response to problems that are reported to the steering committee. Their website www.orphandrugs.nl provided general information.

As of 31 December 2011, the Steering Committee was disbanded by the government: however €880'000 was made available to ZonMw (the Netherlands Organisation for Health Research and Development) for the years 2012-2015 to install a secretariat for rare diseases and orphan medicinal products.

Good practice guidelines

Funding was provided by a Dutch health insurance fund (Innovatiefonds) for the development of guidelines. VSOP also continued to work on 17 standards of care for rare disorders, 4 of which will be finished in 2012, the others will be finished by 2014. Major funding (in total nearly €3million) was provided by the Dutch government.

Training and education initiatives

A course on practical clinical, radiological and pathological diagnosis of skeletal tumours was organised by the European network of excellence EuroBoNeT in collaboration with Leiden University Medical Center (14-16 February 2011).

National rare disease events in 2011

The Dutch Rare Disease Day 2011 was held on 15 May 2011¹⁸⁹ in Artis ZOO, Amsterdam, in conjunction, with the EURORDIS Conference. About 350 people, especially families, attended this meeting and two so called angel awards were granted for excellence in patient advocacy and medical care for rare diseases. This day was organised by the Dutch Steering Committee on Orphan Drugs, the Dutch Rare Disease Fund, the Pharmacists Association KNMP and VSOP. On 12 May 2011 a conference was organised by the Dutch member organisations of EURORDIS in collaboration with the Dutch Steering Committee on Orphan Drugs on care for rare diseases.

On 25 February 2011 the Patient Platform Rare Diseases organised a hearing event on rare diseases in the Dutch Senate in The Hague.

Research activities and E-Rare partnership¹⁹⁰

National research activities

A multi-annual research programme started in 2011 at The Netherlands Organisation for Health Research and Development (ZonMw) with a funding of 13.4€ million. The main objective of this is to stimulate translational research in rare diseases with the aim of developing therapies. For the programme €13.6 million is available. The first call was launched in early 2011. ZonMw has also provided and continues to provide funding through several research programmes for research on rare diseases (e.g. the Innovative Research Incentives Scheme, the Gene Therapy subsidy scheme and the additional research programme on efficiency of Expensive and Orphan Medicines).

In 2011, the Netherlands Organisation for Scientific Research made €22.5 million available to a consortium including 8 Dutch university medical centres and other research institutes and universities in order to establish a national biobanking infrastructure, the Biobanking and Biomolecular Resources Research Infrastructure Netherlands (BBMRI-NL), which will integrate clinical materials and data gathered over many years with the goal of improving access to human samples. Such samples are important to rare disease and orphan medicinal product research. However for practical and cost-effectiveness reasons the infrastructure currently can only accept rare disease samples when they are part of biobanks of 1000 samples or more, so the infrastructure for now mostly concerns, rare diseases samples when they are part of a biobank for a more common disorder¹⁹¹.

¹⁸⁹ www.zeldzameziektendag.nl

¹⁹⁰ This section has been written using the KCE reports 112B : *Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp53-62)*.

¹⁹¹ Another interesting example is the following: VU University Medical Centre in Amsterdam is working together with the Dutch Neuromuscular Diseases Association in the development of an n-of-1 trial service. In the case of chronic conditions and fast-acting medicines for symptomatic treatment, it might be justified to collect evidence of efficacy from a trial treatment of a single patient. A "n of 1" is a clinical trial involving a single patient, i.e., a single case study. Through this service, patients with rare diseases would be able to receive treatment while at the same time testing the effectiveness of certain (expensive) medicines. During such an "n-of-1 trial" the physician alternately treats the patient with the off-label medicine and the medicine with which it is compared, for example, a placebo or treatment-as-usual. Rules are agreed in advance to allow for a fair comparison. The results of the trial treatment indicate whether the patient experiences benefits of the off-label medicine over and above treatment-as-usual. As series of trial treatments together bring more knowledge, these separate n-of-1 trials would be centrally coordinated and combined for analysis by an n-of-1 trial service. The current project is investigating whether such trial treatments, to be facilitated by the n-of-1 trial service, could be reimbursed by the Dutch basic

E-Rare

The Netherlands did not participate in the 3rd E-Rare Joint Transnational Call (2011) but will participate in the 4th focused Joint Transnational Call (2012).

IRDiRC

The Netherlands Organisation for Health Research and Development (ZonMw) and the pharmaceutical enterprise Prosenza, are committed members of the IRDiRC.

Orphan medicinal products^{192,193}

Orphan medicinal product committee

In 2011 the Steering Committee focused on the draft for a national plan in close cooperation with different stakeholders. However, it was decided that the Steering Committee would not be funded by the Dutch government after December 2011 and will no longer exist as a governmental committee from 2012 onwards. Stakeholders in the former Steering Committee on Orphan Drugs will assume more tasks and responsibility in their own area of expertise in the future with the Netherlands Organisation for Health Research and Development ZonMw taking more responsibility (with extra funding) and assuming a number of tasks from the former Steering Committee. Notably, the coordination of the development and implementation of a national strategy will be from 2012 onwards assumed by a secretariat at ZonMw.

Five grants have been awarded at the end of 2011 in the framework of the Orphan Designation Dossier (ODD) subsidy scheme.

D.20. POLAND

National plan/strategy for rare diseases and related actions

Although in 2011 a national plan or strategy for rare diseases was not yet adopted, significant steps have been undertaken towards the goal of adopting this important document in order for Poland to meet the EU Council Recommendation, hopefully by the end of 2012.

The Rare Disease Task Force was established via an order of the Minister of Health as his advisory body in 2008. The setup of the Rare Disease Team changed in July 2011. The Minister of Health recognised rare diseases as a much broader problem, not only limited to orphan drugs, thus it was necessary to create a better tailored Task Force with competence also in healthcare system organisation and doctors' education. According to the new order of the Minister of Health the new Task Force leader was chosen based on his experience in the healthcare management rather than the official position. The sole purpose of the reorganised Task Force is to prepare a National Plan on Rare Diseases (NPRD). In autumn 2011 a new setup of this advisory body was formally constituted to help with the elaboration of a plan, in collaboration with patient organisations, due to be launched by the end of 2012. Due to the new Order of the Minister of Health, the group was reconstituted, and now it includes the following members chaired by a representative of the Ministry of Health: four experts in the field of rare diseases including representative of umbrella patient organisations, representatives of Poland in EU institutions in the field of rare diseases, Directors of the Departments at the Ministry of Health and representatives of National Health Fund (the Payor).

On 7-8 December 2011 the conference "Partnership for the National Plan for Rare Diseases", organised by National Forum for the Therapy of Rare Diseases was held in Warsaw. It was agreed during this conference that a patient's input to the draft concerning a National Plan on Rare Diseases should be prepared by the end of February 2012, based on data from the working-groups, and in accordance with the Europlan project. The draft will encompass different areas and aspects of rare diseases, such as classification and rare diseases registry; diagnostics; medical care; integrated social support; and information and education. Once

health insurance. It is also examining whether the results of this type of research may be sufficient for authorities to decide on the effectiveness of an off-label medicine and its reimbursement for future patients with the rare disease in question. In a follow-up project, researchers hope to actually invite patients to participate in pilot trial treatments for neuromuscular diseases and eventually other diseases as well.

¹⁹² This section has been written using *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp53-62)

¹⁹³ This section was 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)* (pp21-23)

prepared, the document will be presented to the Polish Ministry of Health for further discussion and elaboration.

Based on the above mentioned initiative, with the support of the Chairman of the ministerial Rare Diseases Task Force as well as the Children's Memorial Health Institute, the series of working meetings were organised in order to elaborate the final drafts of each mentioned area of the future national plan. During these several working sessions held in late 2011, it was decided that the working document "The systemic assumptions for the development of the National Plan for Rare Diseases" (a joint initiative of the National Forum for Therapy of Rare Diseases and broad rare diseases medical/scientific community) will be submitted directly to the Rare Diseases Task Force at the Polish Ministry of Health for further official elaboration of the future governmental RD National Plan¹⁹⁴. The entire initiative was launched following the EU Council Recommendation on the involvement of patients and their representatives in the political process and promoting the activities undertaken by rare diseases patient groups and associations.

Sources of information on rare diseases and national help lines

Orphanet activities in Poland

Since April 2011 the Orphanet Poland team maintains a national Orphanet Poland national website¹⁹⁵. In order to improve access to information on rare diseases, orphan drugs and Orphan in Poland, the Polish Orphanet team has translated the documents concerning Orphanet's activities (leaflets), created lists of Polish associations/expert clinics/diagnostics centres and is developing Polish versions of rare disease abstracts. All this information is available on the Orphanet website.

National rare disease events in 2011

In Poland, Rare Disease Day 2011 was marked by an event at the famous King's Palace on the lake in Lazienki Park in Warsaw. The Organising Committee, created for the event, consisted of 16 Polish rare diseases patients' support groups who created a web page (www.dzienchorobrzadkich.pl) and a Facebook page for the Polish Rare Disease Day. Altogether over 150 people took part: patients, their families and friends, health professionals, parliament and Ministry of Health representatives, the Orphanet-Poland coordinator and the media attended this meeting. The Minister of Health Ms. Ewa Kopacz gave a welcome address and she then presented the government plans for dealing with the issue of rare diseases at national level. The participants heard about help which should be provided for all affected families, the national strategy for rare diseases, intensive work in this field starting this year and Orphanet activities. After an official session, consisting of a few important speeches by the hosts, all of the participants went outside where many white balloons with the Rare Disease Day logo were released. A private 'wish list' was attached to the string of each balloon. Copies of these wishes were given to the Minister of Health as the patients' petition to the Polish government. The event was reported on in the press, local radio, national radio and TV with a number of interviews and talks.

On 7-8 December 2011 the conference "Partnership for the National Plan for Rare Diseases" was held in Warsaw. This meeting was organised by "Orphan", the National Forum for Rare Disease Therapy, with participation from representatives of the Ministry of Health, families, patient societies, clinical experts, and the Children's Memorial Health Institute's (CMHI) group on rare diseases. The conference was a symbolic, official launch of the work toward developing and adopting a National Plan for Rare Diseases, based on a formula of social consultations. During the first day the current state of Polish patients with rare diseases (RDs) was discussed. The second day took place in the CMHI with the participation of the patient group representatives and the clinical experts who work with rare diseases. The main aim of the discussion was the exchange of experiences and views on the care and treatment of patients and the creation of working-groups, including clinical experts from the Polish reference centers. It was agreed that a patient's input to the draft concerning a National Plan on Rare Diseases will be prepared by the end of February 2012, based on data from the working-groups, and in accordance with the Europlan project. The draft will encompass different areas and aspects of rare diseases, such as classification; diagnostics; medical care; integrated social support; and information and education. Once prepared, the document will be presented to the Polish Ministry of Health for further discussion. On 20 October 2011 a working meeting took place in Warsaw with the participation of the representatives of European paediatric oncology centres and the Ministers of Health of the European countries. It was dedicated to the care of children with cancer, which are all rare diseases. Among other issues, the participants discussed problems related to the establishment of the European Standards of Care for Children with Cancer. The conference was organised by the Polish Ministry of Health in cooperation with the

¹⁹⁴ The list of parties involved in the preparation of the systemic assumptions as well as results of their common work may be reached at www.rzadkiechoroby.pl

¹⁹⁵ www.orpha.net/national/PL-PL

European Society for Paediatric Oncology (SIOPE) in Brussels, and in relation to the Ministry's participation in the European Partnership for Action Against Cancer.

Other rare disease related events included a Dysmorphology meeting in the Children's Memorial Health Institute (Warsaw, 7 June 2011 and Lublin 14 October 2011), V Polish Conference on the Problems of diagnosis, rehabilitation and development of a disabled child", Lublin (13-15 October 2011), "Advances of genetics in pediatric medicine" Course, Warsaw (30 November - 2 December 2011).

Research activities and E-Rare partnership

E-Rare

Poland is an observer of the E-Rare 2 project.

IRDiRC

Polish funding agencies are not yet committed members of the IRDiRC.

Orphan medicinal products

Orphan medicinal product committee

Accordingly to the new Reimbursement Act (in force since July 2011), the Economic Committee within the Ministry of Health takes responsibility to negotiate market conditions for products applying for reimbursement, including orphan medicinal products.

Orphan medicinal product pricing policy

Following the implementation of the new Reimbursement Act (July 2011), a few changes have been introduced complying with Transparency Directive. The Medicines Management Team was disbanded and the new Economic Committee takes responsibility in the negotiation process. In addition to this, the role of HTA has been strengthened.

Orphan medicinal product reimbursement policy

The reimbursement system will change from 1 January 2012 according to the Act of 12 May 2011 on reimbursement of drugs (in force since July 2011), foods for special dietary use and medical devices. The new system will be unified, application based. The Minister of Health will not be able to introduce reimbursement of a new drug without prior application from the marketing authorisation holder. The application will have to contain among others HTA analyses, information on reimbursement status and pricing in other EU Member States.

D.21. PORTUGAL

National plan/strategy for rare diseases and related actions

In November 12, 2008 the Portuguese Minister of Health approved the National Plan for Rare Diseases ("*Programa Nacional para as Doenças Raras*"). A specific tool is already foreseen for the identification of people with rare diseases, aiming at disclosing clinical information to medical doctors and in emergency situations.

The Directorate General of Health, together with the Office of the High Commissioner for Health, have co-funded, in a total amount of €1.9 million, during the years of 2008 to 2011, a few projects on rare diseases, which are currently being developed by several patient associations, what enabled the implementation of a number of strategies mentioned in the National Plan.

Registries

In 2011 the Portuguese Registry of Paramyloidosis was officially established by Order nº 8812/2011 dated 2 June 2011.

National alliances of patient organisations and patient representation

In 2011, FEDRA organised a Conference on “Patients, research and health policies”. FEDRA also launched in 2011 the third volume of the publication “Rare Diseases from A to Z”, with the collaboration of 36 experts who have reported on around 41 rare diseases, and prefaced by the Director General of Health.

Sources of information on rare diseases and national help lines

Orphanet activity in Portugal

The Orphanet-Portugal team also created and maintains the Orphanet national entry point for Portugal.

An official event, with media coverage, was held on 26 February 2011 to announce the launch of the Orphanet website in Portuguese, as well as the constitution of the new Scientific Advisory Board. This took place during the conference “Rare but Equal” (“*Raros mas Iguais*”), organised by the APADR in collaboration and with the support of Orphanet-PT, with the presence of the Minister and Secretary of Health, the President of INFARMED (National Authority of Medicines and Health Products), and other health authorities.

In 2011, the Orphanet Portugal team created a Facebook page called “The Orphanet in portuguese” (“*A Orphanet em português*”), hoping that it will become a forum for discussion among all Portuguese-speaking professionals, patients and their organisations, and that it will serve to promote Orphanet in their respective countries. It has already proved useful in helping finding expert volunteers for translations/validations of disease abstracts. In addition, the national team manages a considerable number of questions and inquiries, sent by users mostly by email, requesting information or help.

Other sources of information on rare diseases

The APPDH – Portuguese Association of Parents and Patients with haemoglobinopathies (“*APPDH - Associação Portuguesa de Pais e Doentes com Hemoglobinopatias*”), member of APADR, published 3 mini-books about haemoglobinopathies, mainly for children, but also useful for adults.

The APN – Portuguese Association of Neuromuscular Diseases (“*Associação Portuguesa de Doenças Neuromusculares*”) a member of APADR as well, published, in 2011, 2 booklets: “Neuromuscular Diseases Manual: for healthcare professionals” (“*Manual sobre Doenças Neuromusculares: Técnicos e Profissionais de Saúde*”) and “Neuromuscular Diseases Manual: for patients and caregivers” (“*Manual sobre Doenças Neuromusculares em Idade Pediátrica: Doentes e Cuidadores*”).

Training and education

In July 2011, during the post-graduation course “Mental Retardation: from Clinic to Gene and Back” (2nd Edition)¹⁹⁶ a session was about Orphanet services was presented. The audience included molecular and clinical geneticists as well as post-graduation students.

Some patient associations have organised one-day receptions for medical students, so that they are made aware of rare diseases and rare disease patients. Some also organise voluntary rotations for other health professionals, such as social workers and speech therapists.

National rare disease events in 2011

To mark the Rare Disease Day 2011, the Portuguese Alliance of Patients Associations of Rare Disorders (APADR), in collaboration with Orphanet-Portugal, organised a conference on the theme “Rare but Equal”, on 26 February 2011. Patients, families, patient associations’ representatives, industry representatives, policy makers and health authorities (including the Portuguese Ministry of Health and the Secretary of State for Health, the Vice-Director of Directorate-General of Health, the Social Security Director and the President of INFARMED - the National Authority for Drugs and Health Products), health professionals and researchers and several members of the Scientific Advisory Board of Orphanet-Portugal were present. The Ministry of Health recognised officially the importance of Orphanet activities. Both FEDRA (in Lisbon) and APADR (in Porto) hosted Rare Disease Day events in 2011.

On 11-12 March 2011, the Second Symposium of the *NERD* of the Portuguese Society of Internal Medicine was held in Tomar: the proposed development of a National Registry of Rare Diseases was discussed.

On 10-12 November 2011, the 15th Annual Meeting of the Portuguese Society of Human Genetics was held in Lisbon, with a communication and poster about rare diseases and Orphanet.

¹⁹⁶ <http://www.icvs.uminho.pt/postgraduation/MentalRetardation/default.aspx>

Research activities and E-Rare partnership

E-Rare

Portugal did not join the 3rd Joint Transnational Call in 2011.

IRDIRC

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

D.22 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)¹⁹⁷ 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

¹⁹⁷ www.edubolirare.ro

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.

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 Oradea¹⁹⁸. 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.

D.23. SLOVAK REPUBLIC

National plan/strategy for rare diseases and related actions

No national plan or strategy for rare diseases currently exists in Slovak Republic and there is no specific budget currently dedicated to rare diseases. However, a working group was established in January 2011 at the Ministry of Health and work has begun on a “Strategy for improving health care for patients with rare diseases”. This document is being reviewed at the Ministry of Health level. A workshop was also held in December 2011 concerning rare diseases at the Ministry of Health.

Centres of expertise

A small workshop was held in December 2011 concerning rare diseases at the Ministry of Health and this group is now working on the criteria for centres of expertise in line with those issued by the EUCERD. Several specialised and centralised departments would be appointed as centres of expertise in the near future (e.g. oncogenetics, hereditary metabolic diseases).

¹⁹⁸ <http://ziuboliorrare.wordpress.com>

Registries

In 2011 the National child hypertension registry was established as sub register of cardiovascular registry.

National alliances of patient organisations and patient representation

The Slovak Rare Diseases Alliance was established at their first constitutive meeting held in Bratislava in Slovakia on 12 December 2011 and is composed of 12 patient organisations out of the 17 related to rare diseases in the country.

Sources of information on rare diseases and national help lines

Orphanet activities in the Slovak Republic

The team launched in 2011 the Orphanet Slovakia national website¹⁹⁹.

National rare disease events 2011

To mark Rare Disease Day 2011 several events was organised, mainly through mass media presentations. On the website of Slovak Ministry of Health there was a short advertisement about Rare Disease Day. Short films were broadcasted on TV and wider discussions took place on the radio. Several rare diseases related presentations were organised in the context of local medical conferences and seminars.

Izakovic's Memorial is an annual conference organised in Slovak Republic by the Society of Medical Genetics, related to genetic and rare diseases. In 2011 the conference was specially focused on problem of rare diseases.

Hosted rare disease events 2011

The DIABGENE Laboratory from Slovak Academy of Sciences organised from 30 September to 3 October 2011 the meeting "The Genetic of Diabetes in Post-Genome Wide Association Era" devoted to monogenic forms of diabetes and/or hereditary hyperinsulinism.

Research activities and E-Rare partnership

IRDIRC

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

Orphan medicinal products

Orphan medicinal product reimbursement policy

At the end of the year 2011 Slovak Ministry of Health introduced a monthly update of "categorisation list", thus increasing the possibilities for all pharmaceutical companies as well as orphan medicinal product pharma companies to launch their products. The "categorisation list" of all reimbursed drugs is published every quarter.

D.24. SLOVENIA

National plan/strategy for rare diseases and related actions

A working group was created at the Ministry of Health in 2010 which prepared a draft national plan for rare diseases in 2011 which has now passed a professional and lay public consultation phase. The plan was accepted by the Health Council in February 2012 and the next steps will be to elaborate an action plan and its implementation.

Sources of information on rare diseases and national help lines

Orphanet activities in Slovenia

The team launched in 2011 the Orphanet Slovenia national website²⁰⁰.

¹⁹⁹ <http://www.orpha.net/national/SK-SK/index/%C3%BAvod/>

²⁰⁰ <http://www.orpha.net/national/SI-SL/index/domov/>

National rare disease events in 2011

To mark Rare Disease Day, a press conference was organised on 28 February 2011 to raise society's awareness of rare diseases, to inform the general public about rare diseases and to improve cooperation between patients and medical profession for better quality of life of patients.

Research activities and E-Rare partnership

IRDIRC

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

D.25. SPAIN

Definition of a rare disease

Spain accepts the definition of the "Community Action Programme on Rare Diseases (1999-2003)" of a rare, minority, orphan or uncommon diseases as a life-threatening or chronically debilitating diseases with a prevalence of less than 5 cases per 10,000 inhabitants.

National plan/strategies for rare diseases and related actions

The Rare Diseases Strategy of the Spanish National Health System was approved by the Interterritorial Council of the Spanish NHS on 3 June 2009²⁰¹.

The Strategy has been evaluated in 2011 and the results are now to be analysed. This assessment will focus mainly on the implementation of the Strategy over the first two years, although it is too soon to measure quality of life this process could help to update recommendations and objectives.

Centres of expertise

Work continues in other areas of specialisation to define all the pathologies and procedures, among them those related to rare diseases, which should be carried out in Reference Centres, Services and Units (CSUR) of the Spanish NHS. In the areas of congenital metabolic diseases and rare neurological disease a work is currently being developed, being already constituted the groups of experts, scheduled to raise their proposals to the Designation Committee of CSUR and the Interterritorial Council in the first half of 2012. During 2011 FEDER (Spanish Federation for Rare Diseases) participated in the CSUR project with regard to rare diseases, by providing professionals to participate in the groups of experts related to rare diseases.

Registries

Since December 2011, a project on the "Spanish Rare Disease Registries Research Network" is being carried out and coordinated by IIER; all the Autonomous Communities are participating in the project. The main objective is to develop the National and Regional registries for rare diseases.

Sources of information on rare diseases and national help lines

Orphanet activities in Spain

In March 2011, Orphanet Spain signed an Agreement with the AEGH by which the Spanish national team will have access to a compiled list of all the laboratories that have registered in the AEGH.

Other sources of information on rare diseases

A book entitled "Communication strategies and challenges for rare diseases: Medical research as a referent"²⁰² was presented on Rare Disease Day 2011. Social researchers from the Universidad de Almería and Valencia's CEU-Cardenal Herrera University offered, for the first time, a quantitative and discursive analysis of the treatment of rare diseases in the Spanish press over a one-year period. The book, freely downloadable in English and Spanish languages, is intended for students – future researchers, clinicians and journalists- as well as for active professionals in these fields, in addition to patients and patient associations.

²⁰¹ <http://www.msc.es/organizacion/sns/planCalidadSNS/docs/RareDiseases.pdf>

²⁰² http://www.ciberer.es/documentos/Libro_Ingles.pdf

Training and education initiatives

In 2011 CIBERER organised three specific courses on the application of OMICS to rare diseases research, a course on animal models phenotyping and a course intended to health professionals for a general overview of rare diseases.

The Bancaja Foundation and CIBERER and have launched another ‘Becas Lanzadera’ (“Scholarship Shuttle”) to attract the best students to research in the field of rare diseases. These grants a year amounting to €60,000, will enable trainees to work in various research projects in the field of rare diseases (cause birth defects, metabolic disorders, disability, sensorineural disorders and intellectual deficiencies) in order to understand their causes and nature, and to develop diagnostic and therapeutic tools.

National rare disease events in 2011

In 2011, FEDER, in collaboration with its more than 200 patient organisations, coordinated the Rare Disease Day Campaign. A number of activities were organised including, the adoption of an official act in the Spanish Senate (Madrid), the 2nd Solidarity race for the rare diseases (Madrid), Multitudinous march, V Orphan drugs and Rare Disease Congress (Seville), Solidarity fair and Benefit Dinner (Barcelona), Solidarity race for the Rare Diseases (Badajoz), Cultural activities and race (Murcia), and VII Rare Disease Encounter (Valencia).

On the occasion of the Rare Diseases Day 2011, the III Meeting "To Research is To Advance" was held in Madrid on 23 February 2011, organised by the Centre for Biomedical Network Research on Rare Diseases (CIBERER). The event was attended by over 150 people and included the participation of researchers and patient organization representatives, who gave examples of collaboration between multidisciplinary teams and patients in metabolic diseases, amyotrophic lateral sclerosis and fragile X syndrome. Moreover, the book entitled "Communication strategies and challenges for rare diseases: Medical research as a referent"²⁰³ was presented.

Other national events related to rare diseases organised in 2011 included: “Keys for the assistance in primary care on rare diseases Valencia (13 January 2011)”, V International Congress of Rare Diseases and Orphan Drugs, Seville (17-19 February 2011), Masters Course “Current knowledge of rare diseases”, Seville (11 March 2011), National Congress of Human Genetics, Murcia (30 March-1 April 2011), Genome Spain workshop 2011 “Genomics, proteomics and bioinformatics applied to the study of rare diseases”, Malaga (3-4 May 2011), IX Congress of the Spanish Association for the Study of Inborn Errors of Metabolism (AECOM) Valencia (28-30 September 2011), Course on “Rare diseases: research, clinical care and social awareness”, Valencia (5 October 2011), II Spanish Biobank Network Congress, Tarragona (20-21 October 2011), VII Annual Conference of the Spanish Association for the Information and the Research of genetic renal diseases (AIRG-E), Barcelona (19 November 2011).

Research activities and E-Rare partnership

National research activities

The results of CIBERER’s 2010 research activities, which are organised into seven programmes (Genetic Medicine, Inherited Metabolic Medicine, Mitochondrial Medicine, Paediatric and Developmental Medicine, Sensorineural Pathology, Endocrine Medicine and Inherited Cancer and Related Syndromes), were compiled in 2011 Scientific Report. This report²⁰⁴ describes and updates the activity of each of the research groups that comprise the Centre, including their research lines, training and dissemination activities, scientific publications, ongoing projects, clinical trials and clinical guidelines. CIBERER has also defined its strategy for 2012, which has been designed to reinforce compliance with the objectives laid down in the Rare Disease Strategy of the Spanish National Health System and follows the main lines drawn and executed through the 2011 plan of action, while taking into account and accommodating budget cuts. The proposed action plan for 2012 emphasises translation and transfer of research and knowledge and includes two new structures: the Platform of Bioinformatics for Rare Diseases (BIER), whose main mission is to cooperate with the experimental groups working with genomic data for its analysis and interpretation; and the Neurogenetics platform, which will provide service performing genetic analysis of rare inherited neuropathies. Another novelty featured in the CIBERER 2012 Action Plan is the call for Cooperative and Complementary Intramural Actions (ACCI), intended to foster cooperative research with an internal but competitive call for which transfer and translative components will be criteria for the funds assignment.

²⁰³ http://www.ciberer.es/documentos/Libro_Ingles.pdf

²⁰⁴ <http://www.ciberer.es/documentos/Memoria%20Cientifica%20CIBERER%202010.pdf>

ISCIII recently created RetBioH (a network of biobank including biobanks for rare diseases and attached to it with a sustainable funding of €6 million per year, that will be the Spanish leg of BBMRI (the European biobanking infrastructure in process of constitution as an ERIC).

In 2011 the GentxGent Foundation (Comunitat Valenciana) received €175'000 Euros from voluntary donors to fund rare diseases research projects.

E-Rare

Spain participated in the 3rd Joint Transnational Call in 2011 and supports a Spanish team in one of the selected consortia.

IRDiRC

The Carlos III Health Institute, is a committed member of the IRDiRC and will be the funding agency for collaborative research projects awarded by IRDiRC to institutions with the facilities to carry out the project and legal and fiscal address placed in Spain. In 2011 the ISCIII launched a call of Collaborative Research Projects with an overall funding up to €10 million for 5 consecutive years aligned with the IRDiRC scientific objectives, funding level, policies and governance structure. Three proposals have been selected for funding at national level: TREAT-CMT, DRUGS4RARE and a collaborative research joint project to create a National Registry for rare diseases at the IIER. These three projects are national projects, evaluated by an international review panel, but within the scope of IRDiRC, and targeting IRDiRC objectives, and so communicated to and recognised by its secretariat.

D.26. SWEDEN

National plan for rare diseases and related actions

At the end of 2011 National Board of Health and Welfare announced the new *National Focal Point* (NFSD-*Nationella Funktionen för Sällsynta Diagnoser*) for rare diseases. Their work will include the promoting of coherence and coordination of health care resources for people with rare diseases and to accomplish increased coordination with the social insurance, employment services, social services, NGOs and other actors. They will also contribute to the dissemination of knowledge and information and to the exchange of good practice and experiences. An inventory of available resources for people with rare diseases is one of the first tasks for the function. The work will start on 1 January 2012 and the assignment has been entrusted to the non-profit rare disease facility Ågrenska.

The Swedish Government assigned in October 2011 to the National Board of Health and Welfare the mission to develop a strategy for rare diseases. This assignment will be presented in line with the Council Recommendation adapted to the Swedish demands. The National Board of Health and Welfare will develop the strategy with the National Function for rare diseases and other stakeholders. The assignment will be presented to the Government in October 2012. The National Board of Health and Welfare is currently considering how the future work with the national strategy shall proceed.

Training and education initiatives

A number of courses were held on the initiative of patient organizations and knowledge centres for rare diseases. Ågrenska arranged in 2011 twenty-two national family stays such as empowerment programmes, including two educational days for professionals and six empowerment programmes for adults (adult stays) with a rare disease. University hospital teams educate and inform patients and families during educational days. Training is given to professionals and representatives from the social services. The *Orphanet* team helps specialists in training about how to find validated information on rare diseases.

National rare disease events in 2011

A number of events were organised in Sweden to mark Rare Disease Day 2011.

Swedish Orphanet team at Karolinska Institute organised a day-long seminar with the title “Rare Disease Research Forum - Challenges and Solutions” on 21 February 2011 at the Karolinska University Hospital. The purpose of the day was to gather researchers in the field of rare diseases and other stakeholders to meet and discuss rare disease research, its challenges and solutions. The day attracted around 65 attendees, the main group being clinical researchers from the Karolinska Institute. However, also representatives from

Industry, the Medicinal Product Agency, the National Board of Health and Welfare, the Swedish Parliament and patient organisations participated.

Riksförbundet Sällsynta Diagnoser organised activities linked to the Rare Disease Day. In the autumn of 2011 they also launched a road show. They visited the University hospitals in Uppsala, Lund/Malmö, Gothenburg, Stockholm, Linköping and Örebro to raise awareness and to present their vision of coordinated centres for rare diseases in Sweden.

Ågrenska arranged a national conference on narcolepsy to improve holistic competence and build network. The target group was professionals with knowledge and experience of children who has developed the disease as a consequence of the Pandemrix vaccine.

Research activities and E-Rare partnership

IRDIRC

Swedish funding agencies are not yet committed members of the IRDiRC. The progress of the consortium activity programme is followed by Orphanet Sweden and the National Board of Health and Welfare.

D.27. UNITED KINGDOM

National plan/strategies for rare diseases and related actions

Although there are these measures in place, a national plan or strategy for rare diseases in the UK has not yet been adopted in the UK. The plan should be produced by the end of 2013.

Rare Disease UK (RDUK) and EURORDIS organised a UK National Conference on Rare Diseases, in the context of the Europlan conference on 16 November 2010²⁰⁵ in Manchester to examine proposals for a plan which were then launched on Rare Disease Day 2011. The proposals took the form of a report entitled *'Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy'*²⁰⁶, presented at the House of Commons on 28 February 2011. The report outlines 27 broad recommendations from RDUK and over 85 specific recommendations covering five areas which an effective strategy needs to address: the coordination of research, prevention and diagnosis, commissioning and planning, patient care, information and support, and delivering coordinated care. All four health departments across the UK have signalled their willingness to take on board RDUK's recommendations in developing a strategy for rare diseases and to work in collaboration with the group.

The Specialised Healthcare Alliance (SHCA) held on 16 November 2010 the SHCA Conference on Delivering Quality in Specialised Care. The conference was opened by the Minister for Quality at the Department of Health. This conference helped inform the 2011 report *"Leaving No One Behind: Delivering High Quality, Efficient Care for People with Rare and Complex Conditions"*²⁰⁷ (see section on "National patient alliances of patient organisations and patient representation": this report was part of the iterative process seeking to inform the UK's response to the EC Council Recommendation on an action in the field of rare diseases, as well as future arrangements for specialised commissioning.

A national plan, aided by the recommendations made by these groups, was developed during 2011. The public consultation was launched on 29 February 2012 to mark Rare Disease Day 2012²⁰⁸. The UK-wide consultation will be open until 25 May 2012. Responses to the consultation will inform the final plan, due to be produced by the end of 2013. The proposed plan recommends using specialist centres to make exact diagnosis; acknowledges that all doctors should have the right training to be aware of the possibility of a rare disease; and recommends that the care of patients with rare diseases be better coordinated.

Other related actions

Deciphering Developmental Disorders (DDD)²⁰⁹ was launched in 2011: this project aims to improve the diagnosis and care of children in the UK who fail to develop normally due to changes in their genetic makeup. The project seeks to capture the genetic make-up of up to 12 000 children with intellectual or physical delays or who have multiple malformations. A collaborative effort between the National Health Service Clinical Genetics

²⁰⁵ [http://download.EURORDIS.org/europlan/2 EUROPLAN Guidance Documents for the National Conference/final_report_uk_europlan.pdf](http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_uk_europlan.pdf)

²⁰⁶ www.rare-disease.org.uk/documents/RD-UK-Strategy-Report.pdf

²⁰⁷ <http://www.shca.info/PDF%20files/SHCA%20Report%202011%20low%20res.pdf>

²⁰⁸ <http://www.dh.gov.uk/health/2012/02/consultation-rare-diseases/>

²⁰⁹ <http://www.sanger.ac.uk/about/press/2011/110322.html>

Services across the UK and the Wellcome Trust Sanger Institute, the project will provide information for researchers and clinicians into rare chromosomal abnormalities and their possible role in disease. Another interesting facet to be explored by the project are the ethical and social aspects involved in the clinical use of new genomic technologies, including the perceptions and expectations of patients and families. The project is supported by the Health Innovation Challenge Fund, a parallel funding partnership between the Wellcome Trust and the Department of Health.

In 2011, the United Kingdom's first brain tumour tissue bank was created, housed in Southern General Hospital in Glasgow, Scotland. It will provide a large number of samples to researchers, with the goal of accelerating research toward treating this group of rare diseases. The new tissue bank, available to researchers from academia and industry, was made possible by funding from brain cancer charity Brainstrust²¹⁰.

Centres of expertise

Health ministers in England have agreed to national commissioning of services, effective 1 April 2011, for patients with the following disorders: Stickler syndrome; Wolfram syndrome; Lymphangiomyomatosis; Insulin resistance syndromes (e.g. Donohue and Rabson Mendenhall syndromes); Severe and complex forms of osteogenesis imperfecta; and Pseudo-obstruction of gut in young children. National commissioning establishes national centres of expertise for a specific disease and streamlines funding to one centralised source rather than being scattered amongst different local budgets.

Genetic testing

The Clinical Molecular Genetics Society (CMGS) issued an annual audit²¹¹ of in 2011 genetic testing activity. Such information is valuable to understanding the rare disease demand for testing and pre- and post-natal activity in this area. The UK audit includes number of samples, number and type of disease, number and type of tests sent for analysis and staff/workload across laboratories. The 2009-2010 audit "...shows a continued growth in national activity for each of the postnatal, prenatal and predictive testing categories, an improvement in routine reporting times and encouraging data of the capturing and utility of activity...". Prenatal diagnosis reports were recorded for 120 different disorders, with 86% being for common aneuploidies. There were 12839 prenatal reports, of which 1744 were for disorders excluding aneuploidy. Non-invasive foetal sexing testing accounted for 19% of non-aneuploidy screening. Monogenic disorders include sickle cell anaemia (440), beta-thalassaemia (119), SMA type I (61), Duchenne muscular dystrophy (32), Huntington disease (25), craniosynostosis (9), and others. For postnatal activity, there was a 31% increase in single gene disorders for 2009-2010. This jump reflects the inclusion of data from a new large volume provider. There was a mean number of 789 reports for fragile X testing across 18 providers. There was a mean number of 706 cystic fibrosis reports across 20 providers.

A new report²¹² from the Foundation for Genomics and Population Health (commonly known as the PHG Foundation) encourages the mainstream medical specialities to become versed in the field of genetics, incorporating genetic knowledge and technology into their offer. The authors of the report propose "...a shift of the axis of main clinical responsibility for individual patients with inherited disease from clinical genetics to the relevant speciality - cardiology, ophthalmology, renal medicine, neurology or a host of other areas". Evoking a future in which, "...rather than genetics 'moving into mainstream medicine' ... clinical areas develop and expand to integrate new clinical expertise relevant to inherited disease and a new set of genomic technologies into clinical pathways as relatively specialised areas within their own service", the report acknowledges that close cooperation with specialist clinical and laboratory genetics service would be necessary in order to promote and sustain such a shift.

Nowgen, a leading UK centre for genetics seeking to inform and improve genetic medicine via training, education, public engagement, research and innovation, issued its Review and Programme for 2011-2012²¹³ in 2011. Nowgen, working with Orphanet UK, will continue its commitment to facilitating access to high quality information on rare diseases and orphan medicinal products for professionals, patients and the public.

The UKGTN has recommended tests for 536 diseases and 714 genes for NHS commissioning for service from April 2011.

²¹⁰ http://www.gla.ac.uk/news/headline_212335_en.html

²¹¹ http://www.cmgs.org/CMGS%20audit/2010%20audit/secure4Final_Audit09_10.pdf

²¹² <http://www.phgfoundation.org/file/7962/>

²¹³ <http://www.nowgen.org.uk/CubeCore/.uploads/documents/NowgenReviewandWorkProgramme20112012.pdf>

National alliances of patient organisations and patient representation

Rare Disease UK

RDUK launched a new report entitled *'Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy'*²¹⁴ at the House of Commons on 28 February 2011. The report outlines 27 broad recommendations from RDUK and over 85 specific recommendations covering five areas which an effective strategy needs to address: the coordination of research, prevention and diagnosis, commissioning and planning, patient care, information and support, and delivering coordinated care. All four health departments across the UK have signalled their willingness to take on board RDUK's recommendations in developing a strategy for rare diseases and to work in collaboration with the group. Following consultation and production of the strategy, RDUK will then be scrutinising the implementation of a strategy.

Specialised Healthcare Alliance (SHCA)

In 2011 the SHCA published a new report. *"Leaving No One Behind: Delivering High Quality, Efficient Care for People with Rare and Complex Conditions"*²¹⁵ which takes stock of recent developments in specialised commissioning and "identifies a series of key drivers in delivering improved care and value for people with rare and complex conditions". These include building on the Carter Review of Commissioning Arrangements for Specialised Services in 2005/06 (which "...marked a watershed in the development of associated policy and has yielded real benefits for patients in the years that followed); the impetus of the patient organisations as a vehicle to "drive up standards"; improved patient-physician collaborations; the contribution of NICE quality standards; the development of multidisciplinary networks; outcome measures that maximise effectiveness and efficiency; and the development of patient registries with sharply focused datasets.

To produce this report, the SHCA organised a series of nine workshops focussing on quality and productivity in services including rare cancers, haemophilia, blood and marrow transplantation which fed into the report *"Leaving No One Behind"*

Stemming from the recommendation in this report concerning the central importance of patient registries in specialised care, the SHCA has now produced the *Registries Guide 2011*²¹⁶. Intended for use by patient organisations - particularly those representing people with rare and complex conditions – the guide seeks to respond to two key questions: Would it be useful and practicable for a particular patient organisation to set up a registry, and what are the key issues that must be taken into account when setting up a registry. The guide also provides tips, case studies and useful links.

Good practice guidelines

New guidance document²¹⁷ on the initial evaluation of paediatric patients with suspected sex development disorders was published in 2011. The free-access article appearing in *Clinical Endocrinology* provides guidance on the initial evaluation of an infant or adolescence with a suspected disorder of sexual development. The guidance also evokes the utility of networks and registries to support clinicians, and support groups and psychological services to support the patient and parents.

National rare disease events in 2011

To mark Rare Disease Day 2011, RDUK coordinated a number of events across the UK. RDUK also launched a new report entitled *'Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy'*²¹⁸ at the House of Commons on 28 February 2011, which was presented to Earl Howe, Minister at the Department of Health. The event brought together patient organisations, patients, carers, healthcare providers, clinicians, researchers, health workers, industry representatives and policy makers. Over one hundred and fifty delegates attended, representing more than one hundred organisations. The report outlines RDUK's recommendations for a strategy for rare diseases and is a product of a year and a half of work in collaboration with members and the broad rare disease community. Receptions were also organised at the Scottish Parliament (22 February 2011) Northern Ireland and Welsh Assemblies (16 March 2011) by RDUK and Genetic Alliance UK. At each of the events, attendees who participated in RDUK's contact campaign took the opportunity to meet with their local politician. Many other patient organisations mark the day with events.

Other events included the Annual Conference of Genetic Alliance UK (24 May 2011), 6th British Society Human Genetic (BSHG) Conference (5-7 September 2011).

²¹⁴ www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf

²¹⁵ <http://www.shca.info/PDF%20files/SHCA%20Report%202011%20low%20res.pdf>

²¹⁶ <http://www.shca.info/PDF%20files/Registries%20Guide%20-%20FINAL.pdf>

²¹⁷ <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3132446/?tool=pubmed>

²¹⁸ www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf

Research activities and E-Rare partnership

IRDiRC

The National Institute for Health Research is currently a committed member of the IRDiRC.

Orphan medicinal products

Other initiatives to improve access to orphan medicinal products^{219,220}

The National Institute for Health and Clinical Excellence (NICE) will start commissioning expert assessments for off-label medicine use starting spring 2012²²¹. These assessments will not constitute formal guidance, but rather will provide “a summary of available evidence on selected unlicensed drugs to inform local decision-making”. The National Health Service (NHS) in England receives some 1000 specific requests for off-label use annually. The announcement for the off-label product assessments has been met with approval from the rare disease community.

²¹⁹ Written using information from *KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009* (pp 62-66)

²²⁰ Written using information from the *Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision)* (p23).

²²¹ <http://www.nice.org.uk/newsroom/news/BetterInformationOnUnlicensedDrugS.jsp>

E. OTHER EUROPEAN COUNTRIES' ACTIVITIES IN 2011

E.1. CROATIA

National plan/strategy for rare diseases and related actions

During 2011 the National Commission for Rare Diseases met on the regular basis which resulted in some progress in creating the national plan for rare diseases.

The Croatian National plan for rare diseases is being developed around of the following nine priority areas:

1. Promotion of the knowledge and the availability of information on rare diseases;
2. Support of rare disease registries and securing of their sustainability;
3. Facilitation of referral centres and centres of expertise activities;
4. Improvement of the availability and quality of health services for rare disease patients (prevention, diagnosis, treatment);
5. Improvement of access to treatment with orphan medicinal products;
6. Securing the availability of special social services for rare diseases patients.
7. Empowerment of patient's organisations;
8. Encouraging research activities in the field of rare diseases;
9. International networking in the field of rare diseases.

The Second National Conference on Rare Diseases was held on 8 October 2011. Like the previous conference, it was again the meeting of all national stakeholders. Numerous problems were discussed. The need to strengthen efforts and accelerate the activities to fulfill the goals outlined during the previous conference was emphasised.

There is currently no earmarked budget for rare diseases in the national health care budget, but special funding is available however for orphan medicinal products and there is a "List of Especially Expensive Drugs".

Neonatal screening policy

Preliminary activities to extend the newborn screening program by tandem mass spectrometry are underway. The national screening laboratory has been renovated and equipped with tandem mass spectrometry technology. The remaining problems to extend the screening are to clarify legislation and funding of the running costs.

National alliances of patient organisations and patient representation

In 2011 the Croatian Society of Patients with Rare Diseases²²² elected a new president, and was supported by an employee.

Sources of information on rare diseases and national help lines

Official information centre for rare diseases

From 2011 the new office of the Croatian Society for Rare Diseases, part of the Croatian Medical Association, started to function as an information center, financed primarily by donations. This service has the support of the government and is consulted by governmental institutions, but it is not designated as an official information centre.

Help line

The national alliance has started the preparations for the official help line. It should be available in 2012 after the education of volunteers and a media campaign. It will be financed through the project and by donations.

National rare disease events in 2011

In Croatia, there are regular professional meetings dedicated to rare diseases organised by the Croatian Society for Human Genetics, Croatian Society for Rare Diseases, the Section for Metabolic Diseases of the Croatian Paediatric Society and different professional and patient organisations.

²²² <http://www.rijetke-bolesti.hr>

A Rare Disease Day press conference was organised in Zagreb on 23 February 2011, by the Croatian Society for Rare Diseases. The main goal was to emphasise the issues we are dealing with, such as this year's topic - inequality. The press conference was held at the City Zagreb's Forum Venue and was supported by the City Zagreb's Department of Health. Rare Disease Day was once again supported by President Prof. dr. Ivo Josipović, who gave a video message to be conveyed to the public by TV in order to raise the public and media awareness about rare diseases.

In addition to this event, Croatia's four biggest cities (Zagreb, Split, Rijeka and Osijek) marked the Rare Disease Day with a range of activities. Information booths were placed in the square in four major cities informing the public about rare diseases. Public lectures were given in order to bring more clarity to the issue of rare diseases and to share experiences of those affected by rare diseases. A round table meeting took place with the participation of medical professionals, health administration representatives and rare diseases patient in Zagreb on 28 February 2011.

During the Fifth Croatian Congress on Human Genetics from 20 to 24 June 2012, there was a round table discussion dedicated to rare diseases, with participation of the experts and representatives of patients groups.

Research activities and E-Rare partnership

IRDIRC

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

E.2. ISRAEL

National plan/strategy for rare diseases and related actions

A law concerning rare diseases has been submitted to the government for consideration.

National rare disease events in 2011

For the first time, to mark Rare Disease Day 2011, a one day conference was organised by Orphanet Israel at the Schneider Children's Medical Center of Israel on 28 February 2011. There were about 300 participants including parliament and Ministry of Health representatives, physicians and patients.

Research activities and E-Rare partnership

E-Rare

Israel is part of the E-Rare consortium, represented by the CSO-MOH (Ministry of Health) and participated in the first two transnational calls in 2007 and 2009 (Israel is represented in three of the selected projects in the first two calls). Israel participated in the third call in the context of E-Rare2 in 2011 and funds Israeli teams participating in 4 of the selected consortia.

IRDIRC

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

E.3. NORWAY

National plan/strategy for rare diseases and related actions

In 2010 the Ministry of Health requested a report on how to reorganise the centres for rare disorders under one administration. The working group led by the Directorate of Health delivered the report²²³ on 1 December 2010. The recommendations were supported by the Directorate, and the Ministry's conclusion is expected in

²²³ http://www.helsedirektoratet.no/vp/multimedia/archive/00316/Revidert_rapport_Sa_316599a.pdf

2012. In addition to this the Regulation on “*Approval of hospitals and national services*”²²⁴, which includes centres of expertise for rare disorders, was enforced from the start of 2011: this Regulation imposes the same criteria and demands on centres of expertise for rare disorders as on other national centres of expertise. The document has been translated to English and published²²⁵.

Centres of expertise

In Norway centres of expertise are entitled national competence services. The Regulation on “*Approval of hospitals and national services*”²²⁶ (section 4, §4-5 and §4-6) outline the requirements and responsibilities for the national competence services, and §4-3 and §4-4 regulate requirements and responsibilities for national and multi-regional treatment services.

Neonatal screening policy

The Government concurred with the recommendations and sanctioned in October 2010 newborn screening for the following conditions: Propionic acidemia, Methylmalonic acidemia, Isovaleric acidemia, Holocarboxylase synthetase deficiency, Biotinidase deficiency, β -Ketothiolase deficiency, Glutaric acidemia type I, Medium-chain acyl-CoA dehydrogenase deficiency, Long-chain L-3-Hydroxy dehydrogenase deficiency, Trifunctional protein deficiency, Very long-chain acyl-CoA dehydrogenase deficiency, Carnitine uptake defect, Carnitine palmitoyltransferase I deficiency, Carnitine palmitoyltransferase II deficiency, Carnitine acylcarnitine translocase deficiency, Glutaric acidemia type II, Maple syrup urine disease, Homocystinuria, Phenylketonuria, Tyrosinemia type I, Congenital adrenal hyperplasia, Congenital hypothyroidism and Cystic fibrosis. The expansion of the program was to be implemented following a revision of the legal regulation on genetic testing. The new regulation was sanctioned in December 2011 with effect from January 1, 2012. Under this regulation, prior to newborn screening, it is expected that the parents are well informed about tests, methods and possible consequences. Newborn screening will be based on informed consent, and residual samples may be kept in a diagnostic bio bank for 6 years. Consent is also required for later use of demographic data, analytical results and information related to diagnostic follow-up and treatment. This information will be stored in a quality register for evaluation of the screening program. Parents can decline storage or use of remaining samples in research. In general, use of screening samples in research will require an approval from an ethical committee and a signed agreement from the parents.

National rare disease events in 2011

Frambu Resource Centre for Rare Disorders marked the Rare Disease Day 2011 by organizing an interview with two families having a child with a rare disease. The interview was broadcasted by the Norwegian Broadcasting Association in their evening news. The interview was located at Frambu and we also got the possibility to inform about the struggle for people diagnosed with a rare disease. Another interview with a third family was made by the Norwegian News Agency (NTB) who published the story in different newspapers all over Norway.

Research activities and E-Rare partnership

IRDIRC

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

E.4. SWITZERLAND

National plan/strategies for rare diseases and related actions

With the aim of filling this gap in rare disease policy in Switzerland, on 16 December 2010, Ruth Humbel, member of the Health Commission in the Parliament submitted to the National Council a postulate for “*a national strategy for improving the health situation of people with rare diseases*”. The National Council followed the recommendation of the Federal Council and accepted the claim in March 2011. The Federal

²²⁴ Unofficial translation: <http://www.regjeringen.no/upload/HOD/SHA/forskrift-eng-270911.pdf>

²²⁵ Unofficial translation: <http://www.regjeringen.no/upload/HOD/SHA/forskrift-eng-270911.pdf>

²²⁶ Unofficial translation: <http://www.regjeringen.no/upload/HOD/SHA/forskrift-eng-270911.pdf>

Council has consequently assigned the Federal Office of Public Health the task of submitting a proposal. An alliance²²⁷ encompassing patient organisations, the Swiss Medical Association, university hospitals, the rare disease informational portal Orphanet-Switzerland and representatives from the pharmaceutical industry, then joined forces in August 2011 to promote a national strategy for rare diseases in Switzerland. Chaired by National Councillor Ruth Humbel, this newly-formed community of interest for rare diseases (*IG rare diseases*) is actively engaged in advocating the development of a national action plan for the country's rare disease patients.

The Federal Office of Public Health is working on a project that will facilitate the reimbursement of rare disease medicinal products. A round table meeting held on 23 September 2011 gave health professionals, representatives of the biopharmaceutical industry, health insurances, patient organisations and local government representatives the opportunity to exchange views. Amongst the topics broached were strategies for reimbursing products and evaluating their benefits, as well as ways to improve diagnosis, for which the French model of identifying and creating networks of expertise was evoked. Finally, the issue of negotiating prices for rare disease treatments was discussed, as well as the necessity for clinicians and researchers to collaborate to enhance the understanding of rare disease treatments. A second round table was held in early 2012. The project should then be open for consultation later in 2012.

Centres of expertise

In 2011, several centres have been officially appointed in the fields of metabolic diseases, retinoblastoma, primary immunodeficiency in children, surgery of the liver and biliary tract in children, rare medullar tumours, surgery of epilepsy and neurosurgery of complex vascular anomalies of the central nervous system.

Neonatal screening policy

The request to implement the neonatal screening for cystic fibrosis, initiated by the Swiss Cystic Fibrosis Task Force, was approved from the Federal Office of Public Health in December 2010 and a 2-year-pilot project started in January 2011.

Genetic testing

Genetic testing laboratories require formal authorisation²²⁸ to practice from the government; more than 60 public and private laboratories provide genetic testing, although not all tests are reimbursed. Since 2011, interlaboratory comparisons (EQA or other) must be performed at least once per year for every analysis proposed by genetic testing laboratories. Genetic counselling is formally required and is usually provided by doctors specialised in medical genetics or by referring doctors.

The efforts of genetic health professionals led to the approval on 2 December 2010 by the Federal Department of Home Affairs of the introduction (as of 1 April 2011) of an orphan disease regulation for the reimbursement of genetic laboratory testing of rare genetic diseases by the compulsory health insurance even if this test did *not* appear in previous list of approved tests or if the test is carried out abroad. An individual application for reimbursement is required and has to be submitted to the health insurance medical examiner (HIME) responsible.

National alliances of patient organisations

In 2011, ProRaris, as a newly founded Alliance, put all its efforts in the increasing of awareness of rare diseases in Switzerland. In the framework of the 4th International Rare Disease Day, ProRaris organised the first conference on rare diseases in Switzerland addressing the main topic "*Inequal access to health care*" with the lack of coverage by health insurances of genetic testing and orphan medicinal products.

As a patients' representative, ProRaris is part of the *Community of Interest for rare diseases*, founded in August 2011, and is strongly implied in political advocacy for the elaboration of a national plan for rare diseases. Within the framework of the new project supported by the European Commission to support rare disease national plans, the proposal of ProRaris to organise, by 2013, a EUROPLAN conference in Switzerland with all stakeholders, which will be supported by EURORDIS, was selected.

²²⁷ http://www.orphanet.ch/PDF/MEDIENMITTEILUNG_Gruendung_IG_Seltene_Krankheiten_f_def.pdf

²²⁸ Federal Act on Human Genetic Testing (HGTA) of 8 October 2004, <http://www.admin.ch/ch/e/rs/8/810.12.en.pdf>

Sources of information on rare diseases and national help lines

Orphanet activity in Switzerland

As a collaborating partner of the Orphanet Joint Action, Orphanet Switzerland is not entitled to the EU funding and must ensure its funding at national level. In 2011, the president of the Swiss Conference of the Cantonal Ministers of Public Health (GDK/CDS) guaranteed a global budget for 2011 and 2012 for Orphanet. In 2011 the team launched the Orphanet Switzerland national website²²⁹.

National rare disease events in 2011

To mark Rare Disease Day 2011, the first conference on rare diseases in Switzerland was organised on 19 February 2011 in Bern by ProRaris, the new Swiss Alliance, and by Orphanet Switzerland. Around 450 participants, including patients, health professionals, scientists and politicians, met to learn, share and discuss the rare diseases public health issue.

Telethon Switzerland is a regular, annual fixture and organised a fund raising event at the start of December 2011 for rare diseases.

Research activities and E-Rare partnership

National research activities

The *Gebert Rűf Foundation*²³⁰, a Swiss grant programme specifically for rare diseases, announced its third call for projects in 2011. In 2011, the chosen topics were: Prodrug Platform for Rare Colonic Diseases; Treatment for Dysferlinopathies; Vaccination for the Prevention and Cure of Inflammatory Bowel Disease; Host- and Pathogen-Derived Factors in Chronic Mucocutaneous Candidiasis; Rational Targeting of FOXC2 Haploinsufficiency; and Role of snoRNAs in the Development of Prader Willi Syndrome. The knowledge gained should lead to a better understanding of the genetic, molecular and biochemical processes underlying these diseases and pave the way towards new forms of treatment or diagnostics. A further aim is to improve the transfer of basic research findings into clinical practice. The focus must be on innovation, feasibility and effectiveness, while attaining high scientific and technological standards.

IRDiRC

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

Orphan medicinal products

Orphan medicinal product reimbursement policy

As of 2 February 2011 the Federal Council put two new articles of the Federal Ordinance on the Health Insurance into force stipulating that the off label use of drugs and the treatment with drugs not listed on the list of the reimbursed drugs (Spezialitätenliste) is admitted in case of life-threatening diseases if an important therapeutic benefit is expected from the treatment and if there is no reimbursed alternative. The Ordinance gives the insurers the freedom to decide about the maximum amount to be reimbursed.

The Federal Office of Public Health is working on a project that will facilitate the reimbursement of rare disease medicinal products. A round table meeting held on 23 September 2011 gave health professionals, representatives of the biopharmaceutical industry, health insurances, patient organisations and local government representatives the opportunity to exchange views. Amongst the topics broached were strategies for reimbursing products and evaluating their benefits, as well as ways to improve diagnosis, for which the French model of identifying and creating networks of expertise was evoked. Finally, the issue of negotiating prices for rare disease treatments was discussed, as well as the necessity for clinicians and researchers to collaborate to enhance the understanding of rare disease treatments. A second round table will be held in early 2012. The project should then be open for consultation later in 2012.

²²⁹ <http://www.orpha-net.ch/?lng=FR>

²³⁰ <http://www.grstiftung.ch/en.html>

⁶ <http://www.blackswanfoundation.ch/>

E.5. TURKEY

National plan/strategies for rare diseases and related actions

The 1st National Rare Disease Symposium took place on 27 November 2011 in Istanbul. Organised by the Orphanet Turkey team, this event brought together representatives from the Turkish Ministry of Health, Social Security authorities, patient organisations, scientists and industry. The symposium covered 3 main topics: rare disease and orphan medicinal products organisations and databases in EU; International and European Union and legislation on rare diseases and orphan medicinal products, and the current situation in Turkey; and problems and difficulties in the treatment and management of rare diseases in Turkey - how to overcome these obstacles. Participants discussed the current legislation at EU level in the field as well as the current situation in other countries such as Italy, France and Bulgaria. A second symposium is planned for 2012 to discuss the areas to be considered in the scope of a national plan for rare diseases.

Sources of information on rare diseases and national help lines

Orphanet activity in Turkey

The team organised the 6th Eastern European Rare Disease Conference in Istanbul on 24-26 November 2011 and the 1st National Rare Disease Symposium in Istanbul on 27 November 2011.

National rare disease events in 2011

A press bulletin was released for Rare Disease Day 2011. Many web based media portals, daily journals have mentioned the importance and the goals of Rare Disease Day. Orphanet Turkey was featured in four national TV channel programs in the same week. In addition, some rare diseases have an annual designated day (e.g. phenylketonuria day, 1 June) to raise awareness of these diseases.

Research activities and E-Rare partnership

E-Rare

Turkey also participated in the 2011 3rd Joint Transnational Call and will support Turkish research teams in 3 of the selected consortia.

IRDIRC

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

Orphan medicinal products

At the end of 2011, the Directorate General of Pharmaceuticals and Pharmacy (IEGM), attached to the Turkish Ministry of Health, transformed into the independent national competent authority, the Turkish Pharmaceuticals and Medical Devices Agency (TİTCK). In 2010, the Orphan Drug Study Group (ODSG) was formed from officers working at the Directorate-General of Pharmaceuticals and Pharmacy (IEGM), TİTCK from here on. The main purpose of ODSG was to prepare the national Guideline for Orphan Medicines. In the course of activities, ODSG compiled information relating to orphan medicinal products and rare diseases in the European Union (EU), studied Regulations 141/2000/EC and 847/2000/EC, and developed a national approach for orphan medicinal product policies in Turkey. The National Draft Guideline for Orphan Medicines was formed in the first quarter of 2011. The Draft Guideline was open for consultation by the pharmaceutical sector, and responses received by the second half of 2011. The National Draft Guideline is ready to be put into force.

LIST OF CONTRIBUTIONS²³¹

Contributions by country:

Austria

Contributions in 2010

Till Voigtlander and Christine Schragel (*Orphanet Austria, Medical University of Vienna*)

Contributions in 2011

Till Voigtlander and Ursula Unterberger (*Orphanet Austria, Medical University of Vienna*)

Iris Fortmann (*FWF Austrian Science Fund*)

Brigitte Blöchl (*Medical University Vienna*)^a

Claudia Hahl/Christine Leopold (*Gesundheit Österreich GmbH/ Austrian Health Institute*)

Contributions in 2012

Claudia Hahl (*Gesundheit Österreich GmbH/ Austrian Health Institute*)

Till Voigtlander (*Orphanet Austria, Medical University of Vienna*)

National Coordination Centre for Rare Diseases (*CCRD*)

Main Association of Austrian Social Security Institutions (*HVB*)

Austrian Ministry of Health (*BMG*), Ministry of Science and Research (*BMWF*)

Patient Organisation for Rare Diseases (*Pro Rare*)

Austrian Pharmaceutical Association (*Pharmig*)

DEBRA Austria

Medical University Vienna (*MUW*)

Gesundheit Österreich GmbH (*GÖG*)

Pharmaceutical Pricing and Reimbursement Information Network (*PPRI*)

Validated by: Helmut Hintner (*EUCERD Representative Austria, University of Salzburg*)

Belgium

Contributions in 2010

Jean-Jacques Cassiman and Elfriede Swinnen (*Orphanet Belgium, Human Genetics Centre, KU Leuven*)

Herwig Jansen (*Scientific Institute of Public Health*)

Contributions in 2011

The revision and the validation of the report has been carried out by the Public Federal Service of Health in collaboration with the National Institute for Health and Disability Insurance and the Institute of Public Health as well as the Regions and the Communities.

Contributions in 2012

Saskia Van den Bogaert (*Federal Public Service of Health, Food Chain Safety and Environment*)

Bruce Poppe (*Federal Public Service of Health, Food Chain Safety and Environment*)

Viviane Van Casteren (*Scientific Institute of Public Health - WIV-ISP*)

Elfriede Swinnen (*Orphanet Belgium, (Scientific Institute of Public Health - WIV-ISP)*)

Herman Van Oyen (*Scientific Institute of Public Health - WIV-ISP*)

Geneviève Haucotte (*National Institute for Health and Disability - NIHDI*)

Ri De Ridder (*National Institute for Health and Disability -NIHDI*)

André Lhoir (*Federal Agency for Medicines and Health Products - FAGG-AFMPS*)

Gert Matthijs (*KU Leuven*)

Jean-Jacques Cassiman (*Fund for Rare Diseases and Orphan Drugs*)

Freia Van Hee (*Fonds de la Recherche Scientifique - FNRS*)

Jonathan Ventura (*RadiOrg.be*)

Pol Gerits (*EUCERD Representative Belgium, Directorate-General Organisations of health care establishments*)

Validated by: Pol Gerits (*EUCERD Representative Belgium, Directorate-General Organisations of health care establishments*)

²³¹ 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.

Bulgaria

Contributions in 2010

Rumen Stefanov and Ralitzia Jordanova (*Orphanet Bulgaria, Bulgarian Association for Promotion of Education and Science BAPES – Information Centre for Rare Diseases and Orphan Drugs*)

Tsonka Miteva (*Bulgarian Association for Promotion of Education and Science BAPES – Information Centre for Rare Diseases and Orphan Drugs*)

Vladimir Tomov (*President of the National Alliance of People with Rare Diseases*)

Contributions in 2011

Georgi Iskrov, Tsonka Miteva (*Bulgarian Association for Promotion of Education and Science BAPES – Information Centre for Rare Diseases and Orphan Drugs*)

Rumen Stefanov (*Orphanet Bulgaria, Bulgarian Association for Promotion of Education and Science BAPES – Information Centre for Rare Diseases and Orphan Drugs*)

Radka Tincheva (*EUCERD Representative Bulgaria, Chair of the National Advisory Council on Rare Diseases, University Paediatric Hospital Sofia*)

Alexey Savov (*University Hospital of Obstetrics and Gynecology, Sofia*)

Iva Stoeva (*University Pediatric Hospital – Endocrine screening programme*)

Contributions in 2012

Radka Tincheva (*EUCERD Representative Bulgaria, Chair of the National Advisory Council on Rare Diseases, Coordinator of the National Plan for Rare Diseases, University Paediatric Hospital Sofia*)

Rumen Stefanov (*Orphanet Bulgaria, Bulgarian Association for Promotion of Education and Science BAPES – Information Centre for Rare Diseases and Orphan Drugs*)

Vladimir Tomov (*President of the National Alliance of People with Rare Diseases*)

Alexey Savov (*University Hospital of Obstetrics and Gynecology, Sofia*)

Iva Stoeva (*University Pediatric Hospital – Endocrine screening programme*)

Georgi Iskrov, Tsonka Miteva (*Bulgarian Association for Promotion of Education and Science BAPES – Information Centre for Rare Diseases and Orphan Drugs*)

Validated by: Radka Tincheva (*EUCERD Representative Bulgaria, Chair of the National Advisory Council on Rare Diseases, University Paediatric Hospital Sofia*)

Croatia

Contributions in 2010

Ana-Stavljenic-Rukavina (*Orphanet Croatia, Zagreb University School of Medicine*)

Ingeborg Barisic (*Children's University Hospital Zagreb, Croatian Society for Rare Diseases, Croatian Medical Association*)

Contributions in 2011

Ingeborg Barisic (*Children's University Hospital Zagreb, Croatian Society for Rare Diseases, Croatian Medical Association*)

Contributions in 2012

Ivo Baric (*EUCERD Representative Croatia, University Hospital Centre, Zagreb*)

Vlasta Zmazek (*Croatian Society for Rare Diseases*)

Ingeborg Barisic (*Children's University Hospital Zagreb, Croatian Society for Rare Diseases, Croatian Medical Association*)

Validated by: Ivo Baric (*EUCERD Representative Croatia, University Hospital Centre, Zagreb*)

Cyprus

Contributions in 2010

Violetta Anastasiadou and Turem Delikurt (*Orphanet Cyprus, Archbishop Makarios III Medical Centre Clinical Genetics Department*)

Contributions in 2011

Lily Cannon (*Cyprus Alliance for Rare Disorders*)

Violetta Anastasiadou (*Orphanet Cyprus, Ministry of Health – Medical Public Health Services*)

Contributions in 2012

Violetta Anastasiadou (*Orphanet Cyprus, Ministry of Health – Medical Public Health Services*)

Cyprus Alliance for Rare Disorders

Validated by: Violetta Anastasiadou (*EUCERD Representative Cyprus, Ministry of Health – Medical Public Health Services*)

Czech Republic

Contributions in 2010

Milan Macek (*Orphanet Czech Republic, University Hospital Motol and 2nd School of Medicine – Charles University Prague*)
Katerina Kubackova (*COMP Representative*)

Contributions in 2011

Milan Macek (*Orphanet Czech Republic, University Hospital Motol and 2nd School of Medicine – Charles University Prague*)
Katerina Kubackova (*COMP Representative*)
Katerina Podrazilova (*SUKL*)

Contributions in 2012

Milan Macek and Marek Turnovec (*Orphanet Czech Republic, University Hospital Motol and 2nd School of Medicine – Charles University Prague*)
Katerina Kubackova (*Former COMP Representative, University Hospital Motol and 2nd School of Medicine – Charles University Prague*)

Validated by: Milan Macek (*EUCERD Representative Czech Republic, University Hospital Motol and 2nd School of Medicine – Charles University Prague*)

Denmark

Contributions in 2010

Karen Brøndum-Nielsen (*Orphanet Denmark, John F Kennedy Institute*)
Marianne Jespersen (*National Board of Health*)
Lene Jensen (*President, Rare Diseases Denmark*)

Contributions in 2011

Marianne Jespersen and Peter Saugmann Jensen (*National Board of Health*)
Ester Garne (*Eurocat*)
Stense Farholt and John Rosendal- Østegaard (*Center for Rare Diseases - Aarhus*)
Lene Jensen and Birthe Holm (*Rare Disorders Denmark*)
Allan Lund and Flemming Skovby, (*Clinic for Rare Disabilities - Copenhagen*)
Heudrun Bosch-Traberg (*Danish Medicines Agency*)
Karen Brøndum- Nielsen (*The Kennedy Center*)

Contributions in 2012

Marianne Jespersen (*National Board of Health*)
Lene Jensen (*President, Rare Diseases Denmark*)
Heudrun Bosch-Traberg (*Danish Medicines Agency*)

Validated by: Marianne Jespersen (*EUCERD Representative Denmark, National Board of Health*)

Estonia

Contributions in 2010

Andres Metspalu and Merike Leego (*Orphanet Estonia, Tartu University*)
Vallo Tillman (*COMP Representative, University of Tartu*)

Contributions in 2011

Vallo Tillman (*Orphanet Estonia, COMP Representative, University of Tartu*)
Inna Vabamäe (*Ministry of Social Affairs*)

Contributions in 2012

Vallo Tillman (*Orphanet Estonia, COMP Representative, University of Tartu*)
Inna Vabamäe (*Ministry of Social Affairs*)
Riina Žordania and Katrin Õunap (*Department of Genetics under Tartu University Hospital*)

Validated by: Inna Vabamäe (*EUCERD Representative Estonia, Ministry of Social Affairs*)

Finland

Contributions in 2010

Riitta Salonen and Leena Toivanen (*Orphanet Finland, The Family Federation of Finland, Department of Medical Genetics*)
Veijo Saano (*FIMEA*)

Contributions in 2011

Riitta Salonen (*Orphanet Finland, The Family Federation of Finland, Department of Medical Genetics*)
Veijo Saano (*FIMEA*)
Helena Kääriäinen (*National Institute for Health and Welfare, Helsinki*)

Contributions in 2012

Riitta Salonen (*Orphanet Finland, The Family Federation of Finland, Department of Medical Genetics*)
Veijo Saano (*FIMEA*)
Helena Kääriäinen (*National Institute for Health and Welfare, Helsinki*)

Validated by: Helena Kääriäinen (*EUCERD Representative Finland, National Institute for Health and Welfare, Helsinki*)

France

Contributions in 2010

Ségolène Aymé (*INSERM, SC11 – Director of Orphanet*)
Florence Suzan (*Institut national de veille sanitaire*)
Paul Landais (*Necker Children’s Hospital*)
Jean Donadieu (*Armand-Trousseau Children’s Hospital*)
Sophie Koutouzov (*GIS Maladies Rares*)
Odile Kremp (*Direction Générale de la Santé*)
Guillaume Le Henanff (*Direction de l’Hospitalisation et de l’Organisation des soins*)

Contributions in 2011

Ségolène Aymé (*INSERM, SC11 – Director of Orphanet*)
Alain Garcia (*Ministère du travail, de l’emploi et de la santé*)
Odile Kremp (*Direction Générale de la Santé*)
Florence Suzan (*Institut national de veille sanitaire*)
Paul Landais (*Necker Children’s Hospital*)
Jeanne-Marie Brechot (*Institut national du cancer*)
Annie Lorence (*Afssaps*)
Valérie Drouvot (*DGOS*)
Sophie Koutouzov (*GIS Maladies Rares*)

Contributions in 2012

Ségolène Aymé & Odile Kremp (*INSERM, US14 –Orphanet*)
François Meyer (*Haute Autorité de Santé*)
Anne d’Andon (*Haute Autorité de Santé*)
Catherine Rumeau-Pichon (*Haute Autorité de Santé*)
Brigitte Lefeuvre (*Direction Générale de la Santé*)
Patrick Cayer-Barioz (*Direction Générale de la Santé*)
Frédérique Pothier (*Direction Générale de la Santé*)
Rosemary Ancelle-Park (*Direction Générale de la Santé*)
Patrice Dosquet (*Direction Générale de la Santé*)
Lydia Le Bris (*Direction Générale de la Cohésion Sociale*)
Jacqueline Patureau (*Direction Générale de la Cohésion Sociale*)
Thomas Heuyer (*Plateforme Maladies Rares*)
Aymeric Audiau (*Alliance Maladies Rares*)
Hélène Dollfuss (*Vice President, Research, National Rare Disease Plan 2011-2014*)
Nathalie Leporrier (*Agence de la Biomédecine*)
Christine Bouveresse (*Institut de Veille Sanitaire*)
Charles Persoz (*Institut National de la Santé et de la Recherche Médicale*)
Annie Lorence (*Agence Française de Sécurité Sanitaire des Produits de Santé*)

Validated by: Alain Garcia (*EUCERD Representative France, Ministère du travail, de l’emploi et de la santé*)

Germany

Contributions in 2010

Manfred Stuhmann-Spangenberg and Kathrin Rommel (*Orphanet Germany, Medizinische Hochschule Hannover*)
Ralph Schuster (*PT-DLR*)
Georg F. Hoffmann (*Department of Pediatrics, University of Heidelberg*)
Gabriele Dreier
Daniela Eidt-Koch (*First author of the study "Strategies for improving the health care situation of patients with rare disease in Germany"*)
Birgit Schnieders (*Federal Ministry of Health*)

Andreas Reimann (ACHSE)

Contributions in 2011

Manfred Stuhmann-Spangenberg (Orphanet Germany, Medizinische Hochschule Hannover)

Ralph Schuster (PT-DLR)

Georg F. Hoffmann (Department of Pediatrics, University of Heidelberg)

Olaf Hiort (Universitätsklinikum Schleswig-Holstein)

Birgit Schnieders and Véronique Héon-Klin (Federal Ministry of Health)

Contributions in 2012

Birgit Schnieders and Véronique Héon-Klin (Federal Ministry of Health)

Georg F. Hoffmann (Department of Pediatrics, University of Heidelberg)

Olaf Hiort (Universitätsklinikum Schleswig-Holstein)

Ute Rehwald (Federal Ministry Of Research And Education)

Manfred Stuhmann-Spangenberg (Orphanet Germany, Medizinische Hochschule Hannover)

Miriam Mann (ACHSE)

Thomas Wagner (Klinikum der Johann Wolfgang Goethe-Universität)

Validated by: Birgit Schnieders and Véronique Héon-Klin (EUCERD Representative and EUCERD Alternate Representative Germany, Federal Ministry of Health)

Greece

Contributions in 2010

Michael Petersen and Sofia Dougzou (Orphanet Greece, Institute of Child Health, Athens)

Marianna Lambrou and Jan Traeger-Synodinos (PESPA - Greek Alliance for Rare Diseases)

Contributions in 2011

Michael Petersen (Orphanet Greece, Institute of Child Health, Athens)

Jan Traeger-Synodinos (PESPA - Greek Alliance for Rare Diseases)

Lia Tzala (Office of the Hellenic Cancer Registry and Rare Diseases, Hellenic Centre for Disease Control and Prevention - KEELPNO)

The Scientific Committee for Rare Diseases of the Hellenic Centre for Disease Control and Prevention (KEELPNO)

The Office for the Hellenic Cancer Registry and Rare Diseases

Christos Kattamis (EUCERD Representative Greece, Emeritus Professor, First Department pediatrics, University of Athens)

Contributions in 2012

Christos Kattamis (EUCERD Representative Greece, Emeritus Professor, First Department of Pediatrics university of Athens)

Lia Tzala (Office of the Hellenic Cancer Registry and Rare Diseases, Hellenic Centre for Disease Control and Prevention - KEELPNO)

Michael Petersen (Orphanet Greece, Institute of Child Health, Athens)

The Scientific Committee for Rare Diseases of the Hellenic Centre for Disease Control and Prevention (KEELPNO)

Catherine Moraiti (National Organisation for Medicines, COMP representative)

Jan Traeger –Synodinos (PESPA Greek Alliance for Rare Diseases)

Validated by: Christos Kattamis (EUCERD Representative Greece, Emeritus Professor First Department of Pediatrics University of Athens)

Hungary

Contributions in 2010

Janos Sandor (Orphanet Hungary, University of Debrecen, Department of Biostatistics and Epidemiology)

Gabor Pogany (HUFERDIS)

Contributions in 2011

Janos Sandor (Orphanet Hungary, University of Debrecen, Department of Biostatistics and Epidemiology)

Gabor Pogany (HUFERDIS)

Béla Melegh, (Department of Medical Genetics, University of Pécs)

Gyorgy Kosztolanyi (National Coordinator of the Hungarian National Plan)

Contributions in 2012

Janos Sandor (Orphanet Hungary, University of Debrecen, Department of Biostatistics and Epidemiology)

Gabor Pogany (HUFERDIS)

Validated by: Janos Sandor (*EUCERD Representative Hungary, University of Debrecen, Department of Biostatistics and Epidemiology*)

Ireland

Contributions in 2010

Andrew Green (*Orphanet Ireland, Our Lady's Hospital for Sick Children, Dublin*)

Contributions in 2011

Andrew Green (*Orphanet Ireland, Our Lady's Hospital for Sick Children, Dublin*)

John Devlin and Bríd O'Higgins (*Department of Health and Children*)

Idoia Gomez-Paramio (*Orphanet UK and Ireland, University of Manchester*)

Eibhlin Mulroe (*IPPOSI*)

Contributions in 2012

John Devlin (*Department of Health and Children*)

Eibhlin Mulroe (*IPPOSI*)

Kathy Tynan (*Genetic and Rare Disorders Organisation*)

Validated by: John Devlin (*EUCERD Representative Ireland, Department of Health and Children*)

Israel

Contributions in 2011

Lina Basel (*Orphanet Israel, Schneider Children's Medical Center of Israel*)

Joel Zlotogora (*Department of community genetics, Ministry of Health*)

Contributions in 2012

Lina Basel (*Orphanet Israel, Schneider Children's Medical Center of Israel*)

Joel Zlotogora (*Department of community genetics, Ministry of Health*)

Italy

Contributions in 2010

Bruno Dallapiccola and Martina Di Giacinto (*Ospedale Bambino Gesù and Orphanet-Italy, Rome*)

Domenica Taruscio and Luciano Vittozzi (*ISS, Europlan*)

Maria Elena Congiu (*Ministry of Labour, Health and Social Policies*)

A. Schieppati (*Ist. Mario Negri*)

Renza Barbon Galluppi (*UNIAMO*)

Contributions in 2011

Bruno Dallapiccola (*Orphanet Italy, Ospedale Bambino Gesù, IRCCS, Rome*)

Maria Elena Congiu (*Direzione Generale, Ministero della Salute, Rome*)

Renza Barbon Galluppi (*UNIAMO, Venice*)

Domenica Taruscio (*Istituto Superiore di Sanità, Centro Nazionale Malattie Rare, Rome*)

Giovanna Zambruno (*Istituto Dermatologico dell'Immacolata, IRCCS, Rome*)

Simona Giampaoli (*Istituto Superiore di Sanità, Rome*)

Contributions in 2012

Bruno Dallapiccola (*Orphanet Italy, Ospedale Bambino Gesù, IRCCS, Rome*)

Simona Bellagambi (*UNIAMO, Venice*)

Maria Elena Congiu (*Direzione Generale, Ministero della Salute, Rome*)

Rita Mingarelli (*Orphanet Italy, Ospedale Bambino Gesù, IRCCS, Rome*)

Domenica Taruscio (*Istituto Superiore di Sanità, Centro Nazionale Malattie Rare, Rome*)

Validated by: Bruno Dallapiccola (*EUCERD Representative Italy, Ospedale Bambino Gesù, IRCCS, Rome*)

Latvia

Contributions in 2010

Rita Lugovska and Zita Krumina (*Orphanet Latvia, Medical Genetics Clinic of the Latvian State, Children's University Hospital, Riga*)

Monta Forstmane (*Department of Health Care, Ministry of Health*)

Ieva Grinfelde (*Medical Genetics Clinic of the Latvian State, Children's University Hospital, Riga*)

Baiba Lace (*Caladrius and Medical Genetics Clinic of the Latvian State, Children's University Hospital, Riga*)

Contributions in 2011

This report has been compiled in collaboration with members of the Ministry of Health Centre of Health Economics, Health Payment Centre, State Agency of Medicines and Medical Genetics Clinic of the University Children's Hospital, Riga, including:

Dainis Krievins (*COMP Member for Latvia, University of Latvia*)

Rita Lugovska (*Orphanet Latvia, Medical Genetics Clinic of the Latvian State, Children's University Hospital, Riga*)

Antra Valdmane (*EUCERD Representative Latvia, Ministry of Health of the Republic of Latvia*)

Contributions in 2012

This report has been compiled in collaboration with members of the Ministry of Health, the National Health Service, the State Agency of Medicines, the Riga East University Hospital, the Paula Stradins Clinical University Hospital, Caladius (The Latvian Rare Disease Organisation), the Society for People with Disabilities Motus Vitae, the Haemophilia Society and the Pulmonary Hypertension Association.

Validated by: Antra Valdmane (*EUCERD Representative Latvia, Ministry of Health of the Republic of Latvia*)

Lithuania

Contributions in 2010

Vaidutis Kucinskas and Birute Tumiene (*Orphanet Lithuania, Vilnius University*)

Odetta Vitkuniene (*Ministry of Health*)

Contributions in 2011

Algirdas Utkus (*Genetics Center at Vilnius University Santarishkes Hospital*)

Andrejus Zevzikovas (*State Medication Control Agency*)

Romalda Baranauskiene, Birute Kavaliauskiene (*Ministry of Health*)

Contributions in 2012

Algirdas Utkus (*Genetics Center at Vilnius University Santarishkes Hospital*)

Birute Kavaliauskiene (*Chief Specialist of the General Medicine Division in Health Care Department at the Ministry of Health of the Republic of Lithuania*)

Jolanta Gulbinovich (*Chief Specialist of the State Medicines Control Agency under the Ministry of Health of the Republic of Lithuania*)

Validated by: Romalda Baranauskiene (*EUCERD Representative Lithuania, Ministry of Health*)

Luxembourg

Contributions in 2010

Yolande Wagener (*Orphanet Luxembourg, Ministry of Health*)

Contributions in 2011

Yolande Wagener (*Orphanet Luxembourg, Ministry of Health*)

Contributions in 2012

Yolande Wagener (*Orphanet Luxembourg, Ministry of Health*)

Guy Weber (*Ministry of Health*)

ALAN

Validated by: Yolande Wagener (*EUCERD Representative Luxembourg, Ministry of Health*)

Malta

Contributions in 2010

Isabella Borg (*Mater Dei Hospital, Department of Pathology, Genetics Unit*)

Miriam Dalmas (*Ministry for Social Policy*)

Contributions in 2011

Miriam Dalmas (*Director, Policy Development, EU & International Affairs Directorate Strategy and Sustainability Division, Ministry for Health, the Elderly and Community Care*)

Isabelle Zahra Pulis (*Director, Pharmaceutical Policy and Monitoring Directorate, Strategy and Sustainability Division, Ministry for Health, the Elderly and Community Care*)

Patricia Vella Bonanno (*CEO, Medicines Authority, Office of the Prime Minister*)

Christopher Barbara (*Chairman Pathology, Department of Pathology, Mater Dei Hospital*)

Christian Scerri (*Consultant in Genetics, Department of Pathology, Mater Dei Hospital*)

Karl Farrugia (*Director, Materials Management & Logistics, Mater Dei Hospital*)

Contributions in 2012

Miriam Dalmas (*Consultant Public Health Medicine, Office of the Chief Medical Officer, Department of Health, , Ministry for Health, the Elderly and Community Care*)

Christian Scerri (*Consultant in Genetics, Department of Pathology, Mater Dei Hospital*)

Karl Farrugia (*CEO, Central Procurement and Supplies Unit, Ministry for Health, the Elderly and Community Care*)

Christopher Barbara (*Chairman Pathology, Department of Pathology, Mater Dei Hospital*)

Isabelle Zahra Pulis (*Directorate for Pharmaceutical Affairs, Department of Health, Ministry for Health, the Elderly and Community Care*)

Patricia Vella Bonanno (*CEO, Medicines Authority, Office of the Prime Minister*)

Neville Calleja (*Directorate Health Information and Research, Department of Health, Ministry for Health, the Elderly and Community Care*)

Charlene Fenech (*Manager, Treatment Abroad Unit, Department of Health, Ministry for Health, the Elderly and Community Care*)

Hugo Agius Muscat (*National e-Health Coordinator, Ministry for Health, the Elderly and Community Care*)

Gertrude Buttigieg (*Malta Health Network*)

Joseph Camilleri (*Director General, Department of Social Security, Ministry for Justice, Dialogue and the Family*)

Validated by:

Miriam Dalmas (*EUCERD Representative for Malta & Consultant Public Health Medicine, Office of the Chief Medical Officer, Department of Health, , Ministry for Health, the Elderly and Community Care*)

Netherlands

Contributions in 2010

Martina Cornel (*Orphanet Netherlands, VU University Medical Centre*)

Gertjan Van Ommen (*Orphanet Netherlands, Leiden University Medical Centre*)

Walter Devillé (*NIVEL*)

Sonja Van Weely (*ZonWm - Steering Committee on Orphan Drugs*)

Jolanda Huizer (*ZonWm - Steering Committee on Orphan Drugs*)

Laura Fregonese (*ZonWm - Steering Committee on Orphan Drugs*)

Edvard Beem (*ZonWm - Steering Committee on Orphan Drugs*)

Contributions in 2011

Sonja Van Weely (*ZonWm - Steering Committee on Orphan Drugs*)

Jolanda Huizer (*ZonWm - Steering Committee on Orphan Drugs*)

Martina Cornel (*VU University Medical Centre*)

Cor Oosterwijk (*VSOP*)

Gerard Wagemaker (*Erasmus University Medical Center, Rotterdam*)

Bert Bakker (*Leiden University Medical Centre*)

Harry Seeverens (*EUCERD Representative Netherlands, Ministry of Health, Welfare and Sport*)

Contributions in 2012

Harry Seeverens (*EUCERD Representative Netherlands, Ministry of Health, Welfare and Sport*)

Sonja Van Weely (*ZonWm - Steering Committee on Orphan Drugs*)

Cor Oosterwijk (*VSOP*)

Validated by: Harry Seeverens (*EUCERD Representative Netherlands, Ministry of Health, Welfare and Sport*)

Norway

Contributions in 2010

Stein Are Aksnes (*Orphanet Norway, Norwegian Directorate of Health*)

Elin Ostli, Bodil Stokke, Lisbeth Myhre (*Norwegian Directorate of Health*)

Contributions in 2011

Stein Are Aksnes (*Orphanet Norway, Norwegian Directorate of Health*)

Lisbeth Myhre (*Norwegian Directorate of Health*)

Lars Gramstad (*Department of Medical Product Assessment, Norwegian Medicines Agency*)

Lisen Julie Mohr (*Frambu*)

Contributions in 2012

Lars Gramstad (*Department of Medical Product Assessment, Norwegian Medicines Agency, COMP representative*)

Rolf Dagfinn Pettersen (*Oslo University Hospital*)

Elin Østli (*Norwegian Directorate for Health, Department rehabilitation and rare disorders*)

Stein Are Aksnes (*Norwegian Directorate for Health, Department rehabilitation and rare disorders*)

Ingunn Aalvik (*Norwegian Ministry of Health and Care Services*)

Validated by: Stein Are Aksnes (*EUCERD Representative Norway, Norwegian Directorate of Health*)

Poland

Contributions in 2010

Jolanta Sykut-Cegielska (*Children's Memorial Health Institute, Warsaw*)

Mirosław Zielinski (*Polish National Forum on the Treatment of Rare Disorders*)

Jakub Adamski (*Ministry of Health*)

Contributions in 2011

Bożenna Dembowska-Bagińska (*COMP Representative Poland*)

Krystyna Chrzanowska (*Orphanet Poland, Children's Memorial Health Institute, Warsaw*)

Mirosław Zielinski (*National Forum for the Therapy of Rare Diseases*)

Contributions in 2012

Malgorzata Krajewska-Walasek, Krystyna Chrzanowska and A. Jezela-Stanek (*Orphanet Poland, Children's Memorial Health Institute, Warsaw*)

Bożenna Dembowska-Bagińska (*Department of Oncology, The Children's Memorial Health Institute Warsaw, COMP Representative Poland*)

Mirosław Zielinski (*National Forum for the therapy of rare diseases "ORPHAN"*)

Jacek Gralinski (*The Children's Memorial Health Institute, Clinical Director, Chairman of the Committee for Rare Diseases at the Ministry of Health, EUCERD representative Poland*)

Validated by: Jacek Gralinski (*The Children's Memorial Health Institute, Clinical Director, Chairman of the Committee for Rare Diseases at the Ministry of Health, EUCERD representative Poland*)

Portugal

Contributions in 2010

Jorge Sequeiros, Jorge Pinto Basto and Sandra Peixoto (*Orphanet Portugal, Institute for Molecular and Cell Biology, University of Porto*)

Luis Nunes (*Serviço Genética Médica, Hospital Dona Estefânia; President, National Plan for Rare Diseases*)

Contributions in 2011

Jorge Sequeiros, Jorge Pinto Basto and Sandra Peixoto (*Orphanet Portugal, Institute for Molecular and Cell Biology, University of Porto*)

Luis Nunes (*Serviço Genética Médica, Hospital Dona Estefânia; President, National Plan for Rare Diseases*)

Heloisa Santos (*Adviser for Medical Genetics to the Direcção-Geral da Saúde, member of the National Plan for Rare Diseases and head of the committee for the implementation of "Reference centres"*)

Marta Jacinto (*Aliança Portuguesa de Associações das Doenças Raras*)

Paula Costa (*FEDRA*)

Ana Corrêa Nunes (*INFARMED, Portuguese representative at COMP*)

Contributions in 2012

Jorge Sequeiros (*Orphanet Portugal, Institute for Molecular and Cell Biology, University of Porto*)

Fernando Guerra (*DGS - Direcção-Geral da Saúde, Ministry of Health*)

Óscar Carvalho (*INFARMED, Ministry of Health*)

Miguel Sousa (*ACSS – Administração Central Sistema de Saúde, Ministry of Health*)

Anabela Isidro (*FCT - Fundação Ciência e Tecnologia*)

Marta Jacinto (*APADR - Aliança Portuguesa de Associações de Doenças Raras*)

Paula Costa (*FEDRA - Federação Portuguesa de Doenças Raras & RARISSIMAS - Associação Nacional de Deficiências Mentais e Raras*)

Validated by: José Alexandre Diniz (*EUCERD representative Portugal, Ministry of Health – DGS*)

Romania

Contributions in 2010

Mircea Covic, Cristina Rusu and Elena Braha (*Orphanet Romania, „Gr T Popa” University of Medicine*)

Dorica Dan (*Romanian National Alliance for Rare Diseases*)

Contributions in 2011

Dorica Dan (*President Romanian Prader Willi Association, Romanian National Alliance for Rare Diseases*)

Cristina Rusu (*Orphanet Romania, „Gr T Popa” University of Medicine*)
Horia Bumbea (*Consultant in Haematology, Carol Davila University of Medicine, Member of Rare Diseases Operative Group*)
Corin Badiu (*Consultant in Endocrinology, Diabetes, and nutrition disorders, Member of Rare Diseases Operative Group*)
Emilia Severin (*Consultant in Medical Genetics, Carol Davila University of Medicine, Member of Rare Diseases Operative Group*)
Ana-Maria Vlădăreanu (*Consultant in Hematology, Carol Davila University of Medicine, president of Rare Diseases Operative Group and Commission*)
Mihaela Gaman (*Secretary of Rare Diseases Operative Group*)

Contributions in 2012

Ana-Maria Vlădăreanu (*Consultant in Hematology, Carol Davila University of Medicine, president of Rare Diseases Operative Group and Commission*)
Emilia Severin (*Consultant in Medical Genetics, Carol Davila University of Medicine, Member of Rare Diseases Operative Group*)
Corin Badiu (*Consultant in Endocrinology, Diabetes and Nutrition disorders, Member of Rare Diseases Operative Group*)
Horia Bumbea (*Consultant in Haematology, Carol Davila University of Medicine, Member of Rare Diseases Operative Group*)
Dorica Dan (*President Romanian Prader Willi Association, Romanian National Alliance for Rare Diseases*)
Cristina Rusu (*Orphanet Romania, „Gr T Popa” University of Medicine*)
Mihaela Gaman (*Secretary of Rare Diseases Operative Group*)
Carmen Cordea (*President PKU Life Romania Association*)
Claudia Torje (*Executive Director of Romanian Society of Multiple Sclerosis*)

Validated by: Ana Maria Vlădăreanu (*EUCERD Representative Romania, Bucharest Emergency University Hospital*)

Slovak Republic

Contributions in 2010

László Kovács and Ludovit Kádasi (*Orphanet Slovakia, Institute of Molecular Physiology and Genetics, Bratislava*)
Jana Behunova (*University Childrens’ Hospital, Kosice*)

Contributions in 2011

Táňa Foltánová (*Department of Pharmacology and Toxicology, Comenius University, Bratislava*)
Katarína Štěpánková (*Slovak Marfan Association*)
František Cisarík (*EUCERD Representative Slovakia, Expert of the Ministry of Health for Medical Genetics*)

Contributions in 2012

František Cisarík (*EUCERD Representative Slovakia, Expert of the Ministry of Health for Medical Genetics*)
László Kovács and Anna Hlavatá (*Orphanet Slovakia*)
Ľudovít Kádaši (*EUCERD Alternat, President of the Slovak Society for Medical Genetics*)
Beáta Ramljakova (*Slovak Rare Disease Patient Alliance*)
Táňa Foltánová (*Department of Pharmacology and Toxicology, Comenius University, Bratislava, COMP Representative*)
Katarína Štěpánková (*Slovak Marfan Association*)
Michal Konečný (*OUSA*)
Iwar Klimeš (*Institute of Experimental Endocrinology, Slovak Academy of Sciences*)
Jana Behúňová (*University Childrens’ Hospital, Košice*)
Svetozár Dluholucký (*Newborn Screening Centre*)
Anna Baráková (*National Health Information Centre*)

Validated by: František Cisarík (*EUCERD Representative Slovakia, Expert of the Ministry of Health for Medical Genetics*)

Slovenia

Contributions in 2010

Borut Peterlin and Luca Lovrecic (*Orphanet Slovenia, University Medical Centre Ljubljana*)
Mircha Poldrugovac and Robert Medved (*Ministry of Health*)

Contributions in 2011

Mircha Poldrugovac, Robert Medved and Doroteja Novak Gosarič (*Ministry of Health*)

Contributions in 2012

Robert Medved and Doroteja Novak Gosarič (*Ministry of Health*)

Validated by: Borut Peterlin & Robert Medved (*EUCERD Representative Slovenia, Ministry of Health*)

Spain

Contributions in 2010

Francesc Palau, Monica Bescos and Ingrid Mendes (*Orphanet Spain, CIBERER*)
Miguel del Campo (*Istituto de Salud Carlos III ISCIII*)
Manuel Posada (*Istituto de Salud Carlos III ISCIII – Research Institute for Rare Diseases IIER*)
Antonia Ribes (*Servicio de Bioquímica y Biología Molecular, Institut de Bioquímica Clínica, Servicio de Bioquímica y genética molecular, Hospital Clínic y Provincial de Barcelona, Barcelona*)
Pablo Rivero (*Ministry of Health and Social Policy, Directorate General of the Quality Agency of the National Health System. Office of Health Planning and Quality*)
FEDER (*Federación Española de Enfermedades Raras*)

Contributions in 2011

Francesc Palau and Virginia Corrochano (*Orphanet Spain, CIBERER*)
Joan Luis Vives Corrons (*University of Barcelona*)
Rafael De Andres-Medina (*Instituto de Salud Carlos III – ISCIII*)
Carlos Segovia (*Instituto de Salud Carlos III, Deputy Director for International Research Programmes and Institutional Relations, Ministry of Science and Innovation*)
Dolores Vaquero García & María Teresa Sanmiguel Samano (*Directorate General for Pharmaceutical and Health Products, Ministry of Health, Social Policy and Equality*)
Isabel Peña-Rey and Pilar Soler (*EUCERD Representative Spain and alternate, Ministry of Health, Social Policy and Equality*)

Contributions in 2012

This document has been elaborated by representatives *Ministry of Health, Social Services and Equality* with the input of:
Francesc Palau (*Orphanet Spain, CIBERER*)
FEDER (*Federación Española de Enfermedades Raras*)
Rafael De Andres-Medina (*Instituto de Salud Carlos III – ISCIII*)
Ignacio Baanante Balastegui (*Instituto de Salud Carlos III – ISCIII Subdirección General de Evaluación y Fomento de la Investigación*)
Josep Torrent-Farnell (*Fundació Doctor Robert*)
Joan Luis Vives Corrons (*University of Barcelona*)
Susan Webb (*Institut de Recerca de l'Hospital de la Santa Creu i Sant Pau, Barcelona*)
Antonia Ribes (*Servicio de Bioquímica y Biología Molecular, Institut de Bioquímica Clínica, Servicio de Bioquímica y genética molecular, Hospital Clínic y Provincial de Barcelona, Barcelona*)
Miguel del Campo (*Istituto de Salud Carlos III ISCIII*)
Manuel Posada (*Istituto de Salud Carlos III ISCIII – Research Institute for Rare Diseases IIER*)
Carmen Pérez Mateos and María Isabel Moren Portela (*Deputy Director-General of Basic Services Portfolio of the National Health System and Cohesion Fund. Ministry of Health, Social Services and Equality*)

Validated by: Isabel Peña-Rey and Pilar Soler (*EUCERD Representative and alternate from Spain, Ministry of Health, Social Services and Equality*)

Sweden

Contributions in 2010

Désirée Gavhed (*Orphanet Sweden, Karolinska Institut*)
Kerstin Westermark (*Chair of the COMP, Medical Products Agency*)
Jonas Karnström (*National Board of Health and Welfare*)
Elisabeth Wallenius (*President of Rare Diseases Sweden*)
Karolina Antonov (*LIF*)
Karin Forsberg Nilsson (*Swedish Research Council*)
Christina Greek Winald (*The Swedish Information Centre for Rare Diseases*)

Contributions in 2011

Désirée Gavhed (*Orphanet Sweden, Karolinska Institut*)
Kerstin Westermark (*Chair of the COMP, Medical Products Agency*)
Björn Beermann (*Swedish Medical Products Agency*)
Ulf Kristoffersson (*University Hospital, Lund*)
Michael Soop (*EUCERD Representative Sweden, National Board of Health and Welfare*)
Christina Greek Winald (*The Swedish Information Centre for Rare Diseases*)
Elisabeth Wallenius (*President of Rare Diseases Sweden*)
Karolina Antonov (*LIF*)
Anders Olausson (*President of Ågrenska*)

Contributions in 2012

Désirée Gavhed (*Orphanet Sweden, Karolinska Institute*)

Christina Greek Winald (*The Swedish Information Centre for Rare Diseases*)
Anders Olausson (*President of Ågrenska*)
Elisabeth Wallenius (*President of Rare Diseases Sweden*)
Kerstin Westermark (*Chair of the COMP, Medical Products Agency*)
Andor Wagner (*EUCERD Representative Sweden, National Board of Health and Welfare*)

Validated by: Andor Wagner (*EUCERD Representative Sweden, National Board of Health and Welfare*)

Switzerland

Contributions in 2010

Loredana D'Amato Sizonenko (*Orphanet Switzerland, University Hospitals of Geneva*)
Matthias Baumgartner (*University Children's Hospital, University of Zurich*)
Andreas Huber (*Kantonsspital, Aarau*)
Peter Miny (*University Hospital, University of Basel*)
Mike Morris (*Division of Medical Genetics, University Hospitals, Geneva*)
Cristina Benedetti (*Secretary of the Expert Commission for Human Genetic Testing, Federal Office of Public Health*)

Contributions in 2011

Loredana D'Amato Sizonenko (*Orphanet Switzerland, University Hospitals of Geneva*)
Sabina Gallati (*EUCERD Representative Switzerland, University Hospital Inselspital, University of Bern*)
Matthias Baumgartner (*University Children's Hospital, University of Zurich*)
Andreas Huber (*Kantonsspital, Aarau*)
Peter Miny (*University Hospital, University of Basel*)
Mike Morris (*Division of Medical Genetics, University Hospitals, Geneva*)
Cristina Benedetti (*Secretary of the Expert Commission for Human Genetic Testing, Federal Office of Public Health*)

Contributions in 2012

Loredana D'Amato Sizonenko (*Orphanet Switzerland, University Hospitals of Geneva*)
Sabina Gallati (*EUCERD Representative Switzerland, University Hospital Inselspital, University of Bern*)
Matthias Baumgartner (*University Children's Hospital, University of Zurich*)
Andreas Huber (*Kantonsspital, Aarau*)
Peter Miny (*University Hospital, University of Basel*)
Mike Morris (*Division of Medical Genetics, University Hospitals, Geneva*)
Cristina Benedetti (*Secretary of the Expert Commission for Human Genetic Testing, Federal Office of Public Health*)
ProRaris (*Swiss Rare Disease Alliance*)

Validated by: Sabina Gallati (*EUCERD Representative Switzerland, University Hospital Inselspital, University of Bern*)

Turkey

Contributions in 2010

Ugur Ozbek, Fatma Atalar and Tufan Acuner (*Orphanet Turkey, Istanbul University*)
Meral Ozguc (*Hacettepe School of Medicine, Ankara*)
Pelin Kilic (*Turkish Ministry of Health*)

Contributions in 2011

Ugur Ozbek, Fatma Atalar and Tufan Acuner (*Orphanet Turkey, Istanbul University*)
Meral Ozguc (*Hacettepe School of Medicine, Ankara*)
Pelin Kilic (*Turkish Ministry of Health*)

Contributions in 2012

Pelin Kilic (*Orphan Drugs Study Group Coordinator - TITCK*)
Ömer Yemşen (*Orphan Drugs Study Group, Chief of Unit - TITCK*)
Fikriye Handan Öztunca (*Orphan Drugs Study Group Member - TITCK*)
Ugur Ozbek, Fatmahan Atalar (*Orphanet Turkey, Istanbul University*)

United Kingdom

Contributions in 2010

Dian Donnai and Idoia Gomez-Paramio (*Orphanet UK and Ireland, University of Manchester*)
Edmund Jessop (*NHS Specialist Commissioning Group*)
Stephen Nutt (*Rare Disease UK & The Genetic Interest Group*)
Anil Mehta (*University of Aberdeen*)
Christine Lavery (*MPS Society*)

Contributions in 2011

Dian Donnai and Idoia Gomez-Paramio (*Orphanet UK and Ireland, University of Manchester*)
Stephen Nutt (*Rare Disease UK*)
Edmund Jessop (*NHS Specialist Commissioning Group*)
Angela Davis (*Nowgen*)
Kate Dack (*Nowgen*)
Jane Deller and Jacquie Westwood (*UKGTN*)
Andrew Devereau (*NGRL Manchester*)

Contributions in 2012

Edmund Jessop (*NHS Specialist Commissioning Group*)
Jane Deller (*UKGTN*)
John Murray (*Specialised Healthcare Alliance – SHCA*)

Validated by: Edmund Jessop (*EUCERD Representative UK, NHS Specialist Commissioning Group*)

Contributions from the European Commission and European Medicines Agency²³²:

Directorate General Health and Consumers

Antoni Montserrat Moliner (*Unit C-2*)
Mirjam Soderholm (*Unit D-5*)

Directorate General Research and Innovation

Iiro Eerola and Gratiela Dobirta (*Scientific Project Officers*)

Directorate General Industry and Enterprise

Catherine Berens (*Policy Officer, Unit F5*)

European Medicines Agency

Jordi Llinares-Garcia (*Head of Orphan Medicines*)

This report was compiled by Charlotte Rodwell

(*Scientific Secretariat of the European Union Committee of Experts on Rare Diseases, INSERM US14, France*)

²³² Disclaimer: the European Commission is not responsible for the completeness and correctness of the information included in this report.

SELECTED BIBLIOGRAPHY AND SOURCES²³³

1. EUROPEAN SOURCES

WEBSITES

European Commission & EMA websites

- Rare Diseases information on the EC Public Health portal
http://ec.europa.eu/health/rare_diseases/policy/index_en.htm
- Public health initiatives and other institutions responsible for rare diseases on the DG Sanco
http://ec.europa.eu/health/ph_threats/non_com/rare_9_en.htm
- Europe for patients: rare diseases
http://ec.europa.eu/health-eu/europe_for_patients/rare_diseases/index_en.htm
- Eudra-CT (European Clinical Trials Database)
<https://eudract.emea.europa.eu/>
- CORDIS: the gateway to European Research and development
http://cordis.europa.eu/home_fr.html
- European Commission research and innovation
<http://ec.europa.eu/research/index.cfm?lg=en>
- European Medicines Agency Committee for Orphan Medicinal Products
http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000123.jsp&murl=menus/about_us/about_us.jsp&mid=WC0b01ac0580028e32

Other European websites

- Orphanet
<http://www.orpha.net>
- OrphaNews Europe archives
<http://www.orpha.net/actor/cgi-bin/OAhome.php?Ltr=EuropaNews>
- EURORDIS
<http://www.EURORDIS.org>
- Eurocat
<http://www.eurocat-network.eu/>
- EUROPLAN: Final National Conference Reports
http://www.europlanproject.eu/newsite_986987/events22.html

KEY TEXTS

Directives, Regulations, Communications, Council Decisions, Council Recommendations and other related documents

- Regulation (EC) N°141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products
http://ec.europa.eu/health/files/eudralex/vol-1/reg_2000_141/reg_2000_141_en.pdf

²³³ All websites and documents were last accessed in May 2012.

- Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (Clinical Trials Directive)
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:121:0034:0044:en:PDF>
- Commission Directive 2005/28/EC of 8 April 2005 laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products (Good Clinical Practice Directive)
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:091:0013:0019:en:PDF>
- Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2001:311:0067:0128:EN:PDF>
- Regulation on advanced therapies (Regulation (EC) 1394/2007)
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:324:0121:0137:en:PDF>
- Regulation on medicinal products for paediatric use (Regulation (EC) N° 1901/2006)
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:378:0001:0019:en:PDF>
- EMA Public Statement on Fee Reductions for Designated Orphan Medicinal Products
http://www.ema.europa.eu/docs/en_GB/document_library/Public_statement/2009/09/WC500003876.pdf
- Council Decision No 1982/2006/EC of 18 December 2006 concerning the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007-2013)
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:412:0001:0041:EN:PDF>
- Communication from the Commission on Rare Diseases: Europe's Challenge
http://ec.europa.eu/health/ph_threats/non_com/docs/rare_com_en.pdf
- Summary of the Impact Assessment Accompanying the Communication on Rare Diseases: Europe's challenges
http://ec.europa.eu/health/ph_threats/non_com/docs/impact_assessment_exs_en.pdf
- Council Recommendation of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02)
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2009:151:0007:0010:EN:PDF>
- Commission Decision of 30 November 2009 establishing a European Union Committee of Experts on Rare Diseases (2009/872/EC)
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:315:0018:0021:EN:PDF>
- European Commission Communication on Action Against Cancer: European Partnership
http://ec.europa.eu/health/ph_information/dissemination/diseases/docs/com_2009_291_en.pdf
- European Commission Communication on a European initiative on Alzheimer's disease and other dementias
http://ec.europa.eu/health/ph_information/dissemination/documents/com2009_380_en.pdf
- Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare
http://ec.europa.eu/health/ph_information/dissemination/documents/com2009_380_en.pdf

Programmes of Community Action, Work Programmes and Calls

- EU Programme of Community Action in the Field of Health 2003-2008
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2002:271:0001:0011:EN:PDF>
- EU Second Programme of Community Action in the Field of Health 2008-2013
<http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:301:0003:0013:EN:PDF>
- DG Sanco Work Plan 2011
http://ec.europa.eu/health/programme/docs/wp2011_en

- DG Sanco Work Plan 2012
http://ec.europa.eu/health/programme/docs/wp2012_en.pdf
- DG Research and Innovation FP7 Calls
http://cordis.europa.eu/fp7/dc/index.cfm?fuseaction=UserSite.FP7ActivityCallsPage&id_activity=1
- EMA Work Programme 2011
http://www.ema.europa.eu/docs/en_GB/document_library/Work_programme/2011/02/WC500102044.pdf
- EMA Work Programme 2012
http://www.ema.europa.eu/docs/en_GB/document_library/Work_programme/2012/02/WC500122955.pdf

KEY DOCUMENTS

DG Enterprise and Industry

- Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products (2005 revision)
http://ec.europa.eu/health/files/orphanmp/doc/inventory_2006_08_en.pdf
- Final Conclusions and Recommendations of the High Level Pharmaceutical Forum (2nd October 2008)
http://ec.europa.eu/pharmaforum/docs/final_conclusions_en.pdf
- Initial investigation to assess the feasibility of coordinated system to access orphan medicines (Gesundheit Österreich GmbH, May 2011)
http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/access_orphans_initialinvest_052011_en.pdf

DG Health and Consumers

- RDTF Report – Overview of Current Centres of Reference on rare diseases in the EU - 12 September 2005
<http://www.eucerd.eu/upload/file/Publication/RDTFECR2005.pdf>
- RDTF Report: Centres of Reference for Rare Diseases in Europe – State-of-the-art in 2006 and Recommendations of the Rare Diseases Task Force – 1 September 2006
<http://www.eucerd.eu/upload/file/Publication/RDTFECR2006.pdf>
- RDTF Report – State of the Art and Future Directions – 11 March 2008
<http://www.eucerd.eu/upload/file/Publication/RDTFERN2008.pdf>
- RDTF Report: Health Indicators for Rare Diseases: State of the art and future directions – June 2008
<http://www.eucerd.eu/upload/file/Publication/RDTFHI2008.pdf>
- RDTF Report: How many drugs for how many patients – July 2007
<http://www.eucerd.eu/upload/file/Publication/RDTFOD2007.pdf>
- RDTF Report: Health Indicators For Rare Diseases I - Conceptual Framework And Development Of Indicators From Existing Sources – April 2010
<http://www.eucerd.eu/upload/file/RDTFIndicators2010.pdf>
- EUCERD Report: Initiatives and Incentives in the field of rare diseases – July 2010
<http://www.eucerd.eu/upload/file/Reports/2009ReportInitiativesIncentives.pdf>
- EUCERD Report: Preliminary analysis of the outcomes and experiences of pilot European Reference Networks for rare diseases - May 2011
<http://www.eucerd.eu/upload/file/Reports/ERN2011Analysis.pdf>

European Medicines Agency

- European Medicines Agency Annual Report for 2010
http://www.ema.gov.sg/media/files/annual_reports/EMA_Annual_Report_2010.pdf

- COMP Recommendation on elements required to support the medical plausibility and the assumption of significant benefit for an orphan designation (EMA/COMP/15893/2009)
http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2010/07/WC500095341.pdf

DG Research and Innovation

- International Rare Disease Research Consortium (IRDiRC) First Workshop Summary Report
http://ec.europa.eu/research/health/medical-research/pdf/reykjavik-workshop-report_en.pdf
- International Rare Disease Research Consortium (IRDiRC) Second Workshop Summary Report
http://ec.europa.eu/research/health/medical-research/pdf/rare-diseases/executive-summary_en.pdf

OTHER DOCUMENTS

- Orphanet Report Series: Prevalence of reported number of published cases listed by alphabetical order by disease
http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_alphabetical_list.pdf
- Orphanet Report Series: Prevalence by decreasing prevalence or number of published cases
http://www.orpha.net/orphacom/cahiers/docs/GB/Prevalence_of_rare_diseases_by_decreasing_prevalence_or_cases.pdf
- Orphanet Report Series: Patient registries in Europe
<http://www.orpha.net/orphacom/cahiers/docs/GB/Registries.pdf>
- Orphanet Report Series: List of orphan drugs in Europe
http://www.orpha.net/orphacom/cahiers/docs/GB/list_of_orphan_drugs_in_europe.pdf
- Orphanet Report Series: European collaborative research projects funded by DG Research and by E-Rare in the field of rare diseases and European clinical networks funded by DG Sanco and contributing to clinical research in the field of rare diseases
<http://www.orpha.net/orphacom/cahiers/docs/GB/Networks.pdf>
- RDPlatform Report: Rare Disease research, its determinants and the way forward (May 2011)
http://asso.orpha.net/RDPlatform/upload/file/RDPlatform_final_report.pdf
- EURORDIS report: The Voice of 12,000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe
http://www.EURORDIS.org/article.php3?id_article=1960
- EURORDIS report: Rare Diseases: Understanding this Public Health Priority" (November 2005)
http://www.EURORDIS.org/IMG/pdf/princeps_document-EN.pdf
- EURORDIS report: Results of the 4th EURORDIS Survey on Orphan Drug Availability in Europe (2007)
<http://www.EURORDIS.org/IMG/pdf/2007ODsurvey-EURORDIS.pdf>

2. INTERNATIONAL SOURCES

WEBSITES

- International Rare Disease Research Consortium (IRDiRC)
http://ec.europa.eu/research/health/medical-research/rare-diseases/irdirc_en.html
- Topic Advisory Group for Rare Diseases – Revision of the WHO ICD
<http://www.who.int/classifications/icd/TAGs/en/index.html>

REPORTS/ ARTICLES USED FOR THE UPDATE OF THIS REPORT

- *Access Mechanisms for Orphan Drugs: A Comparative Study of Selected European Countries* (2009) (OHE Research Briefing No. 52 October 2009)
<http://www.ohe.org/publications/recent-publications/list-by-title-20/detail/date////access-mechanisms-for-orphan-drugs-a-comparative-study-of-selected-european-countries.html>
- *“European regulation on orphan medicinal products: 10 years of experience and future perspectives”* K. Westermark & COMP/EMA Scientific Secretariat (Nature Reviews: Drug Discovery, Volume 10, May 2011)
<http://www.ncbi.nlm.nih.gov/pubmed/21532564>
- *INESSS Report: Prise en charge des maladies rares - Expériences étrangères (August 2011)*
http://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/OrganisationsSoins/ETMIS2011_Vol7_No6.pdf
- *Orphan Drugs in Europe: Pricing, Reimbursement, Funding & Market Access Issues, 2011 Edition*, Donald Macarthur, June 2011, JustPharmaReports
Summary : <http://www.iustpharmareports.com/images/Orphan%20Drugs%20in%20Europe-%20Pricing,%20Reimbursement,%20Funding%20&%20Market%20Access%20Issues,%202011%20Edition.pdf>

3. NATIONAL SOURCES

Austria

- Gesundheit Österreich GmbH / Austrian Health Institute - Rare Diseases
<http://www.goeg.at/de/Bereich/Koordinationsstelle-NKSE.html>
- Austrian Governmental Health Platform – Rare Diseases
www.gesundheit.gv.at/Portal.Node/ghp/public/content/aktuelles/seltene-erkrankungen-befragung.htm
www.gesundheit.gv.at/Portal.Node/ghp/public/content/aktuelles/koordinationsstelle-seltene-erkrankungen.html
- Information provided by the Main Association of Austrian Social Security Institutions
http://www.hauptverband.at/portal27/portal/hvbportal/start/startWindow?action=2&p_menuid=58215&p_tabid=1
- Orphanet Austria national website
<http://www.orpha.net/national/AT-DE/index/startseite/>
- Newborn screening information (University of Vienna)
<http://www.meduniwien.ac.at/hp/neugeborenen-screening/>

Belgium

- *“Recommendations and proposed measures for the Belgian plan for rare diseases (Phase 1)”*
<http://www.kbs-frb.be/publication.aspx?id=271066&LangType=2060>
- *“Recommendations and Proposed Measures for a Belgian Plan for Rare Diseases (Final Report)”*
<http://www.kbs-frb.be/publication.aspx?id=288128&LangType=1033>
- *KCE 112B «Politiques relatives aux maladies orphelines et aux médicaments orphelins, 2009»* (Report of the Belgian Federal Centre of Healthcare Expertise)
http://www.kce.fgov.be/index_fr.aspx?SGREF=3460&CREF=13646
- Institut national d’assurance maladie-invalidité
http://inami.fgov.be/drug/fr/drugs/orphan_drugs/index.htm
- Orphanet Belgium national website
<http://www.orpha.net/international/OrphanetBE.html?lng=EN>
- Website of RaDiOrg.be
www.radiorg.be

Bulgaria

- *“National Plan for Rare Diseases 2009-2013 (Genetic, congenital malformation and nonhereditary disease)”*
<http://www.raredis.org/pub/events/NPRD.pdf>
- Website of the Information Centre for Rare Diseases and Orphan Drugs
<http://www.raredis.org/>
- Orphanet Bulgaria national website
<http://www.orpha.net/national/BG-BG/index/homepage/>

- *“ICRDOD Report on Access to Orphan Drugs in Bulgaria” (March 2011)*
http://raredis.org/pub/OD_Report_04042011_EN.pdf
- *“Europlan Bulgarian National Conference Final Report”*
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/FINAL%20Report_Bulgarian%20EUROPLAN%20NC%202010%20-%20Report%20Package.pdf

Croatia

- Croatian Society for Rare Diseases
<http://www.rijetke-bolesti.org>
<http://www.idizajn.hr/hlz/linkovi.html>
- Croatian Society of Patients with Rare Diseases
<http://www.rijetke-bolesti.hr/>
- Croatian Agency for Drugs and Medicinal Products
www.halmed.hr
- Orphanet Croatia national website
<http://www.orpha.net/national/HR-HR/index/homepage/>
- *“Europlan Croatian National Conference Final Report”*
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/FINAL%20Report_Croatian_%20EUROPLAN%20NC%202010%20-%20Report%20Package.pdf

Cyprus

- Gene Net Cyprus
<http://www.genenet.org.cy/>
- Orphanet Cyprus national website
<http://www.orpha.net/national/CY-EL/index/homepage/>
- Cyprus Alliance for Rare Disorders
http://www.thalassaemia.org.cy/cyprus_alliance.html

Czech Republic

- Ministry of Health
www.mzcr.cz
- Czech National Strategy for Rare Diseases website
www.vzacnenemoci.cz
- *Czech National Strategy for Rare Diseases*
http://ec.europa.eu/health/rare_diseases/docs/national_czech_en.pdf
- Czech site concerning national rare disease activities
www.vzacna-onemocneni.cz/
- Neonatal screening website
<http://novorozenecky-screening.cz/>
- SUKL State Institute for Drug Control
www.sukl.cz
- Orphanet Czech Republic national website
<http://www.orphanet.cz/national/CZ-CS/index/%C3%BAvod/>

Denmark

- Danish Centre for Rare Diseases and Disabilities
<http://www.csh.dk/>
- Rare Diseases Research in Denmark: Barriers and Prospects (2004 report)
<http://www.sjaeldnediagnoser.dk/documents/00105.pdf>
- Rare Disorders Denmark
<http://www.sjaeldnediagnoser.dk/?lang=uk>
- Rare Citizen
www.sjaeldenborger.dk
- Rarelink Denmark
www.rarelink.dk
- Orphanet Denmark national website
<http://www.orpha.net/national/DK-DA/index/homepage/>

Estonia

- Estonian Agrenska Foundation
<http://www.agrenska.ee/?setlang=15>

- Ravimiamet – State Agency for Medicines
<http://www.sam.ee/>
- Orphanet Estonia national website
<http://www.orpha.net/national/EE-ET/index/avaleht/>

Finland

- Vaestoliitto
http://www.vaestoliitto.fi/in_english/genetics/rare_diseases/
- Harvinaiset
<http://www.harvinaiset.fi/>
- Finnish Disease Database
<http://www.findis.org/main.php?action=disease>
- Finnish Medicines Agency
<http://www.fimea.fi/medicines/fimeaweb>
- Rarelink Finland
www.rarelink.fi
- Orphanet Finland national website
<http://www.orpha.net/national/FI-FI/index/kotisivu/>

France

- French National Plan for Rare Diseases 2005-2008 (Ensuring equity in the access to diagnosis, treatment and provision of care)
http://www.orpha.net/actor/EuropaNews/2006/doc/French_National_Plan.pdf
- Evaluation of the French National Plan for Rare Diseases 2005-2008
http://www.sante.gouv.fr/IMG/pdf/Evaluation_interne_Plan_National_Maladies_Rares_2005-2008.pdf
- French National Plan for Rare Diseases (2011-2014)
http://www.sante.gouv.fr/IMG/pdf/Plan_national_maladies_rares.pdf
- French Health Ministry Dossier on Rare Diseases
<http://www.sante-sports.gouv.fr/les-maladies-rares.html>
- Second French National Plan for Cancers (2009-2013)
http://www.plan-cancer.gouv.fr/images/stories/fichiers/plancancer20092013_english.pdf
- Second French National Plan for Rare Handicaps
http://www.cnsa.fr/IMG/pdf/CNSA_Schema-national-Handicap-rare-2.pdf
- Orphanet France national website
<http://www.orphanet-france.fr/national/FR-FR/index/page-d-accueil/?lng=EN>
- Plateforme Maladies Rares
<http://www.plateforme-maladiesrares.org/>
- Maladies Rares Info Services
<http://www.maladiesraresinfo.org>
- Alliance Maladies Rares
<http://www.alliance-maladies-rares.org/>
- AFM Téléthon
<http://www.afm-telethon.fr/>

Germany

- *Maßnahmen zur Verbesserung der gesundheitlichen Situation von Menschen mit Seltenen Erkrankungen in Deutschland* (Strategies for improving the health care situation of patients with rare disease in Germany)
http://www.bmg.bund.de/fileadmin/dateien/Downloads/Forschungsberichte/110516_Forschungsbericht_Seltene_Krankheiten.pdf
- BMG - German Federal Ministry of Health – Rare Diseases
<http://www.bmg.bund.de/praevention/gesundheitsgefahren/seltene-erkrankungen.html>
- BMG - German Federal Ministry of Health
www.bmg.bund.de
- Rare Diseases – The Networks (BMBF)
<http://www.gesundheitsforschung-bmbf.de/de/131.php>
- NAMSE – Nationales Aktionsbündnis für Menschen mit seltenen Erkrankungen
<http://namse.de/>
- German Institute of Medical Documentation (DIMDI)
<http://www.dimdi.de/static/en/index.html>
- German Clinical Trials Register
<http://www.germanctr.de/>

- Orphanet Germany national website
<http://www.orpha.net/national/DE-DE/index/startseite/>
- BMBF – German Federal Ministry of Education and Research
<http://www.bmbf.de/>
- ACHSE – Allianz Chronischer Seltener Erkrankungen
<http://www.achse-online.de/>
- Europlan German National Conference Final Report
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_german_europlan.pdf

Greece

- Proposal for a Greek National Plan for Rare Diseases (2008-2012)
http://www.ygeianet.gov.gr/HealthMapUploads/Files/SPANIES_PATHISEIS_TELIKO_LOW.pdf
- Hellenic Centre for Disease Control and Prevention – Office for Rare Diseases
<http://www.keelpno.gr/el-gr/voorhματαθέματααυγείας/σπάνιανοσήματα.aspx>
- National Organisation for Medicines
<http://www.eof.gr>
- Institute of Child Health
<http://www.ich.gr/el/>
- Orphanet Greece national website
<http://www.orpha.net/national/GR-EL/index/%CE%B1%CF%81%CF%87%CE%B9%CE%BA%CE%AE-%CF%83%CE%B5%CE%BB%CE%AF%CE%B4%CE%B1/>
- Greek Alliance for Rare Diseases – PESPA
http://www.pespa.gr/en/pespa_en.htm
- Europlan Greek National Conference Final Report
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/FINAL%20Report%20Greece%20EUROPLAN%202010.pdf

Hungary

- National Surveillance Centre for Congenital Anomalies and Rare Diseases
<http://193.225.50.35/ujhonlap/control.php?PAGE=RBK>
- HUFERDIS
www.rirosz.hu
- Orphanet Hungary national website
<http://www.orpha.net/national/HU-HU/index/homepage/>
- Europlan Hungarian National Conference Final Report
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_%20hungary_europlan.pdf
- Hungarian National Conference resources
<http://europlan.rirosz.hu/euroterv-ii-konferencia-1/az-elhangzott-eloadasok>

Ireland

- Genetic and Rare Diseases Organisation – GRDO
<http://www.grdo.ie/>
- Medical Research Charities Group
<http://www.mrcg.ie/>
- National Centre for Medical Genetics
www.genetics.ie
- Orphanet Ireland national website
<http://www.orpha.net/national/IE-EN/index/homepage/>
- Europlan Irish National Conference Final Report
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_ireland.pdf
- IPPOSI Information Document on Rare Diseases (19/02/09)
<http://www.ipposi.ie/index.php/information-centre/rare-diseases>
Rehab Care Report: An investigation into the social support needs of families who experience rare disorders on the island of Ireland
- http://www.rehab.ie/about/PDFS/July2008/RehabCare_RD_Report.pdf

Israel

- Orphanet Israel national website
<http://www.orpha.net/national/IL-HE/index/%D7%93%D7%A3-%D7%94%D7%91%D7%99%D7%AA-%D7%A9%D7%9C-%D7%90%D7%95%D7%A8%D7%A4%D7%A0%D7%98-%D7%99%D7%A9%D7%A8%D7%90%D7%9C/>

Italy

- National Centre Rare Diseases - Istituto Superiore di Sanità
www.iss.it/cnmr/
- National Registry for Rare Diseases
www.iss.it/cnmr
- National Register of Orphan Drugs
www.iss.it/cnmr/
- Italian Ministry of Health – Rare Diseases Information
<http://www.ministerosalute.it/malattieRare/malattieRare.jsp>
- Italian Ministry of Health – Rare Disease Research Programme 2008
http://www.salute.gov.it/bandi/documenti/Bando_malattie_rare.pdf
- Rete Nazionale Malattie Rare
<http://www.ministerosalute.it/malattieRare/paginaInternaMalattieRare.jsp?id=707&menu=rete&lingua=italiano>
<http://www.iss.it/ccmr/>
- Orphanet Italy national website
<http://www.orphanet-italia.it/national/IT-IT/index/homepage/>
- OrphaNews Italia
<http://www.orpha.net/actor/cgi-bin/OAhome.php?Ltr=ItaliaNews>
- UNIAMO
<http://www.uniamo.org/>
- Consulta Nazionale Malattie Rare
<http://www.consultanazionalemalattierare.it/>
- Telethon
<http://www.telethon.it/Pagine/Home.aspx>
- Europlan Italy National Conference Final Report
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_italy_europlan.pdf
- *ISTISAN Report “National Registry and Regional / Interregional Registries for rare diseases”*
<http://www.iss.it/binary/publ/cont/undici20WEB.pdf>

Latvia

- The State Agency of Medicines
www.zva.gov.lv
- National Cancer Control Programme (2009-2015)
<http://polsis.mk.gov.lv/view.do?id=2932>
- Orphanet Latvia national website
<http://www.orpha.net/national/LV-LV/index/homepage/>
- Latvian Rare Disease Organisation - Caladrius
www.caladrius.lv
- Palidzesim.lv
www.palidzesim.lv

Lithuania

- Lithuanian State Medication Control Agency
<http://www.vvkt.lt/>
- Orphanet Lithuania national website
<http://www.orpha.net/national/LT-LT/index/prad%C5%BEia/>

Luxembourg

- Groupe de travail maladies rares
<http://www.maladiesrares.lu/start.html>
- Report *Les maladies rares: Enquête sur la situation des personnes atteintes de maladies rares au Grand-Duché de Luxembourg*
<http://www.sante.public.lu/fr/catalogue-publications/maladies-traitements/maladies-rares/index.html>
- Orphanet Luxembourg national website
<http://www.orpha.net/national/LU-LB/index/homepage/>

- ALAN
<http://www.alan.lu/>

Malta

No additional reported sources.

Netherlands

- Dutch Organisation for Health Research and Development (ZonMw)
<http://www.zonmw.nl/en/>
- National Plan Rare Diseases (NPZZ) website
<http://www.npzz.nl/>
- National Genetic Resource and Information Centre
<http://www.erfocentrum.nl>
- Steering Committee on Orphan Drugs Netherlands
www.orphandrugs.nl
- Orphanet Netherlands national website
<http://www.orpha.net/national/NL-NL/index/homepage/?lng=EN>
- Forum Biotechnologie en Genetica
<http://www.forumbg.nl/documenten>
- Farmanco – List of Orphan Drugs registered in the European Union (in Dutch)
<http://www.farmanco.knmp.nl/tekortweesgeneesmiddel>
- VSOP
<http://www.vsop.nl/>
- Rare Disease Day
www.zeldzameziektendag.nl
- List of genetic diagnostic tests in Netherlands
<http://www.dnadiagnostiek.nl/>
- Europlan Dutch National Conference Final Report
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_netherlands_%20europlan.pdf

Norway

- *A Rare Guide: Information on the Norwegian programme for persons with rare conditions (produced by the National Directorate for Health)*
<http://www.helsedirektoratet.no/publikasjoner/en-sjelden-guide/Sider/default.aspx>
- *Rare Disorders in Norway: How users experience the health services (report produced by SINTEF December 2008)*
<http://www.sintef.no/home/Technology-and-Society/Health-research/Global-Health-and-Welfare/Rare-disorders/>
- *Regulation on the Approval of hospitals and national services*
<http://www.regjeringen.no/upload/HOD/SHA/forskrift-eng-270911.pdf>
- National Directorate for Health
<http://www.helsedirektoratet.no/helse-og-omsorgstjenester/sjeldne-tilstander/Sider/default.aspx>
- Resource Centre for Rare Diseases – SSD
<http://www.sjeldnediagnoser.no/>
- Orphanet Norway national website
<http://www.orpha.net/national/NO-NO/index/kort-om-orphanet/>
- Frambu Centre for Rare Diseases
<http://www.frambu.no/>
- Rarelink
www.rarelink.no

Poland

- National Forum on the Treatment of Orphan Diseases
<http://www.rzadkiechoroby.pl/>
- Rare Disease Day website
www.dzienchorobrzadkich.pl
- Orphanet Poland national website
<http://www.orpha.net/national/PL-PL/index/strona-g%C5%82%C3%B3wna/>
- Europlan Poland National Conference Final Report
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_poland_europlan.pdf and <http://www.europlan.org.pl/>

Portugal

- *Programa nacional para doenças raras: Portuguese National Plan for Rare Diseases*
http://ec.europa.eu/health/ph_threats/non_com/docs/portugal.pdf
- Orphanet Portugal national website
<http://www.orpha.net/national/PT-PT/index/p%C3%A1gina-de-in%C3%ADcio/>
- FEDRA - Portuguese Rare Disease Alliance
<http://www.fedra.pt/>
- Aliança Portuguesa de Associações das Doenças Raras
<http://aliancadoencasraras.org>
- Rarissimas
<http://www.rarissimas.pt/> and www.linharara.pt

Romania

- RONARD - Romanian National Alliance for Rare Diseases
<http://www.bolirareromania.ro/>
- Romanian National Plan for Rare Diseases (Draft)
http://www.eucerd.eu/upload/file/Docs/ROPlan_en.pdf
- Orphanet Romania national website
<http://www.orpha.net/national/RO-RO/index/homepage/>
- Romanian Journal of Rare Diseases
www.rjrd.ro
- E-University of Rare Diseases
www.edubolirare.ro
- Genetic and Rare Disease Information in Romanian
<http://bolirare.ro>

Slovakia

- Orphanet Slovakia national website
<http://www.orpha.net/national/SK-SK/index/%C3%BAvod/>
- SUKL - State Institute for Drug Control
<http://www.sukl.sk/>

Slovenia

- *Work Plan for Rare Diseases in Slovenia (September 2011)*
http://www.mz.gov.si/fileadmin/mz.gov.si/pageuploads/redke_bolezni_2012_-_nactr_dela/Nactr_dela_na_podrocju_redkih_bolezni.pdf
- Orphanet Slovenia national website
<http://www.orpha.net/national/SI-SL/index/domov/>

Spain

- Estrategia en Enfermedades Raras del Sistema Nacional de Salud (National Strategy for Rare Diseases)
<http://www.msc.es/organizacion/sns/planCalidadSNS/docs/RareDiseases.pdf>
- REPIER – Spanish Network of Rare Diseases Research on Epidemiology. Information System on Rare Diseases in Spain
<https://registoraras.isciii.es/Comun/Inicio.aspx>
- CIBERER – Biomedical Research Network on Rare Diseases
<http://www.ciberer.es/>
- Advisory Committee on Rare Diseases Catalonia
<http://www.gencat.cat/salut/depsalut/html/ca/dir3420/doc32521.html>
- National-Provincial Atlas of Rare Diseases
http://ec.europa.eu/health/ph_threats/non_com/Atlas_Nacional_Provincial_ER_LD2_prot.pdf
- Rare Diseases in Extramadura (2004 Report)
http://ec.europa.eu/health/ph_threats/non_com/docs/rare_spain.pdf
- CISATER – Information Centre for Rare Diseases
http://iier.isciii.es/er/html/er_noant.htm
- IIER – Research Institute for Rare Diseases
<http://www.isciii.es/ISCIII/es/contenidos/fd-el-instituto/fd-organizacion/fd-estructura-directiva/fd-subdireccion-general-servicios-aplicados-formacion-investigacion/fd-centros-unidades/fd-instituto-investigacion-enfermedades-raras/presentacion-e-historia-iier.shtml>
- Orphanet Spain national website
<http://www.orpha.net/national/ES-ES/index/inicio/>
- FEDER – Spanish Rare Disease Alliance

- <http://www.enfermedades-raras.org/>
- Europlan Spanish National Conference Final Report
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_spain_%20europlan.pdf

Sweden

- Swedish Information Centre for Rare Diseases
<http://www.socialstyrelsen.se/>
- Agrenska
<http://www.agrenska.se/en/>
- National Quality Register
<http://www.kvalitetsregister.se/>
- Orphanet Sweden national website
<http://www.orphanet.se/national/SE-SV/index/hemsida/>
- Rare Diseases Sweden
<http://www.sallsyntadiagnoser.se/>
- Medical Products Agency
www.mpa.se
- Rarelink Sweden
www.rarelink.se
- Europlan Swedish National Conference Final Report
http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/FINAL%20Report_Sweden%20EUROPLAN%20NC%202010.pdf

Switzerland

- Swiss Telethon
<http://www.telethon.ch/>
- Orphanet Switzerland national website
<http://www.orpha-net.ch/?lng=EN>
- Proraris
www.proraris.ch
- Gebert RUF Stiftung Foundation
<http://www.grstiftung.ch/en.html>
- Black Swan Foundation
<http://www.blackswanfoundation.ch/>
- Association Enfance et Maladies Orphelines
<http://www.aemo.ch/index.php?page=news/afficher&idNew=22>

Turkey

- Turkey Health Transformation Program
<http://www.saglik.gov.tr/EN/BelgeGoster.aspx?17A16AE30572D313AAF6AA849816B2EF1DACD7356F6C2568>
- Orphanet Turkey national website
<http://www.orpha.net/national/TR-TR/index/orphanet-t%C3%BCrkiye/>

United Kingdom

- National Commissioning Group
www.ncg.nhs.uk
- Advisory Group for National Specialised Services (AGNSS)
<http://www.specialisedservices.nhs.uk/info/agnss>
- UK Genetic Testing Network
<http://www.ukgtn.nhs.uk/gtn/Home>
- Screening Programmes in the UK
<http://www.screening.nhs.uk/programmes>
- Orphanet UK national website
<http://www.orphanet.co.uk>
- Genetic Alliance
<http://www.geneticalliance.org.uk/>
- Rare Disease UK
<http://www.raredisease.org.uk/>
- Contact A Family
<http://www.cafamily.org.uk/index.php?section=861>

- Consultation – UK Plan for Rare Diseases
<http://www.dh.gov.uk/health/2012/02/consultation-rare-diseases/>
- Europlan UK National Conference Final Report
[http://download.EURORDIS.org/europlan/2 EUROPLAN Guidance Documents for the National Conference/final report_uk_europlan.pdf](http://download.EURORDIS.org/europlan/2_EUROPLAN_Guidance_Documents_for_the_National_Conference/final_report_uk_europlan.pdf)
- Rare Disease UK Report: *Improving Lives, Optimising Resources: A Vision for the UK Rare Disease Strategy*
www.raredisease.org.uk/documents/RD-UK-Strategy-Report.pdf
- Specialised Healthcare Alliance Report: The Challenge of rarity
<http://www.shca.info/PDF%20files/The%20challenge%20of%20rarity%20-%20FINAL.pdf>
- Specialised Healthcare Alliance Report: *Leaving No One Behind: Delivering High Quality, Efficient Care for People with Rare and Complex Conditions*
<http://www.shca.info/PDF%20files/SHCA%20Report%202011%20low%20res.pdf>

3. OTHER DOCUMENTS/SITES

- **EPPOSI**
Archive of EPPOSI workshop reports in the field of rare diseases
<http://www.epposi.org/index.php/programmes/rare-diseases>
- **European Conference on Rare Diseases 2007**
ECRD 2007 Final Report
<http://www.rare-diseases.eu/2007/IMG/File/ECRD%202007%20report.pdf>
- **European Conference on Rare Diseases 2010**
ECRD 2010 Final Report
<http://www.rare-diseases.eu/2012/ECRD-2010-Krakow>
- **Rare Disease Day**
<http://www.rarediseaseday.org>



ISBN 978-92-79-25357-7

