

2013 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE



PART II: KEY DEVELOPMENTS IN THE FIELD OF RARE DISEASES IN EUROPE IN 2012

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

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ACRONYMS

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

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 2012. 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 the European Commission, its Agencies or national health authorities.

The report is split into six parts:

Part I: Overview of rare disease activities in Europe

Part II: Key developments in the field of rare diseases in 2012

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

Part VI: Activities at National level in each EU Member State 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 EUCERD) and other specialised reports on topics concerning the field of rare diseases and orphan medicinal products. 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 2012 period 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

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>

field of rare diseases, the development of rare disease focused projects funded by the Commission 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 EUCERD⁷ (July 2010), 2011 EUCERD Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases⁸ and the 2012 EUCERD Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases⁹. The methodology for the production of these previous reports is outlined in their respective introductions. In addition, reports from previous workshops of the EUCERD, including the EUCERD Joint Action have been used.

- **Reports of the EUCERD meetings**

The reports of 2012 meetings of the EUCERD 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.

- **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*¹⁰ 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*)¹¹. 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 was added to the 2012 edition thanks to the JustPharma report *Orphan Drugs in Europe: Pricing, Reimbursement, Funding & Market Access Issues, 2011 Edition*¹² by Donald Macarthur: this report is referenced in footnotes when used.

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

The site of EURORDIS, the European Organisation for Rare Diseases¹³ was used to provide information on EURORDIS activities and projects and to collect data concerning umbrella patient organisations in

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> ; and <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/Reports/2012ReportStateofArtRDActivities.pdf> ; and <http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivitiesII.pdf> ; and <http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivitiesIII.pdf>

¹⁰ http://ec.europa.eu/health/files/orphanmp/doc/inventory_2006_08_en.pdf

¹¹ *Politiques relatives aux maladies orphelines et aux médicaments orphelins*

http://www.kce.fgov.be/index_fr.aspx?SGREF=3460&CREF=13646

¹² <http://www.justpharmareports.com/images/Orphan%20Drugs%20in%20Europe-%20Pricing,%20Reimbursement,%20Funding%20&%20Market%20Access%20Issues,%202011%20Edition.pdf>

¹³ <http://www.EURORDIS.org/secteur.php3>

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 2012 site¹⁴, maintained by EURORDIS, also provided information on events at Member State level¹⁵ concerning Rare Disease Day.

- **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, patient organisations and rare disease/orphan medicinal product policies outside of Europe for Part I. Orphanet also provides links¹⁶ 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 national Orphanet websites were also consulted to gather national events and initiatives.

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 European Union Committee of Experts on Rare Diseases, 2011 Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases and 2012 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 2011. 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 2012.

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 2013 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 2012 to be included in Part II. Final validation of Parts II, V, VI concerning their country were sent to the EUCERD Member State representatives for final validation, to the best of their knowledge, in May 2013.

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 and Consumers, Research and Innovation, Enterprise and Industry, and the European Medicines Agency (EMA) respectively: this process was carried out in March/April 2013 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 2012 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 II, III, IV and V. Part I was

¹⁴ <http://www.rarediseaseday.org/>

¹⁵ <http://www.rarediseaseday.org/country/finder>

¹⁶ http://www.orpha.net/consor/cgi-bin/Directory_Contact.php?lng=EN

drafted by the Scientific Secretariat of the EUCERD and then sent to all EUCERD members and their alternates for their input before publication in May 2013.

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 2012 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; Part V provides the content of Parts II and V in individual country-specific reports.

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 2012.

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 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).

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 2012.

Part V concerns the rare disease activities in the field of rare diseases in each of the 27 Member States plus Iceland, Norway and Switzerland in addition to Croatia and Turkey as candidates for EU membership, as well as Israel. 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 expertise¹⁷
- Registries
- Neonatal screening policy
- Genetic testing¹⁸
- 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 2012¹⁹
- Hosted rare disease events in 2012²⁰
- Research activities (National research activities, Participation in European research projects²¹, Participation in E-Rare, Participation in IRDiRC)
- Orphan medicinal products (Orphan medicinal product committee, Orphan medicinal product incentives, Orphan medicinal product availability²², Orphan medicinal product pricing policy, Orphan medicinal product reimbursement policy, Other initiatives to improve access to orphan medicinal products), Other therapies for rare diseases
- 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.

Part VI concerns the rare disease activities in the field of rare diseases in each of the 27 Member States plus Iceland, Norway and Switzerland in addition to Croatia and Turkey as candidates for EU membership, as well as Israel. This section is the same as Parts II and V, except that the information is presented as a separate document for each country to facilitate dissemination at country level.

Each section has two parts: firstly the state of the art up until the end of 2012, and secondly the state of the art of activities in 2012 only so as to easily identify new actions and activities.

¹⁷ The term “official centre of expertise” used in this report means officially designated via a (ministerial) procedure.

¹⁸ This section contains data extracted in December 2012 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).

¹⁹ As announced in OrphaNews Europe.

²⁰ As announced in OrphaNews Europe.

²¹ Past and ongoing participation in DG Research and Innovation financed projects. Some countries have added information on additional European projects.

²² 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 RELATED TO RARE DISEASES AND ORPHAN MEDICINAL PRODUCTS

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

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

A.1.1.1. European Union Committee of Experts on Rare Diseases (EUCERD) (2010)

Until the 29 February 2012 the EUCERD was supported by the Joint Action for the support of the former RDTF/EUCERD Scientific Secretariat: from March 2012 until February 2015, the activities of the EUCERD are supported by a dedicated Joint Action²³.

Meetings and workshops

In 2012 a number of workshops were held with the support of the EUCERD Joint Action: Workshop on National Planning for Rare Diseases (10-11 September 2012, Rome)²⁴, Workshop on European Reference Networks (ERNs)²⁵ (25 & 26 September 2012, Newcastle), Workshop on cross-referencing of terminologies²⁶ (27-28 September 2012, Paris), Workshop on rare diseases registration²⁷ (13 November 2012, Luxembourg), Workshop on Specialised Social Services for RD²⁸ (6-7 December 2012, Zalau, Romania). An additional workshop was organised with the collaboration of the EC's Joint Research Centre in Ispra and Eurogentest on 19-20 November 2012 on the Genetic Testing offer in Europe.

The EUCERD held three meetings in 2012 in Luxembourg on 26-27 January²⁹, 20-21 June³⁰, and 14-15 November³¹. A range of topics were discussed over the year including European Reference Networks, the Clinical Added Value of Orphan Medicinal Products, National Plans and Strategies for Rare Diseases, the activities of the EUCERD Joint Action, Newborn Screening Practices in Europe, and ways to collaborate with other EU initiatives in the field.

Recommendations on CAVOMP Information Flow

In 2012 the EUCERD issued a recommendation on improving the assessment of the Clinical Added Value of Orphan Medicinal Products (CAVOMP) Information Flow³². It has been acknowledged over recent years that, while the EU Regulation on Orphan Medicinal Products has stimulated research and development of orphan medicinal products in the EU, equitable and timely access to authorised orphan medicinal products for rare diseases patients remains an issue. Large disparities in access exist between and even within the European Member State countries.

To address this issue, several policy documents have called for an increased cooperation between EU-level authorities and Member States in order to improve access to Orphan Medicinal Products for people living with rare diseases:

²³ See section on Joint Actions 1.2.1.

²⁴ http://www.euoplanproject.eu/newsite_986987/events6.html

²⁵ http://www.eucerd.eu/?page_id=2019

²⁶ http://www.eucerd.eu/?page_id=1799

²⁷ http://www.eucerd.eu/?page_id=2023

²⁸ http://www.eucerd.eu/?page_id=2191

²⁹ http://www.eucerd.eu/?post_type=document&p=1152

³⁰ http://www.eucerd.eu/?post_type=document&p=1135

³¹ http://www.eucerd.eu/?post_type=document&p=2156

³² http://www.eucerd.eu/?post_type=document&p=1446

- Final Conclusions and Recommendations of the EU High Level Pharmaceutical Forum³³
- The Commission Communication on “Rare Diseases: Europe’s Challenges” (11 November 2008)
- The Council Recommendation on a European Action in the Field of Rare Diseases (8 June 2009).

The EUCERD was asked to make recommendations to the European Commission on potential ways to facilitate scientific information exchange on orphan medicinal products, in order to support the Member States in their processes of making informed decisions on the scientific assessment of the clinical effectiveness of an orphan medicinal product.

This EUCERD recommendation highlights the fact that the lifecycle of an orphan medicinal product is a continuum of evidence generation, which is needed by assessors and decision makers, as well as being necessary to improve the good use of medicines and thereby optimising the use of limited resources.

The EUCERD recommendation encourages the creation of an Information Flow between individual Member States and between Member States and the EU bodies, which would bridge existing knowledge gaps, especially at the time of marketing authorisation. This information flow and sharing fits into existing regulatory, clinical, Health Technology Assessment (HTA), pricing and reimbursement processes, while avoiding additional burdens.

The CAVOMP information flow recommended by the EUCERD includes the four following time points:

- Timepoint 1: Early dialogue
- Timepoint 2: Compilation Report and evidence definition / Evidence Generation Plan (EGP)
- Timepoint 3: Follow-up of the EGP
- Timepoint 4: Assessment of relative effectiveness

The recommendation capitalises on existing mechanisms, procedures and regulatory frameworks, and does not bring new obstacles to the assessment process: each element within the Information Flow would be maintained by the corresponding institution responsible for that activity during each particular point in time.

The EUCERD Recommendation on *Improving Informed Decisions Based on the Clinical Added Value of Orphan Medicinal Products (CAVOMP) Information Flow* will ultimately accelerate access to approved orphan medicinal products, by providing the most robust set of information possible, while encouraging pricing and reimbursement decisions based on the value of the OMP and promoting good medical practices throughout the EU.

The Recommendation has been submitted to the European Commission.

Report on State of the Art of Rare Disease activities in Europe

Each year the Scientific Secretariat of the European Union of Experts on Rare Diseases (EUCERD) elaborates a comprehensive report covering the state of the art of rare diseases activities at European and Member State level.

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* 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.

The report is a comprehensive resource for the rare disease community and has been 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 2012 edition of the report is split into five parts this year:

- Part I: Overview of rare disease activities in Europe³⁴
- Part II: Key developments in the field of rare diseases in 2011³⁵
- Part III: European Commission activities in the field of rare diseases³⁶
- Part IV: European Medicines Agency activities and other European activities in the field of rare diseases³⁷
- Part V: Activities in EU Member States and other European countries in the field of rare diseases³⁸

³³ http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/pharmaforum_final_conclusions_en.pdf

³⁴ http://www.eucerd.eu/?post_type=document&p=1378

³⁵ http://www.eucerd.eu/?post_type=document&p=1381

³⁶ http://www.eucerd.eu/?post_type=document&p=1384

³⁷ http://www.eucerd.eu/?post_type=document&p=1387

³⁸ http://www.eucerd.eu/?post_type=document&p=1390

Part I is a general overview, geared to a more general public, whilst Parts II, III, IV and V provide a more detailed report of the situation for stakeholders who wish to learn more about the situation at European or national level. In addition, an individual document for each country covered by the report, containing the extracted data from the report, have been produced for the first time this year in order to encourage the dissemination of this information at national level.

The 2012 edition of the report been elaborated with the collaboration of the members of the EUCERD in concertation with a wide range of stakeholders at national level. This report is a deliverable of the EUCERD Joint Action (EJA) : Working for Rare Diseases (N° 2011 22 01). All parts of the report are free to download from www.eucerd.eu.

For the first time, the Scientific Secretariat of the EUCERD has produced individual reports for each European country containing an extraction of the data published in the *2012 EUCERD Report on the State of the Art of Rare Disease Activities in Europe* related to activities in that specific country. These country editions of the report provide both an overview of national activities up to the end of 2011, as well as a specific focus on the latest activities and developments in 2011. The reports are intended for use and dissemination at the national level, as an up-to-date source of information and support tool for stakeholders wishing to raise awareness of the field of rare diseases. These reports are now available on the EUCERD website in the pages dedicated to other resources at the national level.

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

The 2012 Work Plan³⁹ 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.

The annual work plan 2013⁴⁰ for the health programme was adopted on 28 November 2012. €2 million has been foreseen in the work plan to establish a sustainable platform to coordinate and maintain registries and networks on rare diseases, and financing is foreseen for a paediatric oncology pilot network in the context of the implementation of the Cross-Border Healthcare Directive.

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 was planned for 2012.

A.1.2. Activities in the field of rare diseases funded by DG Health and Consumers

Joint Action to support the Orphanet database (2011-2013⁴¹)

Key developments achieved within the Joint Action Orphanet Europe in 2012 include the following⁴¹:

- A new Orphanet homepage was launched in the summer of 2012. This new version is intended to meet the needs of site users who asked for a less cluttered, more user-friendly homepage.
- All the countries which constitute the Orphanet consortium have a national website which is either published entirely in their national language or with a layout published in English and the mandatory texts in the national language.
- The consortium has expanded toward Australia: Western Australia joined Orphanet in 2012. Negotiations were initiated with Argentina, Brazil, China, Chile, Japan and Russia.
- So as to better identify patients in the healthcare system and to improve knowledge of their healthcare pathways, as of 1 December 2012, the Orpha number has been implemented in the French information systems for all hospitalised patients.
- The servers hosting Orphanet have moved from Paris to the largest civil data centre in France which is

³⁹ http://ec.europa.eu/health/programme/docs/wp2012_en.pdf

⁴⁰ http://ec.europa.eu/health/programme/docs/wp2013_en.pdf

⁴¹ <http://www.orpha.net/orphacom/cahiers/docs/GB/ActivityReport2012.pdf>

based in Montpellier, the CINES.

- A “suggest and update” button is available at the bottom of the disease pages to allow the experts and/or the users to suggest modifications and comments to the texts available online.
- Diseases are now cross-referenced with UMLS, MeSH, MedDRA and SNOMED CT.
- Genes are now cross-referenced with Ensembl, Reactome and IUPHAR.
- The Orphanet ontology of rare diseases is now available on Bioportal.
- The encyclopaedia of rare diseases has been expanded and updated. As of 31 December 2012, some abstracts are available in Finnish and Polish in addition to English, French, German, Italian, Spanish, and Portuguese.
- The directory of expert centres, medical laboratories, clinical trials, research projects, networks, registries and patient organisations has been expanded and updated.
- A survey of the centres of expertise listed in Orphanet has been organised to check whether they match the quality criteria defined by the European Union Committee of Experts on Rare Diseases (EUCERD).
- The list of rare diseases (in English and French) has been published as an Orphanet Report Series for more effective communication.
- Most of the Orphanet Report Series have been updated (List of rare diseases, Prevalence of Rare Diseases, Lists of Orphan Drugs, Orphanet Activity Reports, and Satisfaction Surveys).
- The Orphanet Activity report 2011 has been translated into French, Italian, Spanish and Polish.

Orphadata is a new website, launched in the context of the Joint Action to make Orphanet data available for re-use in research. Since January 2012, Orphadata products were downloaded more than 57 000 times, with an average of 4 800 times a month.

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 started in March 2012. The Joint Action had its kick-off meeting in mid-March 2012 and will 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 will support identified priority areas of the EUCERD’s work. Specifically, this Joint Action will address the following priority areas of the Council Recommendation:

- Enhancing the visibility and recognition of RD;
- Contributing to the development and dissemination of knowledge on RD, from specialised research, through to the support of the healthcare professionals and the empowerment of patients;
- Contributing to improvements in access to quality services and care, from diagnosis, through to care and social support and innovative therapies.

This Joint Action comprises five main areas of work:

- The implementation of plans and strategies for rare diseases at national level;
- The standardisation of rare disease nomenclature at international level;
- Mapping the provision of specialised social services and integration of rare diseases into mainstream social policies and services;
- The leveraging of the value of EU networking for improving the quality of care for rare diseases;
- The integration of RD initiatives across thematic areas and across Member States.

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. The activities and outcomes of the EUCERD Joint Action are available on the EUCERD website⁴² which has been re-looked during the first year of the Joint Action.

In 2012 a number of workshops were held with the support of the EUCERD Joint Action: Workshop on National Planning for Rare Diseases (10-11 September 2012, Rome), Workshop on European Reference Networks (ERNs) (25 & 26 September 2012, Newcastle), Workshop on cross-referencing of terminologies (27-

⁴² http://www.eucerd.eu/?page_id=54

28 September 2012, Paris), Workshop on rare diseases registration (13 November 2012, Luxembourg), Workshop on Specialised Social Services for RD (6-7 December 2012, Zalau, Romania).

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

European Commission public consultation on criteria for European Reference Networks (2012)

The European Commission launched a public consultation⁴³ on the criteria for the European Reference Networks and healthcare providers wishing to join the network under the framework of article 12 of the Directive on cross-border healthcare (Directive 2011/24/EU) at the end of 2012. A conceptual paper⁴⁴ and a questionnaire were prepared by Directorate General Health & Consumers for this consultation. European Reference Networks are of particular relevance in the field of rare diseases which are mentioned in the Directive as an example of a field of particular need for such networks. The Directive on the application of patients' rights in cross-border healthcare requires the European Commission to support Member States in the development of European Reference Networks between healthcare providers and centres of expertise. The main added value of the European Reference Networks and of the Centres of Expertise 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 (see Recital 54 of the Directive). European Reference Networks could also be focal points for medical training and research, information dissemination and evaluation, especially for rare diseases. Article 12 requires the Commission to adopt a list of criteria that the networks must fulfill, as well as the conditions and criteria which providers wishing to join networks must fulfill. The Commission is also required to develop and publish criteria for establishing and evaluating European Reference Networks: the Commission must also facilitate the exchange of information and expertise on the establishment of the networks and of their evaluation.

The following target groups were encouraged to give their views: patient organisations, health professionals' organisations and healthcare provider's organisations; healthcare providers and centres of excellence, academic and public health and healthcare specialised institutions; public authorities and government-appointed bodies responsible or involved in the definition of criteria and the establishment and evaluation of centres of reference/excellence and reference networks of centres providing highly specialised healthcare.

The aim of the consultation is to receive input and opinion of stakeholders based on evaluated experiences, regional or national models, technical and professional standards, existing criteria or recommendations, needs and feasibility and EU added value.

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

In September 2012, the European Commission issued a Communication⁴⁵ and proposed two Regulations⁴⁶ designed to revise current European Union legislation on medical devices and *in vitro* diagnostic medical devices. The proposed Regulations are in response to the Conclusions of the Council adopted on 6 June 2011 on innovation in the medical device sector as well as the European Parliament Resolution (on defective silicone breast implants) adopted on 14 June 2012. The proposed Regulations seek to adapt current legislation “to the needs of tomorrow” by creating a “suitable, robust, transparent and sustainable regulatory framework” that will serve to encourage the development of innovative medical devices and *in vitro* diagnostic medical devices that are safe, and effective. The European Parliament and Council need to adopt the Regulations in order for them to become law. There are a number of rare diseases that include medical devices as part of their clinical management, particularly in paediatric populations.

⁴³ http://ec.europa.eu/health/cross_border_care/consultations/cons_implementation_ern_en.htm

⁴⁴ http://ec.europa.eu/health/cross_border_care/docs/cons_implementation_ern_concept_paper_en.pdf

⁴⁵ http://ec.europa.eu/health/medical-devices/files/revision_docs/com_2012_540_revision_en.pdf

⁴⁶ http://ec.europa.eu/health/medical-devices/files/revision_docs/proposal_2012_542_en.pdf and http://ec.europa.eu/health/medical-devices/files/revision_docs/proposal_2012_541_en.pdf

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

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

The European Commission has published several calls for proposals covering research on rare diseases in various areas of FP7 Health Theme. For the period 2007–2012, altogether 95 research projects related to rare diseases have been funded with an EU contribution of over €485 million. The Work Programme 2012 for FP7 Health included a major funding package for rare diseases research in the Call for proposals FP7-HEALTH-2012-INNOVATION-1 opened on 20 July 2011. As the result of the call 26 new research projects related to rare diseases were launched with the EU contribution of €144 million.

The European Commission released on 10 July 2012 the content of a new call for proposals⁴⁷: this year, one specific rare disease topic is included: *Development of imaging technologies for therapeutic interventions in rare diseases*.

A.2.2. The International Rare Diseases Research Consortium (IRDiRC⁴⁸)

There is a recognised need for more international cooperation in research on rare diseases: to align taxonomy, diagnosis and treatment options, to optimise scattered and scarce resources (patients, experts, budgets), with a view to accelerate the development of new diagnostic and therapeutic options.

Governance

IRDiRC is governed by the Executive Committee, three Scientific Committees and twelve working groups⁴⁹. Until April 2013, IRDiRC will be run by an Interim Executive Committee with representatives of all participating funding agencies. It is 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. The Interim Executive Committee held two meetings in 2012, one in Brussels in January and another in Evry, France in September. Executive summaries of the meetings are available on the IRDiRC website.

The three Scientific Committees are 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 viewpoint. Members of the three IRDiRC Scientific Committees were appointed in 2012.

The IRDiRC Working Groups are composed of representatives of projects funded within the scope of the 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.

EC 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-2012-INNOVATION-1⁵⁰ call for proposals (Work Programme

⁴⁷

http://ec.europa.eu/research/participants/portal/page/cooperation;efp7_SESSION_ID=m0pTRn7GxnWW8LynmvWxs9w6J1KJQC4ByLwcYvzJhm6GL0qNLOX11982354445?callIdentifier=FP7-HEALTH-2012-INNOVATION-1#wlp_call_FP7

⁴⁸ http://ec.europa.eu/research/health/medical-research/rare-diseases/irdirc_en.html

⁴⁹ http://ec.europa.eu/research/health/medical-research/rare-diseases/governance_en.html

⁵⁰ <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>

2012). The project funded in this topic, SUPPORT-IRDiRC provides a Scientific Secretariat for the IRDiRC since its launch in October 2012. The Secretariat is located at the Rare Disease Platform in Paris, in the same structure housing the Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD), pan-European rare disease and orphan drug information portal Orphanet, and the French Rare Disease Foundation. The contract for the SUPPORT-IRDiRC has been assigned to two partners: the INSERM (the French National Institute for Health and Medical Research) and the French Rare Disease Foundation. With this new resource, it is expected that the IRDiRC will have the means of achieving its ambitions.

The Call FP7-HEALTH-2012-INNOVATION-1 resulted in the funding of a number of projects contributing directly to the IRDiRC objectives. Three large-scale integrating projects were funded in the area of -Omics for rare diseases: EUREnOmics will systematically apply -omics technologies for the molecular characterisation of rare kidney disorders in view of developing new diagnostics and treatments, NEUROMICS aims to use the most sophisticated -omics technologies to revolutionise diagnostics and develop pathomechanism-based treatments for large groups of rare neuromuscular and neurodegenerative diseases and RD-Connect will create an integrated platform connecting registries, biobanks and clinical bioinformatics for rare disease research into a central resource for researchers worldwide. Also 10 new research projects were funded for preclinical and clinical development of orphan drugs with the major involvement of industry and small and medium sized enterprises.

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 Commission⁵¹.

A.2.3. Access to scientific information

Access to scientific data is especially crucial in the field of rare diseases, an area suffering from a lack of knowledge and resources, fragmentation, and duplication of effort. In August 2008, the European Commission launched the Open Access Pilot in the Seventh Framework Programme (FP7) with the aim of providing improved Internet access to EU-funded research results, particularly peer-reviewed articles published in the scientific literature. Under the pilot scheme, articles produced via research funded under FP7 become freely accessible following a specific embargo period. Pushing the momentum to improve access to published scientific research results further, two key documents were adopted by the European Commission on 17 July 2012. The first, a Communication, entitled Towards better access to scientific information: Boosting the benefits of public investments in research⁵² delineates actions that the European Commission intends to take “to improve access to scientific information and to boost the benefits of public investment in research”. Policies to be implemented under Horizon 2020, the next Framework Programme for Research and Innovation (2014-2020), are described. The second document, accompanying the Communication, is a Commission Recommendation on access to and preservation of scientific information⁵³. This document recommends that EU Member States (MS):

- Define clear policies for the dissemination of and open access to scientific publications resulting from publicly funded research;
- Ensure that research funding institutions responsible for managing public research funding and academic institutions receiving public funding implement the policies;
- Define clear policies for the dissemination of and open access to research data resulting from publicly funded research;
- Reinforce the preservation of scientific information;
- Further develop e-infrastructures underpinning the system for disseminating scientific information
- Ensure synergies among national e-infrastructures at European and global level;

⁵¹ http://ec.europa.eu/research/health/medical-research/rare-diseases/committed-members_en.html

⁵² http://ec.europa.eu/research/science-society/document_library/pdf_06/era-communication-towards-better-access-to-scientific-information_en.pdf

⁵³ http://ec.europa.eu/research/science-society/document_library/pdf_06/recommendation-access-and-preservation-scientific-information_en.pdf

- Participate in multi-stakeholder dialogues at national, European and/or international level on how to foster open access to and preservation of scientific information;
- Designate by the end of the year a national point of reference;
- Inform the Commission 18 months from the publication of this Recommendation in the Official Journal of the European Union, and every two years thereafter, of action taken in response to the different elements of this Recommendation, in accordance with formalities to be defined and agreed.

Together with the Communication and Recommendation, the Commission also adopted a Communication on A reinforced European Research Area partnership for excellence and growth⁵⁴ in which it sets out the key priorities for completing the European Research Area, one of which is the optimal circulation, access to and transfer of scientific knowledge. In January 2013 the European Economic and Social Committee gave a favourable opinion on the Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions – Towards better access to scientific information: Boosting the benefits of public investments in research - COM(2012) 401 final⁵⁵.

A.2.4. DG Research consultation on public-private partnership initiatives in health research

Public-private collaboration is considered crucial in the field of rare disease and orphan drug research, an area that suffers from a lack of resources and funding. Under the 7th Framework programme for research, technological development and demonstration activities (2007-2013) (FP7) the European Union (EU) entered into a Public Private Partnership (PPP) with the pharmaceutical industry, represented by its umbrella organisation European Federation of Pharmaceutical Industries and Associations (EFPIA). The Innovative Medicines Initiative (IMI) was established by Council regulation 73/2008 of 20.12.2007. Both partners contribute € 1 billion each to implement IMI. With this funding IMI is Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients – including rare disease medicinal products. Based on the success of IMI the European Commission is now exploring whether under Horizon 2020 a renewed PPP should be launched. The Commission proposal for Horizon 2020 foresees that the priority "societal challenges" is also implemented through PPPs. Selection of PPPs will be based on a set of clearly defined criteria, including the added value of action at the EU level, the scale of impact on industrial competitiveness, sustainable growth and socio-economic issues, and the long-term commitment from all partners based on a shared vision and clearly defined objectives. As part of this process a public consultation was conducted in 2012⁵⁶. The consultation seeks key views relating to the launch of a PPP in the life sciences research area under Horizon 2020 and what areas should be addressed.

A.2.5. Biobanks for Europe: A challenge for governance

A new report issued in 2012⁵⁷, produced by DG Research with the participation of an interdisciplinary group of experts, looks at the regulatory and ethical challenges of international biobank research. In order to link individual biobanks together as part of a pan-European infrastructure supporting medical research and health care, an adequate governance framework needs to be put in place. The development of a biobank infrastructure is seen as critical in the field of rare diseases where difficulties accessing specific rare samples

⁵⁴ http://ec.europa.eu/research/science-society/document_library/pdf_06/era-communication-partnership-excellence-growth_en.pdf

⁵⁵ <http://www.eesc.europa.eu/?i=portal.en.int-opinions.24976>

⁵⁶ http://ec.europa.eu/research/consultations/life_science_h2020/consultation_en.htm

⁵⁷ http://bookshop.europa.eu/en/biobanks-for-europe-pbKINA25302/downloads/KI-NA-25302-EN-C/KINA25302ENC_002.pdf;pgid=y8dlS7GUWMdsR0EAIEMEUUsWb00006naClsSM;sid=vk4G5ut1qt0G-LsRpY6YQYIQuZ0ANeymuJ0?FileName=KINA25302ENC_002.pdf&SKU=KINA25302ENC_PDF&CatalogueNumber=KI-NA-25302-EN-C

can hinder research. This expert report offers a set of recommendations for the effective governance of a pan-European biobank network.

A.2.6. Reform of the EU Data Protection Directive

In January 2012, the European Commission proposed a comprehensive reform of the European Union's 1995 Data Protection Directive, seeking to update and modernise the legislation in view of the major technological advances made in recent years. The overhaul also aims to increase harmony between the 27 EU Member States which have implemented the current Data Protection Directive 95/46/EC differently, resulting in divergences in enforcement. The proposed Regulation will decrease the fragmentation by establishing a single set of rules valid across the EU. Specific provision on processing of personal data for health purposes and on historical, statistical and scientific research purposes will increase legal certainty and clarity on applicable rules for data protection in health research. The Commission's proposal for the Regulation is currently being discussed in the European Parliament and the Council.

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

A.3.1. EU activities under Regulation (EC) No 141/2000 on orphan medicinal products

Orphan Medicinal Product Regulation (16 December 1999)

The Commission adopts decisions on designation based on an opinion from the COMP. In 2012, the Commission granted 150 orphan designations⁵⁸. In addition, the Commission authorised nine orphan medicinal products in 2012. These newly authorised medicines aim at treating severe diseases such as lipoprotein lipase deficiency, short Bowel Syndrome, acute myeloid leukaemia or anaplastic large cell lymphoma⁵⁹.

SMEs will continue to avail in 2013 the free services of protocol assistance (scientific advice); fee waiver for initial market-authorisation applications, pre-authorisation inspections, post-authorisation applications and annual fee waiver in the first year from marketing authorisation. However, Non-SMEs developing orphan medicinal products will have fewer benefits in 2013 in some categories. Fee reductions for non-SME will now include a 40% reduction for non-paediatric protocol assistance (previously 75%) and no fee reductions for initial market-authorisation applications (previously 10%) and pre-authorisation inspections (previously 100%). Protocol assistance for paediatric-related medicines will continue to be free for non-SMEs.

A.3.2. European legislation and activities in the field of clinical trials

Revision of the EC Clinical Trials Directive

On 17 July 2012, the Commission adopted a "Proposal for a Regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC"⁶⁰. The adoption was announced in a press release supported 'questions and answers' document⁶¹ and was accompanied by an impact assessment report⁶². The proposal has been submitted to the European Parliament and the Council.

A.3.3. European legislation and activities in the field of advanced therapies

First regulatory approval for a gene therapy drug in the EU

On 2nd November, 2012, the European Commission announced the authorisation of Glybera (alipogene tiparvovec) for marketing in the European Union. The product is designed to treat patients with lipoprotein lipase deficiency (LPLD), a rare inherited disorder which disrupts fat production in the body. Due to a defective gene, patients with this disorder cannot produce enough lipoprotein lipase (LPL), an enzyme responsible for breaking down fats. Glybera uses an adeno-associated virus to infect muscle cells with working copies of the

⁵⁸ Data provided by DG Sanco.

⁵⁹ Data provided by DG Sanco.

⁶⁰ http://ec.europa.eu/health/files/clinicaltrials/2012_07/proposal/2012_07_proposal_en.pdf

⁶¹ http://ec.europa.eu/health/files/clinicaltrials/2012_07/press-releases/memo-12-566_en.pdf

⁶² http://ec.europa.eu/health/files/clinicaltrials/2012_07/impact_assessment_part1_en.pdf (Volume I) and http://ec.europa.eu/health/files/clinicaltrials/2012_07/impact_assessment_part2_en.pdf (Volume II)

LPL gene to enable production of the enzyme in the cells. Backed by the recommendation of the European Medicines Agency, this is the first regulatory approval of a gene therapy drug in the European Union.

A.3.4. European legislation and activities in the field of medicinal products for paediatric use

Public consultation on the experience gained from five years of the Paediatric Regulation

Five years after the Paediatric Regulation came into being, the European Commission is preparing a general report presenting the experience acquired as a result of the application of the Paediatric Regulation and including an inventory of the medicinal products authorised for paediatric use since the regulation took effect. The Commission has released for public consultation⁶³ the *General Report on Experience Acquired as a Result of the Application of the Paediatric Regulation: Experience Acquired and Lessons Learnt*. The responses⁶⁴ to the public consultation were published in January 2013.

A.3.5. Other EC activities and initiatives relative to the field of orphan medicinal products

Launch of a process on corporate responsibility in the field of pharmaceuticals

The Directorate General for Enterprise and Industry announced⁶⁵ in 2010 the launch of a process on corporate responsibility⁶⁶ in the field of pharmaceuticals. In a press release⁶⁷, Commission Vice President Antonio Tajani stated that it is time “to launch a specific consultation at European level in [the pharmaceutical sector] so that commercial imperatives can be combined with the needs of society”. Three separate platforms: ethics and transparency; access to medicines in Africa; and access to medicines in Europe will “examine the major challenges of access to medicines in Europe and Africa in the light of the issues of price and reimbursement.” A number of projects have been launched: one of these projects will look into the possibility to establish a mechanism of coordinated access to orphan medicinal products. For this project, “Members are invited to develop the concept of a coordinated access to orphan medicinal products based on the set up of programmes between companies and groups of competent authorities and results of the ongoing project on a mechanism for clinical added value on orphan medicinal products. A pilot project could be set up in a second stage”. Other projects that could be relevant to the field of rare diseases include one on capacity building on managed entry agreements for innovative medicines and another on facilitating the supply in small markets. Together with Member States, a number of stakeholder organisations take part in the platform, including the European Patients Forum, the European Hospital and Healthcare Federation, the European Federation of Pharmaceutical Industries and Associations, and the European Association for Bioindustries. Results of most working groups under the platform “Access to medicines in Europe” will be submitted to the Steering Group members for endorsement at their meeting in April 2013.

⁶³ http://ec.europa.eu/health/human-use/paediatric-medicines/developments/index_en.htm

⁶⁴ http://ec.europa.eu/health/files/paediatrics/2012-09_publicconsultation_en.pdf

⁶⁵ <http://europa.eu/rapid/pressReleasesAction.do?reference=MEMO/10/442&format=HTML&aged=0&language=EN&guiLanguage=en>

⁶⁶ http://ec.europa.eu/enterprise/sectors/healthcare/competitiveness/process_on_corporate_responsibility/index_en.htm

⁶⁷ <http://europa.eu/rapid/pressReleasesAction.do?reference=IP/10/1170&format=HTML&aged=0&language=EN&guiLanguage=en>

B. EUROPEAN MEDICINES AGENCY ACTIVITIES

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

European Medicines Agency⁶⁸

Seven scientific committees⁶⁹, composed of members of all EU and EEA-EFTA states, some including patients' and doctors' representatives, conduct the main scientific work of the Agency: the Committee for Medicinal Products for Human Use (CHMP), the Committee for Medicinal Products for Veterinary Use (CVMP), the Committee for Orphan Medicinal Products (COMP), the Committee on Herbal Medicinal Products (HMPC), the Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT), and the Pharmacovigilance Risk Assessment Committee (PRAC). The PRAC started working in 2012 and it is the last Committee being created at the Agency; and is responsible for providing recommendations to the Committee for Medicinal Products for Human Use and the coordination group on any question relating to pharmacovigilance activities in respect of medicinal products for human use and on risk management systems and monitoring the effectiveness of those risk management systems.

Work programme

The European Medicines Agency's Management Board, at its meeting on 15 December 2011, adopted the Agency's work programme⁷⁰ and budget for 2012 which are driven by the implementation of the pharmacovigilance legislation. The work programme forecasted a stable number of applications for marketing authorisation for human and veterinary medicines in 2012. The Agency expected 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 advices 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, were all listed as priority areas in the work plan.

In the document it was noted that orphan medicinal product designations were 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 was also expected. Objectives for 2012 included 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.

The European Medicines Agency's Management Board, at its meeting on 13 December 2012, adopted the Agency's work programme and budget for 2013⁷¹. The Agency's priorities will be to continue to ensure that assessment activities are conducted to the highest scientific levels, to increase efficiency in its activities, and to develop initiatives for greater transparency and communication with stakeholders. Further specific drivers include the continued implementation of the pharmacovigilance legislation and the new falsified-medicines legislation, and the planned revision of the veterinary medicines legislation. In 2013, the Agency expects a

⁶⁸ Information reproduced from

http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000091.jsp&murl=menus/about_us/about_us.jsp&mid=WC0b01ac0580028a42

⁶⁹ http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000217.jsp&murl=menus/about_us/about_us.jsp&mid=WC0b01ac0580028c77

⁷⁰ http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/document/document_detail.jsp?webContentId=WC500122955&mid=WC0b01ac058009a3dc

⁷¹ http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2012/12/WC500136442.pdf

stable total number of applications for human medicines, with 100 applications in 2013. These include some 54 applications for new medicinal products (excluding designated orphan medicines), 20 new orphan medicines and 20 generic applications (2012: 52, 13 and 39 respectively). Some 10 applications for new veterinary medicines are expected, with 3 generic applications (2012: 9 and 3 respectively). The work programme is accompanied by a budget of €231.6 million, an increase of 4.1% over 2012, which includes fee revenue of €179.8 million (3.8% increase compared with 2012, this increase is mainly due to inflation) and a European Union (EU) contribution of €39.2 million.

During 2013 the Agency will continue to foster its approach to communication and transparency in order to strengthen public confidence in the Agency and the EU system of evaluation and supervision of medicines. The publication of the agendas and minutes of all scientific committees' meetings has been already a reality for the Committee for Orphan Medicinal Products since September 2012. Following the successful workshop in November 2012 on access to clinical-trial data and transparency, the Agency will start a consultation with stakeholders at the beginning of 2013 in order to publish a policy on the release of data from clinical trials in early 2014.

EMA annual reports

The European Medicines Agency Annual Report for 2011⁷² was released in mid 2012. The report shows continuously high levels of activities in almost all of the Agency's business areas. There was a slight increase in the number of applications for initial marketing authorisations for medicines for human use, from 91 applications in 2010 to 100 applications in 2011. Most of this increase was due to applications received for new medicines: this number rose by over 40% from 34 in 2010 to 48 in 2011. The number of applications received for initial marketing authorisation for veterinary medicines declined slightly, which is likely to reflect the delayed impact of global recession and the consolidation seen in recent years in the veterinary sector. Significant advances were made in terms of transparency. In March 2011, the European Union Clinical Trials Register went live. The launch of this database was welcomed by patients', consumers' and healthcare professionals' organisations as an important step towards increasing transparency of medical research and facilitating availability of information about clinical trials taking place. Later in the year, the Agency launched a new database of European experts, which allows the public to access an expert's declaration of interests online. However, nowhere was the impact of the Agency's much more proactive approach to transparency more dramatic as in relation to handling of access-to-documents requests. During the course of the first full year of operation of the new access to documents policy, the Agency released more than a million pages in response to requests.

In 2011 the EMA received 166 orphan designation applications, of which 111 positive opinions were issued by the Committee for Orphan Medicine Products (COMP). Of these, oncology products once again were in the majority.

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

EMA Committee for Orphan Medicinal Products (COMP)

Since its implementation, the Orphan Regulation has yielded more than 1120 positive opinions for orphan product designation, adopted from 1630 applications reviewed since 2000. To date, the distribution of the prevalence of conditions for which the designations have been adopted shows that the most frequently designated conditions have been those that affect between 1 and 3 in 10 000 patients, that is between approximately 50 000 and 150 000 people (receiving 51% of all orphan designations). Indeed, 48% of the orphan medicinal products having obtained market authorisation in the EU, are for the treatment of diseases affecting less than 1 in 10 000 patients.

The number of applications has increased steadily each year during the first decade of the Regulation with 197 applications received in 2012. Seventy-eight designated products had received marketing authorisation by the end of 2012, of which oncology is by far the most common therapeutic area (39%). Interestingly, the average time span between designation and authorisation is only 2.8 years, indicating that designated products were at an advanced developmental stage.

⁷² http://www.ema.europa.eu/docs/en_GB/document_library/Annual_report/2012/06/WC500128162.pdf

The COMP has also granted orphan medicinal product designations to various innovative product types (i.e. fusion proteins, monoclonal antibodies, cell and gene therapy products, tissue-engineered products, oligonucleotides): at the end of 2012, the COMP has given more than 80 positive opinions for advanced therapy products out of a total of 1125 positive opinions for orphan medicinal product designation.

Positive opinions on orphan designations in 2012

The COMP adopted 139 positive opinions on orphan designations in 2012. The European Commission granted 148 of orphan designations in 2012. Ten orphan medicinal products received marketing authorisation in 2012 covering 12 conditions (due to variations)⁷³.

EMA's Committee for Orphan Medicinal Products initiative to publish prevalence information (2012)

As part of a general growing trend toward sharing data and resources in the interest of facilitating rare disease and orphan drug information and research, the European Medicines Agency (EMA) has created a table of relevant sources for prevalence data for orphan conditions⁷⁴. The sources included in the document were validated by the Committee for Orphan Medicinal Products (COMP) during the evaluation of orphan designation applications. The table, publicly available, will be updated on a regular basis. While sponsors are still required to submit original, verifiable, current prevalence data with their application for an orphan designation, the table is considered a useful resource for facilitating access to such data. Orphan designated medicinal products are indicated for conditions that affect 5 persons or less per 10 000 of the population in the EU. Determining prevalence can be challenging for stakeholders. The new table lists the sources, such as relevant scientific literature, registries and databases, used to determine prevalence for a condition at the time an orphan designation was sought.

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

CHMP opinions in 2012 concerning orphan medicinal products

In 2012, the CHMP issued positive opinions for marketing authorisation applications for: Revestive (teduglutide) for the treatment of adult patients with short bowel syndrome, and Signifor (pasireotide) for the treatment of Cushing disease in patients who cannot have surgery or for whom surgery has not been successful.

Following review from its Committee for Medicinal Products for Human Use (CHMP), the European Medicines Agency (EMA) has also recommended marketing approval for Kalydeco (ivacaftor), an orphan-designated medicine indicated for the treatment of cystic fibrosis in patients age 6 years and older who have a *G551D* mutation in the cystic fibrosis transmembrane regulator (*CFTR*) gene. The CHMP reviewed Kalydeco in 150 days under the EMA's accelerated assessment scheme, a mechanism created to speed up access to new medicines. Kalydeco, from Vertex Pharmaceuticals Ltd (UK), is the first treatment that targets the underlying mechanism of the disease, by restoring the mutated CFTR protein function. Other existing therapies for cystic fibrosis address the consequences of the disease, rather than the cause.

The CHMP also gave a positive opinion recommending a variation to the terms of the marketing authorisation for the medicinal product Volibris (ambrisentan) (Glaxo Group Ltd). The CHMP adopted a new contraindication for idiopathic pulmonary fibrosis with or without secondary pulmonary hypertension.

Workshop on clinical trial data and transparency (22 November 2012)

The European Medicines Agency (EMA) announced in 2012 that it will proactively publish clinical trial data and enable access to full data sets by interested parties. As there are a number of practical and policy issues that need addressing before complex data sets can be made available, a workshop was held on 22 November 2012 to discuss topics relating to this evolution. The workshop seeks to elicit the views and concerns from a broad

⁷³ Data provided by EMA's COMP,

http://www.ema.europa.eu/docs/en_GB/document_library/Committee_meeting_report/2013/03/WC500140633.pdf

⁷⁴

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/07/news_detail_001576.jsp&mid=WC0b01ac058004d5c1

range of institutions, groups and individuals in order to help the Agency define the modalities of proactive access to clinical trial data. A report⁷⁵ was published after the workshops which presents the debate that was at the heart of the clinical-trial transparency event, and also outlines the Agency's action plan with regard to access to clinical-trial data.

B.4. EMA activities in the field of advanced therapies

Reflection paper on the classification of advanced-therapy medicines (2012)

The European Medicines Agency (EMA) released a reflection paper on the classification of advanced-therapy medicines for public consultation. The paper clarifies the legal basis for the classification of medicines as advanced therapies and provides information on how these medicines are classified as gene therapy, somatic-cell therapy, tissue-engineered or combined medicines. The paper additionally discusses the information required for application for classification. Within the EMA, the Committee for Advanced Therapies is responsible for issuing opinions on whether a medicine should be classified as an advanced therapy. The reflection paper was open for comments until 31 July 2012.

Public website for reports of adverse effects (2012)

The European Medicines Agency (EMA) launched in 2012 a public website⁷⁶ housing reports of adverse effects suspected in medicinal products authorised in the European Economic Area (EEA). The reports originate from national medicines regulatory authorities and the pharmaceutical companies that hold marketing authorisations for the medicines and are extracted from EudraVigilance, the European Union medicinal product safety database. The website launch is in compliance with EudraVigilance⁷⁷ Access Policy, developed to improve public health by supporting the safety-monitoring of medicines and increasing the EMA's level of transparency. According to a press release, the new website houses data on some 650 medicinal products, and gathers various incidents on a given product into one report. The information can be viewed by various features, including age, gender, the nature of the adverse effect, and outcome. There is also information provided on how to report a suspected adverse reaction to a medicine. The website is available in all 23 EU languages.

Pilot for electronic application forms for submission of centralised marketing authorisation applications (2012)

The European Medicines Agency (EMA) has launched a four-month pilot phase of electronic application forms for the submission of centralised marketing authorisation applications. The pilot will allow sponsors to use an interactive PDF form for initial marketing authorisation applications for human medicines as well as variation and renewal applications for human and veterinary medicines. The pilot moves forward the EMA's progression toward the standard use of electronic applications.

Public consultation on a revision of the guideline for the evaluation of human anticancer medicines (2012)

The European Medicines Agency has opened a public consultation on the revised guideline on the evaluation of human anticancer medicines. The guideline seeks to provide guidance on all stages of clinical drug development for the treatment of malignancies, including rare cancers and paediatric cancers, all of which are rare. The guideline revision emphasises exploratory studies to properly define the most appropriate target population as well as the role of biomarkers. Also new, the guideline incorporates disease-specific guidance. Comments on the reflection paper were open until 31 May 2012.

Guideline on use of pharmacogenetics in evaluating pharmacokinetics of medicines (2012)

Following a period of public consultation and the consequent adoption by the Committee for Medicinal Products for Human Use, the *Guideline on the Use of Pharmacogenetic Methodologies in the Pharmacokinetic Evaluation of Medicinal Products*⁷⁸ has now been published by the European Medicines Agency. This guideline

⁷⁵ http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2012/12/WC500135842.pdf

⁷⁶ <http://www.adrreports.eu/index.html>

⁷⁷ <http://eudravigilance.ema.europa.eu/human/index.asp>

⁷⁸ http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/02/WC500121954.pdf

elaborates requirements and recommendations on when pharmacogenetic studies should be performed; how these studies should be designed and carried out; how the clinical impact of genetic differences between patients should be evaluated; how dosing or treatment recommendations for genetic subpopulations should be studied; consequences for treatment recommendations and labelling; and the impact of interactions between medicines and of impaired or immature organ function. Companies applying for marketing authorisation should follow the guideline from 1 August 2012.

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

Paediatric Committee (PDCO)

The Paediatric Committee at the European Medicines Agency (PDCO) is developing an inventory process aiming to identify areas in which further research and development specific to paediatric medicinal products are needed. Such an inventory could assist industry in identifying opportunities, provide a source of information for healthcare professionals and patients, and aid various PDCO assessment processes. The first inventory, in the area of cardiovascular medicines for use in children, was released for public consultation⁷⁹ in 2012.

B.6. International cooperation between regulators in the field of orphan medicinal products

The COMP has established an active international cooperation, which will be expanded in 2013. In 2008, the Committee started collaboration with the United States Food and Drug Administration (FDA), allowing applications for orphan drug designations to be submitted in parallel to the two agencies. The parallel submission process helps rationalise the development of orphan medicines by facilitating access to parallel scientific advice (protocol assistance) from the two regulatory authorities. Based on the success of this collaboration, which led to 62% of applications submitted in parallel in the EU and the FDA in 2012, last year the COMP began to collaborate with the Japanese regulatory authorities. An increase in the number of Japanese orphan-drug designations with prior European designations was observed in 2012. A dialogue with Health Canada has been established and a closer collaboration with this country is anticipated in 2013.

In fiscal year 2012, the Food and Drug Agency (FDA) continued to bring innovative drugs to patients in the United States quickly and efficiently, while ensuring that medicines are safe and effective. Of the 35 novel drugs approved in 2012⁸⁰, nine concerned orphan diseases, continuing FDA's commitment to approve drugs for patients with rare conditions. Again, FDA expedited the review and approval of over half of these innovative medicines by using its several review authorities for important new drugs, including Fast Track, Priority Review, and Accelerated Approval.

Confidentiality agreement with Japan (2012)

The European Medicines Agency and the European Commission announced in 2012 the extension of their confidentiality arrangement with the Ministry of Health, Labour and Welfare and the Pharmaceuticals and Medical Devices Agency of Japan, established in 2007, for another year⁸¹. Under the arrangement, advance drafts of legislation and regulatory guidance documents, scientific advice on medicine development, assessments of applications for marketing authorisations and information concerning the safety of marketed medicines may be exchanged between the two agencies. This is welcome news for the rare disease and orphan drug community, which is striving to reduce duplication of effort and encourage cooperation in the field.

⁷⁹ http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/08/news_detail_001591.jsp&mid=WC0b01ac058004d5c1

⁸⁰ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/UCM330859.pdf>

⁸¹ http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2012/02/news_detail_001429.jsp&mid=WC0b01ac058004d5c1

C. OTHER EUROPEAN RARE DISEASE ACTIVITIES

C.1. E-Rare

In December 2012, E-Rare launched its 5th Joint Transnational Call (JTC 2013) open to participants in 14 countries including Canada, Hungary, Romania and Switzerland, joining the E-Rare call for the first time.

The overwhelming response to the E-Rare joint calls demonstrates the demand and the potential of the rare disease research community to engage in collaborations with complementary expertise.

It is now recognised that E-Rare has become one of the major contributors to transnational rare diseases research funding. To continue and expand its activities in accelerating the development of new diagnostics and therapeutics for patients suffering from rare diseases the "E-Rare Group of Funders" (FWF, Austria; FNRS, Belgium; FWO, Belgium; ANR, France; BMBF, Germany; GSRT, Greece; ISS, Italy; CSO/MOH, Israel; FCT, Portugal; ISCIII, Spain; ZonMw, The Netherlands and TUBITAK, Turkey) recently joined (in September 2012) the International Rare Disease Research Consortium (IRDiRC).

C.2. International Rare Disease Events in 2012

Rare Disease Day 2012 (29 February 2012)

The Fifth edition of the annual Rare Disease Day 2012, organised by EURORDIS, was held on 29 February 2012. Rare Disease Day 2012 included 63 countries (up from 55 in 2011, 46 in 2010, 30 in 2009 and 18 the first year); first-time countries this year included Costa Rica, Chile, Macedonia, Malta, Pakistan, Uruguay, and Venezuela. In 2012, over 300 "Friends of Rare Disease Day" signed up on the Rare Disease Day (RDD) website including the French Ministry of Health and other luminaries such as Harvard Medical School, the Slovenian Ministry of Health, members of the biopharmaceutical industry, numerous patient groups and individuals involved with patients, rare disease research entities, and others.

The official Rare Disease Day (RDD) website⁸², maintained by EURORDIS, received almost 40,000 visits from some in the weeks leading up to the day. The response to social media was strong: the RDD Facebook page received over 13 000 "likes" and thousands of "Tweets" were sent via Twitter. Over 350 photo stories were uploaded to the site and the special Rare Disease Day video has been viewed over 100 000 times. The media played a key role as print, radio and television news sources around the world reported on the happenings, heightening exposure to the rare disease cause significantly.

In 2012, Rare Disease Day put the spotlight on "Solidarity" a value that characterises the rare disease patient movement across diseases and national boundaries. The theme also served to focus on the importance and the need for collaboration and mutual support in an area where patients are rare, expertise is scarce and people affected face similar challenges. At the European level, Rare Disease Day will sought to highlight rare diseases as a model of EU solidarity in today's crisis-stricken Europe. In line with this initiative, EURORDIS organised a symposium with the European Commission, in Brussels on 29 February 2012, to showcase the successes achieved over the last decade and to discuss the way forward. The European Symposium 'Rare Diseases a model of EU Solidarity'. The meeting aimed to demonstrating the value of the EU-wide approach in the area of rare diseases – show it has a positive impact on the health of all EU citizens and can generate a good return to investment, in addition to being a model that is being emulated outside of the EU. Attendees included patients and patient representatives, researchers, health professionals, members of the EU Committee of Experts on Rare Diseases, European Parliamentarians, high-level officials of the European Medicines Agency and the European Commission, as well as representatives of the pharmaceutical and biotech industry.

In addition, EURORDIS held a gala on the evening of the 29 February 2012 in Brussels, presenting awards for excellence and leading work in the field of rare diseases. These prestigious awards are judged by the

EURORDIS Board of Directors based on over 100 nominations received from EURORDIS members, volunteers and staff. The EURORDIS Awards are designed to recognise the outstanding commitment and achievements of patients' advocacy groups, volunteers, scientists, companies, media and policy makers who have contributed - directly or indirectly - to reducing the impact of rare diseases on people's lives.

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.

EC Joint Research Centre workshop on the Genetic Testing Offer in Europe – Ispra, 19-20 November 2012

The EC's Joint Research Centre organised, in collaboration with the EUCERD and Eurogentest, an expert workshop in Ispra at the end of 2012 in order to discuss a number of areas where European cooperation could give added-value in terms of the quality of genetic services and the organisation of genetic services. The topics discussed included the organisation of quality assessment schemes, the challenge presented by next generation sequencing techniques and direct-to-consumer testing. Areas for harmonisation at European level could be envisaged, and the outcomes of the workshop will be considered by the EC. The outcomes⁸³ of the workshop will be considered by the EUCERD as a basis for a possible future EUCERD recommendation in this area.

European Conference on Rare Diseases and Orphan Products – Brussels, 24-25 May 2012

The sixth edition of this biennial conference drew together the rare disease and orphan drug community from across Europe and beyond to share triumphs, address problems, unstop bottlenecks, and move forward on all fronts – regulatory, research, policy, therapeutic, social. Organised by the European Organisation for Rare Diseases (Eurordis) and the DIA Europe, the ECRD was held in Brussels from 24-25 May. Over 650 participants from 45 different countries attended.

Perhaps the largest benefit of the ECRD is its capacity to galvanise stakeholders. The rich exchange between participants – researchers, health professionals, patients and patient organisations, policy makers, members of the biopharmaceutical industry, and bioinformatics specialists, breathes fresh hope and energy into the goals and struggles individual participants bring to the table. This year's event was particularly pivotal for driving forward national rare disease plans, which the *Council Recommendation on an Action in the Field of Rare Diseases* urges EU Member States to create by the end of 2013. This year's ECRD focused on several often complex issues relating to the implementation of the Council Recommendation. The organisation and development of Centres of Expertise for rare diseases was discussed at length, along with similar issues around the European Reference Networks, which still have to be defined and selected within the context of the *Directive on cross-border healthcare*, the adoption of which spurred discussion on how the rare disease community can best benefit from sharing knowledge and resources. While most experts agree that it is the data that must travel as much as possible, many practical questions – especially in the areas of the organisation of expertise and reimbursement – remain to be ironed out. Other topics addressed this year included Health Technology Assessment (HTA) in the EU Member States and how to develop a harmonised approach that will yield greater equity between countries while eliminating unnecessary duplication of effort. Another interesting subject involved the care of patients transitioning from paediatric to adult services. For many rare diseases, comprehensive services available for paediatric populations suddenly dry up when patients reach adulthood. Given that advances in care and treatment are allowing a longer life for many patients, this is an urgent question that needs addressing.

There were many interesting sessions offered within the context of seven distinct themes: *National Plans for Rare Diseases; Centres of Expertise and European Reference Networks; Information and Public Health; Research from Bench to Bedside; Orphan Products and Rare Disease Therapies – Access; Orphan Products and Rare Disease Therapies – Regulatory; and Patients' Empowerment*. Of particular note were the opening Plenary sessions, which featured a keynote address from European Commissioner for Health and Consumer Policy, John Dalli, who set a tone of optimism by announcing that “*action on rare diseases features prominently in the European Commission proposal for the new Health Programme and the new Research Programme for 2014 onwards*” and that he was confident that the EU Member States would “*adopt national plans on rare diseases in due time despite the difficult economic climate*”.

⁸³ http://ihcp.jrc.ec.europa.eu/our_activities/public-health/jrc-publishes-a-report-entitled-genetic-testing-offer-in-europe/at_multi_download/file?name=finalreportWSgenetic%20testing.pdf

Other notable sessions throughout the two day event included the *Introduction to Centres of Expertise; How Rare Disease Research can contribute to innovation; Introduction of European Reference Networks; Making rare diseases visible for research and public health; The Big Picture of Rare Disease Research Policy; The value and specificity of the rare disease business model; Improving Care through Clinical Guidelines; EU Infrastructure & Projects in the field of rare diseases and patient registries; EU Policy Developments in the Field of Access to Orphan Drugs; Health care pathways focusing on transition from childhood to adulthood; Novel reimbursement schemes as a potential way forward; Compassionate Use Programmes; and Ways to look at HTA for Orphan Drugs and Rare Diseases.*

The Executive summary report⁸⁴ of the conference includes the main features and statistics of the Conference, the programme at a glance, a list with photos of the Programme Committee, a list of posters' titles and authors, as well as the poster winner and descriptions of exhibiting companies. The seventh ECRD will be held in Berlin in 2014.

High Level Conference - EU Health Programmes: results and perspectives (2012)

A conference⁸⁵ was held on 3 May 2012 by the European Commission's Directorate-General for Health and Consumers and its Executive Agency to reflect on the results and success stories from the first and second Health Programmes. The conference was also an opportunity to share views and build consensus for the future third programme. More than 400 people have participated in the conference, including policy makers, key actors from the health sector, NGOs, Member States and European institutions, health programmes' beneficiaries, scientists and academics from EU and third countries, participating in the Health Programme.

C.3. Other European activities in the field of rare diseases in 2012

Council of Europe information document on genetic tests for health purposes (2012)

The Council of Europe, with the support of the European Society of Human Genetics and EuroGentest, published in 2012 an information document that aims to "provide objective information on genetic tests, their nature and potential implications of their results". The document also presents different types of tests available, their application in the medical field and the extent and limits" of the test results. The document can be consulted in a range of languages⁸⁶ on the site of the Council of Europe.

European Academies Science Advisory Council and Federation of European Academies of Medicine recommendations on *Direct-to-Consumer genetic testing* (2012)

A lay account of the latest report of EASAC - the European Academies Science Advisory Council, and FEAM - the Federation of European Academies of Medicine, entitled "*Direct-to-Consumer genetic testing for health-related purposes in the European Union*"⁸⁷ was published in 2012. This report details the outcomes of a Working Group set up by EASAC and FEAM to review consumer genetic services in Europe. The report proposes a "*list of recommendations to policy-makers in the European Commission, European Parliament and Council of Ministers, and to Member States in which parallel action may be necessary*".

European Directory of Health Apps (2012)

The first edition of the *European Directory of Health Apps*⁸⁸ was unveiled on 3 October 2012 at the European Health Forum Gastein 2012. The Directory contains information on some 200 health-related smartphone applications that assist patients with the management of their medical conditions – including several rare diseases. Published by UK-based research, publishing and consultancy group, PatientView, with a foreword from Robert Madelin, European Commission Director General for Communications Networks, Content and Technology (DG Connect), the Health Apps selected for the Directory have all been recommended by patient groups and empowered consumers. There is one App for rare diseases in general: ODDT, a crowdsourced content aggregator that collates treatment research data, primarily for scientists. There are also Apps for specific rare diseases, including haemophilia and Huntington disease, an App on Cross-Border Healthcare, and

⁸⁴ <http://www.rare-diseases.eu/2012/ECRD-2012-Conference-Report>

⁸⁵ http://ec.europa.eu/health/programme/docs/ev_20120503_prog_en.pdf

⁸⁶ http://www.coe.int/t/dg3/healthbioethic/Activities/07_Human_genetics_en/Brochure/default_en.asp

⁸⁷ http://www.easac.eu/fileadmin/PDF_s/reports_statements/Easac_12_DTCGT-Lay_Web.pdf

⁸⁸ http://www.patient-view.com/uploads/6/5/7/9/6579846/pv_appdirectory_final_web_300812.pdf

several Apps for communication disability, deafness, visual impairment, physical disability and other conditions frequently associated with rare conditions. The Directory provides a description for each App, including technical details, available languages, and reviews from related patient/consumer groups. The Directory cross-indexes Apps by name, specialisation, and language.

European Patients Academy on Therapeutic Innovation launches as an educational resource on medicinal product research and development (2012)

The European Patients' Academy on Therapeutic Innovation (EUPATI)⁸⁹ launched in 2012 as a patient-led initiative that will develop educational material, training courses and a public Internet library to educate patient representatives and the lay public about the various processes involved in medicines development. Rare disease patient organisation stakeholders will play a prominent role in the five-year effort. Topics will include the design and conduct of clinical trials, drug safety and risk/benefit assessment, health economics, patient involvement in drug development and personalised and predictive medicine. Funded by the Innovative Medicines Initiative (IMI), EUPATI seeks to provide scientifically reliable, comprehensive information that will enable patients to serve as effective advocates and advisors in different capacities, such as working with regulatory authorities and ethics committees. Educational resources will be produced in English, French, German, Italian, Polish, Russian and Spanish languages.

⁸⁹ <http://www.patientsacademy.eu>

D. EUROPEAN MEMBER STATES' ACTIVITIES IN 2012

D.1. AUSTRIA

National plan/strategy for rare diseases and related actions

The main activities of the National Coordination Centre for Rare Diseases (CCRD, Nationale Kontaktstelle für Seltene Erkrankungen, NKSE) were the following:

- Acting as the main driving force in drawing the national plan for rare diseases until the end of 2013 through a participative process of discussing the 9 priorities of the national plan with all representatives of the expert group as well as of the strategic platform;
- Publication of the first report on rare diseases in Austria based on a large scale needs assessment survey involving academics, stakeholders such as patients, physicians, payers and industry. The report (only available in German) can be downloaded on the website of the Ministry of Health⁹⁰ or on the website of the CCRD⁹¹;
- Awareness raising among professionals / experts / doctors / patients on the topic of rare diseases through presentations and dissemination of information;
- Acting as the focal point for European activities in the field of rare diseases through active participation in EU-funded projects and initiatives such as Orphanet and EUCERD and the Cross Border Health Care Directive as well as other European initiatives in the area of Orphan Medical Products (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);
- Continuation of Orphanet activities:
 - Establishment of Orphanet national scientific advisory board;
 - Updating of national Orphanet website;
 - Dissemination of information on rare diseases in Austria ;
- Agreement on eligibility criteria for the establishment and designation of centres of expertise based on EUCERD recommendations; these criteria will be included in the Austrian Health Care Structure Plan, which is a nation-wide planning tool;
- Acting as the communication hub between actors in the field, focussing on health care professionals and other stakeholders.

At the second Austrian National Conference on Rare Diseases, which took place on 4-5 October 2012 in Salzburg among other topics the eligibility criteria for the establishment and designation of centres of expertise were presented.

The National Plan for Rare Diseases will be published in autumn 2013.

Centres of expertise

In 2012 an agreement was reached on the definition of eligibility criteria for the establishment of centres of expertise. These criteria take into account the recommended EUCERD criteria as well as national healthcare regulations. These criteria will be included in the national plan for rare diseases which will be published in autumn 2013. It is therefore expected that the developed criteria will be embedded in the Austrian health care structure plan, which will also specify the designation of future centres of expertise.

National alliances of patient organisations and patient representation

In 2012 Pro Rare Austria achieved the following milestones:

- Development of a cooperate identity for Pro Rare Austria including a logo, claim, banners and roll-ups;

⁹⁰ http://bmg.gv.at/home/Schwerpunkte/Krankheiten/Bericht_Seltene_Erkrankungen_in_Oesterreich

⁹¹ <http://www.goeg.at/de/BerichtDetail/Seltene-Erkrankungen-in-Oesterreich-2012.html>

- Publications in media - more than 30 newspaper articles and TV broadcasts;
- Fundraising for and organisation of the Rare Disease Day 2012 with around 400 participants;
- Development and launch of website: www.prorare-austria.org;
- Out of around 60 rare disease patient organisation, 20 organisations are members of Pro Rare Austria;
- Member of EURORDIS;
- Participation of EURORDIS Summer School in Barcelona in June 2012;
- Active participation at the meetings of the expert committee on rare diseases under the lead of the national coordination centre for rare diseases;
- Questionnaire for patients about the key challenges of patients with rare diseases;
- Establishment of a medical expert committee.

Apart from Pro Rare general alliances of patient organisations (both for rare and non-rare diseases) do exist on the state 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 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".

Training and education initiatives

The Academy of the Epidermolysis Bullosa House AUSTRIA hosts training workshops for epidermolysis bullosa on a regular basis. In addition, the Department of Dermatology of the Paracelsus Medical University Salzburg organised the "Fostering Courses for Genodermatoses" under the auspices of the European Academy of Dermatology and Venerology in 2009, 2010 and 2012.

National rare disease events in 2012

A number of events were held to mark the Rare Disease Day 2012 with Pro Rare leading the organisation of this day in Austria. Events to mark the day included an information day on 26 February 2012 in Salzburg, and a march for rare diseases in Vienna on 3 March 2012.

On 4-5 October 2012, the Second Austrian National Conference on Rare Diseases was organised in Salzburg. The Days of Molecular Medicine (8-10 October 2012 in Vienna) were dedicated to rare genetic disorders, as a professional exchange on latest scientific developments in the field of rare genetic diseases.

Hosted rare disease events in 2012

Amongst the hosted events in 2012 announced in *OrphaNews Europe* was the Days of Molecular Medicine 2012 Conference: The Translational Science of Rare Diseases - From Rare to Care (Vienna, 8-10 October 2012).

Research activities and E-Rare partnership

E-Rare

Austria joined the 4th Joint Transnational Call on Rare Diseases Driven by Young Investigators in 2012 and 2 of the 11 projects selected included a team from Austria.

IRDiRC

The Fonds zur Förderung der wissenschaftlichen Forschung as part of the E-Rare group of funders joined the IRDiRC in 2012.

D.2. BELGIUM

National plan/strategy for rare diseases and related actions

A steering committee appointed by the Minister of Public Health is now in place which will analyse the proposals for a rare disease strategy in terms of financing and the existing plans for cancer and chronic diseases.

Centres of expertise

An additional budget of €2 million has now been allocated for the development and the strengthening of multidisciplinary centres of expertise. A group of experts have developed a tool for prioritisation and the working modalities of the centres of expertise in order to implement this action.

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 conceptual note was written concerning the creation of a Central Registry of Rare Diseases able to collect a small set of basic variables on rare disease patients. The conceptual note, approved by a group of stakeholders was accepted in December 2011 and a budget was allocated for 2012-2013 to the Scientific Institute of Public Health for creation of a Central Registry for Rare Diseases. Objectives for this time period are the mapping of expertise in rare diseases in Belgian hospitals including further mapping and characterisation of rare disease patient databases, defining criteria for prioritisation in elaborating new disease-specific registries, participation in EPIRARE, defining the common data set and developing a business plan and privacy plan for a central registry

Genetic testing

As concerns genetic tests carried out abroad, a list of authorised tests and the foreign reference laboratories is in preparation: this initiative is part of a decree for the creation of a convention between the NIHDI and the genetic centres that is in force since 1 January 2013.

National rare disease events in 2012

To mark of Rare Disease Day 2012, RaDiOrg members visited the university hospitals on an awareness raising campaign, providing information about patient organisations and Orphanet. In the context of the finalisation of recommendations for a national strategy for rare diseases, RaDiOrg.be, in collaboration with the Fund for Rare Diseases and Orphan Drugs, organised a national conference on 29 February 2012⁹²: the event was dedicated to the recommendations concerning the establishment of centres of expertise and brought together a wide range of stakeholders. During this event, Laurette Onkelinx, Minister of Public Health, received the Edelweiss Award from RaDiOrg for her commitment and support for patients with rare diseases.

Hosted rare disease events in 2012

A number of European events were held in Brussels to mark Rare Disease Day. Eurordis held their annual symposium (entitled 'Rare Diseases a model of EU Solidarity') to mark the day. The event, organised with the European Commission, was held on 29 February 2012, and showcased the successes achieved over the last decade and to discuss the way forward. The European Society of PKU launched their Benchmarking Report, 'Closing the Gaps in Care', on 29 February 2012 in the European Parliament.

Other events announced in *OrphaNews Europe* include: International Childhood Cancer Awareness Day Multistakeholder Meeting (Brussels, 9 February 2012), Rare Cancers Conference: Improving the Methodology of Clinical Research (Brussels, 10 February 2012), Roundtable on Organisation of Rare Cancer Care (Brussels, 12 March 2012), 6th European Conference on Rare Diseases & Orphan Products (Brussels, 23-25 May 2012), 7th European Elastin Meeting (Ghent, 1-4 September 2012), 13th International Workshop on Multiple Endocrine Neoplasia (Liege, 5-8 September 2012), First International Symposium on the Ehlers-Danlos Syndrome (Ghent, 8-11 September 2012), 15th Society for the Study of Behavioural Phenotypes International Research Symposium and Education Day: Social Phenotypes in Genetic Disorders (Leuven, 11-13 October 2012), Epossi Conference on an Optimal European Chronic Care Model: Towards Implementation and Benchmarking (Brussels, 5 December 2012), Symposium ATP1A3 in Disease: From Gene Mutations to New Treatments (Brussels,

⁹² http://www.radiorg.be/sites/default/files/RDD2012-%20report_fr.pdf

10-11 December 2012), European Organisation for Research and Treatment of Cancer (EORTC) 50th Anniversary Conference (Brussels, 15-16 March 2012).

E-Rare

The FRS-FNRS participated in the 4th Joint Transnational Call in 2012: a Belgian team will participate in 1 of the 11 projects selected for funding.

IRDIRC

The FNRS and FWO as a member of the E-Rare group of funders joined the IRDiRC in 2012.

Orphan medicinal product reimbursement policy

In 2012 an article⁹³ was published, assessing the system of reimbursement for orphan drugs in Belgium, outlining the official criteria by which reimbursement decisions are achieved: therapeutic value, price, proposed reimbursement tariff, clinical value and budget impact, as well as other negotiable factors including price adjustments, employment incentives for manufacturers, diagnostic test funding by the company, and patient population restrictions. While reimbursement approval is granted to the majority of orphan drugs in the country, the authors identify measures to improve the system, such as good practice principles for analysing budget-impact, further standardisation of applications for reimbursement, and enhanced European cooperation in sharing clinical evidence.

D.3. BULGARIA

National plan/strategy for rare diseases and related actions

On 27 November 2008, the Bulgarian Council of Ministers approved the National Plan for Rare Diseases – genetic disorders, congenital malformations and nonhereditary diseases (2009 – 2013). The Bulgarian National Plan for Rare Diseases started on 1 January 2009 and will last for 5 years.

The National Plan's implementation was greatly disrupted by the country's general economic difficulties and pending healthcare reforms. Nevertheless, individual efforts from medical professionals, university clinics, patient groups and association have greatly contributed for the overall progress of rare diseases issues in Bulgaria. Many new rare diseases activities have been launched by different stakeholders, an excellent rare disease network has been established within the country and rare diseases awareness has been significantly improved. Funded by the National Plan, national newborn screening programmes have been stabilised and improved, which has positively affected the start age of therapy in newborns picked up by mass and selective screening programs, diagnosis and therapy have also moved forward. There is now more mutual confidence and close collaboration among different groups, as well as more active "crosstalk" regarding rare diseases policy (especially rare diseases centres of expertise). Annual rare disease conferences continue to be organised so as to discuss with stakeholders the provisions and advancements of the national plan.

Two major developments concerning the NCCRD and the Bulgarian National Plan took place in 2012. The first one was the Annual National conference for rare diseases⁹⁴ in September 2012, which gathered more than 160 national rare diseases stakeholders to discuss the official designation of rare diseases centres of expertise in Bulgaria. The participation of the Chair of Committee on Healthcare at the Bulgarian Parliament (Dr. Daniela Daritkova), the Director of the National Health Insurance Fund (Dr. Plamen Tsekov) and leading experts from the Ministry of Health was an encouraging sign for all local rare diseases stakeholders. The second one was that NCCRD board was significantly renewed at the beginning of 2013. Its members are now supposed to take more active role in the EU Cross-Border Healthcare Directive transposition in Bulgaria, especially on the matter of rare diseases and centres of expertise.

⁹³ <http://www.ncbi.nlm.nih.gov/pubmed/21905759>

⁹⁴ Brief report of the 3rd National Conference for Rare Diseases and stakeholders feedback in "Rare Diseases & Orphan Drugs" (October 2012, in both Bulgarian and English) http://raredis.org/pub/Newsletter/Newsletter_12_EN.pdf

Centres of expertise

The national plan was supposed to carry out a feasibility study on the necessity, possibility and criteria for the creation of a centre of expertise for rare diseases. However, by the end 2012 no such steps have been undertaken.

Nevertheless, rare diseases centres of expertise for rare diseases were the principle focus of the Bulgarian Third National Conference for Rare Diseases and Orphan Drugs (14-15 September 2012): a panel of experts focused on the EUCERD quality criteria for centres of expertise for rare diseases, with the goal of adopting a set of designation criteria that could be proposed to the Ministry of Health. Given the wide range of rare diseases and problems associated with them, stakeholders agreed that it is difficult to approach uniformly all these issues. However, requirements such as multidisciplinary, recognised expertise and reputation, networking with other similar national and European structures, cooperation with patient organisations were unanimously supported as criteria for designation of these centres. On the other hand, not all Bulgarian experts believe that the criteria for scientific contribution and participation in clinical trials can be fully met, mainly due to the insufficient human and material resources for these activities in the hospitals here.

Registries

The first priority in the National Plan was to provide epidemiological data on rare diseases in Bulgaria through the establishment of a National Registry. By the end 2012 no specific steps for the implementation of this task have been undertaken.

The Bulgarian Information Centre for Rare Diseases and Orphan Drugs (ICRDOD) released a new report⁹⁵ in 2012 listing the epidemiological registries for rare diseases in Bulgaria: the report aimed to provide up-to-date and reliable information on the epidemiological registries for rare diseases in the country. Eight nation-wide epidemiological registries concerning rare diseases have been identified by the ICRDOD: the National registry of Patients with Phenylketonuria, the National Registry of Patients with Primary Immunodeficiencies (PID), the National Registry of Patients with Thalassemia Major, the National Registry of Chronic Myeloid Leukaemia Patients, the National Registry of Crohn Disease Patients, the National Registry of Wilson Disease Patients, the National Registry of Gaucher Disease Patients, the National Registry of Mucopolysaccharidosis type 2 Patients. However, this data are not complete and only include registries whose coordinators have provided feedback. The survey will be organised once again in 2013 in order to catch the missing information, as well as the recent developments in this field.

On 28 October 2009, was In 2012 epidemiological data for the national thalassemia, chronic myeloid leukemia and Crohn disease registries have been updated by BAPES (Bulgarian Association for the Promotion of Education and Science), as well as pilot epidemiological studies for myelofibrosis and neuroendocrine tumors have been started.

The Screening Laboratory of the University Pediatric Hospital in Sofia has also created and is currently maintaining several databases, which are primary sources for analysis and evaluation of neonatal screening programmes in Bulgaria. Several modules are implemented (with no government funding): mass neonatal screening registry, primary congenital hypothyroidism, congenital adrenocortical hyperplasia, hyposomatotropism and Turner syndrome patient registries. There were talks with the Ministry of Health to link the Ministry of Health's birth registry with the mass neonatal screening registry and to co-work in real time. All the University Pediatric Hospital registries have proved to be very efficient for the respective rare diseases patients' follow up, as well as medical professional training.

Neonatal screening policies

The revision and update of the National Medical Genetics Standard (including neonatal screening programmes) started in 2012. It envisages the expansion of the screening panel in accordance with the proposals of screening expert network in Bulgaria. National screening experts even propose to elaborate a separate regulation for neonatal screening, including the designation of the participating laboratories as "centres of expertise" on different sectors (diagnosis, clinical management, consultation, registries, training, etc.). The technological renovation of the centralised screening laboratories, as planned in the National Rare Diseases Plan, has not been carried out yet.

⁹⁵ http://raredis.org/pub/Epi_Reg_Report_2012_EN.pdf

Sources of information on rare diseases and national help lines

Official information centre for rare diseases

ICRDOD published in September 2012 an updated review of the access to orphan medicinal products for rare diseases in Bulgaria⁹⁶: 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.

The Bulgarian Information Centre for Rare Diseases and Orphan Drugs (ICRDOD) released a new report in 2012⁹⁷ listing the epidemiological registries for rare diseases in Bulgaria: the report aimed to provide up-to-date and reliable information on the epidemiological registries for rare diseases in the country.

Help line

ICRDOD is a member of EURORDIS-led European Network of Rare Diseases Help Lines and took part in the Network's Caller Profile Analysis in 2012.

Good practice guidelines

In 2012, rare diseases experts from the University Pediatric Hospital in Sofia took part in the elaboration of "Growth and Endocrine Disorders in Thalassemia: The International Network of Pediatric Endocrinologists in Thalassemia (I-CET) position statement and guidelines".

Training and education initiatives

The second edition of the Eastern European Rare Diseases Summer School⁹⁸ designed for Russian health authorities and legislative institutions was in 2012⁹⁹. The Summer School 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.

Furthermore, BAPES organises each year a two-day rare disease training seminar for medical students. Medical students have 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.

The Screening Laboratory at the University Pediatric Hospital in Sofia also organises a 3-day training workshop for medical professionals each year.

National rare disease events in 2012

In Bulgaria the Rare Disease Day was celebrated through events in Sofia, Plovdiv, Stara Zagora and Pleven, including a release of balloons in solidarity with rare disease patients in the capital. In Sofia and Varna training sessions were held for general practitioners concerning how to relate to people with rare diseases.

The Third Bulgarian National Conference for Rare Diseases and Orphan Drugs¹⁰⁰ was held on 14-15 September 2012. 163 participants, including officials from the Parliamentary Health Committee, the Ministry of Health and the National Health Insurance Fund attended the conference. Centres of expertise for rare diseases were the principle focus: a panel of experts focused on the EUCERD quality criteria for centres of expertise for rare diseases, with the goal of adopting a set of designation criteria that could be proposed to the Ministry of

⁹⁶ http://raredis.org/pub/OD_Report_04042011_EN.pdf

⁹⁷ http://raredis.org/pub/Epi_Reg_Report_2012_EN.pdf

⁹⁸ http://raredis.org/pub/Newsletter/Rare_Diseases_Summer_School_2011.pdf

⁹⁹ http://raredis.org/pub/Newsletter/Newsletter_15_EN.pdf

¹⁰⁰ <http://conf2012.raredis.org/>

Health. Requirements such as multidisciplinary, recognised expertise and reputation, networking with other similar national and European structures, cooperation with patient organisations were unanimously supported as criteria for designation of these centres. On the other hand, not all experts believed that the criteria for scientific contribution and participation in clinical trials can be fully met, mainly due to the insufficient human and material resources for these activities in the hospitals here. Apart from better care and follow-up of patients, the designation of a medical structure as a centre of expertise for rare diseases will provide new opportunities for the development of the institution, such as increasing knowledge and experience of professionals, and attracting additional external funding through participation in European reference networks and research projects. Logically, both doctors and patients are united behind the need for the status of these centres in Bulgaria to be as fast as possible officialised by the Ministry of Health. A proposal for the development of appropriate regulations will be submitted to the Minister of Health. European and international experience has clearly demonstrated the importance and benefits of such public health institutions: better quality of treatment and care, better organisation of medical services, and more efficient use of funds for rare diseases. The designation of centres of expertise at national level is an important topic considering the steps towards the implementation of the Cross-Border Healthcare Directive.

ICRDOD and NAPRD organised for the first time in Bulgaria a workshop on health technology assessment for rare diseases on 1 November 2012 in Sofia. The event was under the auspices of and hosted by the Healthcare Commission at the 41st National Assembly of Bulgaria. The event aimed to advocate for a better comprehension, access and use of innovative health technologies, including orphan medicinal products. Many different rare disease-specific training and scientific events were also organised by different stakeholders. For example, several workshops on thalassemia were held (2nd Workshop on thalassaemia major “Multimodal approach in therapy and follow-up”, Summer Academy “Quality of life of patients with β Thalassemia in Bulgaria – focus on endocrine complications”, etc).

Hosted rare disease events in 2012

The Bulgarian Association for Promotion of Education and Science launched and organised in 2005, 2006, 2008 and 2009, the annual “Eastern European Conference on Rare Diseases and Orphan Drugs”. In 2010 for the very first time the event was hosted and co-organised outside Bulgaria, in Saint Petersburg, Russia, in conjunction with the first All-Russian Conference for Rare Diseases and Rarely Used Medical Technologies. It has proved to be an efficient strategy to foster rare diseases progress in Eastern Europe. In 2011, the sixth edition¹⁰¹ of this initiative was held and co-organised in Istanbul, Turkey. The Bulgarian National Alliance of People with Rare Diseases initiated and organised a Balkan patient meeting on 24 March 2012 in Sofia. Leading rare diseases experts and patients from Balkan countries took part in this event. A second edition is expected in 2013.

Orphan medicinal products

ICRDOD issued an updated report in September 2012 reviewing access to medicines for rare diseases in Bulgaria¹⁰². 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. Subsequently, the Parliament adopted in 2012 new legislation, by which a National Council for Pricing and Reimbursement of Medicinal Products would replace the Commission at the beginning of 2013. The new body would have a status of a State agency and would be responsible for both pricing and reimbursement of all medicinal products. The headquarters would be in Pleven, rather than Sofia. Medicinal products’ safety will continue to be monitored by the Executive Drugs Agency.

Orphan medicinal product market availability situation

By the end of 2012, 24 orphan medicinal products with EMA market authorisation are priced and included in the PDL. 15 of them are reimbursed by NHIF and 9 – by the respective hospital budget. These include: Atriance,

¹⁰² Orphan drugs in Bulgaria: Periodic review of the access to orphan drugs in Bulgaria: http://raredis.org/pub/OD_Report_2012_EN.pdf

Elaprase, Evoltra, Exjade, Fabrazyme, Glivec, Litak, Lysodren, Mozobil, Nexavar, Nplate, Revatio, Revolade, Somavert, Sprycel, Tasigna, Torisel, Tracleer, Ventavis, Volibris, Votubia, Xagrid, Yondelis, Zavesca.

D.4. CYPRUS

National plan/strategy for rare diseases and related actions

The Cyprus National Strategic Plan for Rare Diseases¹⁰³ (CNSPRD) was established following the European Council's Recommendation that each Member State should develop a national plan or strategy on rare diseases, preferably by the end of 2013. The final version of the CNSPRD was developed by a national steering committee for rare diseases, which consisted of Ministry of Health officials, experts in various fields relating to rare diseases as well as patient representatives, following a public consultation (the second) with local stakeholders including patient's representatives, in March 2012. The CNSPRD was approved by the Council of Ministers of the Republic of Cyprus in November 2012.

The main objective of the National Strategic plan is to ensure that patients with rare diseases will have access to high quality care (diagnostics, treatments as well as rehabilitation for those living with the disease). The CNSPRD is based on the following 5 pillars:

- (a) Prevention – Early Diagnosis
- (b) Treatment and Management
- (c) Palliative Care / Social Inclusion / Support
- (d) Registries/Epidemiology
- (e) Research

Following the approval of the CNSPRD, the National Committee for Rare Diseases was appointed by the Council of Ministers with the task of implementing as well as monitoring the progress of the plan. In addition, the National Committee for Rare Diseases is responsible for defining a number of priority actions with objectives and follow-up mechanisms.

Centres of expertise

The procedure for officially designating Centres of Expertise for rare diseases in Cyprus is currently under discussion.

Neonatal screening policy

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. The committee has drafted a report summarizing their findings and highlighting Cyprus's future needs. The report is currently under review by the Ministry of Health officials.

National rare disease events in 2012

The Ministry of Health organised a seminar on 1 March 2012 to honour Rare Disease Day. The seminar was addressed by the Minister of Health and was attended by many health professionals, scientists and stakeholders in the field of rare diseases as well as patients and their representatives. During the seminar, members of the National Steering Committee, presented the first draft of the National Strategic Plan for Rare Diseases, followed by discussion and public consultation. Other rare disease-related events in 2012 included the Inherited Neurological Disorders Seminar organised by the Cyprus Society of Human Genetics and the Neurological Society of Cyprus (2 February 2012, Nicosia), the Familial Cancer Management Seminar organised by the Cyprus Oncological Society and the Department of EM / Molecular Pathology of the Cyprus Institute of Neurology and Genetics (22 March 2012), the Galactosemia seminar organised by the Pediatric Clinic of the Makarios III Hospital and the Biochemical Genetics Department of the Cyprus Institute of Neurology and Genetics (29 March 2012), the 8th Postgraduate Pediatrics Conference (which included topics on rare metabolic diseases and rare genetic diseases) organised by the Pediatric Clinic of the Makarios III Hospital in April 2012.

¹⁰³ [http://www.moh.gov.cy/MOH/MOH.nsf/All/CD61A07312284C0A422579DC0023AF8A/\\$file/Strategic%20Plan%20Rare%20Diseases.pdf](http://www.moh.gov.cy/MOH/MOH.nsf/All/CD61A07312284C0A422579DC0023AF8A/$file/Strategic%20Plan%20Rare%20Diseases.pdf)

Additionally, several events took place combining scientific seminars and public awareness such as the Scleroderma International Day.

Hosted rare disease events in 2012

Cyprus hosted a number of rare disease related events including: the 3rd Pan-European Conference on Haemoglobinopathies and Rare Anaemias organised by the Thalassaemia International Federation in October 2012, the XIIth NeuroMediterrané Conference, organised by the Cyprus Institute of Neurology and Genetics, the Cyprus Neurological Society and the NeuroMediterrané Society in November 2012, the 3rd International Conference of the Cyprus Society of Human Genetics in November 2012, and the 3rd Thalassaemia Conference organised by the Cyprus Institute of Neurology and Genetics and the Cyprus Thalassaemia Centre in November 2012. Furthermore, experts in the management and treatment of various rare diseases presented the latest advancements in their fields of expertise as part of general or more specialised medical conferences.

D.5. CZECH REPUBLIC

National plan/strategy for rare diseases and related actions

A group of stakeholders gathered in 2011 (including the Ministry of Labour and Social Affairs, experts and payers) to elaborate the Czech National Plan for Rare Diseases for 2012-2014¹⁰⁴, which on 29 August 2012, the Czech government adopted via Decree 633. The plan delineates concrete actions identified in the 2010-2020 Czech National Strategy¹⁰⁵. Specific areas include: Improving information; Education; Prevention; Improving screening and diagnosis; Improving the availability and quality of care; Improving quality of life and social inclusion; Support for rare disease science and research; Unification and development of data collection and rare disease biological samples; Supporting and strengthening patient organisations; Interdepartmental and interdisciplinary collaboration; and International cooperation. Besides diagnostics and treatment, the Czech National Plan encompasses research, public information, training for health professionals (both paediatric and adult specialists), and quality of life for patients in collaboration with the Ministry of Social Affairs. The Ministry of Health has opened targeted appropriation funding calls for the implementation of the Czech National Plan in December 2012.

Care for rare diseases is planned to be concentrated in 10 to 20 expert centres. The 2011 EUCERD Recommendations on Quality Criteria for Centres of Expertise for Rare Diseases in Member States were officially adopted by the Interministerial and interdisciplinary commission for rare diseases as a basis for the *de iure* establishment of rare disease expert centres in the country. The Ministry of Health plans to issue a series of public tenders for the establishment of rare diseases expert centres based on these criteria for selected groups of diseases. The aforementioned EUCERD guidelines are intended to serve as basis for the crossborder health care in rare diseases related to the implementation of the 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 healthcare¹⁰⁶

Centres of expertise

Based on the work of the Interministerial and interdisciplinary commission for rare diseases in 2011 and early 2012, including the entry into force of Law 372/2011Sb which in its article 112 provided legal basis for establishment of expert centres (not only for rare diseases), a group of rare disease centres was officially established on 28 May 2012 and published in Bulletin n. 4 / 2012 of the Czech Ministry of Health¹⁰⁷ – section 4 “Basic network of rare disease centres”. These centres include a) the National Coordination Centre for rare diseases in the Prague-Motol Teaching Hospital of Charles University Prague¹⁰⁸ in collaboration with the University Hospital of Masaryk University Brno¹⁰⁹ for the sake of regional representation, b) five regional centres of cystic fibrosis (Prague – Motol Teaching Hospital of Charles University Prague¹¹⁰, Brno Teaching

¹⁰⁴ http://www.eucerd.eu/?post_type=document&p=2105

¹⁰⁵ http://ec.europa.eu/health/rare_diseases/docs/national_czech_en.pdf

¹⁰⁶ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:088:0045:0065:EN:PDF>

¹⁰⁷ http://www.mzcr.cz/Legislativa/dokumenty/vestnik-c4/2012_6288_2510_11.html

¹⁰⁸ www.ublg.lf2.cuni.cz

¹⁰⁹ www.fnbrno.cz

¹¹⁰ www.fnmotol.cz

Hospital of Masaryk University¹¹¹, Olomouc Teaching Hospital¹¹² of Palacky University, Hradec Králové Teaching Hospital of Charles University Prague¹¹³ and Pilsen Teaching Hospital of Charles University Prague¹¹⁴) covering all regions of the country (children and adults with the disease), linked via a dedicated disease-specific registry¹¹⁵, c) national centre for epidermolysis bullosa at the Faculty Hospital Brno of the Masaryk University associated with DebraCZ¹¹⁶ and the d) Centre for inherited metabolic disorders¹¹⁷ at the General Teaching Hospital of Charles University Prague¹¹⁸. These centres received their status for the next three years and could be renewed following audit by the Ministry of Health. In November 2012 negotiations had started with additional centres to be created based on the EUCERD criteria. All of the planned centres operate based on their professional reputation and could be thus considered as *de facto* centres-. The Interministerial and interdisciplinary commission for rare diseases aims to transform them into *de iure* centres in the future.

The value of these centres has been acknowledged by many of the country's major stakeholders including the State Institute for Drug Control, the Czech general insurance company, the Ministry of Health, patient groups, researchers and physicians. Treatment with orphan medicinal products is fully reimbursed in these centres and these centres manage the provision of very expensive orphan medicinal products.

Establishment of centres gives them government recognition, but still does not imply a dedicated budget line from health insurance companies. Treatment and diagnostics will thus continue to be provided within standard health insurance procedures administered by the General Health Insurance company (covering approximately 65% of the general population) and the "Association of Czech health insurance companies¹¹⁹" that comprises six additional smaller health insurance companies that main have regional coverage).

However, in the future and following gradual reform of health care funding (after 2014) it is planned that respective rare diseases or related rare disease diagnostic groups will be concentrated into dedicated centres and that they will receive a dedicated budget line linked to nominal health insurance reallocation (e.g. as in The Netherlands). In this regard it is expected that the major condition for health care reimbursement would be *de iure* established 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 EU Directive on cross-border healthcare sections 54 and 55). Currently, cross-border healthcare falls into the domain of the Centre for International Reimbursements¹²⁰.

Neonatal screening policy

In 2012 the ongoing research grant from the Czech Ministry of Health has enabled a pilot project for broadening of the scope of screened metabolic diseases by mass spectrometry. Its outcomes will be published in 2013. The information portal for lay public and physicians on neonatal screening was established and financed by the Czech Ministry of Health¹²¹.

Genetic testing

In November 2011 a new law On Specific Health Care Services 373/2011 Sb was passed. Act 373/2011 Sb regulates genetic testing for rare diseases and reflects the Council of Europe's Additional Protocol to the Convention on Human Rights and Biomedicine concerning Genetic Testing for Health Purposes (CETS No 203) which regulates Direct to Consumer (DTC) testing via specific informed consent provisions. 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"¹²². Moreover, new law 372/2011 Sb stipulates provisions regarding informed consent procedures in the domain or health care services. This law came into effect in the Czech Republic on 1 April 2012.

¹¹¹ www.fnbrno.cz

¹¹² www.fnol.cz

¹¹³ www.fnhk.cz

¹¹⁴ www.fnplzen.cz

¹¹⁵ www.cfregistr.cz

¹¹⁶ <http://www.debra.cz/>

¹¹⁷ www.udmp.cz

¹¹⁸ www.vfn.cz

¹¹⁹ <http://www.szpcr.cz/>

¹²⁰ <http://www.cmu.cz/en?Itemid=224>

¹²¹ <http://www.novorozeneckyscreening.cz/>

¹²² <http://www.oecd.org/dataoecd/43/6/38839788.pdf>

National alliances of patient organisations and patient representation

In December 2011 the foundations were established for the creation of an overarching Czech National Alliance for Rare Diseases¹²³, which was officially established in February 2012 (received official registration from the Czech Ministry of Interior) and became member of Eurordis in May 2012. As of December 2012 this alliance linked together 24 individual patient support groups via a democratic, bottom-up, activity spearheaded by several larger patient support groups. Its members meet approximately every 3 months, publish a newsletter, run awareness campaign in the media, co-organised one Czech Parliament hearing on rare diseases. The Czech National Alliance also works in association with the Coalition for Health Association¹²⁴, which also has common disease representatives. Both alliances will collaborate on topics of common interest, mainly in the social services domain. The Ministry of Health had issued appropriation schemes for the operation of these alliances in October 2012. In June 2012 representatives of the Czech National Alliance joined the Interministerial and interdisciplinary commission for rare diseases.

Sources of information on rare diseases and national help lines

Orphanet activities in the Czech Republic

Since 2006 there is a dedicated Orphanet team in the Czech Republic, currently hosted by the University Hospital Motol and the Second Faculty of Medicine of Charles University Prague, that has been transformed by the Bulletin n4/2012 into the National Coordination Centre for Rare Diseases (see above).

Official information centre for rare diseases

There is no official information centre for rare diseases in the Czech Republic other than Orphanet and the first steps for the establishment of such a centre were started in Autumn within the framework of the National Coordination Centre for Rare Diseases at University Hospital Motol¹²⁵.

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 and by dedicated appropriations from the Czech Ministry of Health in 2013.

Training and education initiatives

Rare disease information was added into the medical genetics training curriculum at the Masaryk University Brno¹²⁶ (4th year) and Charles University Prague – 2 Faculty of Medicine (5th year¹²⁷).

National rare disease events in 2012

A number of events were organised by rare disease patient organisations in the Czech Republic to mark Rare Disease Day 2012, including the first major meeting on 24 February 2012 of patient organisations and patient representatives with the goal of establishing a Czech Association for Rare Diseases to connect all patients and patient organisations with the aim of raising awareness about rare diseases and their impact on patients' lives amongst the general public and decision-makers. In addition, the Czech National TV station CT1 broadcasted a documentary about rare diseases on 15 February 2012. In September 2012 the second cycle of interviews on rare diseases was initiated at Radio ClassicFM Prague.

Hosted rare disease events in 2012

Amongst the events announced in OrphaNews was: the 6th International Symposium on Childhood MDS and Bone Marrow Failure syndromes (7-9 November 2012, Prague).

Orphan medicinal products

Orphan medicinal product reimbursement policy

Establishment of official expert centres via Bulletin 4/2012 (see above) will facilitate subsequent reimbursement negotiations with health insurance or pharmaceutical companies (e.g. clinical trials, compassionate use programmes, risk sharing strategies etc.). Alternatively, there is the possibility to use art. 16 of Law 48/1997 Sb for the "Individual patient reimbursement scheme". This scheme is applicable only in the

¹²³ www.vzacna-onemocneni.cz/

¹²⁴ www.koaliceprozdravi.cz

¹²⁵ www.vzacnenemoci.cz

¹²⁶ www.muni.cz

¹²⁷ www.lf2.cuni.cz

case of unavailability of alternative treatments. Specialised centres can apply within a revolving application scheme to a commission comprising major stakeholders (e.g. the Czech Ministry of Health, State Institute of Drug Control and Health insurance companies) until the official reimbursement procedure is instituted for the given orphan medicinal product. This measure is mainly intended to “bridge” the period between e.g. phase 3 clinical trials and introduction of a successful drug into health insurance reimbursement schemes.

D.6. DENMARK

National plan/strategy for rare diseases and related actions

The working group with the task to elaborate a national plan for RD has a broad representation of stakeholders and was founded at the end of 2011 and met at the start of February 2012 for the first time. The recommendations in the previous report on rare diseases from 2001 are being 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. The subject of centres of expertise is a key area of consideration. The working groups’ proposal for a national strategy/ plan is scheduled to be ready in Autumn 2013.

National alliances of patient organisations and patient representation

Over 2009 -2012 Rare Disease Denmark (RDD) developed a special training programme for families with children affected by rare diseases under the age of 18 called “Rare Family Days”. Some preliminary results were presented by RDD at the ECRD conference in Brussels and the final results will be published in 2013, along with a new concept for “Rare Family Days”.

RDD cooperates with the Centre of Disability and Social Psychiatry (ViHS). In 2012 RDD through ViHS adopted a Focus Point of Contact for very rare disease patients and relatives with no possibility to join or form a patient organisation/society. More than 500 rare citizens adhere to the Focus Point, representing more than 150 rare diseases.

Also in 2012, RDD contributed to the work of National Board of Health’s working group to elaborate a national strategy for Rare Diseases. When it comes to the internal life of RDD, several activities for RDD’s member organisations have been organised, including seminars, project days and more. A monthly electronic newsletter was published to more than 400 recipients. From December 2012, RDD has established its own secretariat situated in an accessible building, which holds offices for 24 disability- related organisations.

Patients’ organisations are, in general, consulted regarding legalisation concerning issues relevant to rare diseases and, in general, participate in the relevant boards and official bodies/working groups. Rare Disorders Denmark is represented on an advisory board of the Centre for Disability and Social Psychiatry (ViHS) and in the working group of National Strategy for rare diseases, constituted by the National Board of Health in December 2011.

National rare disease events in 2012

Rare Disorders Denmark organised a number of events to mark Rare Disease Day 2012¹²⁸. A conference entitled ‘Welcome to the Land of the Rare’ focused on the provision of social support to the rare patients and their families. This conference aimed to provide input to the ongoing elaboration of the National Plan for Rare Diseases. The 150 participants at the conference included patients, their relatives, professionals and specialists in the area of social services, doctors and relevant authorities and decision makers. In addition a march to mark the day was held in Copenhagen to raise awareness of the cause. The march ended with the awarding of the Rare Disease Day prize to John Rosendahl Ostergaard received Wednesday 29 February Rare Prize for his work for people with rare diseases and disabilities, as well as to the former chair of Rare Diseases Denmark, the late Torben Grønnebæk.

¹²⁸ www.29februar.dk

D.7. ESTONIA

National plan/strategy for rare diseases and related actions

The national plan for rare diseases in Estonia is under development. In September 2012 a working group was set up to discuss the activities on the field of rare diseases which will be added to the implementation plan of ERTA: the working group includes professionals in the field of rare diseases (doctors, medical geneticists, representatives of patient organisations, representatives from the Estonian Board of Disabled People, etc.). A draft plan for rare diseases was drawn up at the end of 2012. The process to finish the plan will be presented to the Minister and management team members of the Ministry of Social Affairs.

Centres of expertise

As the Tartu University Hospital Meets the EUCERD criteria for centres of expertise, there are no plans for a special designation procedure for centres of expertise.

Training and education initiatives

There was a special advanced course for physicians on rare disorders, organised by the Department of Continuing Education at the Tartu Medical University increased in 2012.

National rare disease events in 2012

Due to Estonia's small size, there are no special annual rare disease events, nonetheless rare diseases are given a spotlight during the annual meetings of the Estonian Society of Human Genetics and Estonian Society of Laboratory Medicine.

In August 2012 a meeting "Orphan diseases – today and future" was organised by Agrenska Estonia in Tammistu, Tartumaa, with more than 160 participants from different areas (doctors, nurses, physiotherapists, teachers, patients, social workers, etc).

Specialised social services

In 2012, several respite camps were organized by the Estonian Agrenska Foundation.

D.8. FINLAND

National plan/strategy for rare diseases and related actions

A meeting is planned in March 2013 to advance with the elaboration of the national plan for rare diseases. The aim is to have the plan ready during 2013, the designation of expert centres will be a much longer process to follow.

Planning is also underway for a national plan for cancer treatment and research with the hope that the process for the rare disease and cancer plans to feed into one another.

Centres of expertise

The establishment of centres of expertise and healthcare pathways will be one of the first topics to be dealt with in the elaboration of a national plan for rare diseases, with hope for the first official centres of expertise by 2013.

The Ministry of Social Affairs and Health carried out a nationwide survey in 2011 to identify unofficial centres of expertise which fueled discussions on the subject at the 2012 meeting of the Orphanet Scientific Advisory Board.

Neonatal screening policy

A pilot scheme for screening additional metabolic diseases including congenital adrenal hyperplasia (CAH), MCAD deficiency, LCHAD deficiency, Glutaricaciduria type 1 (GA1), and phenylketonuria was started in 2007 in the Turku area, concerning around 3000 newborns per year. No decision has at present been made concerning the continuation of the pilot beyond the year 2012 or widening of the pilot to other areas in Finland, though experts representing university hospitals now suggest that screening for newborn congenital metabolic

diseases should be widened in 2015, so that the screening practice in Finland would be similar to other western countries. A screening recommendation was handed over to the Ministry of Social Affairs and Health in 2012.

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 held on 21 January 2012. The new alliance, named HARSO, HARvinainen (rare) Sairauksien (diseases) Organisaatio (organisation) welcomes all Finnish patient organisations that represent one or more rare diseases or disabilities. Harso is run by patients themselves. There were 29 organisations out of a total of 51 in Finland present at the launch of the association. The new umbrella group will advocate for the rare disease patients, their families and their organisations in Finland, aiming for the best possible health and social care for the entire rare disease community. One of the main objectives will be to raise awareness of rare diseases and disabilities in order to facilitate diagnosis. Rare diseases and/or disabilities affect the daily lives of approximately 250 000 people in Finland. Harso will provide the rare disease community with strength in numbers for the first time. The organisation unites the rare disease community, creating a common voice and more visibility. So far, some rare disease organisations have chosen to stay outside Harso.

Sources of information on rare diseases and national help lines

Help line

The Norio-centre has a nationwide phone and e-mail service for matters concerning rare diseases, which operates on work-days: the Norio-centre receives part of its funding from Finland's Slot Machine Association (RAY). The main purpose of RAY is to raise funds through gaming operations to promote Finnish health and welfare.

National rare disease events in 2012

International Rare Disease Day 2012 was coordinated by The Finnish Network for Rare Diseases, Harvinaiset-verkosto. Together with the patient organisations the Network organised a webinar entitled "Rare Disease Day 2012" at the Finnish Parliament Annex, called the Little Parliament on 29 February 2012. Ms. Paula Risikko, The Minister of Social Affairs and Health as a guest speaker. Dr Päivi Kaukonen, Ministerial Adviser from the Ministry of Social Affairs and Health, presented survey which has been carried out among university and central hospital chief physicians and Harvinaiset Network member organisations of diagnostics, care and rehabilitation with rare disease patients in Finland. Dr. Kaukonen announced the establishment for April 2012 of a steering group for the preparation of the national plan by the Ministry. The seminar was also an opportunity to hear the results of the Harvinaiset survey launched in January 2012 on rare diseases which received around 700 responses.

Swedish Orphan Biovitrum Finland organised the 4th *Harvinaiset Sairaudet-päivä* (Rare Disease Day) together with stakeholders in Helsinki on 19 October 2012. This day provided a forum for questions concerning research and management for Finnish decision-makers and specialists. The principal goal of the day was to discuss how Finland would become a model country for rare disease research and management and which actions would ensure that patients suffering from rare conditions would be entitled to the same quality of treatment as other patients.

D.9. FRANCE

Second French National Plan for Rare Diseases 2011-2014

Since 1 December 2012, hospitals – in priority Reference Centres – began one of the key actions of the second plan: coding in the National Database of Inpatient Registrations ("PMSI") all hospitalised rare disease patients using systematically Orphanet nomenclature. The goal is to better identify patients in the healthcare system so as to improve knowledge of their healthcare pathways.

An "information and experience sharing meeting" was organised on 19 December 2012 concerning the implementation of the Second Plan for over 300 participants, in particular for all the coordinators of the Reference Centres. The meeting objectives were to share information with the coordinators on the progress of the plan. In particular the new evaluation procedures for Reference Centres were presented and discussed, as

were the future national clinical network organisation and the new method to develop “PNDS” (See section on Good Practice Guidelines).

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

The National Cancer Institute (“*Institut national du cancer*” – INCa) published a report concerning the activity of the expert centres in 2012¹²⁹, as well as a document published in French¹³⁰ and in English¹³¹ describing this specific organisation.

The INCa published two new reports on genetic testing and treatment for hereditary cancers in 2012. The first one summarises the 2011 activities of French oncogenetic platforms. The second one focuses on molecular genetic testing for targeted therapies in France in 2012¹³².

French National Plan for Rare Disabilities 2009-2013

A fourth national “resource centre” for patients with rare disabilities and severe epilepsy was created in 2012. Inter-regional relays of these national centres will be created during 2013. Cooperation between national “resource centres” and inter-regional teams for rare disabilities and “reference centres” for rare diseases is also planned.

Other French national initiatives related to rare diseases

The “dossier medical personnel” (“personal medical record” - DMP) is a national healthcare tool for sharing and exchanging information about individual patients. Two years after the DMP was launched, there were 250 000 DMP at the end of 2012.

Centres of expertise

Up to the end of 2012, the Reference Centres were evaluated over time, first through self-evaluation after 3 years as a designated centre, then through an external evaluation after 5 years. The new process has been in progress in 2012 and will be definitively specified at the beginning of 2013. The evaluation process will be modified: each reference centre will establish an activity report each year and undergo evaluation at 5 years according to modalities still under discussion. When the new process will be published, the missions of the “permanent working group” established by the plan will evolve towards the analysis and the follow-up of the annual activity and 5-year evaluation reports of the Reference Centres. This working group will also monitor the development of the future national clinical networks.

In June 2012, the French General Directorate for Provision of Healthcare launched a position paper¹³³ detailing the conditions for the establishment and renewal of expert centres so as to best respond to requests for designation of such centres. This position paper is not specific to rare disease centres.

In 2012, the Assistance Publique - Hôpitaux de Paris, the consortium of university hospitals of Paris, organised several meetings to set up closer links and common procedures between Paris Reference Centres and social services which assess needs and meet requirements of rare disease patients with disabilities.

Registries

A National Rare Disease Registry Committee was created in October 2006 as part of objective 1 - “Improve knowledge of epidemiology of rare diseases” - of the first National Plan for Rare Diseases. In 2012, one register was qualified for 3 years (2013-2015). At the end of 2012, 12 national registries were qualified: thalassemia, Gaucher disease, histiocytosis, congenital neutropenia, Pompe disease, cystic fibrosis, biliary atresia, esophageal atresia, arterial pulmonary hypertension, hereditary immune system disorders, SDH-dependant hereditary paraganglioma, and inherited deficiencies of coagulation. In 2012, a reflection has begun on the questions of a possible evolution of the Committee’s missions and the needs of the other registries and databases existing in France for support and evaluation.

The Second National Plan for Rare Diseases also foresees the creation of a National Rare Disease Database (BNDMR). Its primary objective is to describe the demand of care for rare diseases at a national level, as well as the offer of care, and to assess whether the offer matches the demand. To achieve these objectives,

¹²⁹ http://www.e-cancer.fr/component/docman/doc_download/9274-bilan-2011-de-la-prise-en-charge-des-patients-adultes-atteints-de-cancers-rares

¹³⁰ http://www.e-cancer.fr/component/docman/doc_download/4692-cancers-rares-de-ladulte-lorganisation-en-centres-experts

¹³¹ http://www.e-cancer.fr/component/docman/doc_download/9266-rare-adult-cancers-organisation-into-expert-centres-septembre-2012

¹³² <http://www.e-cancer.fr/toutes-les-actualites/360-les-soins/7283-genetique-moleculaire-des-cancers-deux-nouveaux-rapports-sur-la-prise-en-charge-personnalisee-des-patients#>

¹³³ http://circulaire.legifrance.gouv.fr/pdf/2012/06/cir_35428.pdf

the first step is to build a minimum data set (MDS): this MDS will be common to all rare disease reference centres and to all rare diseases. In 2012, a working group helped to build the MDS, which will be discussed and validated by the Steering Committee of the Plan at the beginning of 2013. The MDS will be entered through an application called BaMaRa (“Banque Maladies Rares”), either directly by the reference centres, or through their own application if appropriate. It will help gathering data at the reference centre level and linking this information to biobank data and other national databases (medico-economic databases, national health insurance databases etc.). A data warehouse, the National Rare Disease Database (BNDMR), will host several types of de-identified national rare disease data sets in accordance with the Data Protection Act.

Neonatal screening policy

Neonatal screening programme for deafness (of which rare diseases may be a cause) was approved in April 2012. Screening for deafness was already performed in 51% of the French maternity hospitals using different methods. National specifications on screening methods will be published in 2013.

Genetic testing

The French Biomedicine Agency (“*Agence de la Biomédecine*”), a public organisation operating under the supervision of the Ministry of Health, was created under the Bioethics Law of August 2004. The Biomedicine Agency published its 2011 annual report¹³⁴ in 2012. For the third consecutive year, the Agency included data on postnatal genetic testing carried out in France culled via a partnership with Orphanet. The annual report revealed that 387 059 tests were performed in France in 2011. In the domain of molecular genetics (including pharmacogenomics), diagnostic tests were undertaken for 1 012 diseases of a total offer of 1 282 diseases for which testing is possible in France. Of these 1 282 diseases, 726 tests are available in only one French laboratory. As in previous years, two non-rare disease indications (haemochromatosis and non-rare thrombophilia) represented over 40% of the total analyses conducted in 2011.

Sources of information on rare diseases and national help lines

Official information centre for rare diseases

Orphanet is the official source of information on rare diseases in France.

Information on rare cancers organisation is available on the INCa website¹³⁵. Ten national expert centres have elaborated dedicated websites with high quality information available for the patients.

Help line

Maladies Rares Info Services implemented a “rare diseases barometer”. The purpose of this barometer is to collect objective data on the issues to which patients are confronted. Data were collected by means of qualitative and quantitative surveys targeting users of the information and support service. The results of the first round of these surveys were published in 2012¹³⁶. The service also launched a forum for its users in 2012.

Good practice guidelines

Since the beginning of the first national plan, the Reference Centres produced, with the help of the HAS, 49 national good practice guidelines (“PNDS”) for diagnosis, treatment and follow-up of patients with rare disease. At the end of 2012, the HAS published a new simplified method to develop “PNDS”¹³⁷ to help the Reference Centres draft more quickly the PNDS.

National rare disease events 2012

In 2012, the 26th edition of the *Téléthon* took place on 8-9 December, raising 81 million Euros. On 8 December 2012: the AFM launched a new English language website to present the aims of the organisation and the projects the AFM is funding. In 2012, the annual Rare Disease March gathered around 2000 people in Paris. The *Téléthon*¹³⁸ and Rare Disease March¹³⁹ aim to raise awareness about rare diseases in addition to the Rare Disease Day which is celebrated each February.

¹³⁴ http://www.agence-biomedecine.fr/IMG/pdf/ra_biomed_2011_bd_web.pdf

¹³⁵ <http://www.e-cancer.fr/soins/prises-en-charge-specifiques/cancers-rares>

¹³⁶ <http://www.maladiesraresinfo.org/news/observatoire-maladie-rare-maladies-rares.html>

¹³⁷ http://www.has-sante.fr/portail/jcms/c_1340205/fr/methode-d-elaboration-des-protocoles-nationaux-de-diagnostic-et-de-soins-pnds?xtmc=&xtcr=2

¹³⁸ <http://www.afm-telethon.fr/le-telethon/le-telethon-2011>

¹³⁹ <http://www.alliance-maladies-rares.org/article/marche-des-maladies-rares-2011-98>

On 29 February 2012, on the occasion of the Rare Disease Day, the *Fondation maladies rares* (Rare Diseases Foundation) was officially launched at the French Academy of Sciences with a dedicated evening event which gathered 150 participants and welcomed speeches from its founding members. A press release also acknowledged the creation of the Foundation, a unique alliance of actors from research, care and patients' organisations devoted to speeding up and stimulating research in rare diseases. In addition to this, the *Alliance Maladies Rares* and Orphanet organised an awareness-raising day with the French railway company SNCF: they were present on a number of high speed trains leaving Paris for other major towns. On the same day in Paris, members of the Rare Diseases Platform came together in front of the Eiffel Tower to raise their hands in support of patients for the Rare Disease Day. A range of activities were organised in towns across France by patients' organisations to raise awareness of the Day and rare diseases in general.

In September 2012, Orphanet held its 13th Forum for Patient Organisations in Paris, in collaboration with the *Alliance Maladies Rares*. The sessions centred on clinical and emergency online guidelines for rare diseases developed by Orphanet and on personal electronic medical records in the French healthcare system, as well as advances in the area of research, and the recent launch of the French Rare Disease Foundation.

Hosted events in 2012

Amongst the events hosted by France in the field of rare diseases were: EUCERD/Eurogentest workshop on coding rare diseases and describing phenotypes (27 -28 September 2012, Paris), International Symposium on Hepatic Glycogen Storage Diseases (4-6 April 2012, Lyon), Sixth International Alkaline Phosphatases Symposium (16-19 May 2012, Huningue), European Working Group on Gaucher Disease Meeting (28-30 June 2012, Paris), World Federation of Hemophilia World Congress (8-12 July 2012, Paris), Mechanisms of Intellectual Disability: From Genes to Treatment (3-7 October 2012, Roscoff), 7th World Rett Syndrome Congress (22-26 June 2012, Paris, France), OroDysmorphology course (24 May 2012, Strasbourg), ESH-ENERCA Training Course: Diagnosis and Management of Very Rare Anaemias (3-4 February 2012, Paris). The IRDiRC held its Executive Committee Meeting on 25-26 September 2013 in Evry, and the Interdisciplinary Group held a meeting on 9-10 November 2012 in Paris.

Research activities and E-Rare partnership

National research activities

In 2012, the ANR and the DGOS prepared a common call for proposals in translational research, which will be launched at the beginning of 2013 ("*Programme de recherche translationnelle en santé*" – PRTS, Programme for translational research in Health¹⁴⁰). This call for proposals is not specific for rare diseases. The first objective of this programme is to select and fund research projects at the interface between basic research projects currently funded by ANR and clinical research projects currently funded by PHRC.

The "*Fondation maladies rares*¹⁴¹" (*Rare Diseases Foundation*) was approved by a decree of the French Ministry of Research and Higher Education on 6 February 2012, and officially launched on 29 February 2012. The creation of this rare diseases research foundation is a measure delineated in the research objectives of the second French Plan for Rare Diseases 2011-2014. The Foundation is a private non-profit structure endorsed by both the French Ministry of Research and the French Ministry of Health to coordinate, federate and fund rare diseases research. Its main aim is to accelerate and promote technological, medical and social innovations to the benefit of the rare disease patients. The Foundation gathers French rare disease research into one cooperative structure that operates with a sustained source of funding to bring a new synergy to fundamental, clinical and translational research. Its funding bodies represent a unique alliance of research, care and patient organisations. The funding bodies are: the AFM (French Muscular Dystrophy Association), the French Alliance for Rare Diseases Alliance (*Alliance Maladies Rares*), the French National Institute of Health and Medical Research (Inserm), the Conference of General Directors of the University Hospitals and the Conference of University Presidents. The Foundation is administrated by an Executive Board, composed of representatives from each of the funding members and eight renowned experts in research and academia. Furthermore, the Foundation benefits from the guidance of a Scientific Committee composed of French and International leading medical specialists and scientists in the rare diseases field, encompassing both biomedical and social and human sciences fields. The Foundation is based in the "*Plateforme Maladies Rares*" in Paris. It consists of a team of twelve people, including seven regional delegates, who ensure the linking of actors as well as the development of rare diseases research programmes.

¹⁴⁰ www.agence-nationale-recherche.fr/programmes-de-recherche/appel-detail/programme-de-recherche-translationnelle-en-sante-prts-2013/

¹⁴¹ <http://fondation-maladiesrares.org/>

In 2012, several activities have been developed around 6 main objectives that structure the Foundation working programme:

1. Boosting research by facilitating access to technology platforms and launching calls for tenders;
2. Developing research in social and human sciences applied to the rare diseases field;
3. Supporting the setting up and development of preclinical and clinical trials;
4. Participating in and developing European and international rare diseases dedicated research programmes;
5. Being involved and proactive in the public health and research policies and frameworks;
6. Supporting and valorising rare diseases data collection according to state of the art national and international frameworks.

As far as calls for proposals are concerned (Point 1), the French Rare Diseases Foundation is offering funding opportunities both for biomedical research and social and human sciences. In the biomedical field, three different project calls were launched to increase access to High Throughput Sequencing in May 2012, September 2012 and February 2013 respectively. A total of 55 projects have been funded in 2012 with the aim to identify new genes responsible for rare diseases. The Foundation works in close collaboration with state of the art public and private technological platforms and is establishing partnerships to facilitate general access to resources for rare diseases research, also outside its own funded calls. New themes for calls for proposals, especially designed according to the needs identified from the extensive regional coverage of research teams, will be implemented on a regular basis. In addition to exome and genome sequencing calls for proposals, the Foundation also funds animal models through bi-annual call for proposals (the first call will be launched on mice models in February 2013) as well as the screening of innovative molecules.

In addition to the calls for projects, an important milestone has been reached in 2012 with the online release of an extensive mapping of funding opportunities for rare disease research (including institutional funding, charities, private, and EU and international funding). This unique and regularly updated portal, established by the Foundation in collaboration with the ANR and the DGOS, gives a better visibility to researchers seeking funding. Of note, this provides, within a single platform, information to the French rare diseases community on funding opportunities available at the French regional and national levels as well as at the EU level (including for instance programmes such as IMI, COST, FP7, DG SANCO). Information is relayed and extended locally by the Regional Delegates.

In December 2012, a first call for proposals was also launched in the field of human and social sciences (Point 2) jointly by the Foundation, the French National Solidarity Fund for Autonomy (CNSA) and the General Directorate for Health (DGS) to support human and social sciences research while encouraging cross-disciplinary studies by involving patients' organisations and clinicians together with dedicated academics. This call for proposals addressed three different areas: the diagnostic pathway; new technologies in the field of genetics and consequences for patients including ethical issues; and the social, educational and professional pathways for rare disease patients. More than 70 projects have been submitted to this first call for proposals underlying the need of additional calls to be launched on a regular basis.

The Foundation aims to boost clinical trials in rare diseases (Point 3) by identifying and supporting innovative medical devices as well as molecules with therapeutic benefit. Dedicated new public-private partnerships are under development. The objective is to provide guidelines, methodological support and search for partners in the development of preclinical and clinical studies linking academia and industry.

In order to promote French research, increase international collaborations and influence global related policies (Point 4), the Foundation has been actively involved in a number of international programme. In 2012, the Foundation, together with Orphanet, has been awarded the scientific organisational support of the International Rare Diseases Research Consortium (SUPPORT-IRDIRC, coordinated by Orphanet) and has joined the integrated infrastructure programme RD-Connect as an official partner in order to assess the project's impact and the appropriateness of the implementation of shared databases with the needs of the international research community. The Foundation also supported the collaborative Mediterranean Myology School initiative of Saint-Joseph University (Beirut, Lebanon), by funding three traveling grants, hence promoting expertise sharing in the Mediterranean area.

Beyond workshops jointly organised with French National Alliance for Life Sciences and Health (*Alliance nationale pour les sciences de la vie et de la santé - Aviesan*) on timely themes including proteomics and model organisms, the Foundation has initiated collective initiatives (Point 5), in 2012, on rare diseases issues, such as a think-tank of pharmaceutical companies and awareness actions together with the international business school ESSEC, that are to be continued in 2013.

Since its setup, the Foundation has been working closely with the representatives of the national data collection programme respectively initiated by the French Ministry of Health and the French Ministry of Higher Education and Research, namely the National Rare Disease Database (BNDMR) and the RaDiCo Project (Point 6).

In September 2012, the French Institute of Rare Disease Biotherapies was launched, grouping together the actions of Genethon, the French Muscular Institute, I-Stem and the Genetic Therapy Pole of Nantes under the coordination of the AFM, to cover all the stages of research. The Institute will bring together hundreds of experts and researchers.

In the scope of the Second French National Plan for Rare Diseases, €9.6 million were dedicated by DGOS in 2011-2012 to upgrade next generation sequencing platforms.

Other funding opportunities for rare diseases research in 2012 included grants and calls launched by the following organisations/institutes: Agence nationale de sécurité du médicament et des produits de santé (ANSM), International Fund for research on Congenital Adrenal Hyperplasia, Fondation Jérôme Lejeune, Fondation Thierry Latran, Fondation des Entreprises du Médicament, Fondation Imagine, Association Française de l'Atresie de l'oesophage, Association Française de l'Ataxie de Friedreich, Association pour l'information et la recherche sur les maladies rénales génétiques (AIRG-France), Institut de Recherche en Santé Publique (IReSP), Association Française du Syndrome de Rett (AFSR), Fondation Motrice, and l'Agence de la biomedicine.

E-Rare

France participated in the 4th Joint Transnational Call in 2012, with French teams participating in 7 out of the 11 consortia selected for funding.

Orphan medicinal products^{142,143}

The LEEM (French Pharmaceutical Industry Association) presented its annual overview of therapeutic advances with an edition covering 2012. A particular emphasis was put on new orphan drugs in relation to the development of personalised medicine¹⁴⁴.

Initiatives to improve access to orphan medicinal products

Compassionate use for individual patients takes the form of either cohort use (cohort Temporary Authorisation for Use) or named patient supply (nominative Temporary Authorisation for Use) prior MA granted both by the ANSM. Patients can also be treated with drugs before these drugs have received MA through clinical trials or hospital preparations. Reimbursement measures are in place for compassionate use. Innovative drugs are eligible for an ATU ("*Autorisation temporaire d'utilisation*" - Temporary Authorisation for Use) from the ANSM if there is a public health need.

This process was modified in 2012 following the law reinforcing the monitoring of safety of drugs and other healthcare products, published on 29 December 2011 (Law N° 2011-2012). The new law maintains the possibility of an ATU, in particular in the case of rare diseases. The drug must fulfil the following criteria: the treatment cannot be postponed; there is no alternative therapeutic to the drug; the efficacy and security of the drug are strongly presumed from 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.

This law also introduced the concept of "temporary recommendation of use" ("*recommandation temporaire d'utilisation*" - RTU) developed and published under the responsibility of the ANSM. The aim of RTU is to provide a framework for the prescription of a medicinal product beyond the indications of its MA when no other medicinal product with a MA or a cohort ATU is available for the considered indication. The development of RTU is possible when the ANSM considers the available data are sufficient to presume a favourable benefit risks ratio. Prospective data collection concerning safety and efficacy of the drug is mandatory when a RTU is published. In November 2012, the ANSM published a template¹⁴⁵ for the follow-up of patients and collection of data if RTU are available. In order to help the ANSM to prepare the development of RTUs for rare diseases, the

¹⁴² This section has been written using the KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp45-49)

¹⁴³ This section has been written using the Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products. 2005 Revision (pp12-14)

¹⁴⁴ <http://www.leem.org/les-essentiels-maladies-rares>

¹⁴⁵

http://www.legifrance.gouv.fr/jopdf/common/jo_pdf.jsp?numJO=0&dateJO=20121122&numTexte=13&pageDebut=18412&pageFin=18414

Ministry of Health asked the Reference Centres in July 2012 to carry out an inventory of their prescriptions out of the MA of the medicinal products that could be eligible for RTU. The questionnaire was returned by 70% of the Reference Centres. The data were compiled by the ministerial authorities and sent in November 2012 to the ANSM which is now exploiting them.

In hospitals, Temporary Treatment Protocols (*“Protocoles temporaires de traitement”* - PTT) may also be used to extend the indication for a drug or device with reimbursement permitted. Temporary Treatment Protocols are limited to expensive drugs used only in hospitals and registered on a special list.

In 2006, the law for the financing in 2007 of French Social Security system planned a derogative pathway for exceptional coverage of off-label use of medicinal products and of non-covered medical devices or services by the National Health Insurance¹⁴⁶. Orphan or non-orphan medicinal products used off-label, medical devices or services intended for rare diseases are in particular concerned. The complete reimbursement is allowed for a limited renewable period by the Ministry of Health after the HAS has given a positive opinion. Since the law of the 29 December 2011 reinforcing the monitoring of safety of drugs and other healthcare products, the ANSM must publish a RTU before the HAS is allowed to advise the complete reimbursement of a medicinal product used off-label.

D.10. GERMANY¹⁴⁷

National plan for rare diseases and related actions

By the end of 2012, around 60-70 proposed measures had been discussed in a workshop with all members of the *Nationales Aktionsbündnis für Menschen mit Seltenen Erkrankungen* (NAMSE)¹⁴⁸ working groups. In the context of the elaboration of the national plan, the objective is to adopt the proposed measures in 2013 by NAMSE and then to hand them over to the federal government which will adopt the plan.

Centres of expertise

The implementation of national centres of expertise in Germany is challenged by the decentralised, federal structure of the German health care system, since the provision of sufficient structural resources for health care is a matter solely concerning the *Laender* (federal states).

In order to improve further the care of complex diseases – in particular rare diseases – new opportunities were opened by the Act on Care Structures in the Statutory Health Insurance System (*GKV-Versorgungsstrukturgesetz – GKV-VStG*) that entered into force on 1 January 2012. It provides for the gradual establishment of a new specialist care sector aimed to achieve seamless care provision between outpatient and inpatient settings.

Specifically, highly specialised outpatient care can now be provided by both hospitals and non-hospital doctors (office-based specialists) on a high level and at the same conditions in terms of quality and remuneration (Social Code V, Section 116b).

Highly specialised out-patient care comprises the diagnosis and management of complex, hard-to-treat diseases that require special qualifications, interdisciplinary co-operation and appropriate equipment. They include rare diseases and conditions with correspondingly low case numbers such as:

- tuberculosis
- cystic fibrosis
- haemophilia
- malformations, congenital skeletal abnormalities and neuromuscular conditions
- serious immunological disorders
- biliary cirrhosis
- primary sclerosing cholangitis

¹⁴⁶ Article L162-17-2-1 of the Social Security Legal Code.

¹⁴⁷ 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.

¹⁴⁸ <http://namse.de/>

- Wilson's disease
- transsexualism
- caring for children with congenital metabolic disorders
- Marfan's syndrome
- pulmonary hypertension
- short bowel syndrome
- caring for pre- and post-transplant patients and for living organ donors

The sector of highly specialised outpatient care is organised by the Federal Joint Committee (*Gemeinsamer Bundesausschuss, G-BA*) that fleshes out the relevant provisions through binding guidelines. This includes, particularly, the specification of diseases, scope of treatment, technical resources and staff required for service provision as well as referral requirements and quality assurance measures. The Federal Joint Committee (*Gemeinsamer Bundesausschuss, G-BA*) also can extend this list of diseases which has been stipulated by law (Social Code V, Section 116b).

The Federal Joint Committee (*G-BA*) is the supreme decision-making body of the so-called self-governing system of service providers and health insurance funds in Germany¹⁴⁹. In the field of outpatient care for rare diseases provided by hospitals according to Social Code Book V, Section 116b, the *G-BA* has to regulate both the structural and personnel resources needed for outpatient care provided by both hospitals and office-based specialists. Consequently, all of these service providers are subject to the same staffing, equipment and regulatory/contractual requirements as well as special measures for quality assurance. Basically, access is free for service providers that prove compliance with the applicable requirements.

From now on, the Joint Committee will be able to broaden the catalogue of services and diseases in response to an application from one of its member organisations or the organisations on the Federal level that champion the interests of patients, also the self-help organisations of chronically ill and disabled persons.

There are already several self-appointed centres for rare diseases in Germany¹⁵⁰. However, these do not share a nation-wide concept and are not reviewed in respect of any specific quality criteria for rare diseases. Therefore, it falls to the NAMSE process to define and develop national framework conditions for centres and networks dedicated to rare diseases. This process is underway, with a number of meetings organised to discuss criteria and indicators for such centres. This also includes topics such as the setting up of registries and biobanks as it does the drafting of criteria and eligibility procedures for the certification of future centres. The self-appointed centres for rare diseases hold regular meetings to improve networking (coordinated by Prof. Wagner, EUCERD member). The group decided in 2012 to continue the state-wide cooperation of these centres; to share the experiences of the centres, with particular emphasis on their coordinating functions in both the framework of the medical faculties and the administration of the university hospitals ; to share efforts to attain sustainability; to help patients with rare and very rare diseases, and their responsible physicians/experts or clinical departments, to find and use the best expertise available; to coordinate an application for financial support for clinical research; to share information on the participation of National or European institutions for research and clinical care in the field of rare diseases.

Training and education initiatives

The Centre for Rare Diseases Tuebingen (University Hospital Tuebingen) provides continued education for physicians since April 2011 entitled the German Academy for Further Medical Training on Rare Diseases (FAKSE) in April 2011. In 2012, two more courses on rare auto inflammatory diseases and rare tumours were held. Further courses for 2013 are already being planned.

National rare disease events in 2012

The German Society of Human Genetics (GfH) holds an annual conference 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

¹⁴⁹ Physicians, dentists, hospitals and health insurance funds are represented in the *G-BA*. Since 2004 national groups representing patients were given the right to file applications and to participate in the consultations of the *G-BA*. The *G-BA* issues the directives/binding guidelines that are necessary for safeguarding medical service provisions. The latter aims to ensure that medical services for persons ensured under the statutory health insurance in Germany are adequate, appropriate and efficient. The *G-BA* issues directives and thus determines the benefit package of the statutory health insurance (*gesetzliche Krankenversicherung, GKV*) covering about 70 million people. The *G-BA* is responsible for reimbursement decisions in the statutory health insurance (*GKV*).

¹⁵⁰ Listed in <http://www.orpha.net/national/DE-DE/index/zentren-für-se/>

Paediatric rheumatology, all holding yearly meetings often including patient organisations. ACHSE organises meetings for patient organisations twice a year.

In Germany several events were organised to mark Rare Disease Day 2012, coordinated by ACHSE. These events took place in Bielefeld, Dessau, Essen, Flensburg, Halle, Hamburg, Köln, München, Nürnberg and Würzburg. On 28 February 2012, the Eva Luise Köhler prize for research on rare diseases was awarded¹⁵¹. On 29 February 2012 a political symposium on the theme “rare but strong together – finding better ways for people with rare diseases” was organised by ACHSE and attended by the German Minister of Health, Daniel Bahr, and the President of the German Medical Association. Expert panel discussions provided the opportunity for in depth discussion on a number of themes. On 29 February 2012, the 3rd Rare Disease Day Symposium organised by Orphanet Germany was held at the Hannover Medical School. More than 30 different support groups attended the event and manned the stands at the event, providing an opportunity to meet the 350 visitors about. Some patient organisations gave talks together with the professionals from the newly created centre of rare diseases of the Hannover Medical School. This year was also the first time that professionals from the pharma industry presented their activities in the field of orphan medicinal products.

Hosted rare disease events in 2012

Amongst the events hosted in Germany and announced in *OrphaNews Europe* were: 4th International Tuebingen-Symposium on Pediatric Solid Tumors (Tuebingen, 16-18 February 2012), International Meeting on Rare Diseases: Mechanisms and New Therapeutic Approaches (Freiburg, 22-24 February 2012), 5th International Conference on Ectodermal Dysplasia (ED2012) (Erlanger, 1-3 June 2012), 10th International primary hyperoxaluria workshop (Bonn, 22-23 June 2012), European Human Genetics Conference 2012 (Nurnberg, 23-26 June 2012), Retina International World Congress (Hamburg, 14-15 July 2012).

Research activities and E-Rare partnership

National research activities

The Federal Ministry for Education and Research (*Bundesministerium für Bildung und Forschung, BMBF*) funded 12 networks national academic groups, clinical centres, specialised laboratories and patient organisations for basic and clinical research starting in 2012 with more than €21million for three years.

E-Rare

Germany participated in the 4th Joint Transnational Call in 2012 with German research groups participating in 10 of the 11 projects selected for funding of about €3.4 million.

D.11. GREECE

Definition of a rare disease

The definition is for discussion in the agenda of the steering committee for Rare Diseases working on the final revision on national plan for RD.

National plan/strategy for rare diseases and related actions

The Second EUROPLAN Conference, organised by the Greek Alliance for Rare Diseases, on 1 December 2012, was met with great success, with the acceptance and active participation of all the involved stakeholders, as well as an impressive attendance by patients from all over the country. The conference was organised by PESPA with the support of EURORDIS, and was held under the auspices of His Excellency, the President of the Hellenic Republic, Mr. Karolos Papoulias. During the Conference, four working groups were created, in which various stakeholders from EOF, IFET, SFEE, KEELPNO as well as patients, participated. The principle subjects worked upon were predetermined by the EUROPLAN program: Patients' Access to their Diagnosis and Medical/Pharmaceutical Care; Social Security Rights for Patients with Rare Diseases; Reference Centres for Rare Disease; and Rare Diseases Registries in Greece. The results of the working groups focused on present-day problems for Greek patients with rare diseases, changes that need to be made, as well as new suggestions, shaping a complete plan of action for rare diseases, which will form the basis of the final report that will be

¹⁵¹ http://www.achse-online.de/cms/was_tut_achse/forschung_vorantreiben/koehler_forschungspreis.php

sent from Greece to the European Parliament. For example, some of the actions suggested during the conference will be implemented in the official report: establishment of already existing clinics as Reference Centres for Rare Diseases and creation of new ones (i.e. Children's Hospital, Sismanoglio, Evangelismos); participation of patients in the decision-making process for subjects that have to do with their medical/pharmaceutical care; establishment of the mandatory use of the ICD10 codification for rare diseases in the electronic prescription process, so that fully measurable data can be gathered for every disease; and cooperation of all registry stakeholders in Greece, for the creation of a common network.

Centres of expertise

Data has been collected in 2012 concerning centres of expertise but has not yet been evaluated.

Neonatal screening policy

The national of neonatal screening program was not changed in 2012 in the Greek NHS, a Ministerial Decision for the standardisation of the process of Development of execution of the NBS was launched.

National alliances of patient organisations and patient representation

PESPA organised in 2012 events for Rare Disease Day 2012 as well as the Europlan-2 conference on 1 December 2012 to discuss the national plan for rare diseases. In 2012 PESPA created a "Medical Support Fund for financially frail patients with Rare Diseases" to support in the current economic context families when they cannot receive support from their insurer.

National rare disease events in 2012

The Greek Alliance for Rare Diseases (PESPA) organised a series of events with the subject of "Rare but Strong Together" to mark Rare Disease Day 2012.

Members of the Greek Alliance for Rare Diseases, volunteers and the Greek Women Guides Association distributed leaflets regarding Rare Diseases in general as well as Rare Disease Day specific ones during the whole week around Rare Disease Day 2012. Throughout the month of February, Greek TV channels broadcasted video spot regarding Rare Disease Day 2012, as well as a radio spot for radio stations, with a series of interviews and articles regarding rare diseases for the press. Four different Bicycle Races will be held in Ptolemaida, Thessaloniki and Athens, in order to raise awareness and celebrate Rare Disease Day 2012. A Second Europlan Conference was organised by PESPA on 1 December 2012. A range of stakeholders were present for the conference.

Hosted rare disease events in 2012

A meeting entitled "Molecular Genetic Diagnostic Tests" at the Medical School of the University of Patras on 3 February 2012. As in previous years a considerable number of scientific events, national and international conferences and meetings, were held in Greece concerning rare diseases.

Research activities and E-Rare partnership

E-Rare

Greece did not participate in the 4th Joint Transnational Call in 2012.

IRDiRC

The GSRT as a member of the E-Rare group of funders joined the IRDiRC in 2012.

Orphan medicinal products

Orphan medicinal product market availability situation

The Greek Alliance of Rare Diseases (PESPA) expressed in 2012 the anxiety of Greek patients with rare diseases, as they are worried for the access to new medicines as quickly as it is possible after the authorisation of an orphan medicinal product. The main reason for not having a quick and easy access is the delay of giving a price to the orphan medicines as the Ministry of Health and EOF follow the same way for all medicines. There is no differentiation in the process between orphans and ordinary medicines and that means huge delays in pricing procedure. PESPA is asking, orphan medicines to be handled for pricing as quickly as possible exactly after the code number and the "blue box" for the marketing of the orphan medicine has been issued by EOF. PESPA tried to give their reasoning to the Prime Minister Antonis Samaras and the Minister of Health, Mr. Andrea Lykourantzou and explain the necessity for giving prices to orphan medicines as quickly as possible, as deterioration in the health of patients is unavoidable. PESPA argues that the deterioration of the health of

these patients, in addition to the price overcharge (if imported via IFET), will cost much more to the state because the necessary hospitalisation, consultations and other effects.

Orphan medicinal product pricing policy

No specific information reported. Medicinal products pricing policy in general was under continued revision in 2012. During 2013 the same pricing policy is continuing.

D.12. HUNGARY

National plan/strategy for rare diseases and related actions

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 was sought on the plan in March 2012. The third Hungarian Europlan Conference on Rare Diseases¹⁵² (16-17 November 2012) was organised by HUFERDIS, together with the Ministry of National Resources, in Budapest. All stakeholders were present during the two day conference aimed at defining further concrete steps to develop a national action plan for rare diseases.

By the end of 2012 the plan was submitted to the Ministry of Health. The legal status of the document and budgetary considerations are still to be considered. The national conference, organised by HUFERDIS with the participation of the Ministry of Health examined the document and the budgetary question. It was hoped that the text of the plan will be finalised by the middle of 2013. The plan includes a proposal for the designation of centres of expertise in accordance with the EUCERD Recommendations. In 2012 an expert group was also established at the Ministry of Health to identify the technical specification for a pilot study concerning the introduction of Orphacodes into hospital and healthcare centre records.

Centres of expertise

NRDC initiated a collaboration with the National Health Insurance Fund for the listing and transparent accreditation of centres of expertise, hospitals, and laboratories working in the field of rare diseases taking into account existing resources and their concentration, as well as eliminating parallelism and formalising existing informal relations and determining patients' pathways. The research project final report is expected to be published in 2013.

Sources of information on rare diseases and national help lines

Orphanet activities in Hungary

There is a Orphanet national website launched in 2012, in the Hungarian language¹⁵³.

Training and education initiatives

The Department of Medical Genetics at the University of Pécs has organised since 2009 3-day clinical genetics course covering among others the diagnosis and management of selected rare diseases; the meeting is intended for specialists in the field as well as for family practitioners. The course in October 2012 aimed to show the interdisciplinary participation of various disciplines in the diagnosis and care of rare disease patients. The institutions and clinics participating in rare disease care constitute a Rare Disease Network of the University of Pécs established in February 2012.

National rare disease events in 2012

HUFERDIS, the Hungarian rare disease alliance, organised a number of events to mark Rare Disease Day in Hungary on 25 February 2012 in Budapest. As usual, many parallel programmes was arranged: 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. Many videos and report are available¹⁵⁴). The main breakthrough of the programme was the section dealing with social problems of rare diseases for the first time: four leaders of the Ministry of Social Affairs participated and

¹⁵² <http://europlan.rirosz.hu/>

¹⁵³ <http://www.orpha.net/national/HU-HU/index/honlap/>

¹⁵⁴ <http://ritkanap.rirosz.hu/eddigi-ritka-napok/ritka-nap-2012/videok-interjuk-2012>

gave talks¹⁵⁵. For the second time, Rare Disease Day in Hungary was organised in two cities simultaneously. In addition to the events in the capital, Budapest, events were also held in the university town of Pécs, in southwest Hungary. The initiative to organise Rare Disease Day events at multiple locations allows Hungarian rare disease patients to participate in the events nearer to their hometowns. As a joint effort of the Department of Medical Genetics of the University of Pécs, the Életes Mátyás School for Children with Special Needs, and the Pécs Gallery at the Zsolnay Cultural Center, an information day for all rare disease patients in the region was held on 23 February, 2013. The backbone of the program consisted of musical performances by the students of the Életes Mátyás School, many of whom are affected by rare diseases themselves, and information stands of various Hungarian rare disease patient organizations and caregivers from the region. The guest of honour at this year's scientific program was Daria Julkowska, program coordinator of E-Rare2, the ERA-Net on Rare Disease Research Funding. Hungary joined the E-Rare2 network in 2010, and was able to participate through contributions from the University of Pécs, and the Hungarian National Research Fund. Daria Julkowska gave both a broad overview on E-Rare2 activities and achievements, as well a model of rare disease national coordination, using the example of the French Rare Disease Foundation. The broad interest in rare diseases, and the success of the local events strengthened the organizers in their ambition to continue this tradition, and even inspire other regions in Hungary to organise local events on future Rare Disease Days.

The third Hungarian Europlan Conference on Rare Diseases¹⁵⁶ (16-17 November 2012) was organised by HUFERDIS, together with the Ministry of National Resources, in Budapest. All stakeholders were present during the two day conference aimed at defining further concrete steps to develop a national action plan for rare diseases

Hosted rare disease events in 2012

Amongst the events hosted by Hungary and announced in *OrphaNews Europe* was the 8th International Society for Newborn Screening European Regional Meeting (4-6 November 2012, Budapest).

Research activities and E-Rare partnership

E-Rare

Hungary did not participate in the 4th Joint Transnational Call in 2012.

IRDiRC

Hungarian funding agencies have not currently committed funding to the IRDiRC, but as part of the E-Rare group of funders there is the possibility for Hungary to participate in the IRDiRC through the University of Pécs.

Orphan medicinal products¹⁵⁷

Orphan medicinal product committee

There is a new committee for the evaluation of reimbursement inclusion decisions in case of high-value medicines and care. A new system was established at the National Health Insurance Fund for the evaluation of high valued medicines and care, besides professionals caring for patients with rare diseases where high valued therapy is available, the representatives of HUFERDIS were invited to this expert committee. The committee has issued guidelines on the diagnosis, treatment and care of various rare diseases where therapy is available, those guidelines serve as a basis for the individual decision on the reimbursement of high valued orphan drugs to Hungarian rare disease patients.

Orphan medicinal product reimbursement policy

The National Health Insurance Fund established an advisory group to evaluate the applications for expensive medical treatments. The operation rules for this committee have been elaborated. A significant proportion of applications are submitted by rare disease patients' physicians.

Specialised social services

HUFERDIS joined the therapeutic recreational programs of a member association (Hungarian Williams Syndrome Association) and organised programmes for capacity building and training, networking, awareness

¹⁵⁵ In addition, some videos were released by Bach Rezsőo Bach: <http://youtu.be/JKiGdF-fvHg>, and Gábor Pogány: <http://youtu.be/Z-i8R - CzU4> Hungary (Society of Aiders and People suffering from Neurofibromatosis).

¹⁵⁶ <http://europlan.rirosz.hu/>

¹⁵⁷ This section has been written using the Inventory of Community and Member States' incentive measures to aid the research, marketing, development and availability of orphan medicinal products. 2005 Revision (p15)

raising, exchange of information and best practices, during a special development family camp and after. HUFERDIS is also participating in the EUCERD Joint Action activities concerning Specialised Social Services.

D.13. IRELAND

National plan/strategy for rare diseases and related actions

A national consultation¹⁵⁸ was carried out in 2012 on the proposed national plan for rare diseases. The Health Service Executive National Advocacy Unit is supporting the Department of Health in its initiative to develop a national rare disease plan. The patient-centred policy framework will encompass actions targeting the prevention, detection and treatment of rare diseases based on the principles of quality care and equity. The policy will operate over a five-year period and define priority actions, subject to resource availability, in the areas of centres of expertise, orphan drugs and technologies, research and information and patient empowerment and support. A National Steering Group invited stakeholders to participate in a consultation process designed to gather views concerning the plan's various components. A National Consultation Day event was held on 11 June 2012. This was followed by an online consultation process which received almost 500 valid responses. The Institute of Public Health, which is providing support for the development of the Plan, is preparing a report on both aspects of the consultation process which it is intended to publish alongside the Plan itself in 2013.

On 7 March 2012 a motion¹⁵⁹ was heard in the Seanad Éireann (Senate) on the subject of rare diseases: the Minister for Health, Dr. James Reilly, announced the intention of the Health Service Executive (HSE) to develop a Clinical Care Programme for Rare Diseases. The recruitment process for a Clinical Lead in Rare Diseases in the Health Service Executive commenced in late 2012.

Centres of expertise

A policy concerning centres of expertise is under development as part of the national plan for rare diseases.

Registries

The Health Information Bill is expected to be published in 2013 and will address ethical and legal issues concerning data collection and sharing patient data.

National alliances of patient organisations and patient representation

The Rare Disease Taskforce

The Rare Diseases Towards 2013 Taskforce was set up in 2011 by the Medical Research Charities Group (MRCG), the Genetic and Rare Disorders Organisation (GRDO) and the Irish Platform for Patients' Organisations, Science and Industry (IPPOSI). The Taskforce brings the three umbrella organisations together to work collaboratively to ensure that the needs of the Rare Diseases stakeholders are represented in the National Strategy for Rare Disease 2013.

The Minister for Health has established a National Steering Group which is tasked with developing a five year national plan and which will deal with the diagnosis, prevention, management, treatment and research of rare diseases in Ireland. The Rare Disease Taskforce will support this National Steering group and provide input from the appropriate stakeholders. The aim of the 2013 Taskforce is the delivery by the State of a comprehensive, targeted and achievable National Strategy for Rare Diseases by 2013.

GRDO, MCRG & IPPOSI as part of the Rare Disease Taskforce came together in 2012 to plan and organise Rare Disease Day on 28th of February 2013 with the theme of Rare Disorders without Borders which addressed the EU directive on cross border healthcare for Ireland. In keeping with the theme of cross border co-operation this event was organised along with the Northern Ireland Rare Disease Partnership (NIRDPA) and Rare Disease UK. IPPOSI took the lead in co-ordinating and organising this event.

Genetic and Rare Diseases Organisation (GRDO)

At the end of 2011 GRDO launched a survey to gather information relating to patient support and advocacy 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. The results of

¹⁵⁸ <http://www.dohc.ie/press/releases/2012/20120614d.html>

¹⁵⁹ <http://debates.oireachtas.ie/seanad/2012/03/07/00008.asp>

this survey were published on Rare Disease Day 2012, which highlighted the urgent need for development of co-ordinated healthcare pathways and a central information point on rare conditions.

The results also reveal significant difficulties in the areas of access to diagnosis, information and to treatment, as well as a lack of coordination in delivery of services. 13.3% of respondents report waiting more than 10 years for diagnosis and 37.2% report receiving an incorrect diagnosis before the correct one. 73.1% of those surveyed report attending more than one hospital consultant or other medical professional for treatment yet 44.8% report not having a specific point of contact to go to with questions about their condition. 62.5% of respondents list the Internet as their main source of information. The establishment of a National Rare Disease Office in Ireland and the development of co-ordinated healthcare pathways are the two changes to the healthcare system that respondents would most like to see (82%), followed by more information about their conditions (73%). A national office would act as a focal point for the development of a national registry of rare conditions, and a vitally needed information portal for patients and medical professionals. It would help patients to access Centres of Expertise, whether in Ireland or abroad, and ensure the best model of care for patients with faster diagnosis and access to treatment. It would also be cost efficient.

In the context of developing a National Rare Disease Plan and the EU Directive on the Application of Patients' Rights in Cross-border Healthcare, GRDO is working to establish a cross border working group with its equivalent organisation in Northern Ireland, the Northern Ireland Rare Disease Partnership.

National rare disease events in 2012

To mark Rare Disease Day 2012 in Ireland GRDO planned a number of initiatives. The GRDO addressed the Joint Oireachtas Committee^{160&161} on 29 February 2012, which was aimed at providing committee members with an in-depth briefing on the issue in Ireland and provide the groups dealing with various rare diseases with an opportunity to outline the key issues they face in terms of prevention, detection and treatment of rare diseases, access to appropriate medication and the identification of appropriate centres of expertise for rare diseases which is a key priority.

The results of the GRDO-led patient survey on the experiences of people in Ireland with rare conditions were published on Rare Disease Day 2012. The survey highlights the urgent need for development of co-ordinated healthcare pathways and a central information point on rare conditions. The information from the survey will be used by GRDO, together with the Medical Research Charities Group (MRCG) and the Irish Platform for Patients' Organisations, Science and Industry (IPPOSI) and their patient representatives to assist the National Rare Diseases Taskforce ('Towards 2013 - the National Plan for Rare Diseases') to engage with the Rare Diseases Steering Committee of the Irish Government's Department of Health.

In addition, GRDO launched a postcard campaign to highlight Rare Disease Day in Ireland, including images from the official Rare Disease Day video which was filmed in Dublin : the postcards were delivered to politicians and other public figures, as well as to media representatives across Ireland. In addition, GRDO produced a new Easy Guide public information booklet on rare disease in Ireland which was launched on Rare Disease Day 2012, this was accompanied by an awareness-raising campaign.

On 11 June 2012, the Department of Health's Consultation Day on the National Rare Disease Plan took place in Dublin. An online consultation process was also launched, offering all those affected the opportunity to contribute to the formation of the plan.

On 26 March 2012 a workshop hosted by the Health Research Board on behalf of the National Steering Group for Rare Diseases was held to provide an opportunity for stakeholders to input to planning for the future of rare disease research in Ireland and inform deliberations in the area of research for the forthcoming Irish National Plan for Rare Diseases.

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: in June 2012 a roundtable on access to new therapies and treatments¹⁶² was organised.

In June 2012, IPPOSI facilitated a roundtable discussion with its members and invited guests, on the issue of Access to Innovation which was an issue for Rare Diseases and other diseases. The Board of IPPOSI decided to call this meeting in response to reports of treatments which had been approved for reimbursement but were not reaching patients. IPPOSI asked key patient organisations to outline the issues and clarify the

¹⁶⁰

<http://media.heanet.ie/oireachtas/asx.php?Channel=Committee1&Date=20120229&StartTime=05%3A00%3A00.000&Duration=02%3A00%3A00.000>

¹⁶¹ <http://www.oireachtas.ie/parliament/mediazone/pressreleases/name-6924-en.html>

¹⁶² <http://www.ipposi.ie/index.php/news-a-events-mainmenu-28/227-outcome-report-from-ipposi-roundtable-on-access-to-new-treatments-and-therapies->

situation for their patient members. Key contributions were made by the Irish Cancer Society, MS Ireland and Fighting Blindness. IPPOSI also launched the Outcome Report on their website on 11 October 2012, IPPOSI members welcomed the presence of the Secretary General of the Department of Health at the roundtable and IPPOSI has subsequently met with the Secretary General to discuss the issue further. An announcement was made by the Department of Health on 18 June 2012 which saw the HSE give approval to the reimbursement of certain treatments.

On 17 September IPPOSI hosted an event where a well known Broadcaster and the CEO of the Health Research Board, launched a new information campaign aimed at people who have been asked to participate in a clinical trial. The clinical research information campaign includes a new leaflet and dedicated website which will provide patients with independent answers to many of the questions which they may have about clinical trials.

IPPOSI held an information day on the process of Health Technology Assessments (HTA) in Ireland on 11 October 2012. IPPOSI members attending represented key individuals from leading patient organisations, clinicians, researchers and industry. The aim of the event was to explain how pharmaceutical products are assessed to further inform pricing and reimbursement decisions made by the Health Service Executive (HSE) and/or the Department of Health. Patient organisations articulated a willingness to get involved in the HTA process at the earliest stage. The Director of the Irish National Centre for Pharmaco-Economics (NCPE) agreed that this was an area the NCPE are interested in pursuing and indicated that IPPOSI would be an ideal partner in linking his team with relevant patient groups as new applications arrive in to the NCPE office.

Research activities and E-Rare partnership

National research activities

On 26 March 2012 a workshop hosted by the Health Research Board on behalf of the National Steering Group for Rare Diseases, brought together national and international speakers and Irish researchers. This meeting was intended to provide an opportunity to input to planning for the future of rare disease research in Ireland and inform deliberations in the area of research for the forthcoming Irish National Plan for Rare Diseases. This event outlined how Ireland can move forward in the area of rare disease research and participate at an international level. Keynote presentations on the elements involved in successful research in the area of rare disease were followed by a panel discussion on the barriers, solutions and opportunities in rare disease research.

Orphan medicinal products

Orphan medicinal product incentives

This will be covered in the National Rare Disease Plan. The approval of Kalydeco for use in Ireland for patients with cystic fibrosis with at least one copy of the G551D gene alteration is likely to be an indirect incentive to support the development of orphan medicinal products. Ireland, through cystic fibrosis centres, played a key role in supporting the phase three clinical trials for this groundbreaking gene modification therapy.

Orphan medicinal product pricing policy

In the IPPOSI HTA meeting in October 2012, patient organisations articulated a willingness to get involved in the HTA process at the earliest stage. The Director of the National Centre for Pharmaco-Economics (NCPE) agreed that this was an area the NCPE are interested in pursuing and indicated that IPPOSI would be an ideal partner in linking his team with relevant patient groups as new applications arrive in to the NCPE office. This type of engagement happened recently with the cystic fibrosis example mentioned above.

Orphan medicinal product reimbursement policy

This will be covered in the National Rare Disease Plan. The reimbursement of medicines in general is provided for through a number of “Community Drug Schemes” and “National High Tech Drug Schemes”. As a result of the 2012 Industry-Department of Health recent supply terms and pricing agreement, a budget for innovative and new treatments was created and it is the view that emerging high cost drugs will fall into this budget.

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. On 23 February 2012, a conference was held at the Chamber of Deputies, and a white paper presented, with the aim of encouraging the government to put in place the rare diseases plan. Between March and April 2012 both Orphanet and UNIAMO organised public consultation on rare diseases with the aim of providing input from stakeholder into the process. The working group of the Ministry of Health preparing the draft of the national plan concluded in June 2012, and the document was sent by the Ministry of Health to AIFA for comments and subsequently again to the Ministry of Health for final assessment. The document was illustrated officially in December 2012 at the Ministry of Health in the presence of 200 stakeholders. The next step is for the document to be commented on by stakeholders. Their comments will be evaluated and implemented into the document by the Ministry of Health and sent for approval by the permanent Conference for relations between State, Regions and the autonomous provinces of Trento and Bolzano.

Registries

A congress on the National Registry and Regional and Interregional Registries for rare diseases was held in Rome on 22 February 2012, to illustrate the results, to discuss and agree among all actors on actions to improve further the performance of the National Registry.

Neonatal screening policy

According to SIMMESN (Società Italiana per lo Studio delle Malattie Metaboliche Ereditarie e lo Screening Neonatale¹⁶³), about one fifth of the Italian newborn population underwent an expanded screening in 2011. UNIAMO F.I.M.R. sent a position paper on this subject as Memorandum for the XII Social Affairs Commission of the Chamber of Deputies on Draft Law No. 5,440 Conversion into law of Decree-Law of 13 September 2012, n. 158 laying out “urgent measures to promote the development of the country by a higher level of protection of health”, calling for a gradual expansion of neonatal screening programs for all rare diseases for which there is evidence of appropriateness and not just to rare diseases for which a cure already exists. However, it will be mandatory to define a common set of standards, procedures and methodologies at the national level to ensure an effective, fair and appropriate disease screening as well as to assure adequate health and social post screening management.

Genetic testing

In an international context, Italy is one of the few countries to monitor genetic test use (this survey was implemented in the 1980s), and recently this monitoring has expanded to include clinical and laboratory activities carried out by Medical Genetic Institutes and also private laboratories since 2009^{5,6}. This census promoted by SIGU surveys the services provided by Italian Medical Genetic Centres and involves the NHS bodies, the IRCCSs (Excellence Centres for Healthcare and Research), the University Institutes, the CNR (Research National Council) laboratories, and private laboratories. Data collection takes into account the typology of the Institutes, number and functions of the laboratory staff, cytogenetic analyses, genetic-molecular and immunogenetics analyses, and clinical activities, including genetic counselling. Certified quality systems adopted by the Institutes and the adequacy of some genetic tests have been also checked.

The survey concerning the 2011 data was carried out in 2012. The census was made possible thanks to the collaboration of the Bambino Gesù Children Hospital, Orphanet-Italy, and SIGU. On the whole, 517 services hosted by 268 Hospitals or Institutions were surveyed, including 145 clinical genetic services, and 153 cytogenetic, 198 molecular genetics and 21 immunogenetics laboratories. The 53% of services are located in the Northern regions, the 20% in the Central regions, 17% in the Southern regions, and 10% in Sicily and Sardinia. About 74% of these services were accredited and 55% certified.

The CNMR-ISS is in charge of carrying out the National External Quality Control Scheme for genetic tests. As regards molecular genetics, in 2012, national experts have assessed laboratory performance on genotyping, interpretation, and reporting of test results for a total of 404 different DNA samples sent to 68 public and private laboratories. In addition, 75 laboratories participated in one or more schemes of constitutional or cancer cytogenetic quality control.

¹⁶³ www.sismme.it/it/documents/rt_screening/rt_screening_2011.pdf

National alliances of patient organisations and patient representation

In 2012, a framework agreement was signed by UNIAMO F.I.M.R. with the Telethon Foundation Onlus-CTFO, to promote access to TNGB genetic biobanks by members of the associations' federation.

In October 2012, the Ministry of Welfare recognised UNIAMO F.I.M.R. as an Association of Social Utility.

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

- "Knowing to assist", carried out in collaboration with Farindustria and Scientific Societies, is aimed at training general practitioners and paediatricians regarding rare diseases. The project is based on a covenant of understanding signed by several Institutions. The project will cover the whole Italian territory by 2013.
- "Galeno Help" results from a memorandum of understanding between UNIAMO F.I.M.R. and the professional pharmacists federation (UPFARM), with the intention of giving practical support to patients who need drugs which are difficult to find. Many of these drugs can be prepared in the galenic laboratories of the pharmacies in a personalised manner. "Galeno Help-Pharmacist helps for rare disease patients" is a national service offering the possibility to quickly and easily find the nearest participating pharmacy.
- "Mercury", funded by the Ministry of Labour and Social Affairs in cooperation with the signatories of the aforementioned covenant of understanding, has been designed to train the general practitioners and paediatricians in rare diseases. The major goal of the project is to implement and enhance the web site "Malatirari.it" and turn it into a platform to meet the rare disease community's needs along the complex path from a suspected case to diagnosis of rare disease. The site will become a virtual place where information based on direct experience can be shared by patients, relatives and health professionals involved in the diagnosis and treatment of these diseases. In 2012 the data were implemented with an area dedicated to health professionals, with a restricted access.
- "The Atlantis Code" is aimed at fostering the culture of research in rare diseases. Developed in partnership with the Telethon Foundation, it involves rare disease patient organisations in the attempt to identify research priorities and provide answers to the patients' needs. Three seminars were organised. The outcomes of this survey were matched up with the results of a similar investigation carried out by EURORDIS at European level.
- "Momo" intends to bring together, with a unique voice, the demands of different groups of rare disease patients at Regional level. For this purpose, regional UNIAMO delegations were created in the context of a progressive regionalisation of the federation.
- "A Community for Rare Diseases", is aimed at developing a model to assess the quality of expertise centres for rare diseases in Italy. Since many Regions are reorganising their network of expertise centres, it was felt important to share similar inclusion criteria. Participants were the Ministry of Health, the Ministry of Labour and Social Affairs, ISS, Regions, local health authorities, Orphanet Italy, expert centres, municipal districts, general practitioners, primary care paediatricians, biobanks and patients organisations. On September 20, 2012 an agreement was signed with Age.Na.S., the National Agency for Regional Health Care Services, for the implementation of the second phase of the project which will assess some previously defined centres of expertise, with a major emphasis on the geographic distribution of a selected group of centres dedicated to distinct diseases (e.g. haemoglobinopathies).
- "Diaspro Rosso", a pilot project concluded in 2012, has provided an accurate, effective and efficient model for detecting the care needs and the social-economic costs for families with patients affected by rare diseases. The model will be presented to the institutional actors as a decision-making tool to be used to develop policies on social health based on concrete data.
- "Dumbo" was aimed at developing a model for the social reporting of patients' organisations. This model was illustrated to the Associations' members in several meetings and UNIAMO F.I.M.R. used it to present its first Social Report.

In November 2012, the MIR (Movimento Italiano dei Malati Rari) was established by 15 patients' associations.

Sources of information on rare diseases and national help lines

Help line

In 2012, the CNMR-ISS started collaborations and training activities for regional help lines (i.e. Contact Centre of Tuscany Coordination Centre for rare diseases) and with Patients' Associations (i.e. Foundation "W Ale – Alessandra Bisceglia").

Best practice guidelines

In order to promote the development of high quality best practice guidelines and their use in Italy and across Europe, CNMR-ISS organised national and international training courses (9-11 July 2012) providing participants (health care professionals, policy makers, patients) with the opportunity to learn about the core methodology used to develop best practice guidelines. In addition, CNMR-ISS encourages international debate on the role and quality of best practice guidelines in the field of rare diseases. In particular, a workshop on Clinical Practice Guidelines on Rare Diseases was organised on 23-24 February, 2012, aimed at sharing experiences and knowledge and discussing critical methodological issues due to the specificity of rare diseases.

In 2012, CNMR-ISS, 13 institutional partners and one SME have been awarded with a grant by the European Commission, under the Seventh Framework Programme (FP7/2007-2013) for a four-year research project entitled RARE-BestPractices (www.rare-bestpractices.eu), commencing in January 2013. This project will bring together a team of experts in the area of clinical practices guideline, systematic review, health technology assessment, health policy, rare disease epidemiology and public health.

Training and education initiatives

A workshop on Clinical Practice Guidelines on Rare Diseases was organised on 23-24 February 2012, for sharing experiences, knowledge and discussing some methodological related to the specificity of rare diseases.

The Italian Telethon Foundation and Orphanet-Italy joined their respective competences and contact networks in October 2012 to meet the patients' needs and support health professionals via a training course entitled "e-patients, e-parents, e-doctors: le malattie rare via web – opportunità e rischi". Suited for all stakeholders of the rare disease community, this event provided an opportunity to discuss web services and social networks as tools for professionals, patients and their families. During the course, health professionals, journalists, and IT experts presented their experiences to guide the community in using the web as a tool to break the isolation rare diseases can impose. A round table was animated by communication experts on the responsible use of Internet.

On 16 April 2012, the Orphanet team held a training course in Rome for health professionals operating in the Bambino Gesù Children Hospital, aimed at teaching them how to use the Orphanet resources.

National rare disease events in 2012

Since February 2008, UNIAMO F.I.M.R. 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 over one hundred local events, in squares, sports halls and schools and through many articles and interviews on rare diseases in newspapers and on TV. The cartoon "Mamma, cosa sono le malattie Rare? – Mum, what are rare diseases?" promoted by UNIAMO F.I.M.R. was shown on Mediaset TV Channels all through February. The Volley Major League collaborated with UNIAMO F.I.M.R. in distributing dedicated information leaflets on rare diseases during the matches where an awareness raising announcement was also made.

On 29 February 2012, the event "La solidarietà che costruisce" was organised at the Italian Senate to promote the Rare Disease Day in Italy, with the participation of several leading figures in the field of the rare diseases. This event raised awareness on the needs and actions in the field of rare diseases, and promoted dialogue between stakeholders and public institutions. During the event, Orphanet-Italy received a prize for its contribution in the "Mercurio" project (update of the malatirari.it web site) managed by UNIAMO F.I.M.R.

To mark Rare Disease Day, the Bambino Gesù Children Paediatric Hospital, in collaboration with Orphanet launched on 27 February 2012, a pilot project on rare diseases for middle schools. The "Virgilio" public school is hosting the project whose aim is to teach children the basics of familial inheritance. Professionals from Bambino Gesù Hospital will work together with teachers and pupils to produce papers, which will be evaluated in the context of a prize-awarding contest. The award ceremony will be held on Rare Disease Day 2013.

The CNMR-ISS presented two different events: a theatre play dedicated to rare diseases, inspired by real events, and the fourth edition of the event "Il Volo di Pegaso - Raccontare le malattie rare: parole e

immagini" (Pegasus' Flight – Describing rare diseases through words and images), an art contest on rare diseases. The theatre play "Controvento" (Against the Wind) took place at the Quirino theatre in Rome on 27 February 2012 and the art contest prize-giving at the ISS on the same day. Another institutional event, on 29 February was the initiative "La solidarietà che costruisce" (Creating through solidarity): several leading figures in the field of the rare diseases discussed the topic "L'esperienza, il presente e il futuro per le Malattie Rare in Italia", while a white book "Una incompiuta: le Malattie Rare" was presented by the Senator Antonio Tomassini. Flash mobs were also organised to mark the Day with a closing speech by the Italian Minister of Health, Prof. Renato Balduzzi.

On 29 February 2012, the patient association MITOCON organised a round table focused on research, care and policy concerning rare diseases.

On 8 February 2012, in the Rome Campidoglio a press conference was held for the event "Stammi vicino" (Stay close to me), organised by EEC syndrome International Network Word Communication ONLUS. This event, aimed to foster communication on rare diseases through sport.

On 18 February 2012, on the occasion of the Del Monte Italian Cup final tour, before the beginning of the matches, particular attention was given to the importance of funding rare disease research.

On 4 June 2012, an international congress entitled "Narrative Medicine and Rare Diseases" was held in Rome at the ISS.

On 12 June 2012 a press conference was held at the Senate to mark the launch of the book "Malattie rare: alla ricerca di un approdo" (Rare Diseases: in search of a landing place). This book collects the results of the Public Consultation launched in March 2012 on website and includes interviews of the main Italian and European stakeholders belonging to the academic and institutional world, together with the experience of patients and their families. The aim was to provide input on the elaboration of the National Plan for Rare Diseases.

On 12 July 2012, a press conference was organised in Rome to launch the second edition of the project "MALattie raRE NOSTRUM", promoted by "Tender to Nave Italia" a non-profit foundation and the Bambino Gesù Children Hospital. The project aimed at making a group of children affected by rare diseases more independent, fostering sea and navigation as an education instrument.

From 1 September to 6 September 2012, the first edition of the project "GiRare Mangiando", an initiative of the non-profit organisation UNIAMO Goldin, was held in Venice. This project was designed to provide an information path of independent living for patients affected by metabolic rare diseases. Four young patients were given the opportunity to stay in an apartment in Venice owned by UNIAMO Goldin, profiting by the facilities of the Fantasia restaurant, managed by rare disease patients, and following a program of cultural activities on the territory. The young participants have been supported by the healthcare professionals of the Bambino Gesù Children Hospital.

On 18 September 2012, a conference entitled "The State of Art of Rare Diseases: Rare Diseases and Economic Development" was held in Rome at the Ministry of Health. The Conference focused on several issues related to rare diseases: diagnostic difficulties; lack of therapeutic options and structured care pathways; chronic and debilitating course of the disease; emotional impact due to feelings of isolation experienced when living with one of these diseases. The initiative aimed to identify goals and actions to support health services, industry production and drug companies.

Several dozens of events have been organised locally in all Italian Regions.

Hosted rare disease events in 2012

Amongst the events announced in *Orphanews Europe* were: 15th Biennial Meeting of the European Society for Immunodeficiencies (Florence, 3-6 October 2012), EpiRare International Workshop: Rare Disease and Orphan Drug Registries (Rome, 8-9 October 2012), Goldrain Courses in Clinical Cytogenetics and Prenatal Genetic Diagnosis (Goldrain, 15-21 September 2012) .

Research activities and E-Rare partnership

National research activities

In 2012 Telethon was able to fund 260 research projects on rare genetic diseases, thanks to the fundraising activities in 2011.

E-Rare

Italy did not take part in the 4th Joint Transnational Call in 2012.

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. A public consultation of the plan was launched in 2012 and the results were analysed by the Ministry of Health. A number of meetings with different stakeholders were held, and as a result, the plan was further elaborated. The plan should be able to be adopted in 2013.

Registries

There is a plan to pilot use the Orpha code for rare diseases in the register of patients with congenital anomalies.

Sources of information on rare diseases and national help lines

Orphanet activities in Latvia

The Ministry of Health of the Republic of Latvia has designated The Centre for Disease Prevention and Control as the representative of the Republic of Latvia to participate in the Joint Action Orphanet Europe since April 2012. The Orphanet Latvia country site was launched in April 2012 and regularly updated by the Orphanet team.

National rare disease events in 2012

The Rare Disease Association Caladrius, Latvian Association of Hemophilia, PHA Latvia and the Association Motus Vita all marked Rare Disease Day in Latvia on 29 February 2012 with an event entitled 'SOLIDARITY'. The event took place in the EU House Conference Hall in Riga. The event served to highlight a number of issues concerning the quality of care for rare disease patients, as well as access to diagnosis and treatment, and aimed to make suggestions concerning what can be done to improve the situation for rare disease patients in Latvia. The Children's Hospital organised a day to raise awareness of cystic fibrosis dedicated to the parents and primary care providers.

Orphan medicinal products

Orphan medicinal product market availability situation

The following orphan medicinal products were marketed in Latvia in 2012: Aldurazyme, Cystadane, Diacomit, Gliolan, increlex, Jakavi, Kuvan, Litak, Mozobil, Myrin, Nexavar, Pedea, Revatio, Sprycel, Tassigna, Ventavis, Volibris, Wilzin, Yondelis. In 2012, compared to 2011, 3 new orphan drugs were launched on the market: Aldurazyme, Jakavi, Yondelis and 3 orphan drugs were no longer available on the market in 2012: Arzerra, Nplate, Revolade. Medicinal product Glivec which was originally designated as an orphan medicine and was placed on the market in 2011 is no longer designated as an orphan drug in Europe.

D.16. LITHUANIA

National plan/strategy for rare diseases and related actions

On 18 October 2012, the national plan for rare diseases was approved by the Order No V-938 of the Minister of Health, and a national rare diseases coordination committee was formed, including delegated experts from university hospitals, universities, non-governmental organizations, state institutions representatives to oversee the plan. The plan aims to establish a common approach on rare diseases, to raise public awareness, and to ensure prevention, early diagnosis, efficient treatment, improvement of quality of life and social support for patients suffering from rare diseases. It also includes the optimisation of health care services and rational allocation of available resources, as well as measures for improving the assessment of medicinal products and medical devices.

In 2012 12,97 million litas (about 3,6 million of euro) were allocated to reimbursing rare medicinal products and devices.

Centres of expertise

At the Centre for Medical Genetics at Vilnius University Hospital Santariškių Klinikos, an expert centre for diagnosis, treatment and management of rare diseases was established in November 2012. A coordination centre for children with rare diseases has been established at Vilnius Children's Hospital¹⁶⁴.

Registries

Establishment of various diseases is quite long and costly process, this is why Lithuania is looking to innovate by establishing electronic, platform-based registries during the period of implementation of E-Health project 2013-2015. Registries of separate diseases (rare included) will function as subsystem of National E-Health information system and will be integrated into common data network.

Neonatal screening policy

An Order of the Minister of Health (2012-05-28 No V-470) in 2012 approved obligatory screening of newborns' vision.

National rare disease events in 2012

A press conference was held on 28 February 2012 to mark Rare Disease Day 2012: this event was organised by the Lithuanian Society of Human Genetics. On 29 February 2012, a conference entitled "Rare children's diseases: problems and decisions" was held Children's Hospital, Affiliate of Vilnius University Hospital Santariskiu Klinikos, to mark Rare Disease Day 2012. A number of press releases and informative documents were provided by the Ministry of Health on the day (e.g. the Ministry of Health of Republic of Lithuania published an annual press release on the policy on rare diseases; the calendar of the Ministry of Health marked 29 of February as Rare Disease Day).

A conference on rare diseases was also organised on 28 September 2012 to mark the 75th anniversary of the Paediatrics Society of Lithuania. The event was supported by the European Academy of Paediatrics, and the conference was attended by its President, as well as foreign representatives, geneticists, paediatric surgeons, family doctors and other physicians.

Hosted rare disease events in 2012

No specific activity reported.

Specialised social services

A recreational camp for haemophilia patients and their family members entitled "Barger 2012" took place in May 2012.

D.17. LUXEMBOURG

National plan/strategy for rare diseases and related actions

Concertation on a plan was reinforced at Ministry level in 2012.

Centres of expertise

There are currently no official centres of expertise for rare diseases in Luxembourg. However a new system for referrals has recently been introduced which should improve access to healthcare.

National rare disease events in 2012

To mark Rare Disease Day 2012, a week of awareness-raising activities were organised by ALAN absl from 22 to 29 February 2012 at the Belle Etoile shopping centre: this event included a photo exhibition including photos of

¹⁶⁴ <http://www.vaikuligonline.lt>

people with rare diseases posing next to celebrities from Luxembourg. A number of personalities participated, including the Deputy and Bourgmestre of the town of Luxembourg Mr. Bettel.

D.18. MALTA

National plan/strategy for rare diseases and related actions

An advanced first draft of the National Plan on Rare Diseases was completed in 2012. An internal consultation exercise was also completed. A public consultation on the plan will take place in 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.

Centres of expertise

Since 2012 Malta is sending patients to centres in Italy for specialised investigation and treatment such as lung transplants. From 2014 onwards it is also planned to house the new Oncology Hospital which is currently under construction on the Mater Dei Hospital site.

National rare disease events in 2012

In 2012 to mark Rare Disease Day, an expression of the solidarity event, in collaboration between the Malta Health Network and the Malta Health Authorities, was held at Mater Dei Hospital, on 29 February 2012.

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 Dutch government regarding rare diseases for the years 2012-2015¹⁶⁵. 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 (and centres of expertise);
- Funding (only university hospitals) 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 in 2013). This new policy will not hinder the accessibility of orphan medicinal products;
- 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 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 screening¹⁶⁶.

¹⁶⁵ <http://www.government.nl/issues/health-issues/documents-and-publications/reports/2013/01/24/strategy-of-the-netherlands-in-the-field-of-rare-diseases.html> (English Translation Strategy)

¹⁶⁶ 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. The minister responded constructively to several points that were addressed by VSOP.

In addition to this strategy preparations for a national plan on rare diseases for all stakeholders have started. The Netherlands Organisation for Health Research and Development (ZonMw), has been commissioned by the Ministry of Health, Welfare and Sport to coordinate the input for a National Plan following up on the initial work of the Dutch Steering Committee on Orphan Drugs.

The input of all stakeholders was collected via information from different meetings organised in the last year and via working groups and the website, coordinated by ZonMw/NPZZ and under the auspices of a sounding board especially formed for this task (<http://www.npzz.nl/>). The website will make public the preparatory documents for the National Plan. In January-March 2012, stakeholders started collecting possible solutions for the issues raised and discussing these on the website and in a public hearing in April 2012. A meeting was organised on 28 August 2012 in Amsterdam to present the first draft of the national plan for rare diseases¹⁶⁷.

A second draft was presented on the website in January 2013. The National Plan for Rare Diseases with input from all stakeholders is in an advanced stage of preparation, anticipated to be ready before September 2013. The national plan will consist of issues on information, care, research, availability of knowledge (education), availability of therapy, awareness and the role of Patient's organisations.

Centres of expertise

The Dutch Federation of University Medical Centres (NFU) presented their plan at the Conference on the National Plan in August 2012. Here it was stated that the NFU will present their 'list' with centres of expertise early 2013. This list with identified centres will be checked with the information in the Orphanet database and the information collected by the National Patient Alliance for Rare and Genetic Disease (VSOP) after consultation of patient organisations. If the NFU does not complete this procedure, the Ministry of Health will do so on their behalf. The government has also decided that only University Hospitals can be reimbursed for orphan drugs, so centres are unofficially designated at the moment in this way.

Registries

The expertise of several partners involved in the research of rare inborn errors of metabolism (IEM) has been assembled in the Orphan Disease Registry Consortium. Pooling of expertise will greatly support registry of these metabolic diseases in The Netherlands and will lead to improved guidelines for treatment and monitoring as well as a better understanding in the future. This project delivered one thesis in 2012: Fabry disease; studies on diagnosis, screening and patient's perspective. Another result of this project is that the national web-based facilitating registry for inborn errors of metabolism has been further developed¹⁶⁸.

To assist patient organisations in the setting up of patient registries and biobanks, VSOP launched the website www.biobanken.net.

Neonatal screening policy

The Dutch Health Council has been asked by the Ministry of Health for advice on expanding neonatal screening for other rare diseases.

National alliances of patient organisations and patient representation

VSOP continues the development of several 'standards of care' for rare diseases and treatment guidelines for general practitioners. Amongst the meetings organised by VSOP, a meeting for patient organisations was organised on 10 October 2012, to discuss the draft National Plan for Rare Diseases presented in August 2012. VSOP and 16 other patient organisations started voucher-funded projects, three rare disease projects started aiming a.o. at improving diagnosis, centralisation of expertise, registries and quality of life.

Sources of information on rare diseases and national help lines

Orphanet activities in the Netherlands

Starting February 2012, the entry of new specialised Dutch clinics in the Orphanet database is now validated by the Scientific Advisory Board of Orphanet the Netherlands, also including the consultation of patient organisations.

¹⁶⁷ <http://www.npzz.nl/wp-content/uploads/2012/08/conceptverslag-28-augustus02.pdf>

¹⁶⁸ <https://ddrmd.nl/index.php/>

Official information centre for rare diseases

As of 31 December 2011, the Steering Committee was disbanded by the government: however ZonMw (the Netherlands Organisation for Health Research and Development) was stimulated to install a general information desk at the secretariat for rare diseases with as main objective to coordinate the plan on RD (NPZZ). With a small financial incentive (€30.000) ZonMw has stimulated the development of new information portals for researchers and small pharmaceutical companies about OD. After this project this portal should be embedded within the Dutch Pharmaceutical Umbrella organisations: Biofarmind and Nefarma.

Other sources of information on rare diseases

The website www.erfelijkheid.nl contains a database of approximately 400 rare diseases with information for both lay-persons and professionals. In 2013, 50 new rare diseases (all chromosome disorders) will be added to the database. In addition, public information is available on genetic, biomedical and pregnancy related issues¹⁶⁹.

Good practice guidelines

VSOP hosts a website dedicated to good practice guidelines for rare diseases. On this website: www.zorgstandaarden.net, standards of care for rare diseases developed by VSOP are published, to be used especially by healthcare providers. Both generic themes and disease-specific standards are provided. In addition, in 2012 VSOP finished 33 treatment guidelines for general practitioners carried out in close collaboration with the related patient organisations and the Dutch College of General Practitioners (NHG). Ten additional guidelines are in preparation.

Clinical guidelines on mitochondrial diseases and on Guillain-Barré syndrome (GBS) were launched in 2012. The alliance for Neuromuscular Diseases developed in cooperation with medical specialists specific information for GBS which patient can take with them (to the GP and others), in line with the project 'Patient as information carrier'.

National rare disease events in 2012

Several parties (ZonMw, Rare Disease Fund ZZF, KPMG and VSOP) worked together to organise the fifth national Rare Disease Day, on 25 February at the Dolfinarium in Harderwijk, as part of the international rare disease day. Angel Awards were granted to a patient representative and a medical specialist) as a recognition, reward and encouragement. Over 500 people attended this day, which generated a lot of media attention. At the yearly congress of Dutch paediatricians, paediatricians and VSOP organised a workshop on rare diseases, focussing on the diagnosis and proper referral of children with rare disease.

Hosted rare disease events in 2012

In 2012 the following rare disease related events were hosted by the Netherlands and reported in *OrphaNews Europe*: Eurogentest2 General Assembly (Nijmegen, 18 January 2012), Joint Eurogentest/Techgene Scientific Symposium (Nijmegen, 19 January 2012), Symposium on Neurocognitive Developmental Disorders (Rotterdam, 25 May 2012), 11th Conference of the International Association of Bioethics: Bioethics and the Future, and the Future of Bioethics (Rotterdam, 26-29 June 2012), The Second Joint International Symposium on Neuroacanthocytosis and Neurodegeneration with Brain Iron Accumulation (Ede, 26–27 October 2012), 12th International symposium on MPS and related diseases (Noordwijkerhout, 28 June - 1 July 2012).

Research activities and E-Rare partnership

National research activities

A multi-annual research programme started in 2011 at The Netherlands Organisation for Health Research and Development (PM Rare at 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. Three projects were each awarded a €3 million grant under this ZonMw Priority Medicines for Rare Diseases and Orphan Drugs (PM Rare) research programme¹⁷⁰.

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

¹⁶⁹ These sites provide further web based information: www.biomedisch.nl; www.zwangernu.nl; www.zwangerwijzer.nl; www.slikeerstfoliumzuur.nl; www.prenatalescreening.nl

¹⁷⁰ <http://www.zonmw.nl/nl/programmas/programma-detail/priority-medicines-zeldzame-ziekten-en-weesgeneesmiddelen-rare/algemeen/>

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. In 2011 26 new projects started. In the databank are (October 2012) 191 Dutch Biobanks and over 500 000 participants. In 2013 new projects will be able to be granted.

In November 2012, BBMRI-NL had its congress. VSOP presented the patients and parents role in the governance of biobanks for rare and paediatric disorders.

E-Rare

The Dutch Organisation for Health Research and Development (ZonMw) participated in the 4th Joint Transnational Call in 2012: teams from the Netherlands participate in 8 out of the 11 consortia selected for funding

Orphan medicinal products

Orphan medicinal product committee¹⁷¹

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 no longer existed 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 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 and the sounding board on the National Plan. This plan will not only cover orphan drugs but also rare diseases.

Orphan medicinal product incentives

The programme for Expensive and Orphan Medicines (2007-2014) aims to investigate the effectiveness of expensive drugs and of expensive orphan medicinal products and the development of HTA methodology to help the Dutch Health Care Insurance Board in its advice on reimbursement. In the scope of this programme, several projects on registered orphan medicinal products have already been selected.

Orphan medicinal product pricing policy

The minister will start the negotiation with pharmaceutical companies about pricing (*see evaluation of conditional reimbursement in the section below*).

Orphan medicinal product reimbursement policy

In 2012, the Dutch Health Care Insurance Board (CvZ) addressed the country's Minister of Health concerning the conditional reimbursement of three rare disease products deemed "too expensive". Both products target lysosomal storage disorders: a treatment for Pompe disease and Fabry disease treatment. Health Minister Edith Schippers has been advised to cut public funding for the treatments, although babies diagnosed with Pompe disease would continue to have their treatment supported by State funding under the proposal. The minister will start the negotiation with pharmaceutical companies about pricing. During this negotiation the drugs will be reimbursed (in 2013).

D.20. POLAND

National plan/strategy for rare diseases and related actions

By the end of 2012 a strategic document "National Plan for Rare Disease – the roadmap" was prepared and handed to the Minister of Health. A broad consultation process started, and it is scheduled for completion by June 2013 in order to meet the recommendations of the EU Council by the end of 2013.

Upon the occasion of International Rare Disease Day celebration in Warsaw (29 February 2012), the National Forum for the Therapy of Rare Diseases handed the proposals for the National Rare Diseases Plan to the Minister of Health, expecting its further elaboration and adoption. The Minister of Health declared, that by the end of 2012 the draft paper "National Plan for Rare Disease – the roadmap" will be completed by Rare

¹⁷¹ Also the former Dutch Steering Committee OD had a broader assignment than only OD

Disease Task Force. On the same day the Parliamentary Group on Rare Diseases met to contribute to the drafting process.

In Spring of 2012 another initiative of the self-organised "Partnership for the National Plan for Rare Diseases" (RD think-tank, consisting of representatives of patients groups, academia, clinicians, health politics, payer, providers, suppliers and communication) started its work. Actively supported by the Chairman of the ministerial Rare Diseases Task Force as well as the Children's Memorial Health Institute, the series of working meetings took place in order to broadly discuss the final draft of each area of the National Plan. During six workshops and number of satellite meetings, the final text was elaborated.

Between February and December 2012, the Rare Disease Task Force met eight times to elaborate and draft 12 consecutive versions of the paper. Parallel work in Parliamentary Group on Rare Diseases as well as Partnership for the National Plan for Rare Diseases group was a significant support.

The entire initiative was launched following the recommendation of the the EU Council on the involvement of patients and their representatives in the political process and promoting the activities undertaken by rare diseases patient groups and associations.

In summary, during entire 2012, a total of 42 meetings, consultations, workshops and conferences were held, with active participation of group of ca 400 experts (clinicians, scientists, patients groups, providers, payers, industry, Members of Parliament, Government Officials, health politicians) to work on the document entitled "The National Plan for Rare Diseases – the roadmap". The final version (no 12.2) was submitted to the Ministry of Health in December 2012, as scheduled. Accordingly to the project plan, the final paper should be signed by the Minister of Health before June 2013. Later on work on organisational, budgetary and legal framework will take place, based on the strategic paper "The National Plan for Rare Diseases – the roadmap" which has been accepted by the Ministry of Health and the Government.

Centres of expertise

There is the intention to establish a designation policy for centres of expertise.

Registries

There is no national committee dealing with registries, however the Centre of Information Systems has the responsibility to facilitate the Parliament Act of April 2011 on information systems in healthcare, which is in force since January 2012. It states that all registries have to comply with strict requirements, including data safety and protection. Registries had to comply with its requirements by June 2012 including measures for data safety and protection. The Minister of Health in the field of monitoring of healthcare needs, patients health status, prophylaxis and monitoring of health programs, may establish a dedicated registry, issuing a particular Regulation, which may also state a public source of funding. Although this legal regulation is in force, there is no designation process for a unified rare disease registry at the moment.

Sources of information on rare diseases and national help lines

Orphanet activities in Poland

Orphanet Poland took part in elaborating "The National Plan for Rare Diseases – the roadmap" by participating in Ministry of Health Rare Disease Task Force, and a series meetings with patient organisations and workshops dedicated to rare diseases which took place in September 2012 in the Children's Memorial Health Institute. Polish Orphanet Coordinators were group leaders of two workshops "Support activities for the preparation of applications for research projects related to rare diseases" and "Exchange of information to gather knowledge about centers of expertise in Poland; Creation of centers of expertise for group of rare diseases based on currently operating centers treating patients with rare diseases; Support for the creation of reliable registries for rare diseases".

National rare disease events in 2012

Rare Disease Day was marked in Warsaw on 29 February 2012 with a conference entitled "Strong Together". Around 120 people participated (including Minister of Health) and the media were present. There was a special portal opened for the occasion: www.dzienchorobrzadkich.pl . There was also a photo exhibition depicting people with rare diseases. A social media campaign entitled "Hope. It's in your genes" was launched that day for at least 1 year run. It still operates as the biggest national rare diseases awareness campaign at www.nadziejawgenach.pl . During the Day, there was also the opportunity to educate students about rare diseases by lectures and information points around Poland in many medical high schools and universities. These activities continued nationwide during 2012.

Other events included: Selected Aspects of the Genetics of Metabolic Diseases (9-13 January 2012, Warsaw), unknown dysmorphological cases (20 April 2012, Warsaw), Polish Smith-Lemli-Opitz syndrome Society Conference (30 April - 3 May 2012, Warsaw), Pediatric cardiology course (7-11 May 2012, Warsaw), 10th European Conference on Rare Diseases (6-9 July 2012, Cedzyna). Dysmophologic meeting during Conference "Options to support the development of people with Duechenne'a disease and other muscular dystrophies" (30 November, 2012, Sobieszewo/Gdańsk).

Hosted rare disease events in 2012

Amongst the hosted events organised in 2012 was the 9th European inborn errors of metabolism course in Warsaw, Poland (in collaboration with the Children's Memorial Health Institute) (Warsaw, 25-29 September 2012), and the Fourth International Meeting on Primary Central Hypoventilation Syndromes (Warsaw, 13-14 April 2012).

Research activities and E-Rare partnership

E-Rare

Poland is an observer of the E-Rare 2 project. The Polish partner for E-Rare ERA-NET is The National Center for Research and Development. Poland joined the 2012 Joint Transnational Call but did not receive funding.

Orphan medicinal products

Orphan medicinal product reimbursement policy

The system of drug reimbursement changed on 1 January 2012 accordingly to the Reimbursement of drugs, food for special dietary use and medical devices Act, issued 12 May 2011. The new system is unified and application based. The Minister of Health is not able to introduce reimbursement of a new drug without prior official request from the Marketing Authorisation Holder. The application process is costly and has to be supported with comprehensive data (including reimbursement status, price data in other EU Member States, and health technology analysis).

Orphan devices

Since 1 January 2012, according to the Reimbursement Act, the national healthcare package has been continuously supplemented by new medical devices dedicated also to patients with rare diseases. Orphan devices are regularly presented during dysmorphological meetings, national conferences and trainings.

D.21. PORTUGAL

National plan/strategy for rare diseases and related actions

An important step in terms of implementing the National Plan for Rare Diseases took place in 2012: a specific card for the identification of people with rare diseases ("*Cartão para a Pessoa com Doença Rara*") was developed along this year, aiming at disclosing clinical information to medical doctors and also in emergency situations. This card, to be issued by DGS is currently being tested and will be progressively distributed along 2013.

Genetic testing

In 2012, the number of clinical cases sent abroad for referral amounted to 354, especially for molecular study and laboratorial genetic testing.

National alliances of patient organisations and patient representation

In 2012, RARÍSSIMAS (the largest Association within FEDRA) launched a series of events and meetings in order to raise awareness on rare diseases and to achieve several goals. Among these initiatives, they published in February "*Vidas Raras*" (Rare Lives), a book telling stories about patients and their families. Moreover, they also signed a protocol aiming to find a place to install the "*RarÍSSIMO Centre*" in Pico Island, Azores. In November they also organized in Oporto the first Meeting on '*Angelman Syndrome*' with Portuguese and international specialists. RARÍSSIMAS continues to publish its magazine 'Rare Pages', disclosing important information on rare diseases to the whole population.

Sources of information on rare diseases and national help lines

Orphanet activity in Portugal

By the end of 2012, nearly 400 abstracts of rare disease and 18 emergency guidelines had been translated and validated into Portuguese and entered in the international database; about 150 new abstracts were also translated and validated, waiting to be inserted.

During 2012, Orphanet-Portugal continued to collect and validate and significantly increased the information available in the country on national resources and activities related to rare diseases and orphan drugs. These included 133 specialised centres, 114 diagnostic laboratories, 705 diagnostic tests, 157 research projects, 21 clinical trials, 73 patient organisations and 21 patient registries and databases, by December 2012; the list of the orphan drugs available in the country (currently 51, in a total of 88 different presentations and/or dosages) is regularly updated by INFARMED and provided in our national website, together with the annual uptake for each one.

The Orphanet-Portugal team also contributed to the development (in English) and subsequent translation and validation into Portuguese of a leaflet on "Genetic Testing Related Health", produced by the Council of Europe and prepared by EuroGentest (a network of excellence funded by the European Commission) and the PPPC (Public and Professional Policy Committee) of the ESHG (European Society of Human Genetics). This brochure (in Portuguese) is to be released during the Rare Disease Day 2013.

The national scientific advisory board of Orphanet-Portugal proved to be a valuable resource, providing important information as well as the validation of some data whenever requested; it met once, before the DNA Day event with Ségolène Aymé, leader of the Joint Action Orphanet Europe.

In addition, as in previous years, the national team has been committed to the diffusion of the Orphanet portal and services to professionals involved in rare diseases, as well as to patients, families and the general public. This was done both through the organization of specific events, and the participation in several scientific meetings and courses with oral or poster communications and lectures. In 2012, 11 presentations about Orphanet were made at such meetings, and 2 conferences were organised (together with APADR) by Orphanet-Portugal (the Rare Disease Day 2012 and a special DNA Day Conference).

Help line

The 'Rare Line' ("*Linha Rara*")¹⁷², throughout the year of 2012 provided relevant information to 2 137 requests.

Good practice guidelines

DGS, in collaboration with the Portuguese Medical Association ("*Ordem dos Médicos*") has been developing a number of clinical guidelines; among these, and in the specific area of rare diseases, three guidelines were issued in 2012, which refer, specifically, to the diagnosis and follow-up of Cystic Fibrosis and Pulmonary Hypertension.

National rare disease events in 2012

The Portuguese Alliance APADR, in collaboration with Orphanet-Portugal, organised a conference to mark Rare Disease Day in 2012. Many patients, relatives, patient associations' representatives, industry representatives, policy makers and health authorities, health professionals and researchers, including several members of the Scientific Advisory Board of Orphanet-Portugal were present at this event. The conference included presentations of Orphanet tools and activities.

On 20 April 2012, the Orphanet-Portugal team organised a national meeting on rare diseases and orphan medicinal products. This event was part of the DNA Day 2012 and was preceded by the 1st meeting of the National Advisory Board of the Orphanet-Portugal. The topics of the main meeting included: the current status of the Portuguese Rare Disease Plan, the future Reference Centres and Networks for Rare Diseases and Cards for Persons with a Rare Disease, as well as the current status of legislation and regulation of genetic testing and its quality, including the licencing, certification and accreditation of genetic laboratories.

Other events included: Lysosomal Disorders Day conference (28 May 2012), International Day of Ataxias event (22 September 2012), Solidarity Dinner for the International Day of Amyotrophic Lateral Sclerosis (21 June 2012), events for the European Week for Hemochromatosis (7-10 June 2012), events for the International Day of Osteogenesis Imperfecta (6 May 2012), 3rd Symposium of the Study Group of Rare Diseases of the Portuguese Society of Internal Medicine (12-13 October 2012), Annual Meeting of the Portuguese Society of Human Genetics (22-24 November 2012), Symposium on Rare Diseases of the Metabolism (Lisbon, 14 December 2012).

¹⁷² www.linharara.pt

Hosted rare disease events in 2012

Amongst the rare disease related events announced in *Orphanews Europe* in 2012 was: the First International Primary Immunodeficiencies Congress (IPIC), (Estoril, 7-8 November 2013).

Research activities and E-Rare partnership

National research activities

The Foundation for Science and Technology ("*Fundação para a Ciência e Tecnologia*" - *FCT*) runs several programmes to fund research on rare diseases. In 2012, *FCT* funded scientific projects in a total amount of € 583,000.

Participation in European research projects

In 2012, *INSA* participated in ten Research & Development projects on rare diseases, namely the haemoglobinopathies, lysosomal storage diseases, muscular dystrophies, cis-irruption (genomic) disorders and genetic dyslipidaemia. *INSA* also points out its participation in the EUCERD Joint Action, and as member of the ERA-Net on Rare Diseases (E-Rare-2) project.

E-Rare

During 2012 *FCT* has funded research projects in the amount of €342,000. Portugal joined the 4th Joint Transnational Call in 2012 with Portuguese teams participating in 2 out of the 11 research projects.

IRDIRC

Portuguese funding agencies have not yet committed funding to the *IRDIRC*, however the *FCT* through the E-Rare Group of Funder, Portugal will be represented at the *IRDIRC* as of the end of 2012.

Orphan medicinal products

In 2012, the delivery of enzyme replacement therapy amounted to € 47.5 million. A list of enzymatic diseases, which benefit from free of charge treatment in public hospitals, is also available.

D.22 ROMANIA

National plan/strategy for rare diseases and related actions

The National Committee for Rare Diseases met five times in 2012 with the representatives of the Health Ministry to discuss the government's decisions in order to support the further development of a RD national plan (NP) and national strategy (NS) for the next period of time. The meetings prioritised the areas and actions of intervention in the field of RD, such as, the harmonisation of European and national criteria for establishing centers of expertise at the national/regional level and permanent monitoring and assessment of pathways for patients from contact with the help lines to integration into society.

At the request of the Ministry of Health - Romania, RONARD (Romanian National Alliance for Rare Diseases) has carried out an impact study for implementation of the National Plan for RD in Romania and a strategy proposal to be included in the National Strategy for Health 2014-2020.

During the last four years the National Health Programme for diagnosis and treatment for rare diseases included more patients affected by rare diseases and, so far, 17 rare diseases were included in the programme funded and supported by Romanian Ministry of Health. In spite of worldwide economic crisis Romania tried to maintain the same level of funding for RD as in 2011.

Centres of expertise

The criteria and the designation procedure for centres of expertise have been provided in the National Plan for RD, using the EUCERD Recommendations on Quality Criteria for Centres of Expertise adapted to the situation in Romania. A national policy for establishing centres of expertise is not yet clearly stated. An Expert Advisory Committee is established and waiting for the confirmation of Ministry of Health. This Committee will select the criteria, define the policy in the country and organise the national competition for expertise centres.

The number of total national/regional centres of expertise is still debatable based on population size. Following the competition the Centres of Expertise designed will participate in the future European Reference Network.

Registries

Although the Health Ministry plans to organise a national registry for RD but there is not yet a national committee dedicated to dealing with registries and no public financial resources are allocated so far.

Neonatal screening policy

In 2012 Romania joined contributed to the efforts aimed at the preparation of European guidelines on diagnostic tests or population screening (in the scope of the Tender on New Born Screening European Network of Experts) respecting national decisions and competences.

National alliances of patient organisations and patient representation

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

In 2012 the alliance organised:

- Meetings of the National Committee for RD with the representatives of the Health Ministry to discuss the priorities of the National Plan for RD and how to organise the competition for the designation of centres of expertise;
- The Rare Disease Day in Bucharest and helped with the organisation in major university centres;
- The EUCERD Joint Action Workshop – Guiding Principles for Specialised Social Services;
- Helpline for the patients with RD;
- Lectures in the field of RD for the patients, as well as for the specialists (they are accredited for doing this);
- The patient organisations component of the alliance organised activities in their field and they are supported by the Romanian National Alliance for RD (ANBRaRo).
- Moreover, the Alliance will organise the Europlan Conference in 2013.

Several new organisations for patients with rare diseases have been established and joined the national alliance.

Sources of information on rare diseases and national help lines

Orphanet activity in Romania

An Orphanet country site for Romania was launched in 2012.

Training and education initiatives

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

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

National rare disease events in 2012

The Romanian National Alliance for Rare Diseases has marked Rare Disease Day with many events since 2008. The alliance is coordinates efforts and collects the information about the campaign events organised by the member organisations. In 2012, Rare Disease Day was an opportune event to support efforts to advocate at the

Ministry of Health level for the Romanian National Plan for Rare Diseases to be included in the National Strategy for Public Health and to keep maintain collaborations with other Ministries (ex. Education and Research, Work and Social Affairs). The Romanian National Alliance for Rare Diseases is organising a meeting of the National Committee for Rare Diseases in Bucharest on 16 February 2012 to this effect. On 17 February 2012 a round table was organised in Bucharest, focusing on the topics of the national plan, the framework for organising the centres of expertise, the quality criteria for centres of expertise, the possibilities for organising and accrediting the centres of expertise in Romania, and Romania's participation in European Reference Networks for Rare Diseases.

Member organisations held events to mark the day in Bucharest, Timisoara, Cluj-Napoca, Iasi, Zalau, Targu Mures and Oradea. These events were for patients and their families, for specialists involved in the management of rare diseases and for the general public, and took the form of marches, conferences, workshops, PlayDecide sessions, ability workshops, lessons on rare diseases in schools, and artistic events.

The Orphanet Romania team helped organise the annual conference of the Romania Society of Medical Genetics.

Hosted rare disease events in 2012

The EUCERD Joint Action workshop on Specialised Social Services was hosted in Zalau, Romania (6-7 December 2012).

Research activities and E-Rare partnership

National research activities

In 2012 there was a general call for projects (non-rare disease specific). There are currently no other fundraising initiatives for rare disease research in Romania.

D.23. SLOVAK REPUBLIC

National plan/strategy for rare diseases and related actions

A working group was established in January 2011 at the Ministry of Health to work on a strategy for improving health care for patients with rare diseases. This strategy includes the basic concepts for the plan, and was adopted in April 2012 by the Ministry of Health, before being adopted by the Government of the Slovak Republic on 24 October 2012. The Interministerial Committee for the National Plan will organise a Europlan national conference including specialists in the field in February 2013 and also a National conference on 28 February 2013. There is hope of adopting the Plan by the end of 2013.

Neonatal screening policy

In 2012 a document on newborn screening was adopted, expanding the panel of screened diseases from 4 to 13, to include hyperphenylalaninemia(HPA),leucinosi s (MSUD), MCAD, LCHAD, VLCAD, CPT I., CPT II.A,CACT, glutaric aciduria type I (GA I), and isovaleric aciduria(IVA).

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. Close cooperation with the National Working Group for Rare Diseases in Slovakia and the National Coordinator of Orphanet Slovakia and other professionals was also established. The main activities and goals of the Slovak Rare Disease Alliance were presented at the First Slovak Conference on Rare Diseases, held in Bratislava on 29 February 2012. The fundamental challenge for the Slovak Rare Disease Alliance is to raise public awareness for the conditions of people with rare diseases and to participate in the formation of National Plan for Rare Diseases.

Sources of information on rare diseases and national help lines

Orphanet activities in the Slovak Republic

The Slovak Orphanet team initiated and organised the First Slovak Conference on Rare Diseases to commemorate the 2012 Rare Disease Day. The Conference was organised in close cooperation with EUCERD representative and Slovak National Alliance of Rare Disease Patient Groups.

Good practice guidelines

National guidelines for genetic testing were developed and adopted by the Slovak Society of Medical Genetics (SSLG) in June 2012. SSLG, oncogenetics laboratories and Association of Health Insurance Companies developed guideline for diagnostics and clinical management of HBOC.

National rare disease events 2012

To mark Rare Diseases Day, the first Slovak Conference of Rare Diseases¹⁷³, organised by Orphanet Slovakia, was held on 29 February 2012: the conference was held under the auspices of the Minister of Health of the Slovak Republic and the Deans of the Comenius University Medical School and Faculty of Pharmacy in Bratislava. The aim of the conference was to raise awareness about diseases that most people will not know of, as well as to improve access to treatment. Together 150 invited participants attended from health care providers, patient organisations, scientific institutions, public insurance companies and social affairs institutions. The English abstracts from presentations and posters were published in the official journal of the Faculty of Pharmacy, Comenius University in Bratislava and are freely available¹⁷⁴.

In addition, a press conference/round table on the subject of orphan drugs¹⁷⁵ was held with experts in the field on 20 February 2012 in Bratislava with the aim of providing information on the subject of orphan drugs, addressing the question of why orphan drugs are so expensive and considering the Slovak Republic's approach to rare diseases. The first three sections were concerned with recent European actions in the field followed by invited talks on the role of centres of expertise and cross-border collaboration. The third part of the conference will concentrated on social, health and community policy. A poster section was also organised to map the country's resources in diagnosis, treatment and patient care.

Izakovic's Memorial is an annual conference organised in Slovak Republic by the Slovak Society of Medical Genetics, related to genetic and rare diseases. The 23rd conference had international attendance and was held in Bratislava on September 2012 welcoming over 200 participants. The main topics included Genetics and Biology of Neurological Disorders, Cytogenetics, Oncogenetics, Prenatal Diagnostics, Clinical Genetics, Molecular Pathology, Syndromology, Trends and Research.

Hosted rare disease events 2012

Amongst the hosted events announced in *OrphaNews Europe* in 2012 was the 6th International Workshop on Alkaptonuria (Piestany, 1-2 November 2012).

Orphan medicinal products

Orphan medicinal product market availability situation

All orphan medicinal products registered at EU level are available in the Slovak Republic. Directly available on the Slovak market at the end of 2012 were 25 orphan medicinal products: Myozyme, Aldurazyme, Naglazyme, Zavesca, Kuvan, Ventavis, Revolade, Nplate, Firazyf, Volibris, Tracleer, Revatio, Somavert¹⁷⁶), Increlex, Litak, Nexavar, Sprycel, Tassigna, Torisel, Revlimid, Lysodren, Vidaza, Inovelon, Exjade, Tobi podhaler. The rest can be provided at named-patient basis. For this the physician has to submit a special application at the Ministry of Health. The information about the amount of OMP distributed at named-patient basis is not published for now.

Orphan medicinal product pricing policy

No specific information reported.

Orphan medicinal product reimbursement policy

At the end of 2012 out of the 25 orphan medicinal products, 6 orphan medicinal products require patients' participation towards costs (Myozyme plc ifo 10x50 mg, plc ifo 25x50 mg, Tobi podhaler plv icd 224x28 mg, Firazyf sol inj 1x3ml, Inovelon tbl flm 50x200 mg, tbl flm 50x400 mg). The highest copayment was for Tobi podhaler plv icd (€529.84, which means 21.68% of the total price). The average copayment is 4.62% of the total price (0.87 – 21.86%). The orphan medicinal products are distributed mainly through pharmacies as well as on a centre basis, depending on the reimbursement category which is also set in the "categorisation list"¹⁷⁷.

¹⁷³ www.zriedkavechoroby.sk

¹⁷⁴ <http://www.degruyter.com/view/j/afpuc.2012.vii.issue-0/issue-files/afpuc.2012.vii.issue-0.xml>

¹⁷⁵ <http://zbierka.sk/news/default.aspx?itemid=1202200230>

¹⁷⁶ Orphan status withdrawn in 2012.

¹⁷⁷ Foltánová, T. / Konečný, M. / Hlavatá, A. / Štěpánková, K. / Cisárik, Orphan drugs used for treatment in Paediatric patients in the Slovak Republic, <http://www.degruyter.com/view/j/afpuc.2012.lix.issue-0/issue-files/afpuc.2012.lix.issue-0.xml>

D.24. SLOVENIA

National plan/strategy for rare diseases and related actions

In 2012 a national plan for rare diseases was accepted by the Health Council and the next steps will be to elaborate an action plan and its implementation, as well as to identify funding. The Work Plan for Rare Diseases¹⁷⁸ is designed to serve as a roadmap until 2020 and is qualified as “... an opportunity for better coordination of efforts of all partners involved, establishing health care that will be comprehensive, accessible, timely and patient-focused”. The major objectives of the plan centre around the identification and monitoring of rare diseases; improving early diagnosis and access to appropriate medical treatments; mechanisms to improve an integrated approach to rare diseases; and improving access to information for patients, the general public, and professionals. Amongst identified actions include the establishment of a national registry for rare diseases; establishment of national reference centres integrated with international networks; examining cross-border cooperation for genetic testing and other services; introducing a system of evidence-based clinical guidelines; defining orphan drug policy and developing decision guidelines for competent authorities; identifying additional funding sources for orphan drugs; establishing an umbrella organisation of patient groups; and establishing a national centre for rare diseases in the country.

Centres of expertise

The establishment of centres of expertise is foreseen in the national plan for rare diseases.

Registries

There is currently no national registry for rare diseases in Slovenia. A new Healthcare Databases Act, which sanctions the establishment of national registries, is under preparation, and the inclusion of registries in the area of rare diseases is expected.

Sources of information on rare diseases and national help lines

Official information centre for rare diseases

Establishment of national contact point for patients and professionals to get some extensive information on rare diseases diagnosis and treatment is foreseen. This will be the first action to be implemented in the Work Plan for Rare Diseases. There are on-going negotiations with the stakeholders.

National rare disease events in 2012

On 29 February 2012 a press conference was organised by Ministry of Health as a way to raise awareness of rare diseases to mark Rare Disease Day 2012. The event was also the opportunity to inform the general public on rare diseases and to improve cooperation between patients and medical professions for a better quality of life. On the same day gathering of different stakeholders on the field of rare diseases (patient organisations, health care providers, medical doctors, ministry representatives, representatives of local community, press) was carried out by one of patient organisations.

Orphan medicinal products

Orphan medicinal product committee

In 2012 The Health Insurance Institute of Slovenia put on positive hospital list both orphan medicinal products: clofarabine (Evoltra) and busulfan (Busilvex) that were in 2011 covered by additional funding. The Strategic Council for Drugs in 2012 provided additional government budget funds of 794.537,00 € to finance two orphan medicinal products: eculizumab (Soliris) for 2 patients and idrusulfase (Elaprase) for 1 patient.

Orphan medicinal product reimbursement policy

The expenditure for orphan medicinal products increased by 44,9 % from 2010 to 2012, whereas total expenditure for other drugs was in 2012 lower in comparison to 2010 due to systematic price regulation.

Other therapies for rare diseases

In Slovenia other therapies for rare diseases are also available, for example: implantation of subdermal pump for treatment of epilepsy, surgical corrections of rare inborn heart defects, cranial synostosis, inborn facial defects and transplantation of hematopoietic stem cells.

¹⁷⁸ http://www.mz.gov.si/fileadmin/mz.gov.si/pageuploads/redke_bolezni_2012_-_nact_dela/Nact_dela_na_podroczju_redkih_bolezni.pdf

D.25. SPAIN

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 2009¹⁷⁹.

Indicators have been defined for the evaluation of the Strategy and it was evaluated in 2012. This assessment focused mainly on the implementation of the Strategy over the first two years, although it is too soon to measure health results, this process could help to update recommendations and objectives. The results, and consultation with the Stakeholders, could help update the Strategy. As a result of the evaluation, it can be confirmed that the Strategy has been implemented in the majority of the Regional Governments (RG). In addition, 70.7 % of the specific objectives evaluated have been achieved by more than 50% of the RG.

The main achievements have been, amongst others: the establishment of the National Registry for Rare Diseases, availability of an inventory of services and tests of prenatal diagnosis and derivation protocols for pregnant women at risk or foetal RD, to raise awareness and recognition of rare diseases, and to promote socio-health care and research for children under three with rare diseases. Moreover, the evaluation has also showed that it is necessary to implement actions aimed at collecting and disseminating information and resources available on rare diseases, to increase training of primary care professionals on suspected diagnosis of rare diseases and to establish adequate criteria for referral, to improve the availability of basic health information to the teaching staff that attends children with rare diseases, to develop initiatives of joint coordination and planning for the adaptation of jobs and for the management of the reintegration and continued employment of family members of persons affected by rare diseases, to carry out initiatives to facilitate keeping persons with Rare diseases in their surroundings such as home care services, home hospitalization, day centres, and so on, to develop integration activities in the community (leisure activities) for those with Rare diseases, and to promote participation of patients associations in participation-decision bodies in the area of health of the Regional Governments.

The Spanish Minister of Health, Social Services and Equality, declared 2013 the Spanish Year of Rare Diseases. With this initiative, the government expects to raise knowledge and awareness for rare conditions, and establish stronger ties of mutual support. The operation will focus on the health, research and social perspective of rare diseases¹⁸⁰.

Centres of expertise

Currently, the annual follow-up of 132 CSUR of the NHS is being carried out. These CSUR serve 35 diseases and procedures, and they have been operating in 2009, 2010, 2011 and 2012. Each year collected data and indicators are analysed by professionals from CSUR and expert groups in each area of expertise, and if required, appropriated improvements are introduced.

Genetic testing

At the present time, the MSSSI is working together with Regional Governments and Scientific Societies defining the genetic portfolio of services for the NHS and HTA agencies which are involved in the description of the Spanish map of genetic test offered by the NHS.

National alliances of patient organisations and patient representation

FEDER, the Spanish Rare Disease Federation, was established in 1999 as a non-governmental organisation (NGO). Currently, FEDER with its 190 members is recognised as an umbrella organisation for the 3 million people with rare diseases in Spain and their families. In 2012, FEDER organised along with the company Fluor the collection of used mobile phones to go towards fundraising for rare diseases.

Sources of information on rare diseases and national help lines

Other sources of information on rare diseases

FEDER also promotes social and sanitary studies on rare diseases such as the 2012 “Estudio ENSERio 2 “Por un modelo sanitario para la Atención a las personas con Enfermedades Raras en las Comunidades Autónomas”

¹⁷⁹ <http://www.msc.es/organizacion/sns/planCalidadSNS/docs/RareDiseases.pdf>

¹⁸⁰ <http://www.msc.es/gabinete/notasPrensa.do?id=2611>

Training and education initiatives

The Universidad Internacional de Andalucía (UNIA) and the Universidad Pablo de Olavide de Sevilla (UPO) in collaboration with the CIBERER, offers an official Master in 'Rare Disease Diagnosis and Therapy' since 2010. In 2012 the third edition took place.

Each year FEDER and CREER organise a training school aimed at empowering rare disease patients groups.

National rare disease events in 2012

FEDER has organised various National Conferences on rare diseases and Regional Conferences. Many other rare disease specific patient associations hold their annual meetings where some time is dedicated to comment on general questions concerning rare diseases. Some Medical and Scientific Societies include round table discussions and conferences related to rare diseases in their annual meetings.

Every year, the Spanish Federation of rare diseases (FEDER) celebrates Rare Disease Day, with hundreds of patient organisations organising a wealth of events. In the build up to Rare Disease Day 2012, the Orphanet Spanish team also contacted with all the associations registered in Orphanet asking them to collaborate and obtaining a list of around 20 different events.

Amongst the events in Spain organised to mark the Day included a number of round tables, workshops and exhibitions across Spain, as well as the passing of an act recognising rare disease day in parliament. FEDER also marked the day with an official prize-giving to honour people working in the field.

The Fifth National Rare Disease Congress was organised in October 2012 by the Spanish Rare Diseases Alliance (FEDER) and D'Genes Association in Totana, Murcia. The Spanish Minister of Health, Social Services and Equality, Ana Mato, declared 2013 the Spanish Year for Rare Diseases at this conference. The objective of this initiative is to raise awareness of rare diseases and to make them more visible to society, as well as to stir the interest of new researchers, health professionals and the industry in order to continue developing treatments and advancing the knowledge of these diseases. At the meeting, the Minister spoke about her commitment to develop a coordinated strategy to tackle rare diseases with a multidisciplinary approach that includes health, social and scientific perspectives.

Hosted rare disease events in 2012

Every two year since 2000, the Royal College of Pharmacists in Seville has organised the International Congress on Orphan Drugs. The last one has been in February, 2013. All stakeholders have participated in this event. Other events announced in *OrphaNews Europe* in 2012 included: BioSpain Conference (Bilbao, 19-21 September 2012), 8th International Congress on Autoimmunity (Granada, 9-13 May 2012), World Pulmonary Hypertension Day-Scientific Symposium (Madrid, 4-5 May 2012) , 2nd Annual Orphan Drug Congress 2012 (Barcelona, 7-8 June 2012).

Research activities and E-Rare partnership

National research activities

The results of CIBERER's 2011 research activities, organised into seven programmes (Genetic Medicine, Inherited Metabolic Medicine, Mitochondrial Medicine, Paediatric and Developmental Medicine, Neurosensorial Pathology, Endocrine Medicine and Inherited Cancer and Related Syndromes) were made available in 2012 in CIBERER's 2011 Scientific Report. The report 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. In 2011 a reorganisation based on the modifications of the Centre's statutes, greater knowledge of the groups' potentials and the definition of new strategic objectives was undertaken. The structure of Scientific Areas was replaced by the organisation of groups in Research Programmes. The 2011 Action Plan defined certain instrumental measures with a scientific, technical, translational and training slant. A principle network scientific endeavour in 2011 was the start of the Programme for "Genes in undiagnosed Rare Diseases", a major project for applying exome sequencing to many rare diseases in order to discover new genes and variants involved in this kind of pathologies. The report also details actions in the area of translational research, technology transfer, training, outreach, scientific publication, and public awareness.

CIBERER had also defined its strategy for 2012, which was 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 translational components will be criteria for the funds assignment.

CIBERER (part of the Institute of Health Carlos III) was given funding by ISCIII amounting to €5.1 million in 2012 (basic, clinical, epidemiological and translational) in the field of rare diseases.

E-Rare

Spain participated in the 4th Joint Transnational Call in 2012: 3 teams from Spain participated in the Consortia funded through the call.

D.26. SWEDEN

National plan for rare diseases and related actions

In November 2012, the Swedish national strategy for rare diseases was transmitted to the government. For the moment the financial implications have not been considered.

On 26 November 2012, a Europlan national conference was held in Stockholm bringing together 140 stakeholders, to follow the elaboration of the national plan for rare diseases. The conference was organised by the Rare Diseases Sweden and focused on how to transform the strategy proposed by the National Board of Health and Welfare into a concrete plan of action to improve care for rare diseases. Health care providers, policy makers and user representatives from across the country signed up to take part in the discussion about how to put the strategy into action.

Centres of expertise

The new NFSD will collect information concerning centres of expertise in Sweden. Criteria for expert centres are under development.

Registries

During 2012 a working group was established for the purpose of developing national registries for rare diseases which will provide a tool to measure and monitor relevant patient care activities for patients with rare diseases.

Sources of information on rare diseases and national help lines

Orphanet activities

Orphanet Sweden started a close cooperation during 2012 with the recently installed National Function Point for Rare Diseases and the Information Centre of Rare Diseases to optimise the national information resources. In 2012 Orphanet arranged conferences related to the Rare Diseases Day.

National rare disease events in 2012

Rare Diseases Sweden organised a number of events to mark Rare Disease Day. The campaign kicked off in the months prior to the Day and included a photography exhibition and a lecture tour over the winter of 2011-2012 to establish contact between the Swedish Alliance of Rare Diseases and hospitals working with rare disease patients.

On 29 February 2012, volunteers organised an event at the Central station of Stockholm to reach the general public and raise awareness. On the same day, a number of meetings and think tanks were held: a range of stakeholders were invited to discuss the content of the national plan/strategy of rare diseases.

A rare disease scholarship was bestowed to a young volunteer in a rare disease patient organisation to mark the day. In addition a flash mob was organised to mark the Day.

On 22 February a regional meeting to celebrate the Day organised by Orphanet in Stockholm together with the Swedish Alliance of Rare Diseases under the auspices of the Karolinska University Hospital and the Karolinska Institutet. The theme of the meeting was "Shaping regional centres for rare diseases" and was attended by about hundred representatives of health care professionals, researchers, patients, pharma industry, health authorities and politicians. The regional meeting was one of a series of Regional meetings across Sweden to mark Rare Disease Day

On 26 November 2012, a Europlan conference was held in Stockholm, to follow the elaboration of the national plan for rare diseases.

Rare Diseases Sweden held their annual meeting on 24-25 November 2012, welcoming 50 participants.

Orphan medicinal products

Orphan medicinal products incentives

The Medical Products Agency (MPA)¹⁸¹ is responsible for the regulation and surveillance of the development, manufacturing and marketing of medicinal products in Sweden. Regarding orphan medicinal products, centralised marketing authorization application to the European Medicines Agency (EMA) is mandatory. The applications are assessed by the Committee for Human Medicinal Products (CHMP) at the EMA and the decision, valid for the whole of the EU, is granted by the Commission.

The MPA can waive the fees for clinical trial applications and provide scientific advice for researchers, applicants and companies lacking support from the pharmaceutical industry. Concerning the provision of free of charge IMP by clinical trial sponsors, Swedish law allows exemptions: should an obligation to perform a trial after marketing have been a condition of the marketing authorisation being granted for an orphan drug. The same could apply for all clinical trials and IMPs, not just orphan drugs on the condition that the clinical trial is performed without the participation of the pharmaceutical industry or that the clinical trial is special importance to public health.

Orphan medicinal product market availability situation

According to the MPA, out of the 78 orphan medical products (OMPs) authorised by December 2012 The Dental and Pharmaceutical Benefits Agency had decided to reimburse the following 38 OMPs (some with restrictions): Fabrazyme**, Replagal**, Glivec** (for CML), *(withdrawn from registry of OMPs for remaining orphan designated conditions), Tracleer**, Somavert, Zavesca (for Niemann-Pick's disease), Carbaglu, Aldurazyme, Ventavis, Onsenal (withdrawn register medicinal products human use), Wilzin, Xagrid, Orfadin, Prialt, Revatio, Nexavar, Sutent*, Thelin (withdrawn register medicinal products human use), Exjade, Sprycel, Diacomit, Inovelon, Cystadane, Revlimid, Increlex, Tasigna, Thalidomide Celgene, Volibris, Firazyr, Ceplene, Mepact, Afinitor*, Cayston, Nplate, Revolade*, Esbriet, TOBI Podhaler, Votubia. The DPBB decided not to reimburse the following 21 OMPs: Busilvex, Litak, Lysodren, Pedeia, Xyrem*, Naglazyme, Myozyme, Evoltra, Savene, Elaprase, Soliris, Atriance, Glilolan, Yondelis, Torisel, Kuvan, Vidaza, Mozobil, Ilaris*, Arzerra, VPRIV¹⁸². Of note, Zavesca** for treatment of Gaucher's disease has been removed from the list of reimbursed OMPs by the DPBB. Reimbursement information is lacking for a number of OMPs, some of which have been withdrawn from the market but the majority being products authorised late in 2011 and 2012. Several OMPs are marketed in Sweden without general reimbursement.

D.27. UNITED KINGDOM

National plan/strategies for rare diseases and related actions

Current organisation of health care for rare diseases in the UK

In the past, the basic concept in the National Health Service is not that of 'rare diseases' but rather that of 'specialised services'. However, this changed as of 1 December 2012, in preparation for the new framework for healthcare delivery in England. Whilst all aspects of specialised service provision remain under the control of the NHS, for the first time, rare diseases policy (including the development of the UK Plan for Rare Diseases) is now the responsibility of the genetics and genomics team in the Health Science and Bioethics Division of the Department of Health England.

In 2012, proposals were developed to disband the Advisory Group on National Specialised Services (AGNSS). This will take effect as of April 2013. The services currently commissioned on a national basis will continue to be commissioned by a new NHS Commissioning Board. The Clinical Reference Groups during the transition of specialised services to the new NHS Commissioning Board will continue to be the source of clinical advice as the NHS Commissioning Board moves forward in its direct commissioning role. The Clinical Advisory

¹⁸¹ www.mpa.se

¹⁸² *The product has been withdrawn by the sponsor from the Registry of Orphan Medical Products, **The product has been removed from the Registry of Orphan Medicinal Products since its 10 years of market exclusivity has expired. For Glivec the applies to the acute lymphatic leukaemia indication only.

Group (CAG) for Prescribed Services took evidence from these Clinical Reference Groups and has released a report¹⁸³ outlining which services should be directly commissioned by the new NHS Commissioning Board (many of these are services for rare diseases). A public consultation¹⁸⁴ on specialised services to be commissioned nationally by the NHS Commissioning Board was launched in December 2012, with the results to be published in early 2013.

Steps towards a national plan/strategy for rare diseases

The Department of Health launched a consultation on a UK Plan for Rare Diseases on 29 February 2012 (Rare Disease Day). The consultation ran for 12 weeks and showed strong support for a UK Plan for Rare Diseases. Over 350 consultation responses were received from a range of sources including patients, carers, academics, clinicians, researchers and patient support groups. A summary of the consultation responses was published on 16 November 2012¹⁸⁵.

Throughout 2012, healthcare services in England were making preparations in readiness to transfer to a new delivery and governance system. As part of the changes, patient services for those with rare disease continued to be part of specialised services, led by the NHS Commissioning Board. However, for the first time, there is now a nominated lead for rare diseases policy within the Department of Health (DH). The DH rare diseases policy lead will have responsibility to deliver the UK Plan for Rare Diseases in line with EU recommendations.

A new report entitled *Forgotten Conditions: Misdiagnosed and Unsupported, How Patients are Being Let Down*¹⁸⁶ issuing from a roundtable of stakeholders from government, academia, and medicine held in June 2012, finds that low prevalence disorders are little understood and frequently misdiagnosed in the United Kingdom. The report also evokes the “postcode lottery” rare disease patients face, in which access to service and treatment depends upon the part of the UK in which one resides, with patients in Wales and Scotland enjoying greater access for certain conditions than those in England. The report offers several recommendations to remedy the current state of affairs, including: developing shared care pathways for best practice clinical guidance and expertise; education for medical students that broadens the scope of rare disease diagnostics; harnessing new technology to improve diagnostics; encouraging and supporting self-diagnosis and self-care for patients; and ensuring that the National Commissioning Board takes rarer conditions into account when developing guidance for Clinical Commissioning Groups.

Other related actions

On 25 January 2012, the Human Genomics Strategy Group, which was set up in 2010 as part of the Government’s response to the House of Lords Science and Technology Select Committee’s report on Genomic Medicine with a remit to develop strategic options for genomics in the NHS and to oversee broader developments in relation to genetics in NHS services, produced its report: *Building on our inheritance: genomic technology in healthcare*. This presented a vision for the development and adoption of genomic technology in healthcare and made recommends on its implementation. The report and its recommendations were welcomed by the UK Government.

Following on from the report, on 10 December 2012 the Prime Minister announced that the UK will sequence 100,000 whole genomes of NHS patients at diagnostic quality over the next three to five years, earmarking £100 million:

- to train a new generation of British genetic scientists to lead on the development of new drugs, treatments and cures, building the UK as the world leader in the field.;
- to pump-prime DNA sequencing for cancer and rare inherited diseases; and,
- to build the NHS data infrastructure to ensure that this new technology leads to better care for patients

The Department of Health has earmarked up to £100 million for the genomics initiative, which will support development of skills and data infrastructure within the NHS and will pump prime the sequencing work. Rare diseases is one of the three priority areas of the initiative, along with cancer and infectious disease.

¹⁸³ <http://www.dh.gov.uk/health/2012/09/cagreport/>

¹⁸⁴ <http://www.commissioningboard.nhs.uk/ourwork/d-com/spec-serv/consult/>

¹⁸⁵ <http://www.dh.gov.uk/health/2012/11/response-rare-disease/>

¹⁸⁶ <http://www.2020health.org/2020health/Publication/Wellbeing-and-Public-Health/forgotten-conditions.html>

Centres of expertise

The Department of Health issued a report¹⁸⁷ in September 2012 specifying which specialised services for rare diseases should be commissioned at the national level from April 2013. 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.

An article¹⁸⁸ appearing in the *Orphanet Journal of Rare Diseases* applies the Systematic Component of Variation (SCV) in order to look at access to nationally commissioned services in England, particularly for highly specialised healthcare, generally affecting fewer than 500 people in England or involving services where “fewer than 500 highly specialised procedures are undertaken each year”. Centralising specialised services in a few centres ensures a volume high enough to maintain excellence, although there is an obligation to ascertain that patients geographically far from such centres are not disadvantaged. The authors applied the Systematic Component of Variation, taking “access” (measured as “service use”) in order to study access to services commissioned by the National Specialised Commissioning Team (NPCT) in England. The results of this study suggest that “...equity of access can usually be achieved at about five years after establishing a service, and this is not dependent, within the geography of England, on the number of centres designated”.

The UK Genetic Testing Network (UKGTN – see page 7 under “Genetic Testing”) has been reviewing genetic testing rates for rare conditions, by geographical regions, based on information from the UKGTN member laboratories. It finds variation in genetic testing rates over the past four years although it is suggested that this is likely due to data quality. This is improving and should yield results for 2011/12 that will be published.

A report¹⁸⁹ of the Joint Committee on Medical Genetics released in 2012 identifies the challenges inherent in integrating genomic medicine into the wide range of existing clinical areas. Amongst the points raised in the report, is the need for genetics sub-specialist training in existing clinical areas such as paediatrics and antenatal care. The report encourages the development of such training to complement and collaborate with existing genetics infrastructures. To combat inequity in the availability of access to specialist centres for heritable disorders, the authors recommend “the formal inclusion in the new commissioning structures of resourced, multidisciplinary expert groups, which may be specialty or disease specific depending on the context, able to give advice (via Public Health England or otherwise) on specifications for quality assured pathways to assist commissioners”.

Registries

In England, a government-backed initiative will allow researchers unprecedented access to anonymised patient health records. The Clinical Practice Research Datalink (CPRD) is a new observational data and interventional research service of the National Health Service (NHS), jointly funded by the NHS National Institute for Health Research (NIHR) and the Medicines and Healthcare products Regulatory Agency (MHRA). The CPRD is “... designed to maximise the way anonymised NHS clinical data can be linked to enable many types of observational research and deliver research outputs that are beneficial to improving and safeguarding public health”. Data confidentiality is a top priority for the new service and several mechanisms are in place to protect patient privacy. Access to patient data could help rare disease researchers advance knowledge and understanding of rare conditions.

Neonatal screening policy¹⁹⁰

The National Health Service revised its screening programme standards in 2011 for sickle cell disease and thalassaemia: the revised screening standards provide new material relating to objectives and performance indicators and will take effect from April 2012.

Genetic testing

The Government response to the House of Lords inquiry into genomic medicine (the inquiry took place in 2008 and the Government response was published in 2009) states that the Department of Health will “continue, via the UKGTN, to monitor commissioning structures within genetics and genomics and to establish the Human Genomic Strategy Group. The Board and three working groups met during 2010 and 2011 and a report was published in January 2012. The report referenced UKGTN in supporting commissioning, including ongoing

¹⁸⁷ <http://www.dh.gov.uk/health/files/2012/09/Clinical-Advisory-Group-for-Prescribed-Services.pdf>

¹⁸⁸ <http://www.ojrd.com/content/7/1/85/abstract>

¹⁸⁹ <http://www.phgfoundation.org/reports/12093/>

¹⁹⁰ <http://www.screening.nhs.uk/programmes>

collaboration with NICE, genetic test evaluation, monitoring quality of member laboratories and supporting the medical genetics Clinical Reference Group.

Between 2004 and 2012 the UKGTN had evaluated 371 gene dossiers and made recommendation for 293 tests to be available for NHS service. During this time 312 testing criteria were developed. There are more testing criteria than Gene Dossiers approved because some TC have been developed for tests already provided by laboratories prior to the introduction of TC. A long term goal for the UKGTN is to draw up TC for all conditions available through the UKGTN including those that pre-date the development of TC in 2006. The Clinical Molecular Genetics Society also develops best practice guidelines which are available from their website. Individually laboratories may develop referral guidelines for local use.

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 2011-2012¹⁹¹ 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.

National alliances of patient organisations and patient representation

Specialised Healthcare Alliance (SHCA)

The Specialised Healthcare Alliance (SHCA) arranged further workshops in 2012 looking at some of the key issues raised *Leaving no one behind*, notably around the role which shared decision-making with patients could play in assisting earlier diagnosis of rare conditions and the integration of specialised services with local aspects of care. For the rest, the Alliance has been largely focused on seeking to ensure that the major changes in specialised commissioning in England are tailored to the best interests of all those needing specialised care

Genetic Alliance UK

A project supported by Genetic Alliance UK, and facilitated by the Welsh Institute for Health and Social Care, examines the benefit/risk ratio of new medicinal products for rare and serious diseases. The report¹⁹² published in 2012 exposes the findings determined by a Citizen's Jury composed of twelve rare and/or serious genetic disease patients or family members, who explored certain key questions: How do patients with rare and/or serious conditions perceive the risks and benefits of new medicines? To what extent should regulators be more permissive in their marketing authorisation decisions? How should patients be involved in the assessment of risks and benefits, and regulatory decision making? After exploring hypothetical case studies and hearing from expert and advocate witnesses on the existing regulatory system and its various strengths and weaknesses, followed by a period of reflection and debate, the jury was able to establish four key recommendations: Regulators should include psychosocial factors in their decision making; Regulators should be more permissive for people with rare and/or serious conditions; Patients should be more involved from setting the research agenda, to post-marketing authorisation decisions; and Patients should be supported in their decision making.

The Northern Ireland Rare Disease Partnership (NIRDP) was formally launched on Rare Disease Day 2012 with support from patients, families, health professionals and government representatives. A non-profit organisation, the NIRDP seeks to bring together rare disease patients and organisations with clinicians and other health professionals, researchers and producers of specialist medicines and equipment, health policy makers and academics to find *"...practical ways of improving the quality of life, treatment and care for those with rare diseases in Northern Ireland"*. The new association will work closely with the Patient Client Council, with other Health and Social Care Agencies in Northern Ireland, with RDUK, IPOSSI, and GRDO in the Republic of Ireland.

National rare disease events in 2012

The UK based charity 'Jeans for Genes' holds an annual awareness day to raise funds for genetic disorders¹⁹³.

Rare Disease UK and their member organisations planned a number of events to mark Rare Disease Day 2012 across the United Kingdom. This included a contact campaigns aimed at politicians in each of the UK parliaments/assemblies, as well as a specific Rare Disease Day event at Royal Holloway University and a Northern Ireland Rare Disease Partnership event at Stormont Estate where the group launched a report looking into experiences of obtaining a diagnosis of a rare disease in Northern Ireland.

¹⁹¹ <http://www.nowgen.org.uk/CubeCore/uploads/documents/NowgenReviewandWorkProgramme20112012.pdf>

¹⁹² <http://www.geneticalliance.org.uk/docs/citizens-jury-report.pdf>

¹⁹³ <http://www.jeansforgenes.com/about>

An event entitled, "Rare Diseases in the UK - Vision 2020" was held in Cambridge on 4 July 2012, bringing together to discuss the application of exome sequencing technologies.

Hosted rare disease events in 2012

Amongst the rare disease related events hosted by the UK and announced in *OrphaNews Europe* were: 3rd Annual Orphan Drug Summit (London, 25-26 July 2012), 8th International Prader-Willi Syndrome Conference (Cambridge, 17-21 July 2013), 4th International DSD (Disorders of Sex Development) Symposium (Glasgow, 7-9 June 2013), Translating Genomics Conference (Cambridge, 4 December 2012), Genomic Disorders 2012 (Cambridge, 21-24 March 2012), 13th International Conference on Neuronal Ceroid Lipofuscinosis and 1st Worldwide Meeting of Batten Disease International Alliance (London, 28-31 March 2012), CILIA 2012 - Cilia in Development and Disease (London, 16-18 May 2012), International Ataxia Research Conference (London, 1-3 November 2012), Joint DIA/ EFGCP/ EMA Medicines for Children Conference on Development of Paediatric Medicines: From Learning to Adapting (London, 26-27 September 2012), Orphan Drugs & Rare Diseases Conference (London, 8-9 October 2012), Epidermolysis Bullosa – An Introduction and Advanced Management courses (London, September 2012).

Research activities and E-Rare partnership

National research activities

Rare diseases research has been supported in the UK. Government funding is mostly available through the Research Councils (e.g. the Medical Research Council) and the National Institute for Health Research (NIHR). Many of the NIHR-funded Biomedical Research Centres (BRCs) and Biomedical Research Units (BRUs) undertake translational health research into rare diseases, and in April 2012 a new round of BRCs and BRUs commenced with £800 million investment over 5 years. In addition, as announced in *the Strategy for UK Life Sciences*, the Department of Health is creating a new NIHR BioResource, to provide a national cohort of healthy volunteers, patients and their relatives who wish to participate in experimental medicine research, and are willing to provide clinical information and samples that will enable them to be recalled for specific studies. These studies will have the potential to rapidly advance the understanding of disease mechanisms, identify potential drug targets, and improve insight into the therapeutic potential and limitations of existing and emerging therapies. The BioResource is on track to be launched in early 2014, however it is already supporting translational research into rare diseases, which is one of its 4 themes of focus. On the basis of the research into rare diseases being undertaken in the NIHR, the Department of Health has confirmed NIHR's membership of the International Rare Disease Research Consortium (IRDiRC) this consortium.

In 2012, a new funding mechanism was created by global charitable foundation the Wellcome Trust. The Pathfinder Awards support academic-industry partnerships dedicated to early-stage applied research in the field of rare and neglected diseases. Open to international participation, the Pathfinder Awards seek to kick-start pilot research initiatives showing potential for developing innovative medicinal products for rare or neglected diseases. The first two awards were granted in 2012, both for rare diseases.

In 2012, the Medical Research Council awarded the University of Edinburgh's MRC Human Genetics Unit and the MRC Institute of Genetics and Molecular Medicine £60 million (£74.2 million) in funding over a five-year period to study illnesses and inherited disorders, including cystic fibrosis, retinitis pigmentosa, anophthalmia, and other rare conditions.

Orphan medicinal products¹⁹⁴

Orphan medicinal product committee

The Advisory Group for National Specialised Services (AGNSS) recently developed a new framework for evaluating "ultra-orphan" drugs: ultra-orphan diseases affect less than 500 people in England. Ultra-orphan medicinal products are not subject to NICE appraisals, but to those of the AGNSS: applications are evaluated for clinical desirability on the information received from clinicians on a case-by-case basis¹⁹⁵. However, Health Ministers in England announced in 2012 that from April 2013 NICE will take on the role of appraising drugs for ultra-rare conditions, defined as those affecting fewer than 500 patients in England (equating to a prevalence of 1 in 100 000 or fewer).

¹⁹⁴ Written using information from KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp 62-66)

¹⁹⁵ EMINET Initial investigation to assess the feasibility of a coordinated system to access orphan medicines, C. Hahl, F. Bachner (2011) p61

Orphan medicinal product pricing policy

Value-priced pricing will come into effect from 2014 for newly launched branded medicines¹⁹⁶.

Other initiatives to improve access to orphan medicinal products^{197,198}

The National Institute for Health and Clinical Excellence (NICE) started to commissioning expert assessments for off-label medicine use from spring 2012¹⁹⁹. These assessments do not constitute formal guidance, but rather 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.

On 18 February 2012 an evidence session was held in the Scottish Parliament a result of the petition sent by Rare Disease UK for the government to address two issues in relation to access to orphan medicinal products in Scotland, namely that the Scottish Medicines Consortium (SMC) appraisal process is not suitable for orphan medicines, and that the Individual Patient Treatment Request (IPTR) process discriminates against patients affected by rare diseases, due to the difficulty in proving exceptionality. Whilst the session was looking at issues of access broadly, access to orphan medicines was also discussed.

¹⁹⁶ Orphan Drugs in Europe : Pricing, Reimbursement, Funding & Market Acces Issues, Donald Macarthur (2011) pp.86-7

¹⁹⁷ Written using information from KCE reports 112B : Politiques relatives aux maladies orphelines et aux médicaments orphelins – 2009 (pp 62-66)

¹⁹⁸ 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).

¹⁹⁹ <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 and 2012 the National Commission for Rare Diseases Committee 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 draft was presented to the Croatian Society of Patients with Rare Diseases in December 2012 before public consultation and presentation to the Parliament.

National alliances of patient organisations and patient representation

The Croatian Alliance for Rare Diseases, replacing the Croatian Society of Patients with Rare Diseases was established in 2012 as the umbrella organisation for rare diseases that gathers 14 other non-profit organisations and more than 200 patients with rare diseases and members of their families who do not have patient organisation representation. At present there are more than 110 different rare diseases registered in the association.

Sources of information on rare diseases and national help lines

Orphanet activities in Croatia

There is an Orphanet national website which was launched in 2012²⁰⁰.

Help line

A rare disease helpline was established in Croatia in 2012 by the Croatian Alliance for Rare Diseases. It will be financed through the project and by donations.

National rare disease events in 2012

To mark Rare Disease Day 2012, a symposium on rare diseases took place on 24 February 2012 at Hotel Dubrovnik in Zagreb, organised by the Croatian Society for Rare Diseases of the Croatian Medical Association. In addition, information stands were present in Zagreb on 25 February 2012, an event attended by the Mayor of Zagreb, and other events took place the same day in Osijek, Rijeka, Split and Dubrovnik. On 29 February 2012 representatives from rare disease patient organisations dealing with rare diseases held a meeting with the Minister of Health Rajko Ostojić at the Ministry of Health, and educational events were held at the Zagreb Health School.

In collaboration with the European Organisation for Rare Diseases (EURORDIS) and the City Office for Health and War Veterans; under the auspices of the Croatian President Prof. Ivo Josipovic and with the support of the Croatian Medical Students' International Committee (CroMSIC) and the Coalition of Healthcare Associations, the events were held in six cities: Krizevci, Osijek, Rijeka, Split, Dubrovnik and Zagreb.

²⁰⁰ <http://www.orpha.net/national/HR-HR/index/homepage/>

Orphan medicinal products

Orphan medicinal product market availability situation

In 2012 Croatian Institute for Health Insurance released an update (Decision, 2012, May 24) of the List of Especially Expensive Drugs which includes drugs for several rare diseases (drugs for multiple sclerosis, some cancers, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, home treatment of hemophyllia, peginterferon, growth hormone, enzyme replacement therapy). Orphan medicinal products approved for treatment of rare and severe diseases can be found on the web pages of the Croatian Agency for Drugs and Medicinal Products²⁰¹. There is a detailed procedure regulating the inclusion of a drug on the List of Especially Expensive Drugs. The final decision is taken by the Board of the Croatian Institute for Health Insurance, based on the report of Committee for drugs and medicinal products.

E.2. ICELAND

National plan/strategy for rare diseases and related actions

In 2012, for the first time, Iceland was able to send a representative to a EUCERD meeting, which already has increased discussion and awareness of rare diseases in Iceland at the level of the Ministry, stakeholders and rehabilitation services. Representatives from these organisations now meet regularly with the purpose to increase awareness of rare diseases within the country. A strategy for disabilities was launched in 2012 and the plan is to revise this document next year and include a chapter on rare diseases within it. Currently, there is no specific funding in place for rare diseases. In 2012 Iceland hosted a Nordic meeting on rare diseases with 120 attendees from all the Nordic countries.

Registries

In 2012, a centralised database on causes of deaf blindness (combined hearing and visual impairment) among Icelandic children and adults was established in cooperation of three national centres servicing people with disabling conditions. These administrative databases are financed by the state.

National alliances of patient organisations and patient representation

In 2012, collaboration was initiated between representatives from the organisation “Unique children”, the Ministry of Welfare and the national habilitation centre with the aim to increase awareness of rare diseases at all service levels in the country.

Sources of information on rare diseases and national help lines

Other sources of information

In autumn 2011 the homepage www.rarelink.is was launched and in 2012 information regarding several rare diseases and syndromes was translated into the Icelandic language and published on this website.

National rare disease events in 2012

The patient organisation “Unique children” celebrated Rare Disease Day for the first time in 2012. The main event was the fund raising event “Rare Run” where people ran a certain distance and raised money for the organisation. In the radio there was an hour long program dedicated to children with rare diseases. In the program children were interviewed and their favourite songs were played.

Hosted rare disease events in 2012

On 31 May and 1 June 2012 Iceland hosted a Nordic meeting on rare diseases with 120 attendees from all the Nordic countries²⁰².

Specialised social services

A new information centre for children with rare disease and their families was opened in autumn 2012. The centre is called Leiðarljós (Guiding Light) and offers parents of children with rare diseases nursing support and detailed information regarding available services.

²⁰¹ www.halmed.hr

²⁰² <http://www.greining.is/media/nordic-conference-2012/nordicconfrence2012linkar.pdf>

E.3. ISRAEL

Genetic testing

All screening tests will be provided free from the beginning of 2013 including cystic fibrosis, SMA and fragile X.

National rare disease events in 2012

On Wednesday, February 29 2012, the Second National Conference was held to mark the International Rare Disease Day, organised by Orphanet Israel, at the Felsenstein Medical Research Center of the Schneider Children's Medical Center of Israel (SCMCI). Around 300 people participated in the conference including physicians, nurses, social workers, researchers and patients. Dr. Zelina Ben-Gershon, Office of the Chief Scientist, Ministry of Health, closed the conference speaking about the importance of promoting research of rare diseases and the necessity for public funding for the recognition of diagnostic characteristics of such diseases in order to develop treatment and cures, since the patients and researchers are few and scattered in different places and therefore cooperation and multinational coordination are essential. The conference successfully presented the topic of rare diseases from a variety of disciplines and points of view, and raised public awareness about the changes taking place in the diagnosis and possible treatment of rare diseases and emphasised the need to examine the entire system for changes and to prepare for them.

Research activities and E-Rare partnership

E-Rare

Israel participated in the 4th Joint Transnational Call in 2012, with teams from Israel participating in 4 out of the 11 projects selected for funding.

IRDiRC

The CSO-MOH as member of the E-Rare Group of Funders joined the IRDiRC in 2012.

E.4. NORWAY

National plan/strategy for rare diseases and related actions

In March 2012 the Ministry announced that the South-Eastern Norway Regional Health Authority (SE-RHF) should establish a national competence service for rare diagnosis and disabilities to administrate all the national services in this field today, except the services for dual sensory impairment (for which there is established a new national service at Northern Norway Regional Health Authority). The SE-RHF chose to establish a project in 2013, to organise the unit from 1 January 2014.

Centres of expertise

National competence service

In 2013 a project is funded for the organisation of one administrative body for the units dealing with rare diseases. This unit will be located at Oslo University Hospital. The services will be evaluated through annual and five-year reports.

Neonatal screening policy

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 1 January 2012. Under this regulation, prior to newborn screening, it is expected that the parents are well informed about tests, methods and possible consequences. Information brochures to parents were produced in close collaboration between The Directorate of Health and Oslo University Hospital before the program was launched on 1 March 2012. Screening is to 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 alliances of patient organisations and patient representation

The Norwegian Directorate for Children, Youth and Family Affairs (BUFdir) is now considering to change the regulations on governmental support to patient organisations, e.g. to make it possible for people with rare disorders and their family to establish organisations.

National rare disease events in 2012

There are meetings organised at all the resource centres, and annual contact meetings between each centre and their respective regional health authority. Conferences and congresses are organised on special occasions such as Rare Disease Day.

A conference²⁰³ was organised to mark Rare Disease Day at the Norwegian Directorate for Health on 29 February 2012. The event welcomed all stakeholders and several of the Norwegian Centres of Expertise (or rare disorders attended and provided information via stands

Hosted rare disease events in 2012

Amongst the hosted events in 2012 announced in *OrphaNews Europe* was the 1st European Conference on Aniridia (Oslo, 8-10 June 2012).

E.5. SWITZERLAND

National plan/strategies for rare diseases and related actions

In September 2012, National Councillor Guy Parmelin requested information concerning the state of advancement of the national strategy for rare diseases. The answer of the Federal Council included the information that a formal meeting between the IG and the Federal Office of Public Health took place on 4 June 2012 to define the expectations and priorities for the development of a national plan. Issues such as financing diagnostic tests and defining the criteria for centres of expertise have been broached. A report on the advancement of the elaboration is due in Spring 2013 so as to determine the next steps in collaboration with the Swiss Academy of medical Sciences.

The Federal Office of Public Health is working on a project that will facilitate the reimbursement of rare disease medicinal products. A second round table was held in early 2012 and the project should then be open for consultation later in 2012.

Centres of expertise

In 2012, no new centres have been officially appointed, however, the procedure of official appointment is still ongoing.

Registries

There are a number of registries for specific rare diseases in Switzerland. Switzerland contributes to the following European registries: AIR, CAPS, E-IMD, TREAT-NMD, EURO CARE-CF and EUROCAT.

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, with screening to be introduced in 2013.

²⁰³ <http://www.helsedirektoratet.no/Om/kurs-konferanser/Sider/en-sjelden-dag-2012.aspx>

National alliances of patient organisations

At the end of August 2012 ProRaris submitted a case study on the unequal treatment of the reimbursement of drugs for patients with rare diseases among various insurance companies in different cantons to the director of the Federal Office of Public Health, Mr. Pascal Strupler. In his answer he announced a close monitoring of the interpretation of articles 71 a and b of the ordinance on health insurance (Krankenversicherungsverordnung) on which the decisions of the insurance companies are based until the end of 2013.

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.

Sources of information on rare diseases and national help lines

In 2011, the Swiss Conference of the Cantonal Ministers of Public Health (GDK/CDS) guaranteed a global budget for 2011 and 2012 for Orphanet.

Help line

A joint venture between the University Hospital of Lausanne (CHUV) and the University Hospital of Geneva (HUG) with the support of Orphanet Switzerland was initiated in 2012 in order to create a regional portal on rare diseases and to establish a helpline. The services are planned to be available in 2013.

National rare disease events in 2012

ProRaris organised events for Rare Disease Day, including an event with 350 participants from all stakeholder groups to learn about, discuss and share about the rare disease public health issue. The event was supported by the main University Hospitals (Geneva, Lausanne, Zurich and Bern), the children's hospitals of Zurich and Basel, Orphanet Switzerland, the BNP Paribas foundation and Gebert RUF Stiftung. The event included the participation of Mr Pierre-Yves Maillard, President of the Conference of Cantonal Health Ministers and the cantonal Minister of Health of the Canton de Vaud, and Mr Pascal Strupler, the Director of the Federal Office of Public Health. Mr. Strupler announced the elaboration of a National Plan for Rare Diseases.

The 25th edition of the Swiss Telethon was held on 6-7 December 2012 in Lausanne²⁰⁴.

Hosted rare disease events in 2012

A number of rare disease events were hosted by Switzerland in 2012 and announced in *OrphaNews Europe*: RE(ACT) Congress 2012 - International Congress on Research of Rare and Orphan Disease (Basel, 29 February 2012), 3rd Annual World Orphan Drug Congress (Geneva, 29-30 November 2012), Autoinflammation 2013: 7th International Congress of the International Society of Systemic Auto-Inflammatory Diseases (Lausanne, 22- 26 May 2013), International Congress on Research of Rare and Orphan Diseases (Basel, 29 February - 2 March 2012).

Research activities and E-Rare partnership

National research activities

The *Gebert RUF Foundation*²⁰⁵, a Swiss grant programme specifically for rare diseases, announced its fourth call for projects in 2012. In 2012, the chosen topics were: Molecular Basis of *Pseudomonas Aeruginosa* Persistence during Chronic Infections of Cystic Fibrosis Airways; Transient Neonatal Diabetes and ZFP57 as a Paradigm for the Exporation of Imprinting Disorders; Inducing Immunological Tolerance to Galsulfate as an Example in Enzyme Replacement Therapies; Uromodulin-associated Kidney Diseases; Optogenic Vision Restoration and Neuroprotection in Retinitis Pigmentosa. 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.

²⁰⁴ <http://www.telethon.ch/>

²⁰⁵ <http://www.grstiftung.ch/en.html>

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

E.6. TURKEY

Research activities and E-Rare partnership

IRDiRC

With a Memorandum of Understanding (MoU) documenting, the commitment of the indicated E-Rare group of funders, who agree on making every reasonable effort to fulfil the intents expressed in their participation in IRDiRC, has been signed between each Party including TÜBİTAK. EC responded positively to this demand that the group of E-Rare funders joins IRDiRC in 2012.

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²⁰⁶ 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.

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²⁰⁷ Disclaimer: the European Commission is not responsible for the completeness and correctness of the information included in this report.

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